

2,6-Diazasemibullvalenes: Synthesis, Structural Characterization, Reaction Chemistry, and Theoretical Analysis

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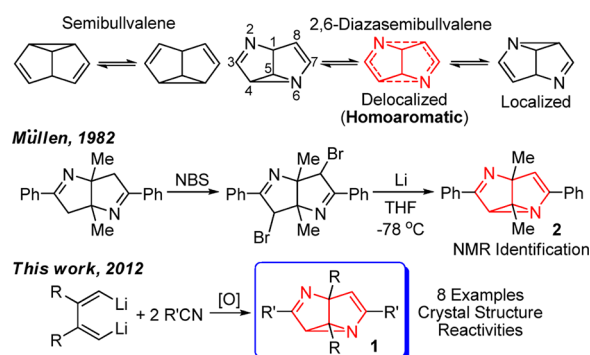
S Supporting Information

ABSTRACT: A series of 2,6-diazasemibullvalenes (NSBVs) were synthesized and isolated from the reaction of 1,4-dithio-1,3-dienes with nitriles via oxidant-induced C–N bond formation. For the first time, the activation barrier and an X-ray crystal structure of a substituted 2,6-diazasemibullvalene were determined. All NSBVs show extremely rapid aza-Cope rearrangement in solution, but the rapid aza-Cope rearrangement is “frozen” in the solid state, as shown by solid-state NMR measurements and X-ray single-crystal structural analysis. Insertion of unsaturated compounds or a low-valent metal center into the NSBV C–N bond gave diverse and interesting ring-expansion products. Theoretical analysis showed that the localized structure is predominant and that the homoaromatic delocalized structure exists as a minor component in the equilibrium.

2,6-Diazasemibullvalene (NSBV) and its all-carbon analogue semibullvalene (SBV) have long been of fundamental interest both theoretically and experimentally^{1–5} because of their unique strained ring systems, their intramolecular skeletal rearrangements, their rapid degenerate Cope rearrangement,⁶ and the predicted existence of a homoaromatic delocalized structure.^{1d,7} Synthesis and structural studies of these highly strained ring systems have been a great challenge in organic chemistry. Reaction studies and synthetic applications of their nonclassical bonding have long been attractive.

For SBVs, there have been many reports and remarkable achievements on the synthesis, structures, and reaction chemistry² as well as theoretical studies³ since Zimmerman and co-workers reported the first synthesis in 1966.^{2a} It has been predicted theoretically that NSBVs should undergo a more rapid aza-Cope rearrangement with a lower activation barrier than the all-carbon SBV analogues and that potentially they should approach a delocalized homoaromatic structure. However, little is known experimentally.^{4,5} In fact, as the only experimental *in situ* NMR identification of an NSBV to date, 1,5-dimethyl-3,7-diphenyl-2,6-diazasemibullvalene (**2**) was reported by Müllen and co-workers as a breakthrough in 1982 (Scheme 1).^{5a} In 1985, the Müllen group reported the thermal rearrangement of **2** to give a 1,5-diazocine, which is the only recorded example of the reaction chemistry of NSBVs.^{5b}

Scheme 1. Semibullvalenes and 2,6-Diazasemibullvalenes



During the past 30 years, no further report have followed in the literature, leaving the structure and reaction chemistry of NSBVs almost totally unknown.^{5c} In this paper, we report (1) the synthesis and isolation of a series of NSBVs, (2) the first single-crystal structure of an NSBV (**1a**), (3) the insertion reaction chemistry of NSBVs, and (4) theoretical/computational calculations and analysis.

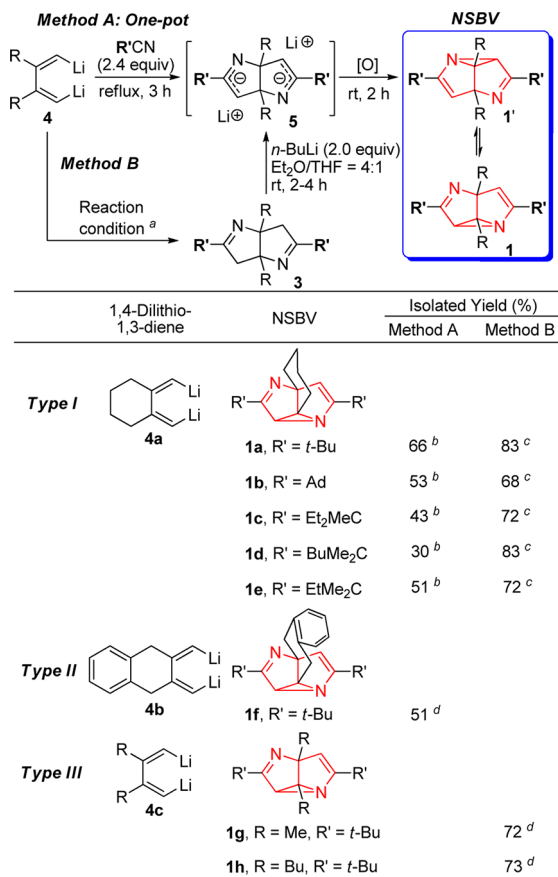
We have developed two preparative methods (A and B) for the efficient synthesis of NSBV derivatives **1** from the reaction of dithio reagents **4** with nitriles (Scheme 2).⁸ Both methods involve lithiation and oxidant-induced intramolecular C–N bond formation.⁹ Method A is a one-pot synthesis of **1**. In the type-I synthesis, **4a** was generated *in situ* from its corresponding 1,4-diiodo compound and *t*-BuLi. Reaction of **4a** with 2.4 equiv of trimethylacetonitrile (*t*-BuCN) readily afforded dianion **5a**.⁸ Addition of di-*tert*-butyl peroxide [(*t*-BuO)₂, 4.0 equiv] as oxidant led to 1,5-bridged NSBV derivative **1a** via intramolecular C–N bond formation. Decomposition of **1a** occurred when the normal workup procedure and column chromatography using silica gel or alumina were used to purify the product. Bulb-to-bulb distillation (220 °C, 0.01 kPa) was found to be an efficient purification procedure, and pure **1a** was obtained in 66% isolated yield as light-yellow crystals. The reactions of **4a** with different nitriles followed by treatment with (*t*-BuO)₂ afforded moderate yields of 1,5-bridged NSBVs **1b–e** with different

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Scheme 2. Synthetic Strategies for NSBVs 1



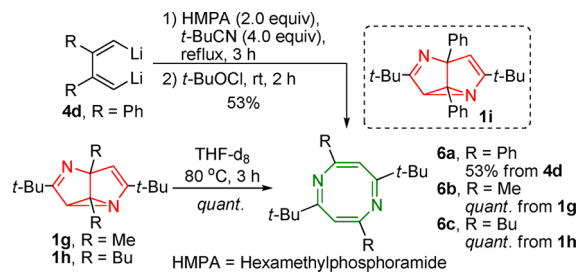
^aConditions for obtaining **3** in method B: HMPA (2.0 equiv), rt, 0.5 h; R'CN (2.4 equiv), reflux, 3 h; NaHCO₃(aq). ^b[O] = (*t*-BuO)₂ (4.0 equiv). ^c[O] = PhI(OAc)₂ (1.0 equiv). ^d[O] = *t*-BuOCl (1.0 equiv).

substituents at the 3- and 7-positions. In the type-II synthesis, dilithio reagent **4b** was successfully applied for the one-pot formation of NSBV derivative **1f** in 51% isolated yield.

Method B is a stepwise synthesis of NSBVs **1**. Dianions **5** could be readily generated in situ via dilithiation of Δ^1 -bipyrrolines **3**. Sequential addition of phenyliodine diacetate [PhI(OAc)₂] as oxidant afforded the corresponding NSBVs **1** in good isolated yields. The use of (*t*-BuO)₂ led to a slightly lower yield. With method B, **1a–e** could all be obtained in higher isolated yields. The 1,5-dialkyl-substituted Δ^1 -bipyrrolines **3** obtained from type-III reagent **4c** could also be converted to the corresponding non-bridged NSBVs **1g** and **1h** in 72 and 73% isolated yield, respectively. For the synthesis of type-I NSBV derivatives, method B was found to be more efficient than method A. All of the NSBV derivatives are stable in an inert atmosphere at room temperature.

However, when 2,3-diphenyl-1,4-dilithio-1,3-butadiene (**4d**) was applied using method A (Scheme 3), 1,5-diazocine **6a** was obtained in 53% isolated yield and structurally characterized. We assumed that the expected NSBV derivative **1i** might be unstable at room temperature and readily transformed into the thermodynamically more stable **6a**, which was also obtained via method B [see the Supporting Information (SI)].^{5c} The nonbridged NSBV derivatives **1g** and **1h** could be quantitatively converted to their corresponding 1,5-diazocines **6b** and **6c**, but a higher temperature was required.^{2g,5b} On the contrary, 1,5-bridged NSBVs **1a–f** showed good thermal stability under 200

Scheme 3. Thermolysis of NSBVs 1 to 1,5-Diazocines 6



°C and did not undergo the transformation. These results show that the substituents at the 1- and 5-positions of **1** play an important role in their thermal stability.^{2c} Notably, thermal conversion of the all-carbon SBV analogues to cyclooctatetraenes (COTs) occurs at higher temperatures in most cases.^{2g} 1,5-Diazocines are interesting aza analogues of COTs, but efficient methods for synthesizing such compounds are very rare.^{5b,10}

The solution NMR spectra of the isolated NSBVs **1a–h** showed a rapid equilibrium between two localized structures, **1** and **1'**. In **1a**, for example, the aziridiny H4 and vinyl H8 displayed only one singlet at 4.79 ppm in the ¹H NMR spectrum in THF-*d*₈ and C1/C5, C3/C7, and C4/C8 displayed singlets at 79.2, 162.9, and 99.1 ppm, respectively, in the ¹³C NMR spectrum in THF-*d*₈ as a result of the rapid degenerate aza-Cope rearrangement. The chemical shift of C4/C8 in **1a** is comparable to those found in NSBV **2** (99.4 ppm for C4/C8).^{5a} Low-temperature ¹H and ¹³C NMR data for **1a** in THF-*d*₈ recorded on a 600 MHz spectrometer unambiguously showed that **1a** continued to undergo rapid aza-Cope rearrangement even down to −100 °C. However, at −110 °C, with addition of CS₂ in the solvent, line broadening of the singlet peak for C4/C8 was observed (width at half-height *W*_{1/2} = 41.9 Hz), while no obvious line broadening of the peak for the CH₃ carbon on the *t*-Bu group took place (*W*_{1/2} = 8.8 Hz), suggesting that the aza-Cope rearrangement was slowed. These experimental observations indicate that **1a** is not a static homoaromatic form but instead is dynamically balanced by the rapid degenerate aza-Cope rearrangement, in good agreement with Müllen's report. Through line-shape analysis of the low-temperature ¹³C NMR spectra as reported by Quast and co-workers,^{2f} the upper limit of the activation barrier of the aza-Cope rearrangement at 163 K ($\Delta G_{163K}^\ddagger$) was found to be 4.4 kcal/mol, which is indeed lower than those of their corresponding all-carbon analogues.^{2b,f}

The solid-state ¹³C NMR spectrum of **1a** at room temperature showed a “frozen” unsymmetrical structure. C4 and C8 showed two broad singlets at 74.7 and 125.3 ppm, respectively. Other peaks of **1a** (e.g., C1/C5 and C3/C7) all showed different chemical shifts from one another, indicating that the degenerate aza-Cope rearrangement was “frozen” in the solid state.

A single crystal of **1a** suitable for X-ray structural determination, obtained at −20 °C in hexane/diethyl ether solution, provided the first example of a single-crystal structure of an NSBV. In sharp contrast to its solution behavior, the single-crystal structure shows a localized structure with a strained aziridine ring (Figure 1a). This is in good agreement with the solid-state ¹³C NMR data. The 1,5-bridge exists as a distorted boatlike cyclohexane ring. The C4–N6 bond (1.628 Å) is much longer than that in simple aziridine compounds

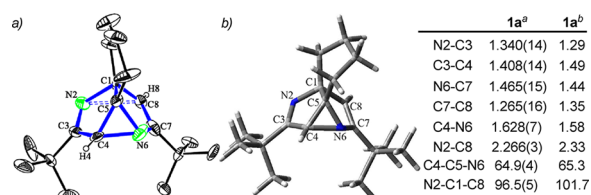


Figure 1. (a) X-ray structure of **1a** (30% thermal ellipsoids; H atoms except H4 and H8 omitted for clarity). (b) B3LYP/6-31G*-optimized localized structure of **1a**. Selected bond lengths (Å) and angles (deg) in the two structures are shown.

(1.520 Å), indicating enhanced strain and through-bond coupling in the NSBV molecule.¹¹ The other bond lengths in the NSBV core are all in the normal range, comparable to those in the calculated localized structure of unsubstituted NSBV.^{4b}

The structures of both localized NSBV **1a** and delocalized NSBV **1a^{deloc}** were optimized using DFT calculations. At the B3LYP/6-31G* level,¹² the ground states of **1a** and **1a^{deloc}** were found to be energy minima, as confirmed by frequency calculations (Figure 1b). The (GIAO)B3LYP/6-311+G**_{calc} calculated ¹³C NMR spectrum of the localized structure was similar to the solid-state ¹³C NMR spectrum of **1a**. The Gibbs free energy of **1a^{deloc}** at 163 K was 1.8 kcal/mol higher than that of the calculated localized **1a**. This trend is consistent with the calculations on unsubstituted NSBV at the MP2/cc-pVDZ level by Greve.^{4b} In addition, the transition state **1a*** for the aza-Cope rearrangement was optimized. The calculations indicated that **1a*** and **1a^{deloc}** are very close in energy, and the potential energy surface has a broad, flat transition-state region (Figure 2). The value of $\Delta G_{163K}^\ddagger$ was calculated to be only 2.1 kcal/mol,

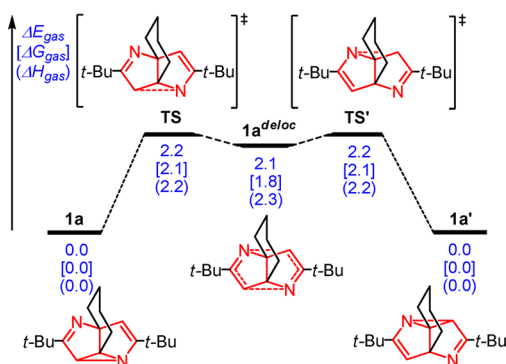


Figure 2. Calculated gas-phase relative energies, Gibbs free energies, and enthalpies (all in kcal/mol) at 163 K, 1 atm.

which is comparable with the experimental result. Because of the small activation barrier from **1a^{deloc}** to **1a**, the rearrangement of **1a^{deloc}** to **1a** should be extremely fast. These results show that the **1a** is the predominant form in solution and the gas phase, with the homoaromatic delocalized **1a^{deloc}** existing as a minor component in the equilibrium. For details of the DFT calculations, including optimized structures and selected bond lengths and angles in **1a^{deloc}** and **1a***, see the SI.

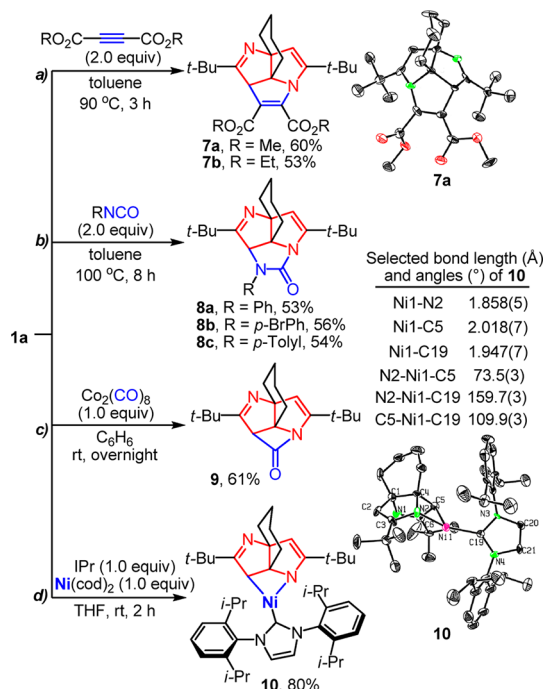
The B3LYP/6-311+G**_{calc}-calculated nucleus-independent chemical shift (NICS) values for **1a^{deloc}** were NICS(0) = −19.0 ppm and NICS(−1) = −14.2 ppm, whose magnitudes are larger than those of **1a** [NICS(0) = −8.4 ppm, NICS(−1) = −7.8 ppm].^{4b,13} In addition, the NICS(0) and NICS(−1) values of the transition-state **1a*** were −17.6 and −13.3 ppm,

respectively. Thus, both **1a^{deloc}** and **1a*** could be homoaromatic on the basis of their NICS values.

The reaction chemistry of NSBVs is unknown except for the thermolysis of **2** to give 1,5-diazocine as reported by Müllen and co-workers.^{5b} Although all of the isolated NSBVs **1** are stable in an inert atmosphere, they are sensitive to acid, base, and silica gel and decompose slowly when exposed to moisture. These observations indicated their highly reactive nature and suggested that the reaction chemistry of such fluxional molecules should be very interesting.

The insertion of unsaturated compounds or low-valent transition metal centers into the weakened C–N bonds interrupt the rapid Cope rearrangement and lead to the diversified ring-expansion products (Scheme 4).^{14,15} Regiospe-

Scheme 4. Insertions into the Weakened C–N Bonds



cific cycloaddition of **1a** with the activated alkynes dimethyl and diethyl acetylenedicarboxylate in toluene at 90 °C readily afforded the 1,5-diazatriquinacenes **7a** and **7b** in 60 and 53% isolated yield, respectively (Scheme 4a).¹⁶ To the best of our knowledge, the syntheses of triquinacenes and azatriquinacenes generally require multistep procedures; thus, this straightforward synthesis of 1,5-diazatriquinacenes should be useful for the construction of structurally interesting yet otherwise unavailable “bowl-shaped” polycyclic frameworks.^{15,17} The cycloaddition of **1a** with isocyanates without any catalyst led to tetracyclic imidazolidinone derivatives **8a–c** in moderate yields (Scheme 4b). It is noteworthy that all reported reactions of simple aziridines with isocyanates require a catalyst such as a transition-metal salt,¹⁸ indicating that the C–N bonds in NSBVs might be more reactive than those in simple aziridines because of the enhanced ring strain caused by the rigid ring system as well as through-bond coupling. The structures of **7a** and **8a** were determined by X-ray diffraction (see the SI).

Carbonylation of **1a** using $\text{Co}_2(\text{CO})_8$ at room temperature gave the tetracyclic β -lactam **9** in 61% yield (Scheme 4c). In contrast, carbonylation reactions of simple aziridines all occur only at elevated temperatures, at high CO pressures, or in the

presence of promoters.¹⁹ Insertion of a low-valent transition metal into the weakened C–N bond was demonstrated by the reaction of **1a** with an N-heterocyclic carbene-ligated Ni(0) complex (Scheme 4d). Addition of **1a** to a 1:1 mixture of bis(1,5-cyclooctadiene)nickel(0) [Ni(cod)₂] and 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) in THF resulted in a rapid color change from dark brown to red. The three-coordinated, four-membered azanickelacycle **10** was isolated in 80% yield, and its structure is shown in Scheme 4. Only one IPr ligand coordinates to the Ni(II) center, probably because of steric hindrance. The angles N2–Ni1–C19 (159.7°) and C5–Ni1–C19 (109.9°) reveal a distorted T-shaped Ni coordination environment.²⁰ Clearly, the enhanced ring strain and through-bond coupling in NSBV molecules in solution weakens the C–N bonds, leading to reactivities different from those of simple aziridine analogues.

In summary, we have successfully established experimental models for structurally and theoretically interesting 2,6-diazasemibullvalenes (NSBVs). The efficient one-pot synthesis and isolation of a series of NSBVs was performed by oxidant-induced C–N bond formation. For the first time, the single-crystal structure of an NSBV (**1a**) was determined, revealing a localized structure. The C₂-symmetric structure of **1a** in solution along with line broadening of the NMR signal at –110 °C indicates an extremely low barrier for the rapid degenerate aza-Cope rearrangement. Theoretical analysis showed that the localized structure is predominant, and the homoaromatic delocalized structure exists as a minor component in the equilibrium. Insertion reactions of unsaturated compounds and a low-valent metal center into the NSBV C–N bond generated diverse ring-expansion products, demonstrating the unusual reactivity of NSBVs. Further studies of the chemical and physical properties of these otherwise unavailable azasemibullvalenes are in progress.

■ ASSOCIATED CONTENT

■ Supporting Information

Experimental and computational procedures, NMR spectra, and crystallographic data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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