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Synthesis of α,α,α′,α′-Tetrachloro-Δ[1]-bipyrrolines and 4,8-Dichloro-2,6-diazasemibuvallenes

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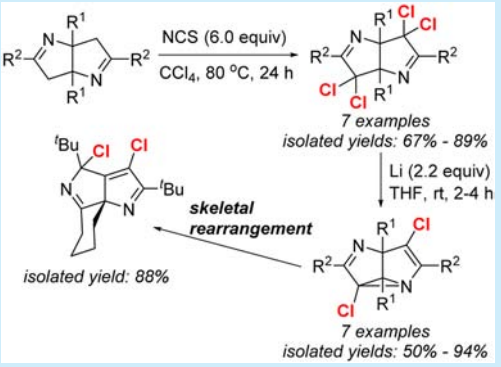
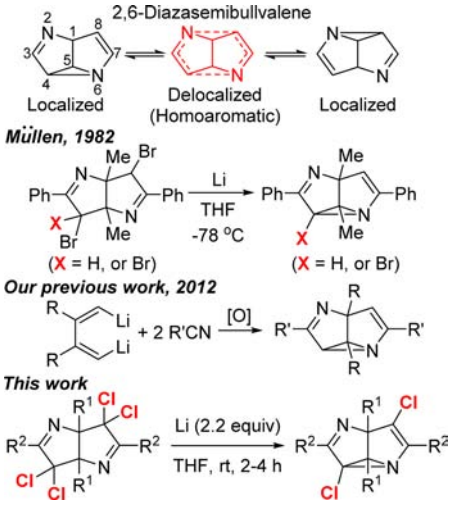
Supporting Information

ABSTRACT: A series of 4,8-dichloro-2,6-diazasemibullvalenes were synthesized and isolated from the reaction of α,α,α′,α′-tetrachloro-Δ[1]-bipyrrolines with lithium via C−N bond formation. All those dichlorodiazasemibullvalene derivatives demonstrated extremely rapid aza-Cope rearrangement in solution. An unprecedented skeletal rearrangement of 4,8-dichloro-2,6-diazasemibullvalene derivatives took place, resulting in the formation of a new bipyrroline skeleton.



2,6-Diazasemibullvalenes (NSBVs) are interesting both theoretically and experimentally (Scheme 1) because such highly strained ring systems demonstrate extremely rapid aza-Cope rearrangement and have been predicted to possess homoaromatic delocalized structures.[1−6] However, due to their inherent structural instability, the studies on NSBVs including their synthesis, reaction chemistry, and synthetic application are very limited.

Scheme 1. 2,6-Diazasemibullvalene and Halogenated Derivatives



The first NSBV derivative, 1,5-dimethyl-3,7-diphenyl-2,6-diazasemibullvalene, was reported by Müllen and co-workers in 1982 (Scheme 1).[5a] Formation of 4-bromo-1,5-dimethyl-3,7-diphenyl-2,6-diazasemibullvalene as the only example of halogenated NSBVs was also achieved by treatment of its corresponding α,α,α′-tribromo-Δ[1]-bipyrroline with lithium.[5a] In 2012, we established two synthetic methods for NSBVs and studied their structures and reaction chemistry (Scheme 1).[6a] However, more diversified NSBV derivatives with different substituents are needed to investigate their physical and chemical properties.

Halogenated NSBVs attracted our attention because the electron-withdrawing halide substituents might have an unprecedented effect on both the rate of aza-Cope rearrangement and their further reaction chemistry, which would make such compounds different from the corresponding non-halogenated ones.[7]

In this work, an efficient synthetic method for α,α,α′,α′-tetrachloro-Δ[1]-bipyrrolines was first developed. Δ[1]-Bipyrrolines are important compounds in many aspects.[8,9] Multiply halogenated Δ[1]-bipyrrolines are expected to have further synthetic applications. Treatment of α,α,α′,α′-tetrachloro-Δ[1]-bipyrrolines with lithium afforded their corresponding 4,8-dichloro-2,6-diazasemibullvalenes in good to excellent isolated yields. Preliminary experimental investigation disclosed that such 4,8-dichloro NSBVs not only demonstrated extremely rapid aza-Cope rearrangement in solution but also underwent unprecedented skeletal rearrangement.

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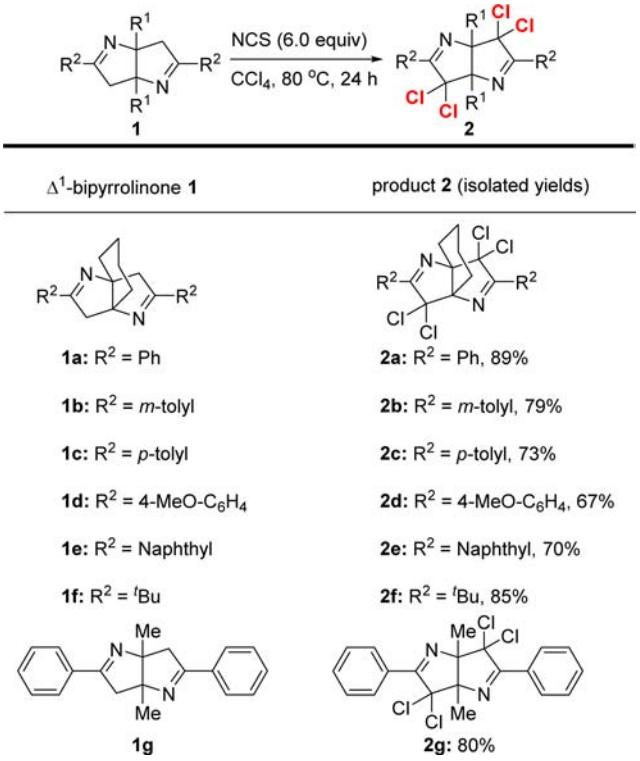
Δ^1-Bipyrroline derivatives **1** could be readily obtained from the reaction of 1,4-dilithio-1,3-butadienes with 2 equiv of nitriles as we previously reported.[6a,8] When Δ^1-bipyrroline **1a** was treated with 6 equiv of *N*-chlorosuccinimide (NCS) at 80 °C for 24 h, the $\alpha,\alpha,\alpha',\alpha'$-tetrachloro-$\Delta^1$-bipyrroline **2a** was obtained in 89% isolated yield (Scheme 2).[9] Similarly, a series

Scheme 2. Synthesis of $\alpha,\alpha,\alpha',\alpha'$-Tetrachloro-$\Delta^1$-bipyrrolines



of $\alpha,\alpha,\alpha',\alpha'$-tetrachloro-$\Delta^1$-bipyrrolines (**2b**−**g**) could be prepared in moderate to excellent isolated yields. The carbon resonance of the C═N bond shifted from 166 ppm for **1a** to 170 ppm for **2a** in the ^{13}C NMR spectrum in $CDCl_3$ solution, indicating the more electron-poor nature of the Δ^1-bipyrroline core due to the multiple chloride substituents. The structure of **2g** was determined by single-crystal X-ray structural analysis (Figure 1).

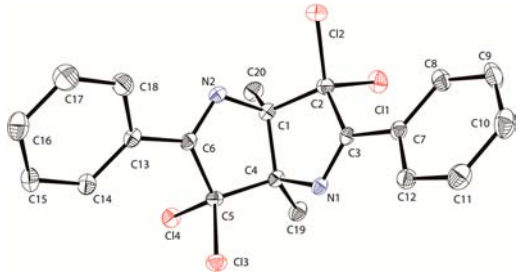
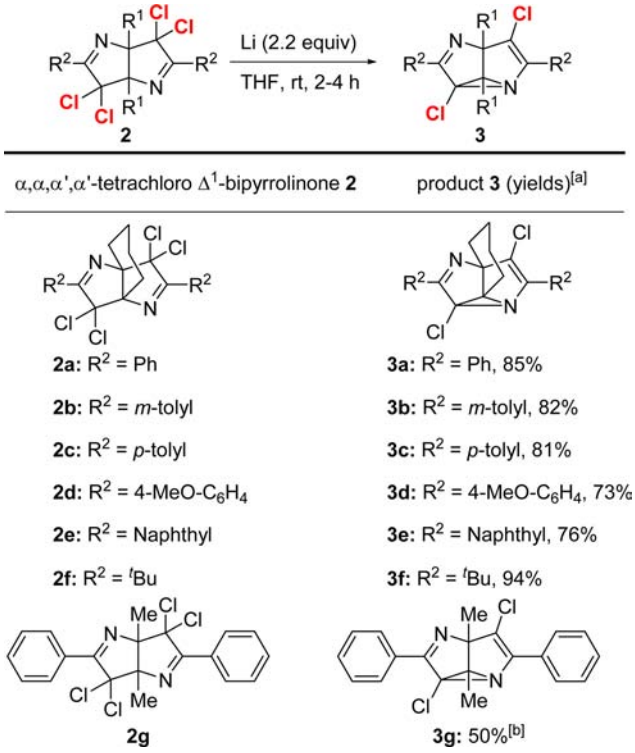


Figure 1. ORTEP drawing of **2g** with 30% thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C(1)−N(2) 1.478(3), C(1)−C(2) 1.550(3), C(2)−C(3) 1.523(3), C(3)−N(1) 1.271(3), C(4)−N(1) 1.476(3), C(4)−C(5) 1.548(3), C(5)−C(6) 1.519(3), C(6)−N(2) 1.274(2), C(2)−Cl(1) 1.797(2), C(2)−Cl(2) 1.777(2), C(5)−Cl(3) 1.780(2), C(5)−Cl(4) 1.795(2).

As shown in Scheme 3, 4,8-dichloro-2,6-diazasemibuvallenes **3** were successfully synthesized and isolated from the reaction

Scheme 3. Synthesis of 4,8-Dichloro 2,6-diazasemibuvallenes



[a]Isolated yield. [b]In situ NMR yield.

of $\alpha,\alpha,\alpha',\alpha'$-tetrachloro Δ^1-bipyrrolines **2** with lithium in THF at room temperature via C−N bond formation.[5a,10] Reductive C−N bond formation has been applied in the synthesis of dibromosemibullvalene derivatives.[11] The in situ NMR experiments indicated that $\alpha,\alpha,\alpha',\alpha'$-tetrachloro-$\Delta^1$-bipyrrolines **2** transformed to their corresponding 4,8-dichloro-2,6-diazasemibuvallenes **3** quantitatively, except for the reaction from **2g** to **3g**.

As indicated by their solution NMR spectra, all these dichlorodiazasemibullvalene derivatives demonstrated extremely rapid aza-Cope rearrangement in solution. The low-temperature NMR of **3a** at −60 °C still showed averaging, symmetrical NMR signals without obvious line broadening, indicating a rapid aza-Cope rearrangement (see details in the Supporting Information). For example, C3/C7 of dichloro diazasemibullvalene **3f** showed a singlet at 157.2 ppm in the ^{13}C NMR spectrum in THF-d_8, which is more downfield shifted than the value of corresponding C3/C7 of the nonchlorinated diazasemibullvalene (163.3 ppm) and the imine carbon of $\alpha,\alpha,\alpha',\alpha'$-tetrachloro-$\Delta^1$-bipyrrolines precursor **2f** (174.8 ppm).[6a] Moreover, the chemical shift (108.3 ppm) of C2/C6 of **3f** is more upfield shifted than the value of C2/C6 of the nonchlorinated diazasemibullvalene (99.6 ppm).[6a] The remarkable chemical shifts of the diazasemibullvalene core of **3** disclosed that the electron-withdrawing chloride substituents would have interesting impact on both the structures and reaction chemistry of dichloro diazasemibullvalene derivatives **3**. Although further full investigation into their physical and chemical properties will be reported in due course, the

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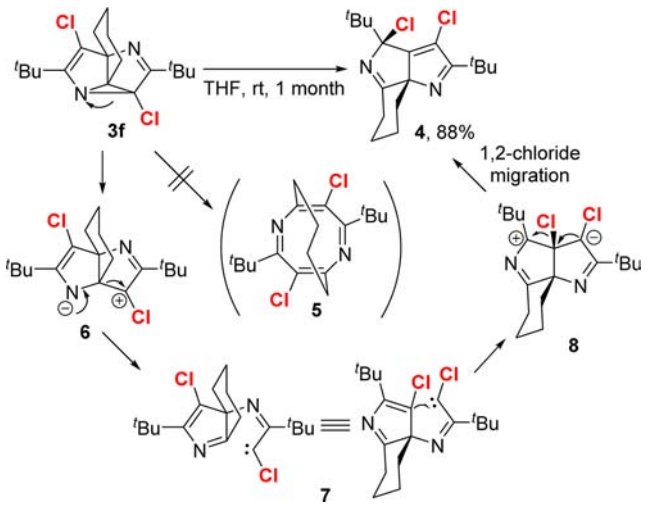
following thermal skeletal rearrangement of **3f** indicated an unprecedented transformation.

It was known that some diazasemibullvalene derivatives could undergo thermal skeletal rearrangement to form their corresponding 1,5-diazocines.[5a,6a] However, when **3f** was heated in THF, a slow skeletal rearrangement was observed, affording an unexpected bipyrroline derivative **4**, along with some unknown products (Scheme 4). The expected corresponding 1,5-diazocine derivative **5** was not observed. When the THF solution of **3f** was kept at room temperature, a clean skeletal rearrangement took place and was completed in one month, affording **4** in 88% isolated yield. As a comparison, the noncholorinated 1,5-bridged diazasemibullvalene was thermally stable.[6a] Thus, this result indicated that the chloride substituents might destabilize the NSBV core and decreased the activation barrier of further transformation. The structure of **4** was determined by single-crystal X-ray structural analysis (Figure 2).

Scheme 4. Skeletal Rearrangement of 4,8-Dichloro-2,6-diazasemibuvallene



A proposed mechanism for the skeletal rearrangement leading to **4** is given in Scheme 4. First, due to the presence of the chloride substituent, ring opening of the three-membered ring took place to give **6**, which generated the chlorine-stabilized carbene intermediate **7**. Similar fragmentation of C–C bond in NSBV derivatives had been illustrated in our previous reports.[6b,e] Electron-withdrawing groups were proposed and found to destabilize the three-membered cyclopropane ring in semibullvalene derivatives.[1c–e] The ring-closure intermediate **8** would be formed from the carbene intermediate **7**.[12] Subsequent 1,2-chloro shift in **8** gave the product **4**.

In summary, we have developed an efficient synthetic method for $\alpha,\alpha,\alpha',\alpha'$-tetrachloro-$\Delta^1$-bipyrrolines, which are expected to have further synthetic applications. A series of 4,8-dichloro-2,6-diazasemibullvalenes were synthesized and isolated from the reaction of $\alpha,\alpha,\alpha',\alpha'$-tetrachloro-$\Delta^1$-bipyrrolines with lithium via C–N bond formation. Further detailed studies of the chemical and physical properties of these otherwise unavailable multiply halogenated Δ^1-bipyrrolines and diazasemibullvalenes are in progress.

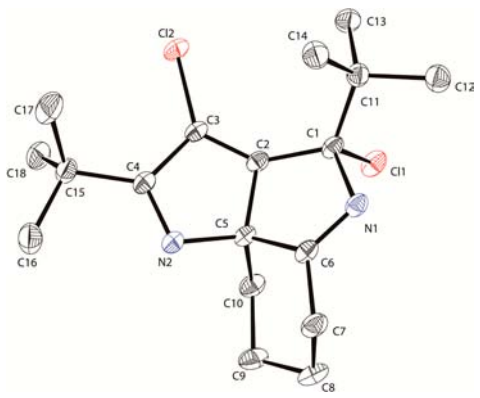


Figure 2. ORTEP drawing of **4** with 30% thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C(1)–N(1) 1.489(3), C(1)–C(2) 1.509(4), C(2)–C(3) 1.341(4), C(3)–C(4) 1.496(4), C(4)–N(2) 1.291(3), N(2)–C(5) 1.462(4), C(5)–C(6) 1.501(4), C(6)–N(1) 1.285(4), C(1)–Cl(1) 1.841(3), C(3)–Cl(2) 1.725(3).

■ ASSOCIATED CONTENT

Supporting Information

Experimental details; X-ray data for **2g** (CCDC 1036087) and **4** (CCDC 1036088); scanned NMR spectra of all new products. 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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