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Communication

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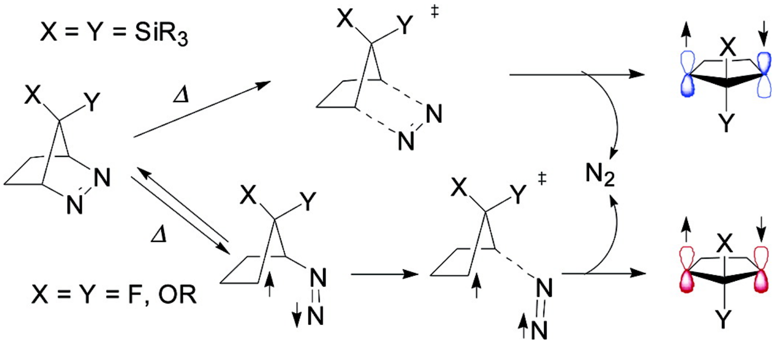

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Novel Substituent Effects on the Mechanism of the Thermal Denitrogenation of 2,3-Diazabicyclo[2.2.1]hept-2-ene Derivatives, Stepwise versus Concerted

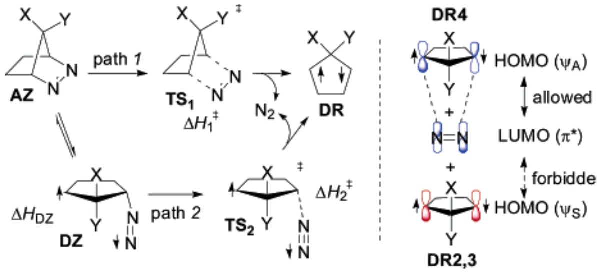
Manabu Abe,* Chizuko Ishihara, Satoshi Kawanami, and Araki Masuyama

Department of Applied Chemistry, Graduate School of Engineering, Osaka University (HANDAI),
Suita 565-0871, Osaka, Japan

Received September 20, 2004; E-mail: abe@chem.eng.osaka-u.ac.jp

A significant debate[1] on the mechanism of the denitrogenation of diazabicyclo[2.2.1]hept-2-enes **AZ** continues since the discovery[2] of the selective formation of doubly inverted bicyclo[2.1.0]pentanes. Recent computational studies[1c,d] on the parent **AZ1** (X = Y = H) disclosed that the concerted denitrogenation is favored over the stepwise denitrogenation (Scheme 1, entry 1 in Table 1). In this study, we found novel substituent effects at C(7) in the denitrogenation mechanism of the 7,7-disubstituted 2,3-diazabicyclo[2.2.1]hept-2-enes **AZ2−4**, in which the two C−N bonds are equivalent.

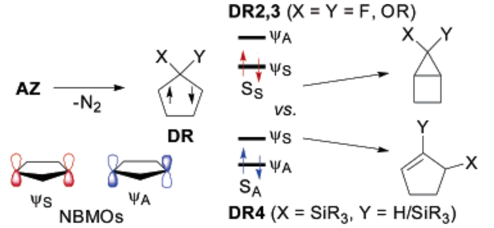
Scheme 1. Possible Denitrogenation Mechanisms: Concerted (Path 1) versus Stepwise (Path 2)



1: X = Y = H, **2**: X = Y = F, **3**: X = Y = OR, **4**: X = SiR$_3$, Y = H or SiR$_3$

Over the past decade, Borden and our group have disclosed that the substituents X and Y determine the electronic configuration of the lowest singlet state of the cyclopentane-1,3-diyls **DR**, S_S versus S_A (Scheme 2).[3] Thus, the selective occupancy of the in-phase nonbonded molecular orbital (ψ_S) is found in the lowest singlet state (S_S) of the diradicals **DR2,3** that possess electron-withdrawing substituents (X, Y = F or OR). In contrast, the out-of-phase ψ_A is energetically located below the in-phase ψ_S in the lowest singlet state (S_A) of the diradicals **DR4** that possess electron-donating substituents (X or/and Y = SiR$_3$). The notable substituent effects on the electronic configuration significantly affect the reactivity of the singlet diradicals: a selective silyl migration was found to occur in **DR4** to produce 5-silylcyclopentene,[3c] while the quantitative formation of bicyclo[2.1.0]pentanes was observed in the reaction of **DR2,3**.[3b] The substituent effects are also expected to affect the denitrogenation mechanism of the azoalkanes **AZ**, i.e., concerted versus stepwise (Scheme 1). The concerted path 1 from **AZ4** is a symmetry-allowed process, since the phases of the diyl HOMO (ψ_A) and the N$_2$ LUMO (π*) match. Thus, the energy barriers of the concerted denitrogenation in **AZ2,3** should be significantly higher than that in **AZ4**, because the diyl HOMO of the lowest singlet state of **DR2,3** is ψ_S. When the energy barrier of the stepwise path 2 is not significantly affected by the substituents X and Y, the substituent-dependent change in the mechanism would be operative.

Scheme 2. Substituent Effects on the Electronic Configuration of the Lowest Singlet State of Cyclopentane-1,3-diyls **DR** and Their Reactivity



First, to obtain information about the substituent effects, three-dimensional potential energy surfaces (PESs) along the two C−N bond breakings were calculated at the UB3LYP/6-31G(d) level of theory[4] (Figures 1 and 2). Apparently, the shape of the 3D plots is mostly dependent on the substituents X and Y. As shown in Figure 1 for **AZ3a**, the stepwise path 2 was calculated to be the energetically more favored process by ca. 10 kcal/mol over the concerted path 1, $\Delta E_1 > \Delta E_2$ (entry 3 in Table 1). In contrast, the energy barrier of the concerted path 1 was predicted to be lower by 7 kcal/mol than that of the stepwise denitrogenation of the azoalkanes **AZ4a**, $\Delta E_1 < \Delta E_2$ (Figure 2, entry 6 in Table 1). The PES analyses clearly indicate that the substituent effects on the energy barrier of the stepwise mechanism are small (ΔE_2 = 32−36 kcal/mol, Table 1). However, as expected, dramatic substituent effects were calculated for the energy barriers of the concerted pathways (ΔE_1 = 25−46 kcal/mol, Table 1). The transition-statestructures for the denitrogenation of the azoalkanes **AZ2−4** were calculated at the UB3LYP/6-31G(d) level of theory (Table 1). As reported for the parent **AZ1**,[1c,d] the transition states for connecting **AZ** and the diazenyl diradicals **DZ** could not be found for **AZ2−4** (Scheme 1); stretching the single C(1)−N(2) bond of the azoalkanes gives rise to a Morse-like potential. The transition states **TS2$_2$** and **TS3a$_2$** for the N$_2$ loss from **DZ2** and **DZ3a** could be located, and the activation enthalpies ($\Delta H_2^‡$) were calculated to be almost zero (entries 3, 4). The transition state from **DZ4b** could not be located at the same level of theory (entry 7). The transition states **TS4$_1$** for the concerted N$_2$ loss from **AZ4** were successfully located, and the activation energies $\Delta H_1^‡$ were closely consistent with ΔE_1 estimated from the PES analyses (entries 6, 7). The transition states for the concerted denitrogenation of **AZ2,3a** could not be found at the same level of theory (entries 3, 4). These computational studies predict that the stepwise denitrogenation of the dialkoxy-substituted **AZ3** is much slower than the concerted denitrogenation of the silyl-substituted **AZ4**.

To confirm the computational prediction of the substituent-dependent change in the denitrogenation mechanism, the thermal

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Table 1. Summary of the Experimental and Computational Activation Parameters, $\Delta H^{\ddagger}$ (kcal/mol) and $\Delta S^{\ddagger}$ (e.u.), for the Denitrogenation of **AZ**[a]

					computational							
		experimental			concerted: path 1			stepwise: path 2				preferred mechanism
entry	**AZ** (X,Y)	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	k_{rel}[b]	ΔE_1[c]	$\Delta H_1^{\ddagger}$[d]	$\Delta S_1^{\ddagger}$[d]	ΔE_2[c]	ΔH_{DZ}[d,e]	$\Delta H_2^{\ddagger}$[d,f]	$\Delta S_2^{\ddagger}$[d,f]	
1	**AZ1** (H,H)	36.5 ± 0.3[g] 36.0 ± 0.2[h]	8.7 ± 0.4[g] 5.8 ± 0.5[h]			36.6[i]	9.1[i]		39.0[i]	2.8[i]	2.5[i]	concerted
2	**AZ1**	36.2 ± 0.6	5.8 ± 0.2	347	38			36				
3	**AZ2** (F,F)				46	*	*	36	32.5	0.0	1.8	stepwise
4	**AZ3a** (OH,OH)				46	*	*	36	33.3	0.4	0.9	stepwise
5	**AZ3b** (OEt,OEt)	39.1 ± 1.0	1.3 ± 0.1	1								
6	**AZ4a** (SiH_3,SiH_3)				25	25.0	2.9	32				concerted
7	**AZ4b** (SiH_3,H)				30	28.5	4.6	33	32.5	*	*	concerted
8	**AZ4c** ($SiMe_2Ph$,H)	26.0 ± 0.5	0.48 ± 0.1	4×10^6								

[a] The calculated values are the UB3LYP/6-31G(d) energies. [b] The relative rate constants are calculated at 150 °C. [c] The energies ΔE_1 and ΔE_2 (kcal/mol) are from the PES analyses (see Figures 1 and 2). [d] All the activation parameters are calculated at 298 K. [e] The energies are reported relative to the corresponding azoalkanes AZ. [f] The activation parameters are relative to the corresponding **DZ**. [g] Reference 5a. [h] Reference 5b. [i] The energies are calculated at 445 K by the method of the CASPT2//UB3LYP, see ref 1d. The * indicates that the transition states were attempted but not successfully located at the UB3LYP/6-31G(d) level of theory.

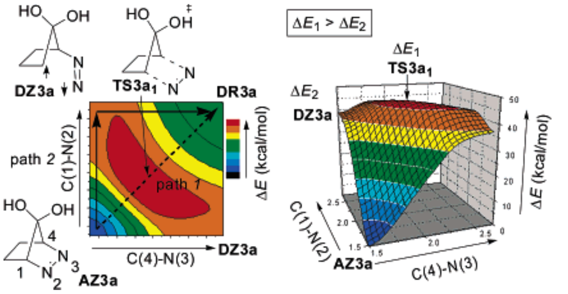

Figure 1. Potential energy surfaces (PES) along the C(1)−N(2) and C(4)−N(3) bond breakings for the denitrogenation of **AZ3a**. The shape of the PES plots for **AZ2** is similar to that for **AZ3a**. See Supporting Information.

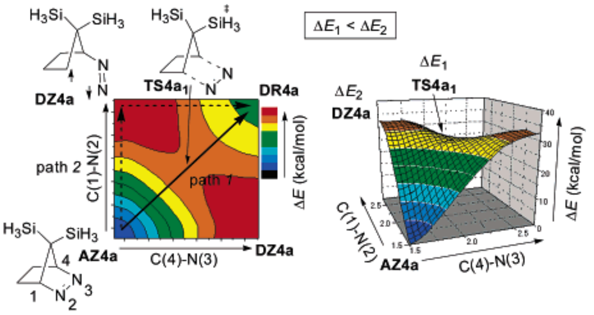

Figure 2. Potential energy surfaces (PES) along the C(1)−N(2) and C(4)−N(3) bond breakings for the denitrogenation of **AZ4a**. The shape of the PES plots for **AZ4b** is similar to that for **AZ4a**. See Supporting Information.

decomposition of **AZ3b** (X = Y = OEt) and **AZ4c** (X = $SiMe_2Ph$, Y = H) was performed in a sealed tube as described in the Supporting Information. The activation parameters, i.e., $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, for the denitrogenation reactions are listed in Table 1 (entries 5, 8), together with the known values[5] for **AZ1** (entry 1). The energies for the **AZ1** decomposition, which were determined in this study, were consistent with those previously determined (entries 1, 2). As predicted by the theory, the rate of the decomposition of **AZ3b** was found to be much slower than that of **AZ4c** (k_{rel}, entries 5, 8). Thus, the dramatic substituent effects on the rate retardation of the **AZ3b** decomposition are reasonably proposed to be due to the mechanistic change from the concerted path 1 to the stepwise path 2. Since the UDFT method is known to underestimate the activation energy by ca. 6 kcal/mol for the stepwise denitrogenation of the parent **AZ1**,[1d] the experimentally obtained activation enthalpy ($\Delta H^{\ddagger}$ = 39.1 kcal/mol) for the decomposition of **AZ3b** is quite consistent with the value calculated for the stepwise path of **AZ3a**, $\Delta H_{DZ} + \Delta H_2^{\ddagger} = 33.7$ kcal/mol (entries 4, 5). Alternatively, the energy ($\Delta H^{\ddagger} = 26.0$ kcal/mol) for the decomposition of **AZ4c** fits that obtained by the calculation for the concerted path of **AZ4b**, $\Delta H_1^{\ddagger} = 28.5$ kcal/mol (entries 7, 8). The UDFT method is known to closely reproduce the energy for the concerted denitrogenation of the parent **AZ1**.[1d]

In summary, in this combined experimental and computational study, novel substituent effects on the mechanism of the thermal denitrogenation of azoalkanes **AZ** were found: a stepwise mechanism is favored by electron acceptors at the methano bridge, but the concerted mechanism operates for electron donors. The dramatic change of the denitrogenation mechanism is attributed to the substituent effects on the electronic configuration of the lowest singlet state of the 1,3-diradicals **DR**. This remarkable finding should stimulate future calculations and experiments on the mechanistically fascinating stereoselectivity[2] in the formation of bicyclo[2.1.0]pentanes from **AZ**.

Supporting Information Available: Experimental and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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