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Investigation of the Rearrangement in Alkyl-Bridged Bis(carbamoyldiaziridine) Derivatives

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The thermal treatment of alkyl-bridged bis(carbamoyldiaziridine) derivatives in toluene at 100 °C led to the formation of new saturated five- and six-membered 1,3-diaza-heterocyclic compounds from ethylene- or propylene-bridged bis(carbamoyldiaziridine) derviatives, respectively. Detailed experimental investigations of this reaction revealed an unprecedented intramolecular eliminative rearrangement, involving the two adjacent diaziridine moieties. The loss of a three-carbon fragment by elimination of acetone during the reaction was confirmed by GC–MS measurements. The products of the rearrangement were fully characterized, and their structures were confirmed by X-ray crystal structure analysis. Furthermore, a reaction mechanism of the eliminative rearrangement was proposed, and the reaction pathway was corroborated by DFT calculations of gas-phase model structures at the B3LYP/6-31G** level.

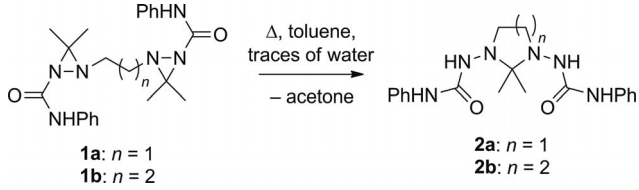
Introduction

Diaziridines (1,2-diazacyclopropanes)[1] are an intriguing class of compounds and have been intensively characterized and investigated, since the pioneering synthetic work of Schmitz et al. in 1959.[2,3] Similar to aziridines, diaziridines contain chirotopic nitrogen atoms and typically show relatively high interconversion barriers[4–6] because of the nitrogen atoms incorporated into the strained three-membered ring and the electronic and steric effects, which destabilize the transition state of the interconversion process. Furthermore, a double interconversion[7] of the chirotopic N-centers is necessary. These properties allow the separation and isolation of single stereoisomers, for example, by chromatographic separation techniques, and make the investigation of the stereochemistry and stereodynamics of these compounds feasible.[8] Depending on the sterics and electronics of the *N*-substituents in aziridines and diaziridines, the free activation energy $\Delta G^{\ddagger}$ for the interconversion of the chirotopic nitrogen atoms is in a range between approximately 90 kJ/mol and 130 kJ/mol.[8b,8d,8f,9] Furthermore, diaziridines show pronounced neurotropic activity.[10]

Despite the relatively weak N–N bond and the highly strained three-membered ring system, diaziridines are thermodynamically stable. Diaziridines are highly reactive and often undergo electrocyclic ring-opening reactions with electron-deficient alkenes, alkynes, or electrophilic reagents such as ketenes, isocyanates, isothiocyanates, and acylating reagents at elevated temperatures. Under such conditions, they are prone to ring-expansion reactions, yielding heterocyclic systems.[11]

Results and Discussion

Herein, we report a new intramolecular eliminative rearrangement reaction of alkyl-bridged bis(diaziridines) to form new saturated five- and six-membered 1,3-diaza-heterocyclic compounds (see Scheme 1).



1a: *n* = 1
1b: *n* = 2

2a: *n* = 1
2b: *n* = 2

Scheme 1. Rearrangement of alkyl-bridged bis(carbamoyldiaziridine) derivatives to give 1,1′-(2,2-dimethylimidazolidine-1,3-diyl)-bis(3-phenylurea) (**2a**) and 1,1′-(2,2-dimethyldiazinane-1,3-diyl)bis-(3-phenylurea) (**2b**).

The reactants 2,2′-(ethane-1,2-diyl)bis(3,3-dimethyl-*N*-phenyldiaziridine-1-carboxamide) (**1a**) and 2,2′-(propane-1,3-diyl)bis(3,3-dimethyl-*N*-phenyldiaziridine-1-carboxamide) (**1b**) were synthesized according to a procedure published by Makhova et al.[12] by starting from acetone through the preparation of acetone oxime *O*-sulfonic esters according to the method of Oxley and Short.[13] The oxime esters were then treated with α,ω-diaminoalkanes to give α,ω-bis(3,3-dimethyldiaziridin-1-yl)alkanes.[12a] The reaction of phenyl isocyanate with both diaziridine-NH groups yielded the corresponding carbamoyl-substituted bis(diaziridine) derivatives (see Scheme 2).[12b]

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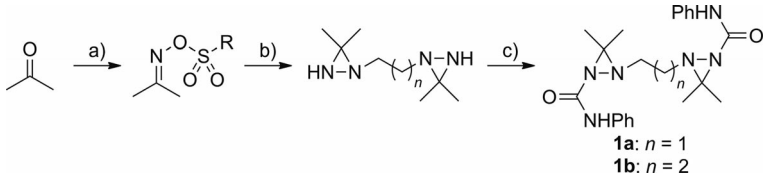
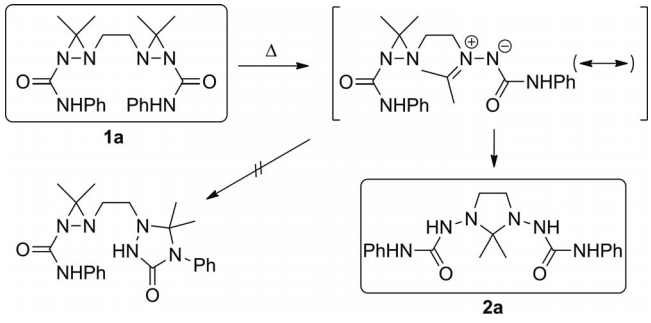


Scheme 2. Synthesis of the reactants for the rearrangement reaction. Reagents and conditions: (a) NaOH (5 M solution), $HONH_3Cl$, RSO_2Cl (R = phenyl or *p*-tolyl), 0 °C, 1 h;[13] (b) dichloromethane, $H_2NCH_2(CH_2)_xNH_2$ (*x* = 1, 2, or 3) (0.5 equiv.), NEt_3, 25–30 °C, 5–11 d;[12a] (c) anhydrous dichloromethane, PhN=C=O (2.4 equiv.).[12b]

We observed that compounds **1a** and **1b** underwent rearrangement in toluene when heated at 100 °C for 18 h. The products were formed by a sigmatropic rearrangement reaction occurring with the formal elimination of C_3H_4 (see Scheme 1). Previously reported rearrangements of diaziridines and, in particular, of *N*-carbamoyl-substituted diaziridines describe rearrangement pathways involving carbamoyl groups, which is not the case with our investigated reactions (see Scheme 3).[14] The unsubstituted bis(diaziridine) 1,2-bis(3,3-dimethyldiaziridin-1-yl)ethane (tetramezine) did not react under the reported conditions herein and was completely reisolated. This indicates that the electron-withdrawing carbamoyl group was essential for the rearrangement, which is explained by the effective stabilization of the proposed reaction intermediate (see Mechanistic Insights). This is also corroborated by the rearrangement of 2,4-dinitrophenyl-substituted 1,2-bis(3,3-dimethyldiaziridin-1-yl)-ethane (**3a**, see Scheme 4 and Figure 4).



Scheme 3. Proposed reaction pathway of the rearrangement reaction. The alternative rearrangement pathway, as described in the literature,[14] was not observed.

The isolated yields of the rearrangement product deceased with the length of the alkylene bridge and the ring size. The reaction proceeded in 67% isolated yield for the five-membered ring and 55% for the six-membered ring product. The reaction leading to the seven-membered ring was not observed. The obtained compounds were soluble in DMSO (dimethyl sulfoxide) and slightly soluble in DMF (*N*,*N*-dimethylformamide), but almost insoluble in less polar solvents such as acetonitrile, dichloromethane, chloroform, toluene, or diethyl ether. The rearrangement product **2a** was unambiguously identified by X-ray crystal structure analysis (see Figure 1).

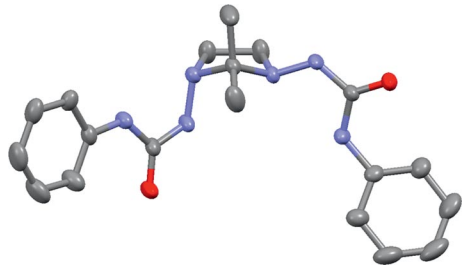


Figure 1. X-ray crystal structure of **2a**. The compound crystallized in racemic form. The enantiomers were formed because of the chirotopic nitrogen atoms in the heterocyclic ring system.

The extended system **2b** obtained by the rearrangement of **1b** shows a similar X-ray crystal structure, where the compound crystallized as a racemic mixture because of the chirotopic nitrogen atoms in the heterocyclic ring system (see Figure 2).

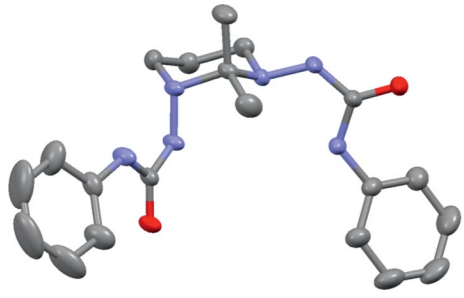
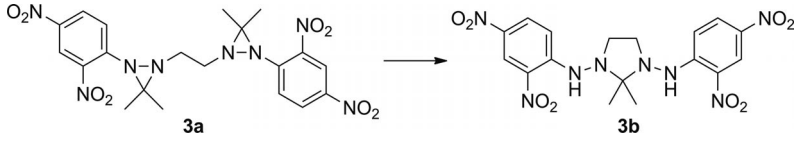


Figure 2. X-ray crystal structure of **2b**.

The crystal structure of the bis(phenylurea)-substituted heterocyclic molecules was stabilized by a network of intermolecular hydrogen bonds (see Figure 3). This network also



Scheme 4. Rearrangement of 2,4-dinitrophenyl-substituted bis(diaziridine) **3a** to *N*,*N*-bis(2,4-dinitrophenyl)-2,2-dimethylimidazolidine-1,3-diamine (**3b**).

stabilized the enantiomeric forms of the molecules in the crystal. The corresponding *meso* form with the *cis*-oriented phenylurea groups was not observed in the solid state.

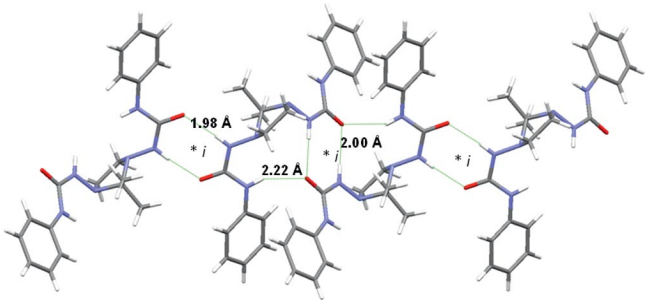


Figure 3. Hydrogen-bond network stabilizing the crystal structure of racemic **2a**. Bond lengths of hydrogen bonds and inversion centers (*i*) are depicted in the structure.

However, in solution the heterocyclic ring system and the chirotopic nitrogen centers were prone to rapid conformational change and inversion, respectively. These processes resulted in a pronounced peak-broadening at room temperature and –50 °C for all of the NMR signals of the ring groups. In particular, the ^{13}C NMR signals for all of the ring carbon atoms were greatly broadened because of the longer relaxation times.

To probe the hypothesis that an electron-withdrawing group is essential for this type of rearrangement reaction, we prepared 2,4-dinitrophenyl-substituted bis(diaziridine) **3a** and subjected this compound to our described rearrangement conditions. Indeed, the same rearrangement proceeded with the electron-withdrawing 2,4-dinitrophenyl groups (see Scheme 4).

The rearrangement product *N*,*N*-bis(2,4-dinitrophenyl)-2,2-dimethylimidazolidine-1,3-diamine (**3b**) was isolated and characterized by X-ray crystal structure analysis (see Figure 4).

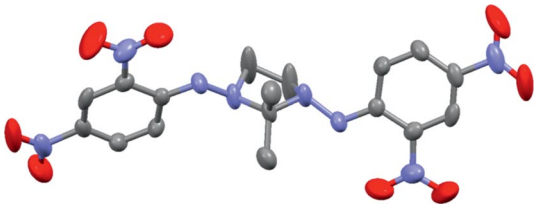


Figure 4. X-ray crystal structure of **3b**. The compound crystallized in racemic form.

Mechanistic Insights

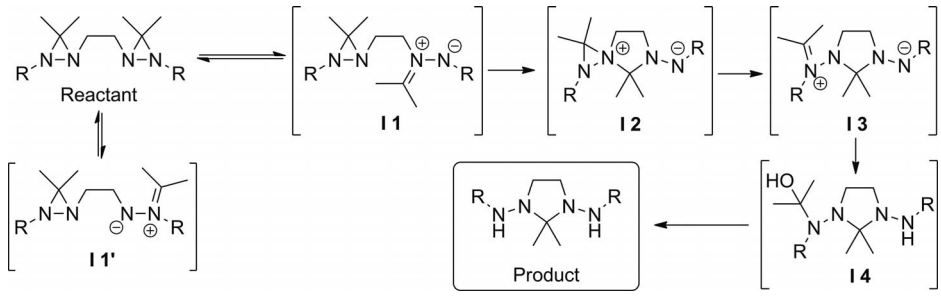
To investigate the mechanism of the rearrangement reaction, we focused first on the formation of the elimination product. Therefore, we performed the rearrangement reactions in a sealed flask using DMF, a less volatile solvent. Upon completion of the reactions, all of the samples were analyzed by GC–MS. We identified acetone as the elimination product, showing significant EI-MS signals at *m*/*z* = 58 $[H_3C(CO)CH_3]^+$ and 43 $[H_3CCO]^+$ at a retention time of 3.11 min. This suggested that the small traces of water (18 μL/mmol) in the solvent were sufficient to produce acetone.

To corroborate our proposed reaction mechanism we performed DFT calculations of gas-phase model structures at the B3LYP/6-31G** level for possible reaction intermediates for the rearrangement of **1a** to **2a**.

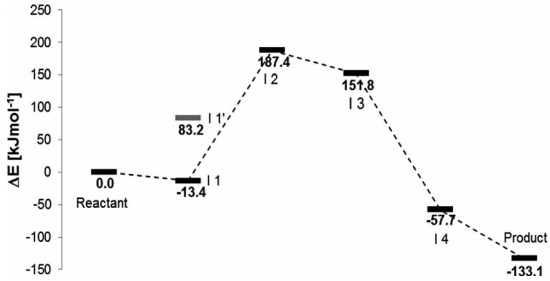
We assume that the first step of the reaction mechanism is a thermal electrocyclic ring opening[15] of one of the diaziridine moieties, which results in an azomethine imine group isoelectronic to an allyl anion. The formation of an azomethine imine intermediate had been previously suggested for the interconversion of diaziridines and for the electrocyclic reactions of diaziridines (see Schemes 3 and 5).[8f,11a,11b,14,16] Furthermore, these structures are stabilized in compounds such as 1-(arylylidene)pyrazolidone 3-betaines.[17] Such compounds are cyclized by UV irradiation to give the corresponding diaziridines.[18] Upon heating, they can be retransformed into the azomethine imines. The stability of these compounds can be attributed to the presence of the carbonyl group next to the nitrogen atom. We anticipate in our investigated reactions that the carbonyl group stabilizes the ring-opened intermediate in a similar fashion. Additional stabilization is expected because of hyperconjugation.

According to our calculations, the ring opening to intermediate **I1** was clearly favored over the bond cleavage to form **I1′** (see Schemes 5 and 6). In the case of **I1** and with the observed five-membered ring product (Scheme 4), this reasoning is in line with the more efficient stabilization of the heteroallyl system by the adjacent carbamoyl group (R). Similar results were found by DFT calculations for the opening of the diaziridine ring in 1,2-diazabicyclo[3.1.0]-hexane-2-ones.[19]

A detailed analysis of the natural bond orbitals (NBOs) of **I1** revealed that the LUMO is located at the N=CMe$_2$



Scheme 5. Proposed mechanism of the rearrangement reaction.



Scheme 6. Energy diagram of the calculated energies of the reactant, product, and proposed reaction intermediates.

group, which can easily be attacked by the lone pair of the diaziridine nitrogen atom located next to the CH_2 group. Both orbitals are depicted in Figure 5.

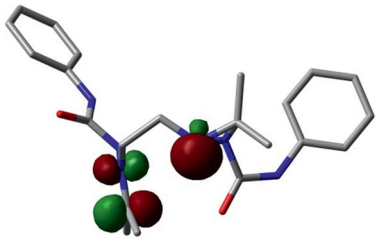


Figure 5. LUMO (left) and nitrogen lone pair (right) of intermediate **I1** revealed by NBO analysis at isosurface values of 0.1.

Through an intramolecular attack of the lone pair at the LUMO, spirocyclic intermediate **I2** is formed, followed by a ring-opening reaction to give intermediate **I3**. The addition of a water molecule leads to intermediate **I4**. In the last step of the reaction, acetone is eliminated to form the product. The total energy balance is exothermic (about 130 kJ/mol in the gas phase). It is noteworthy that the lattice energy from the crystalline product formation, caused by the formation of the strong hydrogen bonds (see Figure 3), has an additional exothermic contribution to the overall energy balance.

Another possible mechanism includes a simultaneous electrocyclic ring-opening reaction of both diaziridine rings followed by cyclization to form **I3**. However, the probability for the simultaneous opening of both diaziridine moieties is highly unlikely.

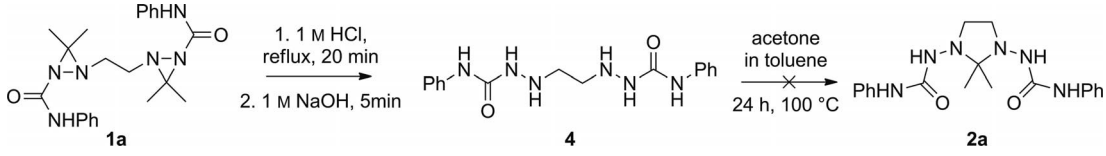
An alternative mechanism can be proposed by hydrolysis of the two diaziridine moieties, which would yield a bis(hydrazine) derivative and 2 equiv. of acetone. Recondensation of the bis(hydrazine) derivative with acetone would result in the observed product (see Scheme 7). To probe this mechanism, we prepared the bis(hydrazine) **4** by hydrolysis of **1a**. Product **4** was subjected to the same reaction conditions as the rearrangement reaction, that is, adding 10 equiv. of acetone to a sealed vial to avoid evaporation of acetone at elevated reaction temperatures. The formation of 1,1′-(2,2-dimethylimidazolidine-1,3-diyl)bis(3-phenylurea) (**2a**) was not observed, bis(hydrazine) **4** was completely reisolated. From these results, we conclude that the simple decomposition and recondensation of the bis(hydrazine) with acetone can be excluded.

Conclusions

We presented a new type of an eliminative rearrangement reaction involving alkyl-bridged bis(carbamoyldiaziridine) derivatives. This rearrangement represents the first example of an intramolecular reaction involving two diaziridine groups. The reaction mechanism was investigated experimentally by GC–MS as well as theoretically by using DFT calculations of gas-phase model structures. The reaction may be expanded to other bis(diaziridine) derivatives with electron-withdrawing substituents and provides a synthetic pathway towards previously unknown substituted heterocyclic compounds.

Experimental Section

General Methods: All of the reagents and solvents were obtained from Acros, ABCR, Alfa Aesar, Sigma–Aldrich, or VWR and were used without further purification unless otherwise noted. Anhydrous dichloromethane was prepared by using an MBRAUN MB SCS-800 solvent purification system. The handling of moisture-sensitive materials was carried out under nitrogen by using Schlenk techniques. Deuterated solvents were purchased from Sigma–Aldrich. The NMR spectroscopic data were recorded with Bruker Avance 500, Bruker Avance 400, or Bruker Avance 300 spectrometers at room temperature. The chemical shifts (in ppm) were referenced to the residual solvent protons. The multiplicity of the signals was assigned as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). The ^{13}C NMR assignments were achieved by using HSQC (heteronuclear single quantum correlation) experiments. Infrared (IR) spectra were recorded with a Bruker TFS66 (Rheinstetten, Germany) or a Thermo Fisher Scientific Nicolet 6700 Advanced FTIR Spectrometer equipped with a Smart iTR ATR Diamond (Madison, WI, USA). HR (ESI) mass spectra were recorded with a Bruker ApexQe hybrid 9.4 T FT-ICR-MS instrument. HR (EI) and HR [FAB (fast atom bombardment)] mass spectra were recorded with a JEOL JMS-700 magnetic sector instrument. GC–MS measurements were performed with a Thermo Trace GC PolarisQ (San Jose, CA, USA) equipped with a split injector (250 °C), a flame-ionization detector (250 °C), and a quadrupole ion trap mass spectrometer. An HP5-MS column was used for separating the analytes (30 m × 0.25 mm i.d., 250 nm film thickness). Helium was



Scheme 7. Alternative reaction pathway through the hydrolysis of the two diaziridine moieties to form bis(hydrazine) **4**. Attempted recondensation of **4** with acetone does not yield 1,1′-(2,2-dimethylimidazolidine-1,3-diyl)bis(3-phenylurea) (**2a**).

used as an inert carrier gas at 80 kPa. All of the measurements were isothermally performed at 80 °C. EI mass spectra were recorded at an ion-source temperature of 200 °C and an electron energy of 70 eV. The data acquisitions were performed by using the Xcalibur software package (Thermo, San Jose, CA, USA). The crystal structures were recorded with a Bruker APEX or a Bruker Smart CCD. The intensities of the reflections were corrected for Lorentz and polarization effects. An empirical absorption correction was applied by using SADABS (2008/1)[20] based on the Laue symmetry of the reciprocal space. The structures were solved by direct methods and refined against F^2 with a full-matrix least-squares algorithm by using the SHELXTL software package (2008/4).[21] The hydrogen atoms were treated by using appropriate riding models.

General Method for the Synthesis of 2,2′-(Alkane-α,ω-diyl)bis(3,3-dimethyldiaziridine): Acetone oxime *O*-benzenesulfonate or acetone oxime *O*-*p*-toluenesulfonate are prepared from acetone according to the synthesis by Oxley and Short.[13] The oxime ester was then treated with α,ω-diaminoalkane in dichloromethane with triethylamine according to the method of Makhova et al.[12a]

General Method for the Synthesis of 1: Compounds **1a** and **1b** were synthesized according to the method of Makhova et al.[12b] 1,2-Bis(3,3-dimethyldiaziridin-1-yl)ethane (851 mg, 5.00 mmol) or 1,3-bis(3,3-dimethyldiaziridin-1-yl)propane (921 mg, 5.00 mmol) were dissolved in anhydrous dichloromethane (20 mL). A solution of phenyl isocyanate (1.30 mL, 12.0 mmol) in anhydrous dichloromethane (35 mL) was added dropwise at 0 °C. The solution was stirred at 0 °C for 1 h and then at room temperature for 10 min. The solvent was removed under high vacuum. The white precipitate formed was washed with diethyl ether (2 × 5 mL) and dried under high vacuum.

2,2′-(Ethane-1,2-diyl)bis(3,3-dimethyl-*N*-phenyldiaziridine-1-carboxamide) (1a): White solid (1.99 g, 97%), m.p. 144–147 °C. ^{1}H NMR (500 MHz, CD_2Cl_2, 25 °C): δ = 8.76 (s, 2 H, NH), 7.51 (d, $^3J_{H,H}$ = 7.5 Hz, 4 H, *o*-CH^{Ar}), 7.29 (dd, $^3J_{H,H}$ = 7.5 Hz, $^3J_{H,H}$ = 7.5 Hz, 4 H, *m*-CH^{Ar}), 7.06 (t, $^3J_{H,H}$ = 7.4 Hz, 2 H, *p*-CH^{Ar}), 3.32 (dq, $^2J_{H,H}$ = 2.8 Hz, $^3J_{H,H}$ = 4.8 Hz, 2 H, CH_2^a), 2.75 (dq, $^2J_{H,H}$ = 2.6 Hz, $^3J_{H,H}$ = 4.7 Hz, 2 H, CH_2^b), 1.58 (s, 6 H, CH_3^a), 1.42 (s, 6 H, CH_3^b) ppm. ^{13}C NMR (125 MHz, CD_2Cl_2, 25 °C): δ = 160.19 (C=O), 137.87 (*ipso*-C^{Ar}), 128.91 (*m*-C^{Ar}), 123.92 (*p*-C^{Ar}), 119.39 (*o*-C^{Ar}), 65.10 (C^{ring}), 53.11 (CH_2), 23.07 (CH_3^b), 18.44 (CH_3^a) ppm. HRMS (ESI): calcd. for [M + H]$^+$ 409.23456; found 409.23477; calcd. for [M + Na]$^+$ 431.21660; found 431.21674; calcd. for [M + K]$^+$ 447.19053; found 447.19069; calcd. for [2 M + K]$^+$ 839.44397; found 839.44429.

2,2′-(Propane-1,3-diyl)-bis(3,3-dimethyl-*N*-phenyldiaziridine-1-carboxamide) (1b): White solid (2.01 g, 95%), m.p. 122–124 °C. ^{1}H NMR (300 MHz, CD_2Cl_2 25 °C): δ = 8.03 (s, 2 H, NH), 7.46 (d, $^3J_{H,H}$ = 8.4 Hz, 4 H, *o*-CH^{Ar}), 7.30 (dd, $^3J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 8.2 Hz, 4 H, *m*-CH^{Ar}), 7.09 (t, $^3J_{H,H}$ = 7.4 Hz, 2 H, *p*-CH^{Ar}), 2.99–2.86 (m, 2 H, NCH_2^a), 2.82–2.69 (m, 2 H, NCH_2^b), 2.18–2.05 (m, 2 H, CH_2), 1.51 (s, 6 H, CH_3^a), 1.37 (s, 6 H, CH_3^b) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2, 25 °C): δ = 160.50 (C=O), 137.44 (*ipso*-C^{Ar}), 129.04 (*m*-C^{Ar}), 124.12 (*p*-C^{Ar}), 119.39 (*o*-C^{Ar}), 66.73 (C^{ring}), 51.00 (NCH_2), 28.79 (CH_2), 22.00 (CH_3^b), 18.64 (CH_3^a) ppm. HRMS (ESI): calcd. for [M + H]$^+$ 423.25030; found 423.25059; calcd. for [M + Na]$^+$ 445.23225; found 445.23255; calcd. for [M + K]$^+$ 461.20618; found 461.20651; calcd. for [2 M + Na]$^+$ 867.47527; found 867.47392; calcd. for [2 M + K]$^+$ 883.44921; found 883.44886.

General Method for the Rearrangement of 1 to 2: 2,2′-(Ethane-1,2-diyl)bis(3,3-dimethyl-*N*-phenyldiaziridine-1-carboxamide) (**1a**, 409 mg, 1.00 mmol) or 2,2′-(propane-1,3-diyl)bis(3,3-dimethyl-*N*-phenyldiaziridine-1-carboxamide) (**1b**, 423 mg, 1.00 mmol) was suspended in toluene (20 mL), and the resulting solution was heated to 100 °C as it was stirred. The suspended reactant dissolved after a few minutes. After that time, the stirring was stopped, and the heating was continued at 100 °C for 18 h. Then, the suspension was slowly cooled to room temperature. The precipitate was collected on a suction filter, washed with dichloromethane (10 mL), and dried under high vacuum.

1,1′-(2,2-Dimethylimidazolidine-1,3-diyl)bis(3-phenylurea) (2a): Colorless crystals (247 mg, 67%), m.p. 206–207 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 8.71 (s, 2 H, PhNH), 7.96 (s, 2 H, NNH), 7.51 (d, $^3J_{H,H}$ = 7.6 Hz, 4 H, *o*-CH^{Ar}), 7.26 (dd, $^3J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 7.3 Hz, 4 H, *m*-CH^{Ar}), 6.97 (t, $^3J_{H,H}$ = 7.3 Hz, 2 H, *p*-CH^{Ar}), 3.80–2.60 (br. m, 4 H, CH_2), 1.15 (s, 6 H, CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 156.14 (C=O), 139.47 (*ipso*-C^{Ar}), 128.38 (*m*-C^{Ar}), 121.93 (*p*-C^{Ar}), 119.30 (*o*-C^{Ar}), 81.90 (C^{ring}), 49.95 (CH_2), 20.15 (CH_3) ppm. HRMS (ESI): calcd. for [M + H]$^+$ 369.20335; found 369.20332; calcd. for [M + Na]$^+$ 391.18530; found 391.18527; calcd. for [M + K]$^+$ 407.15923; found 407.15924; calcd. for [2 M + H]$^+$ 737.39942; found 737.39959; calcd. for [2 M + Na]$^+$ 759.38137; found 759.38136; calcd. for [2 M + K]$^+$ 775.35531; found 775.35552. $C_{19}H_{24}N_6O_2$ (368.43): calcd. C 61.94, H 6.57, N 22.81; found C 62.17, H 6.49, N 22.53. IR (KBr): $\tilde{\nu}$ = 3094, 3063, 2979, 2938, 1680, 1601, 1530, 1447, 755, 693 cm^{-1}.

1,1′-(2,2-Dimethyldiazinane-1,3-diyl)bis(3-phenylurea) (2b): Colorless crystals (210 mg, 55%), m.p. 201–203 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 8.67 (s, 2 H, PhNH), 8.09 (br. s, 2 H, NNH), 7.55 (d, $^3J_{H,H}$ = 7.7 Hz, 4 H, *o*-CH^{Ar}), 7.26 (dd, $^3J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 8.1 Hz, 4 H, *m*-CH^{Ar}), 6.97 (t, $^3J_{H,H}$ = 7.3 Hz, 2 H, *p*-CH^{Ar}), 3.17–2.92 (br. m, 2 H, NCH_2^a) 2.94–2.74 (br. m, 2 H, NCH_2^b), 2.10–1.72 (br. m, 2 H, CH_2), 1.29 (s, 6 H, CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 156.00 (C=O), 139.44 (*ipso*-C^{Ar}), 128.26 (*m*-C^{Ar}), 122.03 (*p*-C^{Ar}), 119.90 (*o*-C^{Ar}), 77.91 (C^{ring}), 48.60 (NCH_2), 20.85 (CH_2), 20.85 (CH_3) ppm. HRMS (ESI): calcd. for [M + H]$^+$ 383.21900; found 383.21923; calcd. for [M + Na]$^+$ 405.20095; found 405.20119; calcd. for [M + K]$^+$ 421.17488; found 421.17515; calcd. for [2 M + Na]$^+$ 787.41267; found 787.41256; calcd. for [2 M + K]$^+$ 803.38661; found 803.38664. IR (KBr): $\tilde{\nu}$ = 3059, 2940, 1677, 1601, 1529, 1447, 1313, 1232, 753, 692 cm^{-1}.

Hydrolysis of 1a to 4: 2,2′-(Ethane-1,2-diyl)bis(3,3-dimethyl-*N*-phenyldiaziridine-1-carboxamide) (**1a**, 204 mg, 500 μmol) was suspended in hydrochloric acid (1 M solution, 5 mL), and the mixture was heated at reflux for about 20 min. After cooling to room temperature, sodium hydroxide (1 M solution, 10 mL) was added. After 5 min of stirring, the product was collected on a suction funnel, washed with water (20 mL), and dried under high vacuum in a desiccator over P_4O_{10}.

2,2′-(Ethane-1,2-diyl)bis(*N*-phenylhydrazinecarboxamide) (4): White solid (155 mg, 94%), m.p. 178–179 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO, 25 °C): δ = 8.68 (s, 2 H, PhNH), 7.60 [s, 2 H, R(CO)NH], 7.52 (d, $^3J_{H,H}$ = 7.9 Hz, 4 H, *o*-CH^{Ar}), 7.21 (dd, $^3J_{H,H}$ = 7.6, 8.2 Hz, 4 H, *m*-CH^{Ar}), 6.91 (dd, $^3J_{H,H}$ = 7.3, 7.4 Hz, *p*-CH^{Ar}) 5.06 (s, 2 H, N*H*CH_2), 2.83 (s, 4 H, CH_2) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO, 25 °C): δ = 156.64 (C=O), 139.83 (*ipso*-C^{Ar}), 128.48 (*m*-C^{Ar}), 121.49 (*p*-C^{Ar}), 118.43 (*o*-C^{Ar}), 49.10 (CH_2) ppm. HRMS (ESI): calcd. for [M + H]$^+$ 329.17205; found 329.17214; calcd. for [M + Na]$^+$ 351.15400; found 351.15408; calcd. for [M + K]$^+$ 367.12793; found 367.12809; calcd. for [2 M + H]$^+$ 657.33682; found 657.33746; calcd. for [2 M + Na]$^+$ 679.31877; found 679.31907; calcd. for [2 M + K]$^+$ 695.29271; found 695.29360. IR: $\tilde{\nu}$ = 3328, 3294, 3232, 3012, 2925, 2863, 1631, 1592, 1569, 1542,

1496, 1444, 1314, 1298, 1276, 1244, 1078, 1050, 910, 889, 846, 789, 737, 693 cm^{-1}.

X-ray Crystal Structure Analyses

Crystal Data of 2a: $C_{19}H_{24}N_6O_2$, M = 368.44 $g\,mol^{-1}$, triclinic, space group $P\bar{1}$, a = 8.8194(8) Å, b = 9.9670(10) Å, c = 12.6762(12) Å, α = 106.504(2)°, β = 105.951(2)°, γ = 103.066(2)°, V = 969.72(16) $Å^3$, Z = 2, $d_{calcd.}$ = 1.262 $g\,cm^{-1}$, μ = 0.086 mm^{-1}, crystal size 0.26 × 0.17 × 0.14 mm, number of reflections: 10393, number of independent reflections: 4788, R_{int} = 0.0208, R_1 = 0.050 [from 4007 unique reflections with $I > 2\sigma(I)$] and wR^2 = 0.118 (from all 4788 unique reflections).

Crystal Data of 2b: $C_{20}H_{26}N_6O_2$, M = 382.47 $g\,mol^{-1}$, triclinic, space group $P\bar{1}$, a = 8.8974(3) Å, b = 10.3608(4) Å, c = 12.2434(5) Å, α = 104.666(1)°, β = 104.697(1)°, γ = 100.356(1)°, V = 1019.61(7) $Å^3$, Z = 2, $d_{calcd.}$ = 1.246 $g\,cm^{-1}$, μ = 0.084 mm^{-1}, crystal size 0.42 × 0.18 × 0.07 mm, number of reflections: 10278, number of independent reflections: 4633, R_{int} = 0.0549, R_1 = 0.049 [from 3376 unique reflections with $I > 2\sigma(I)$] and wR^2 = 0.120 (from all 4633 unique reflections).

Crystal Data of 3b: $C_{17}H_{18}N_8O_8$, M = 462.39 $g\,mol^{-1}$, monoclinic, space group $C2/c$, a = 13.492(3) Å, b = 6.9933(14) Å, c = 22.711(4) Å, β = 105.827(4)°, V = 2061.7(7) $Å^3$, Z = 4, $d_{calcd.}$ = 1.490 $g\,cm^{-1}$, μ = 0.121 mm^{-1}, crystal size 0.26 × 0.20 × 0.06 mm, number of reflections: 11203, number of independent reflections: 1951, R_{int} = 0.0442, R_1 = 0.073 [from 1728 unique reflections with $I > 2\sigma(I)$] and wR^2 = 0.181 (from all 1951 unique reflections).

CCDC-874715 (for **2a**), -874716 (for **2b**), -876725 (for **3a**), -874717 (for **3b**), -874710 (for acetone oxime *O*-benzenesulfonate), -874711 (for acetone oxime *O*-*p*-toluenesulfonate), -874712 [for *meso*-1,2-bis(3,3-dimethyldiaziridin-1-yl)ethane], -874713 [for racemic 1,2-bis(3,3-dimethyldiaziridin-1-yl)ethane], and -874714 [for *meso*-1,4-bis(3,3-dimethyldiaziridin-1-yl)butane] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Computational Calculations: A conformational search was achieved by using MM+ implemented with the HyperChem 7.1 software package.[22] The geometry optimizations of gas-phase model structures were achieved by DFT calculations at the B3LYP/6-31G** level using Gaussian 09.[23] The GaussView[24] software package was used for the visualization of the results.

Supporting Information (see footnote on the first page of this article): Synthetic procedures and ^1H and ^{13}C NMR spectra of all compounds.

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