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Ion Association Assisted Lithium Ion “Claw”

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N-Methoxycarbonyl-1*H*-azepine-2,7-dicarboxaldehyde (**I**) was synthesized via the SeO_2-mediated oxidation of *N*-methoxycarbonyl-2,7-dimethyl-1*H*-azepine. The reductions of **I** in tetrahydrofuran with ^6Li or ^7Li resulted in anion radicals, which are tightly associated with the lithium cations. EPR and ab initio calculations both show a nonequivalency in all of the protons in $\mathbf{I}^{-\bullet},Li^+$ due to the closer approach of the Li^+ to one of the carbonyls and a twist of the ester carbonyl group (slow rotation of the carbamate group) toward the Li^+. Further, as predicted by the MO calculations, $\mathbf{I}^{-\bullet},Li^+$ appears to exist with the nitrogen puckered above the twisted ring system, and the lithium cation is asymmetrically complexed between the two electronegative aldehydic oxygen atoms and the carbamate carbonyl oxygen. It is also Coulombically attracted to the puckered and twisted ring system.

Introduction

The development of host−guest receptors in the form commonly referred to as molecular tweezers has been a very active area of endeavor.[1] This, coupled with our interest in ion association,[2] prompted us to search for an analogous anionic host for the lithium cation.[3] Unlike the host−guest chemistry involving lithium and the lariat ethers,[4] the lithium cation “claw” system would utilize ion association to greatly amplify the host−guest interaction.

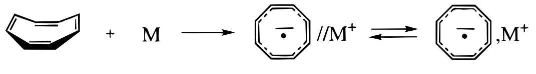
It has been known for over a quarter century that, in ethereal solvents, carbanions exist as an equilibrium mixture of contact ion pairs and solvent-separated ion pairs, reaction 1.[5] The equilibrium constant controlling

$$A^{\cdot-}//M^+ \rightleftarrows A^{\cdot-},M^+ \qquad (1)$$

reaction 1 varies as a sensitive function of the structure of the anions, the nature of the cation, the solvent, and the temperature.[6] When the anionic species is a radical, EPR spectroscopy can add unique insight into the ion pairing situation. When EPR is used to its fullest advantage, in the case of a polarizable anionic radical, it is almost like having access to an enlarged image that can be used to monitor changes in electron distribution as association takes place.[7]

The most tightly ion-associated anion radicals are those in which the cation is attached in a chelatelike fashion to the nonbonding electrons of carbonyl oxygen atoms in the anion radicals, as is the case for *o*-dimesitoylbenzene.[8] In this case, the cesium splitting in dimethoxyethane (DME) is 10.2 G, which is still not as large as the values recently reported for the smallest hydrocarbon anion radicals, those of the di-*tert*-butylbutadienes ($a_K = 25.7$ G in THF at 320 K).[9] It was our motivation to generate a system in which the alkali metal cation would be chelated between two oxygen atoms, as in the case of the *o*-dimesitoylbenzene system, and simultaneously be interacting with the face of the ring portion of the anion radical. This approach necessarily renders the ring portion of the anion radical in a different plane relative to the carbonyl oxygen atoms and the metal cation. Hence, the resulting loss of conjugation would necessitate the use of a very stable anion radical ring system.

Some of the most thermodynamically stable anion radicals can be generated via the reduction of cyclic 4n π-electron systems, because the addition of the extra electron to these systems leads to an approach toward aromatic character.[10a] Cyclooctatetraene (C_8H_8) is the smallest stable nonaromatic annulene, and C_8H_8 and its derivatives represent one of the most intensively studied systems in terms of its reduction chemistry and its anion radical.[10b−f] The 4n π-electron nature of the D_{2d} ground state and the antiaromatic nature of the D_{8h} neutral molecule renders C_8H_8 particularly vulnerable toward electron reduction yielding the (4n + 1 π-electron) D_{4h} anion radical, reaction 2.[10b]



(2)

If the lone pair from the nitrogen is considered part of the π-system, the formerly unknown anion radical of azepine can, in principle, be envisioned as an analogous 4n + 1 π-electron system. The desired “claw” aspect of

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[1] (a) Takeuchi, M.; Imada, T.; Shinkai, S. *J. Am. Chem. Soc.* **1996**, *118*, 10658. (b) For a review, see: Rebek, J., Jr. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245.

[2] For example, see: (a) Stevenson, C. D.; Echegoyen, L.; Lizardi, L. R. *J. Phys. Chem.* **1972**, *76*, 1439. (b) Stevenson, C. D.; Echegoyen, L. *J. Phys. Chem.* **1973**, *77*, 2339. (c) Stevenson, C. D.; Echegoyen, L.; Lizardi, L. R. *J. Phys. Chem.* **1972**, *76*, 2058. (d) Stevenson, C. D.; Wagner, E. P.; Reiter, R. C. *Inorg. Chem.* **1993**, *32*, 2480.

[3] The lithium cation was chosen as the cationic guest, because it is amenable to molecular orbital calculations.

[4] Gokel, G. *Crown Ether and Cryptands*; The Royal Society of Chemistry: Cambridge, 1991.

[5] Szwarc, M. In *Ions and Ion Pairs in Organic Reactions*; Szwarc, M., Ed.; John Wiley and Sons: New York, 1974; Vol. 2, Chapter 1.

[6] Abbotto, A.; Streitwiesser, A.; Stratakis, M.; Krom, J. *J. Am. Chem. Soc.* **1998**, *120*, 1718.

[7] Reiter, R. C.; Stevenson, C. D.; Wang, Z. Y. *J. Phys. Chem.* **1990**, *94*, 5717.

[8] Herold, B. J.; Neiva Correia, A. F.; dos Santos Veiga, J. *J. Am. Chem. Soc.* **1965**, *87*, 2661.

[9] Gerson, F.; Hopf, H.; Merstetter, P.; Mlynek, C.; Fischer, D. *J. Am. Chem. Soc.* **1998**, *120*, 4815.

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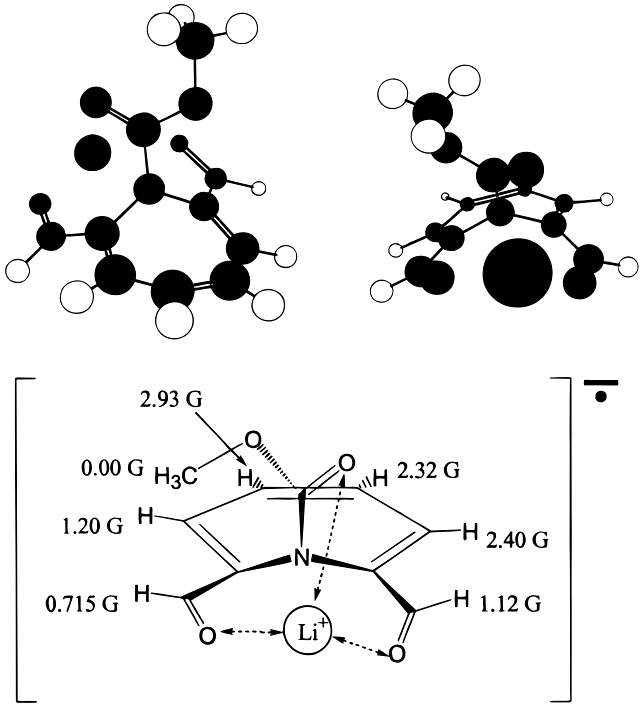


Figure 1. UHF/6-31G* perspectives of the *N*-methoxycarbonyl-1*H*-azepine-2,7-dicarboxaldehyde anion radical acting as a host for the lithium cation (upper). The bottom structure depicts the actual proton EPR coupling constants that are tentatively assigned in accordance with the UHF/6-31G* calculation. The calculations suggest that the Li^+ has a primary interaction with one carbonyl (Li^+-O bond length = 1.80 Å). However, the interactions with the other carbonyls are significant (the other aldehydic $O-Li^+$ bond length = 2.11 Å, and the ester carbonyl $O-Li^+$ bond length = 2.13 Å) according to this calculation. This calculation is consistent with the inability of the crown ethers to extract the Li^+.

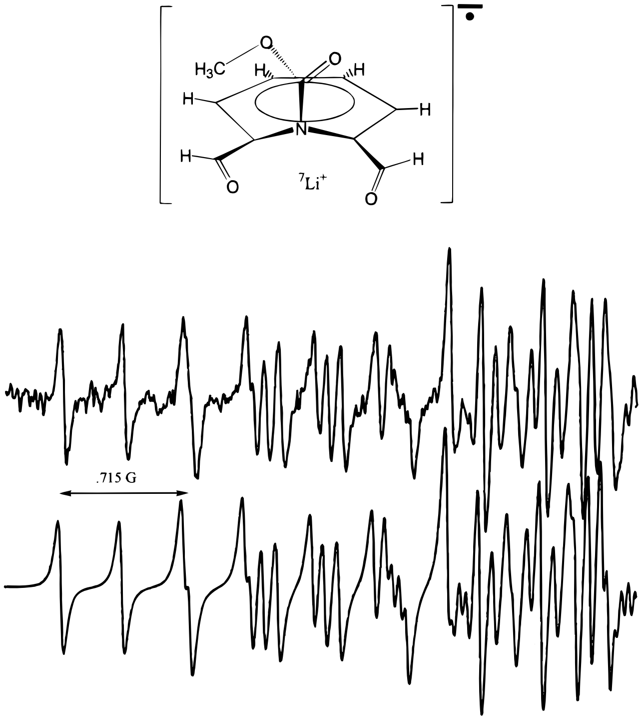
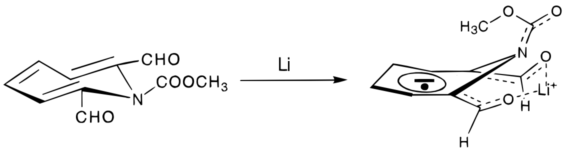


Figure 2. The first 3.5 G of the EPR spectrum of $\mathbf{I}^{-\bullet}$,Li^+ generated via lithium-7 reduction of **I** in THF at ambient temperature. Directly below this spectrum is the computed simulation generated utilizing coupling constants of 0.338 G (^7Li), 2.14 G (^{14}N), and 6 single protons with couplings constants of 2.93, 2.40, 2.32, 1.20, 1.12, and 0.715 G and a peak to peak line width of 0.04 G. The eight splittings visible in this 3.5 G expansion clearly illustrate the asymmetric structure of the anion radical.

the system could be constructed from carbonyl groups in the 2 and 7 positions. As alluded to above, carbonyl groups are ideal for this application, as they are known to serve as excellent sites for ion association.[11] A molecule fitting all of the requirements is represented by *N*-methoxycarbonyl-1*H*-azepine-2,7-dicarboxaldehyde (**I**, shown reaction 3). A possible precursor for this molecule (*N*-methoxycarbonyl-2,7-dimethyl-1*H*-azepine) was synthesized several years ago by Paquette and co-workers.[12a] Although no reference to **I** could be found in the abstracted literature, Vogel[12b] noted in a published lecture that the transformation from *N*-methoxycarbonyl-2,7-dimethyl-1*H*-azepine to **I** could be accomplished with selenium dioxide. In our laboratory, **I** was obtained in this manner.[13] We envisioned the desired claw system via the reduction of **I** to the corresponding anion radical with lithium metal (reaction 3). Herein, we report the resulting ion association assisted-ion claw system.



(3)

I $\mathbf{I}^{-\bullet}$

Results and Discussion

MO Calculations. The geometry optimizations (Figure 1) of the anion radical of *N*-methoxycarbonyl-1*H*-azepine-2,7-dicarboxaldehyde (**I**) gave nearly identical results using the UPM3, UHF/3-21G*, or 6-31G* protocols, Figure 1. The UHF/6-31G* (the highest level of theory used in this study) geometry optimization calculations predict that the nitrogen is puckered above the twisted plane of the ring by 24° in both the neutral molecule and the ion pair ($\mathbf{I}^{-\bullet}$,Li+). As in the case of COT, the planarity of the ring system is perturbed by electron addition. However, in this case the puckering of the nitrogen is not eliminated upon electron addition. In fact,

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(10) (a) Stevenson, C. D.; Peters, S. J.; Reidy, K. A. *Tetrahedron Lett.* **1990**, *31*, 6149. (b) Wenthold, P. G.; Hrovat, D. A.; Borden, W. T.; Lineberger, W. C. *Science* **1996**, *272*, 1456. (c) Hrovat, D. A.; Hammons, J. H.; Stevenson, C. D.; Borden, W. T. *J. Am. Chem. Soc.* **1997**, *119*, 9523. (d) Katz, T. J.; Strauss, H. L. *J. Chem. Phys.* **1960**, *32*, 1873. (e) Katz, T. J. *J. Am. Chem. Soc.* **1960**, *82*, 3785. (f) Strauss, H. L.; Katz, T. J.; Fraenkel, G. K. *J. Am. Chem. Soc.* **1963**, *85*, 2360.

(11) (a) Stevenson, C. D.; Alegria, A. *J. Phys. Chem.* **1973**, *77*, 3100. (b) Stevenson, C. D.; Alegria, A. E. *J. Phys. Chem.* **1975**, *79*, 1042. (c) Stevenson, C. D.; Alegria, A. E. *J. Phys. Chem.* **1976**, *80*, 69. (d) Stevenson, C. D.; Reiter, R. C.; Burton, R. D.; Halvorsen, T. D. *Inorg. Chem.* **1995**, *34*, 1368.

(12) (a) Paquette, L. A.; Kuhla, D. E.; Barrett, J. H.; Haluska, R. J. *J. Org. Chem.* **1969**, *34*, 2866. (b) Vogel, E. In *Lectures in Heterocyclic Chemistry*; Castle, R. N., Snieckus, V., Eds.; HeteroCorporation: Tampa, 1985; Vol. III, p 107.

(13) Dialdehydes of this type are also of great value in ongoing synthetic studies of novel aromatic porphyrynoid systems; see: (a) Hayes, M. J.; Lash, T. D. *Chem. Eur. J.* **1998**, *4*, 504. (b) Lash, T. D.; Chaney, S. T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 839. (c) Lash, T. D.; Hayes, M. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 840. (d) Lash, T. D.; Chaney, S. T. *Chem. Eur. J.* **1996**, *2*, 944. (e) Lash, T. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2533.

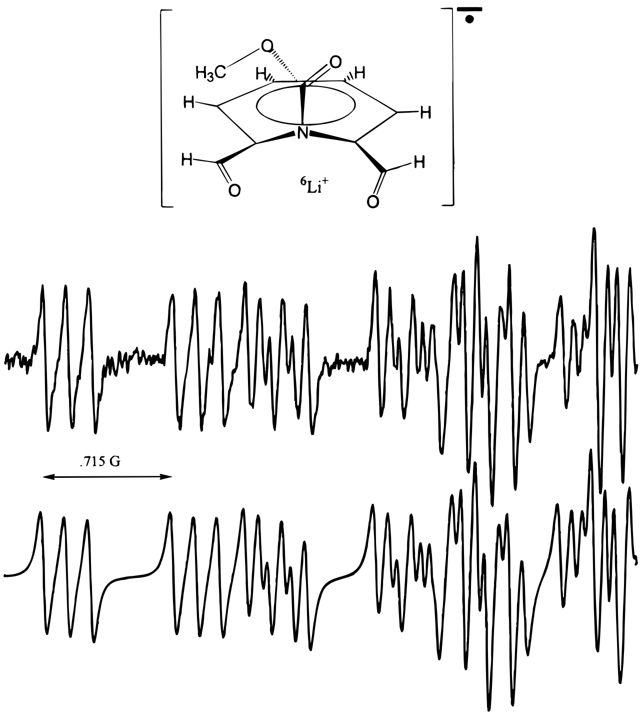

Figure 3. The first 3.5 G of the EPR spectrum of **I**$^{-\bullet}$,Li^{+} generated via lithium-6 reduction of **I** in THF at ambient temperature. Directly below this spectrum is the computed simulation generated utilizing the same proton and nitrogen coupling constants shown in Figure 1. The ^{7}Li splitting was, however, replaced by a 0.129 G ^{6}Li splitting.

the twist in the ring system, represented by the dihedral angle generated by carbons 3, 4, 5, and 6, is increased from 0.9° to 4.1° upon electron addition and simultaneous association with the lithium cation, as suggested by the MO calculations.

In the anion radical, the Li^{+} is predicted to be 1.80 and 2.11 Å from the aldehydic carbonyl oxygens. One might expect that the ester carbonyl oxygen would strongly coordinate with and point directly toward a centrally located Li^{+}. However, under these conditions, the ester carbonyl oxygen is too close to the cation. The resulting unfavorable steric interaction results in the ester carbonyl oxygen pointing toward the aldehyde group closest to the lithium cation, Figure 1.

Despite the asymmetry, the lithium cation is predicted to be bound tightly (asymmetrically complexed) between the two aldehydic oxygens and further locked in place by the ester carbonyl group. Hence, it is predicted that upon EPR analysis the system will reveal an asymmetry that should not modulate on the EPR time scale. Further, an equilibrium involving a solvent-separated ion pair (reaction 1) should not be favorable, thus rendering any lithium hyperfine splitting thermally independent.

EPR Studies. When 0.01−0.001 mM solutions of **I** in tetrahydrofuran (THF) are exposed to lithium metal under high vacuum, dark green solutions result which exhibit strong, well-resolved signals upon EPR analysis. The most obvious features of the resulting EPR signals are the complexity due to the lack of symmetry and the splitting from the ^{7}Li nucleus, Figure 2. Both of these features were predicted by the MO calculations. The lack of symmetry coupled with the four hyperfine components from the lithium-7 nucleus renders the EPR spectrum of **I**$^{-\bullet}$,Li^{+} very complex.

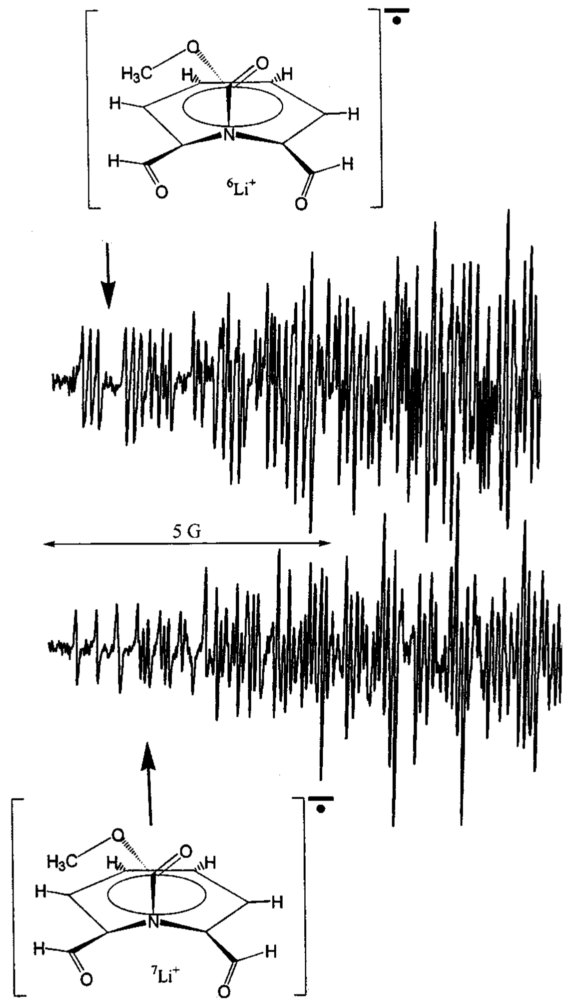

Figure 4. The low field half of the real EPR spectrum of **I**$^{-\bullet}$,^{6}Li^{+} (upper) and the low field half of the real EPR spectrum of **I**$^{-\bullet}$,^{7}Li^{+} (lower).

Usually, metal hyperfine splittings can be reduced or eliminated by lowering the temperature, which shifts reaction 1 to the right.[5,14] However, in this case, the cation is locked into position, rendering a_{Li} (0.338 G) invariant with temperature. This is further evidenced by the fact that the addition of neither 18-crown-6 nor 15-crown-5 results in alteration of a_{Li}, whereas the addition of crown ethers to ion associated anion radicals generally causes the loss of the metal splitting.[15]

The complexity of the EPR pattern could be reduced to manageable dimensions by replacement of the ^{7}Li with ^{6}Li; compare Figure 2 with Figure 3. The lighter isotope has a nuclear spin of only 1 as opposed to $^{3}/_{2}$, and its gyromagnetic ratio is smaller. When ^{6}Li^{+} serves as the counterion, a_{Li} falls to 0.129 G, in quantitative accord with its gyromagnetic ratio. Hence, very precise hyperfine coupling constants for the anion radicals of **I** with its guest lithium cations have been obtained, Figures 2, 3, and 4.

The nonequivalency of all of the protons in **I**$^{-\bullet}$,Li^{+} results from a combination of several interrelated factors: (1) the twist in the ring system, (2) the closer approach of the Li^{+} to one of the carbonyls, and (3) slow

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(14) Hirota, N. *J. Phys. Chem.* **1967**, *71*, 127.

(15) Watts, M. T.; Lu, M. L.; Eastman, M. P. *J. Phys. Chem.* **1973**, *77*, 625.

rotation (on the EPR time scale) of the carbamate group. All of these factors are predicted by UPM3, UHF/3-31G*, and UHF/6-31G* calculations. Further, as predicted by the MO calculations, $\mathbf{I}^{-\bullet}$,Li^+ appears to exist with the nitrogen puckered above the twisted ring system, and the lithium cation is bound between the two electronegative aldehydic oxygen atoms. The nonplanarity of the system and the resulting weakened conjugation between the ring system and the aldehydic carbonyl groups renders the lithium splitting (0.338 G) relatively small compared to that found in the anion radical of *o*-dimesitoylbenzene (3.75 G).[8]

Upon conception of this project, it was anticipated that the carbonyl oxygen in the ester moiety would point toward the centrally located cation, and the puckered ring would become more planar upon electron addition, as in the case of COT. Neither of these conditions prevail. The lithium cation is so strongly held in place between the two carbonyl groups that sufficient displacement to allow symmetrical coordination with the ester carbonyl oxygen is unfavorable, Figure 1. This condition results in even more twisting of the ring system upon one electron reduction and consequent association with the Li^+. This is the condition that ultimately leads to the Li^+ being asymmetrically placed between the two aldehydic groups. This crowding becomes too destabilizing in the case of the larger Na^+. Analogous reductions with sodium metal lead to only a very fleeting, kinetically unstable anion radical for which an EPR spectrum could not be recorded.

Experimental Section

***N*-Methoxycarbonyl-1*H*-azepine-2,7-dicarboxaldehyde (I).** In a 50 mL round-bottom flask fitted with a condenser and a drying tube was placed *N*-methoxycarbonyl-2,7-dimethyl-1*H*-azepine (500 mg) in dioxane (16 mL), and the mixture was heated until all the solid had dissolved. At this point, selenium dioxide (1.24 g) was added, and the mixture was stirred under reflux overnight and then filtered through Celite. The solvent was removed under reduced pressure, and the residue was crystallized from water to produce the dialdehyde (324 mg, 56%) as a yellow powder, mp 144−145 °C. ^{1}H NMR ($CDCl_3$): δ 3.76 (3 H, s, CO_2CH_3), 6.82−6.84 (2 H, m), 6.95−7.06 (2 H, m) (4 × azepine-H), 9.42−9.44 (2 H, s, 2 × CHO). ^{13}C NMR ($CDCl_3$): δ 48.85, 128.56, 128.78, 129.27, 134.71, 134.92, 148.54, 182.28, 182.54. Anal. Calcd. for $C_{10}H_9NO_4$: C, 57.97; H, 4.38; N, 6.76. Found: C, 57.34; H, 4.33; N, 6.29. EIMS (70 eV): *m/z* 207 (32) [M^+], 193 (6.5), 175 (18), 163 (63), 148 (89), 134 (38), 106 (28), 92 (45), 77 (21), 65 (100). HRMS (EI): calcd for $C_{10}H_9NO_4$ 207.0532, found 207.0531.

Reductions, Computations, and EPR Analysis. EPR samples were prepared by adding the azepine (I) and a piece of Li metal to a small bulb with an attached 3 mm EPR sample tube. This bulb was subsequently evacuated. THF was then distilled from a vessel containing NaK_2 alloy directly onto this mixture while high vacuum was maintained. The resulting solution was then poured into the attached EPR sample tube and submitted to EPR analysis. All EPR spectra were recorded on a Bruker EMX 6/1 x-band EPR spectrometer with the following settings: modulation amplitude = 0.05 G, power = 0.20 mW, and a 30 G sweep width.

The molecular orbital calculations were carried out using the Spartan 5.0 program from Wavefunction Inc. (Irvine, CA 1997). The structures were preoptimized using the Merck force field. The structures were subsequently optimized via the UPM3, UHF/3-21G*, and UHF/6-31G* levels of theory.

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