

# Substituent Effect on Reactivity of Triplet Excited State of 2,3-Diazabicyclo[2.2.1]hept-2-enes, DBH Derivatives: $\alpha$ C–N Bond Cleavage versus $\beta$ C–C Bond Cleavage

Manabu Abe,<sup>†,‡,§,\*</sup> Shinji Watanabe,<sup>†</sup> Hiroshi Tamura,<sup>†</sup> Srikanth Boinapally,<sup>†,§</sup> Kousei Kanahara,<sup>†</sup> and Yoshihisa Fujiwara<sup>†</sup>

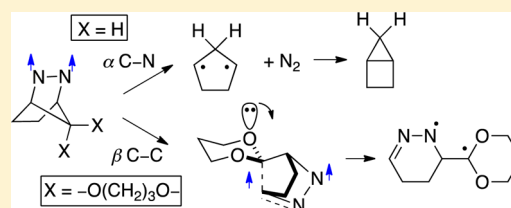
<sup>†</sup>Department of Chemistry, Graduate School of Science, <sup>‡</sup>Department of Mathematical and Life Science, Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima, Hiroshima 739-8526, Japan

<sup>‡</sup>Institute of Molecular Science, Okazaki 444-8787, Japan

<sup>§</sup>CREST, JST, K's Gobancho, 7, Gobancho, Chiyoda-ku, Tokyo 102-0076, Japan

## Supporting Information

**ABSTRACT:** The photoreaction of a series of 2,3-diazabicyclo[2.2.1]hept-2-ene (DBH) derivatives, in which various substituents (X) were introduced at the methano bridge carbon of C(7), was investigated under direct (>290 nm) and triplet-sensitized (Ph<sub>2</sub>CO, >370 nm) irradiation conditions of the azo chromophore (–C<sub>β</sub>–C<sub>α</sub>–N=N–C<sub>α</sub>–C<sub>β</sub>–). The azo compounds offered a unique opportunity to see the substituent X effect at the remote position of the azo chromophore on the reactivity of the triplet excited state of bicyclic azoalkanes. The present study led to the first observation of the unusual C<sub>α</sub>–C<sub>β</sub> bond-cleavage reaction without the ring stiffness, that is, the structural rigidity, in the triplet state of the cyclic azoalkanes. The stereoelectronic effects were found to play an important role in lowering the activation energy of the C<sub>α</sub>–C<sub>β</sub> bond-cleavage reaction. NBO analyses at the M06-2X/cc-PVDZ level of theory confirmed the stereoelectronic effect.

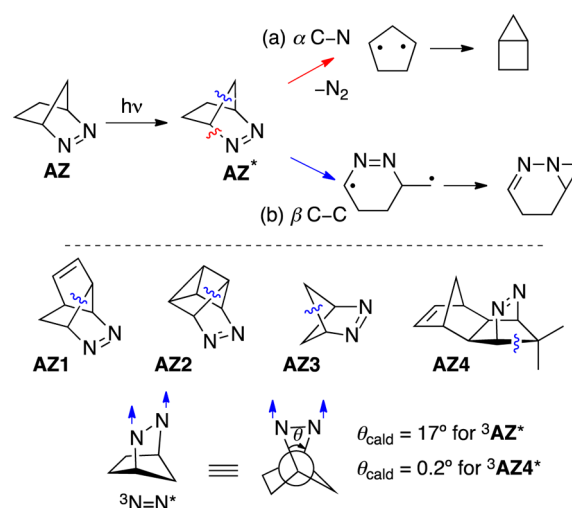


## INTRODUCTION

The chemistry of azo compounds (–N=N–), including the denitrogenation<sup>1</sup> and isomerization with molecular motion,<sup>2</sup> has long been under intensive investigation. Photoreactions of cyclic azoalkanes, AZ, such as 2,3-diazabicyclo[2.2.1]hept-2-ene (DBH), have been utilized to synthesize strained molecules. Molecular nitrogen is efficiently evolved in a high quantum yield ( $\phi_{N_2} \sim 1$ ) to generate the intermediary diradicals by the  $\alpha$  C–N bond cleavage (Scheme 1a).<sup>3</sup> The simple photochemical reaction has attracted much attention not only in synthetic organic chemistry but also in mechanistic organic chemistry. Thus, a number of discussions have focused on the denitrogenation mechanism.<sup>1a,4</sup>

Alternative interest in the reactivity of the excited state of azoalkanes involves the  $\beta$  C–C bond-cleavage reaction (Scheme 1b). So far, only a few reports on the unusual reactivity have appeared in the literature.<sup>5–10</sup> The ring stiffness and strained structure are proposed to be essential for the unusual reactivity of the azo compounds AZ1–4. The  $\beta$  C–C bond-cleavage reaction has typically been found in the triplet-sensitized reaction of the polycyclic azoalkanes. Although the triplet state of the parent AZ (<sup>3</sup>AZ\*, triplet energy =  $E_T = \sim 62$  kcal mol<sup>–1</sup>) was reported to quantitatively produce the  $\alpha$  C–N bond-cleavage product,<sup>3a</sup> the  $\beta$  C–C bond-cleavage product was mainly formed in the triplet state of the strained AZ4 (<sup>3</sup>AZ4\*,  $E_T \sim 63$  kcal mol<sup>–1</sup>).<sup>10</sup> Yamamoto et al.<sup>11</sup> reported in their computational study that the

Scheme 1



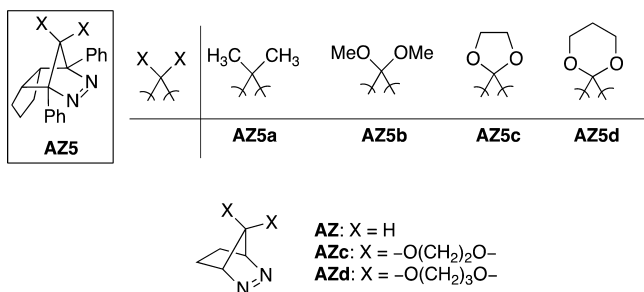
molecular rigidity decreased the dihedral angle  $\theta$  (C–N–N–C) of the triplet excited state of the DBH derivatives (<sup>3</sup>N=N\*). The dihedral angles of <sup>3</sup>AZ\* and <sup>3</sup>AZ4\* were reported to be 17° and

**Special Issue:** Howard Zimmerman Memorial Issue

**Received:** September 10, 2012

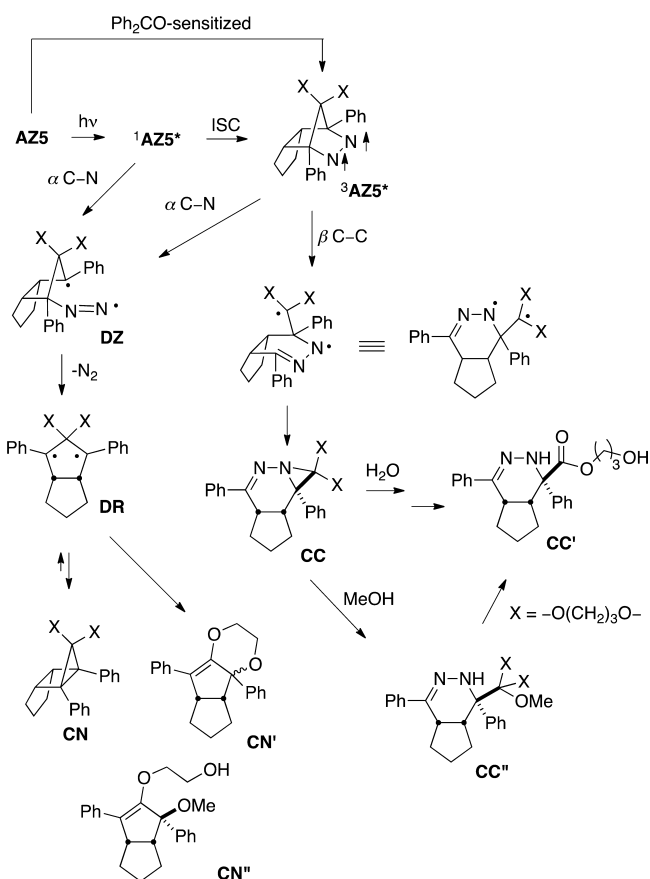
**Published:** September 17, 2012

0.2° at the unrestricted Hartree–Fock (UHF) level of theory, respectively. The computational results using complete active space self-consistent field (CASSCF) method suggested that the  $\beta$  C–C bond cleavage occurred from the triplet excited state with a mixed character of  $n,\pi^*$  with  $\pi,\pi^*$ .



Herein, a novel substituent (X) effect at the methano bridge carbon was found on the reactivity ( $\alpha$  C–N versus  $\beta$  C–C) in the triplet excited state of azo compounds **AZ5a–d**. Thus, the direct irradiation ( $h\nu > 290$  nm) of **AZ5a–d** quantitatively produced the denitrogenation products CN or CN' and/or CN'' by the  $\alpha$  C–N bond-cleavage reaction (Scheme 2). In contrast, the

Scheme 2



product selectivity under the benzophenone-sensitized irradiation conditions was largely dependent upon the substituents (X) (Scheme 2 and Table 1). The ring stiffness seems to be similar among **AZ5a–d**. When **AZ5d** (X =  $-\text{O}(\text{CH}_2)_3\text{O}-$ ) was irradiated in the presence of benzophenone as a triplet sensitizer, the selective  $\beta$  C–C bond-cleavage product CC' was obtained in nonpolar solvent benzene (Scheme 2). The  $\beta$  C–C bond-cleavage reaction was not observed for **AZ5a–c** under similar

**Table 1. Photoreaction of Azoalkanes AZ5a–d (60 mM) at Room Temperature, ca. 20 °C<sup>a</sup>**

entry	AZ5 (X)	$h\nu$ (nm)	sol ( $E_{\text{T}}^{\text{N}}$ ) <sup>b</sup>	products and yields (%) <sup>c</sup>	
				$\alpha$ C–N	$\beta$ C–C
1	<b>AZ5a</b> (Me)	direct (>290)	C <sub>6</sub> H <sub>6</sub> (0.111)	CN (94)	<i>d</i>
2	<b>AZ5b</b> (OMe)	direct (>290)	C <sub>6</sub> H <sub>6</sub>	CN (96)	<i>d</i>
3	<b>AZ5c</b> ( $-\text{O}(\text{CH}_2)_2\text{O}-$ )	direct (>290)	C <sub>6</sub> H <sub>6</sub>	CN' (81) <sup>e</sup>	<i>d</i>
4	<b>AZ5d</b> ( $-\text{O}(\text{CH}_2)_3\text{O}-$ )	direct (>290)	C <sub>6</sub> H <sub>6</sub>	CN (99)	<i>d</i>
5	<b>AZ5a</b> (Me)	Ph <sub>2</sub> CO <sup>g</sup> (>370)	C <sub>6</sub> H <sub>6</sub>	CN (91)	<i>d</i>
6	<b>AZ5b</b> (OMe)	Ph <sub>2</sub> CO <sup>g</sup> (>370)	C <sub>6</sub> H <sub>6</sub>	CN (98)	<i>d</i>
7	<b>AZ5c</b> ( $-\text{O}(\text{CH}_2)_2\text{O}-$ )	Ph <sub>2</sub> CO <sup>g</sup> (>370)	C <sub>6</sub> H <sub>6</sub>	CN' (90) <sup>f</sup>	<i>d</i>
8	<b>AZ5d</b> ( $-\text{O}(\text{CH}_2)_3\text{O}-$ )	Ph <sub>2</sub> CO <sup>g</sup> (>370)	C <sub>6</sub> H <sub>6</sub>	CN (32)	CC' (60)
9	<b>AZ5d</b> ( $-\text{O}(\text{CH}_2)_3\text{O}-$ )	direct (>370)	C <sub>6</sub> H <sub>6</sub>	<i>d</i>	<i>d</i>
10	<b>AZ5d</b> ( $-\text{O}(\text{CH}_2)_3\text{O}-$ )	Ph <sub>2</sub> CO <sup>g</sup> (>370)	DMSO (0.444)	CN (23)	CC' (71)
11	<b>AZ5d</b> ( $-\text{O}(\text{CH}_2)_3\text{O}-$ )	Ph <sub>2</sub> CO <sup>g</sup> (>370)	CH <sub>3</sub> CN (0.460)	CN (23)	CC' (74)
12	<b>AZ5d</b> ( $-\text{O}(\text{CH}_2)_3\text{O}-$ )	Ph <sub>2</sub> CO <sup>g</sup> (>370)	MeOH (0.762)	<i>d</i>	CC' (88)
13	<b>AZ5c</b> ( $-\text{O}(\text{CH}_2)_2\text{O}-$ )	Ph <sub>2</sub> CO <sup>g</sup> (>370)	MeOH (0.762)	CN' (38) <sup>e</sup> + CN' (8)	CC' (54)
14	<b>AZ5c</b> ( $-\text{O}(\text{CH}_2)_2\text{O}-$ )	direct (>290)	MeOH (0.762)	CN' (80) <sup>f</sup> + CN'' (16)	<i>d</i>
15	<b>AZ5d</b> ( $-\text{O}(\text{CH}_2)_3\text{O}-$ )	direct (>290)	MeOH (0.762)	CN (85)	<i>d</i>

<sup>a</sup>A solution of **AZ5** (60 mM) was degassed by N<sub>2</sub> bubbling for 10 min. The photochemical reaction was performed with a high-pressure Hg lamp through a glass filter (>290 or >370 nm) at room temperature for 6 h. <sup>b</sup>Solvent parameter, see ref 15. <sup>c</sup>Products yields were determined on the basis of <sup>1</sup>H NMR (500 MHz) peak areas (error  $\pm 3\%$ ). Triphenylmethane (Ph<sub>3</sub>CH) was used as a standard sample. <sup>d</sup>Not detected using <sup>1</sup>H NMR (500 MHz) spectroscopic analysis. <sup>e</sup>The isomer ratio of cis/trans was 32/68. <sup>f</sup>The isomer ratio of cis/trans was 44/56. <sup>g</sup>Benzophenone (Ph<sub>2</sub>CO, 600 mM) was used.

benzophenone-sensitized conditions. The  $\beta$  C–C bond-cleavage reaction of **AZ5c** (X =  $-\text{O}(\text{CH}_2)_2\text{O}-$ ) was observed only in polar solvents, such as MeOH, to give CC''. Computational studies on the model azo compounds **AZ**, **AZc**, and **AZd** were conducted to understand the notable substituent effect and the solvent effect on the product selectivity. In the combined experimental and computational studies reported here, a stereoelectronic effect was found to play an important role on lowering the energy barrier of the unusual  $\beta$  C–C bond-cleavage process in the triplet state of the bicyclic azoalkanes.

## RESULTS AND DISCUSSION

### Direct and Ph<sub>2</sub>CO-Sensitized Photolyses of AZ5a–d.

Azoalkanes **AZ5a–d** ( $\lambda_{\text{max}} \sim 360$  nm,  $\epsilon \sim 100$ ) were synthesized according to the method reported previously.<sup>12</sup> The absorption maxima ( $\lambda_{\text{max}}$ ) and the molar extinction coefficient ( $\epsilon$ ) of the forbidden excitation ( $n,\pi^*$ ) of the azo chromophore ( $-\text{N}=\text{N}-$ ) were found to be nearly the same as those of **AZ** and **AZa**,  $\lambda_{\text{max}} \sim 350$  nm. As shown in Table 1 (entries 1–4) and Scheme 2, the direct photolysis (>290 nm) of the azo chromophores **AZ5a–d** at room temperature in benzene produced the denitrogenation products CN or CN' in high yields.  $\beta$  C–C

bond-cleavage products such as **CC** or **CC'** were not detected in the  $^1\text{H}$  NMR (500 MHz) spectra of the photolysate. The quantum yields of the denitrogenation processes were determined to be  $\phi_{\text{N}_2} = \sim 0.90 \pm 0.05$ . The denitrogenation reaction of **AZ**,  $\phi_{\text{N}_2} = 1.0$ ,<sup>13</sup> was used as a chemical actinometer to determine the quantum yields of the denitrogenation reactions. No significant fluorescence was observed from **AZ5a–d** at room temperature in benzene. Thus, the  $\alpha$  C–N bond cleavage is initiated from the singlet excited state  $^1\text{AZ5}^*$  to produce the denitrogenation products **CN** or **CN'** through the diazenyl diradicals **DZ** and the following diradicals **DR** (Scheme 2). The product selectivity of the azoalkanes was not affected by the substituents (**X**) under the direct photolysis conditions, that is, in the singlet excited state chemistry (entries 1–4).

In contrast to the direct photochemical reactions, a significant substituent (**X**) effect on the product distribution was observed in the triplet-sensitized reaction ( $>370$  nm) of **AZ5a–d** (60 mM) using benzophenone (600 mM) as a triplet sensitizer,  $^3\text{Ph}_2\text{CO}^*$  ( $E_{\text{T}} \sim 70$  kcal mol $^{-1}$ ) (entries 5–8). Thus, the  $\beta$  C–C bond-cleavage product **CC'** (60%), which is the hydrolysis product of **CC**, was observed together with the denitrogenation product **CN** (32%) in the triplet-sensitized photolysis of **AZ5d** in benzene (entry 8). The quantitative formation of the  $\alpha$  C–N bond-cleavage products **CN** or **CN'** was observed for other azoalkanes **AZ5a–c** in benzene (entries 5–7). The quantitative recovery of the starting azoalkane **AZ5d** ( $\lambda_{\text{max}} = 361$  nm,  $\epsilon = 91$ ) was found in the photochemical reaction ( $>370$  nm) in the absence of benzophenone (entry 9), at which wavelength the direct excitation of azoalkane **AZ5d** is not efficient. Thus, the control experiment clearly indicates that the  $\beta$  C–C bond-cleavage product **CC'** is derived from the triplet state of **AZ5d**.

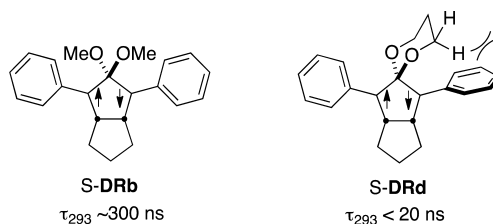
It should be noted that the ring-closed compound **CNd** (**X** =  $-\text{O}(\text{CH}_2)_3\text{O}-$ ), which is the  $\alpha$  C–N bond-cleavage product, was isolated as a stable product in the photolysis of **AZ5d** (entries 4 and 8). However, the corresponding ring-closed compound **CNc** (**X** =  $-\text{O}(\text{CH}_2)_2\text{O}-$ ) in the photochemical reaction of **AZ5c** was unstable at room temperature and afforded the migrated product **CN'** (entries 3 and 7).<sup>12b</sup> The experimental results clearly suggest that the molecular strain in **CNc** is higher than that in **CNd**. Thus, the ring stiffness and molecular strain of **AZ5c** is expected to be higher than that of **AZ5d**. This suggests that the selective formation of the  $\beta$  C–C bond-cleavage product in **AZ5d** is due to the substituent **X** effect at the methano bridge carbon, rather than due to the molecular rigidity (stiffness) of the azoalkanes.

The formation of the  $\beta$  C–C bond-cleavage product **CC'** increased in polar solvents such as DMSO,  $\text{CH}_3\text{CN}$ , and MeOH (entries 10–12).<sup>14</sup> The solvent polarity effect<sup>15</sup> on the product distribution was also examined in the triplet-sensitized reaction of **AZ5a–c** in MeOH. The  $\beta$  C–C bond-cleavage product was observed only for the reaction of **AZ5c**. The compound **CC''** (**X** =  $-\text{O}(\text{CH}_2)_2\text{O}-$ ) was obtained in 54% chemical yield together with the denitrogenation products **CN'** and **CN''** (entry 13). **CC''** is the methanolysis product of **CC**. The hydrolysis product such as **CC'** was not detected for the dioxolane-substituted case. McClelland et al. reported that the hydrolysis rate constant of ortho esters containing 1,3-dioxane was faster than that of ortho esters containing 1,3-dioxolane because of the anomeric effect.<sup>16</sup> Thus, the ortho ester **CC''** (**X** =  $-\text{O}(\text{CH}_2)_2\text{O}-$ ) containing 1,3-dioxolane was supposed to be stable during our isolation procedure using flash column chromatography on silica gel. The quantitative formation of the  $\alpha$  C–N bond-cleavage product **CN**

was observed for the triplet-sensitized reaction of **AZ5a,b** even in MeOH. The data are not shown. Thus, the solvent effect is not enough to change the product selectivity of the triplet excited state of **AZ5a,b**. Under the direct irradiation of **AZ5c,d** in MeOH (entries 14 and 15), the  $\beta$  C–C bond-cleavage product **CC'** or **CC''** was not detected. Only the  $\alpha$  C–N bond-cleavage products **CN** or **CN'+CN''** were observed in the direct photolysis in MeOH (entries 14 and 15). Thus, the solvent effect on the product selectivity was observed only for the triplet state of azoalkanes.

**Transient Absorption Spectroscopy.** In 1995, Adam, Nau, and Wirz et al. reported the generation of the long-lived triplet state of **AZ4** (Scheme 1),  $\sim 0.6$   $\mu\text{s}$  at room temperature, even in the direct photolysis of **AZ4**. They suggest that the unusual  $\beta$  C–C bond cleavage occurs from the long-lived triplet azoalkane.<sup>10b</sup> The transient absorption spectroscopic analysis was conducted for the photolysis of **AZ5d** in order to examine whether a long-lived triplet species is generated or not. The transient absorption spectra and decay traces of the photolysis of **AZ5d** were measured in a degassed benzene solution by means of laser flash photolysis ( $\lambda_{\text{exc}} = 355$  nm, 6 ns pulse) at room temperature, ca. 298 K. No significant signals were observed in the region from 320 to 600 nm at the nanosecond time scale, that is,  $>20$  ns after the flash photolysis. The transient absorption spectroscopic analysis suggests that the singlet excited state of **AZ5d** is quite reactive to evolve molecular nitrogen, producing the  $\alpha$  C–N bond-cleavage product **CN** through the singlet diradical **S-DRd** (**X** =  $-\text{O}(\text{CH}_2)_3\text{O}-$ ) (Scheme 2). The observation is consistent with the high quantum yield of the formation of **CN** in the direct photolysis of **AZ5d**,  $\phi_{\text{N}_2} = \sim 0.90$ .

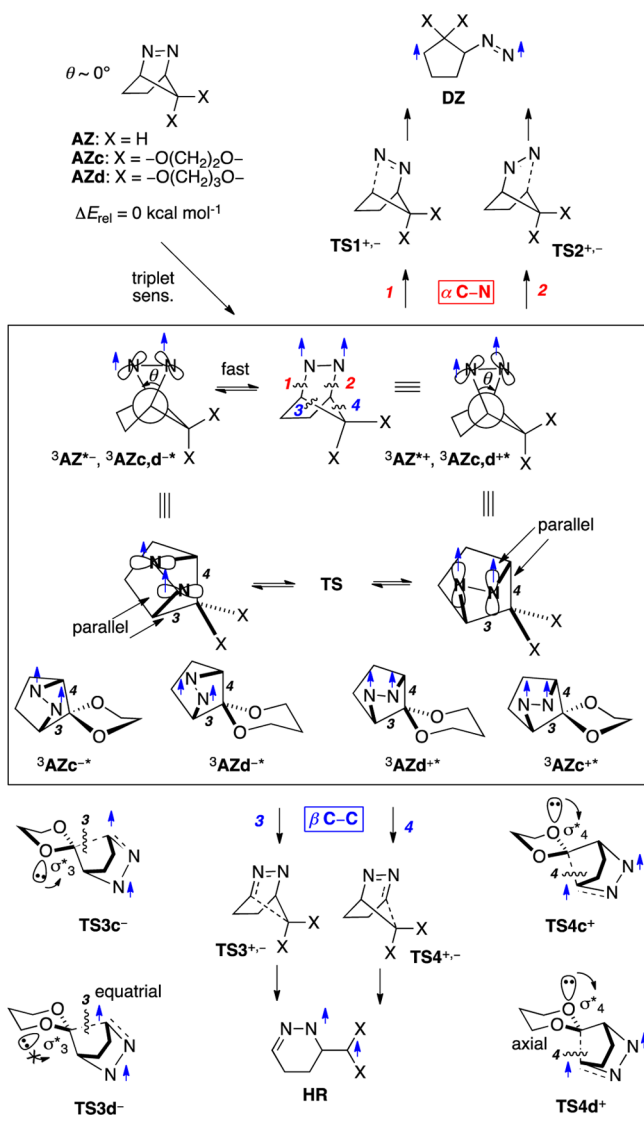
Another question quickly arose; why could the singlet diradical **S-DRd** not be detected at nanosecond time scale, although the lifetime of the singlet state of **DRb** (**X** = OMe) was found to be  $\sim 300$  ns at 293 K?<sup>12c,17,18</sup> The optimized structure of **S-DRd** at the UB3LYP/6-31G(d) level of theory provided a clear-cut answer for the notable substituent effect on shortening the lifetime of the singlet diradical. One of the phenyl rings was found to be twisted to avoid the severe steric repulsion between the ketal moiety with the phenyl ring. Thus, the short-lived singlet diradical is due to the twisted conformation of the phenyl ring. The planar conformation of the two phenyl rings is necessary for the thermodynamic stabilization of the diradical.



**Computational Studies on the Triplet State of AZ, AZc, and AZd.** To gain insight into the notable substituent effect on product distribution in the triplet-sensitized reaction, quantum chemical calculations were performed for azoalkanes **AZ** (**X** = H), **AZc** (**X** =  $-\text{O}(\text{CH}_2)_2\text{O}-$ ), and **AZd** (**X** =  $-\text{O}(\text{CH}_2)_3\text{O}-$ ) as model compounds using the Gaussian 09 suite of programs<sup>19</sup> (Scheme 3 and Table 2). The calculated dihedral angle ( $\theta$ ) of the triplet state of azo chromophore C–N–N–C, the relative energies ( $\Delta E_{\text{rel}}$ ) of the triplet state to the singlet ground state of azoalkanes, the difference of the relative energies ( $\Delta\Delta E_{\text{rel}}$ ), the dipole moments, and the imaginary frequencies ( $\nu$ ) are summarized in Table 2.



Scheme 3



First, the triplet state of the parent DBH AZ was calculated at the UB3LYP/cc-PVDZ, UM06-2X/cc-PVDZ, UM06-2X/aug-cc-PVDZ, and UCCSD/cc-PVDZ//UB3LYP/cc-PVDZ levels of theory (entries 2–5). The calculated triplet energies after the zero-point energy corrections were compared with the triplet energy of  $E_{\text{T}} = \sim 62 \text{ kcal mol}^{-1}$  determined experimentally (entry 1).<sup>13</sup> The triplet energy of AZ at the UB3LYP/cc-PVDZ level of theory was calculated to be  $E_{\text{T}} = \Delta E_{\text{rel}} = 56.9 \text{ kcal mol}^{-1}$  (entry 2). The UB3LYP method significantly underestimated the triplet energy determined experimentally. The triplet energies calculated by other methods, UM06-2X/cc-PVDZ, UM06-2X/aug-cc-PVDZ, and UCCSD/cc-PVDZ//UB3LYP/cc-PVDZ, reproduced well the experimental value within  $1 \text{ kcal mol}^{-1}$  (entries 3–5). Thus, further calculations were done at the UM06-2X/cc-PVDZ level of theory in consideration of the speed and accuracy.

Although the dihedral angles (C–N–N–C,  $\theta$ ) of the singlet ground state molecules were calculated to be almost  $0^\circ$ , twisted conformations were found for the triplet states  ${}^3\text{AZ}^*$  ( $\theta = +28.1^\circ$ , entry 2),  ${}^3\text{AZc}$  (entries 10 and 11), and  ${}^3\text{AZd}$  (entries 21 and 22). The twisted conformation suggests that the triplet states have a character of the  $\pi, \pi^*$  excited state of the double bond of the azo chromophore.<sup>11</sup> The similar twisted conformation of the triplet

state of DBH (AZ) was also reported at the ab initio level of theory.<sup>11,20</sup> The two twisted conformations of  ${}^3\text{AZc}^{+*}$  ( $\theta = +26.2^\circ$ , entry 10) and  ${}^3\text{AZc}^{-*}$  ( $\theta = -26.3^\circ$ , entry 11) were optimized for the triplet state of AZc due to the asymmetric structure based on the envelop conformation of the 1,3-dioxolane substituent (Scheme 3). The two twisted conformations of  ${}^3\text{AZd}^{+*}$  ( $\theta = +26.1^\circ$ , entry 21) and  ${}^3\text{AZd}^{-*}$  ( $\theta = -24.2^\circ$ , entry 22) were also optimized for  ${}^3\text{AZd}^*$  due to the chair conformation of the 1,3-dioxane substituent (Scheme 3). The symbols + and – were used to denote the dihedral twisting in the clockwise (+) or counterclockwise (–) direction. For  ${}^3\text{AZ}^*$ , the structure of  ${}^3\text{AZ}^{+*}$  is the enantiomer of  ${}^3\text{AZ}^{-*}$ . Thus, the energy of  ${}^3\text{AZ}^{+*}$  is equal to that of  ${}^3\text{AZ}^{-*}$ . On the basis of the calculated dihedral angles, the ring stiffness of  ${}^3\text{AZc,d}^*$  should be nearly identical to  ${}^3\text{AZ}^*$ .

Among the four possible reaction pathways from the twisted conformation of  ${}^3\text{AZ}^*$  (X = H), that is, the bond cleavages 1–4 (Scheme 3, 1 and 2 for the  $\alpha$  C–N bond cleavage, 3 and 4 for the  $\beta$  C–C bond cleavage), two transition states **TS1**<sup>+</sup> (entry 6,  $\nu = {}^{\text{im}}676 \text{ cm}^{-1}$ ,  $\Delta E_{\text{rel}} = 70.3 \text{ kcal mol}^{-1}$ ) and **TS2**<sup>+</sup> (entry 7,  $\nu = {}^{\text{im}}769 \text{ cm}^{-1}$ ,  $\Delta E_{\text{rel}} = 73.5 \text{ kcal mol}^{-1}$ ) for the  $\alpha$  C–N bond-cleavage path, and one transition state **TS4**<sup>+</sup> (entry 9,  $\nu = {}^{\text{im}}717 \text{ cm}^{-1}$ ,  $\Delta E_{\text{rel}} = 82.9 \text{ kcal mol}^{-1}$ ) for the  $\beta$  C–C bond-cleavage path, were found at the DFT level of theory. Thus, the activation energy (**TS4**<sup>+</sup>,  $\Delta \Delta E_{\text{rel}} = 20.3 \text{ kcal mol}^{-1}$ , entry 9) of the  $\beta$  C–C bond-cleavage process was calculated to be higher by ca.  $12.6 \text{ kcal mol}^{-1}$  than that of the  $\alpha$  C–N bond-cleavage process (**TS1**<sup>+</sup>,  $\Delta \Delta E_{\text{rel}} = 7.7 \text{ kcal mol}^{-1}$ , entry 6). The computational results were consistent with the exclusive formation of the denitrogenation product in the triplet-sensitized reaction of AZ in benzene.<sup>3a</sup> Yamamoto et al. reported an energy of  $64.8 \text{ kcal mol}^{-1}$  for **TS1**<sup>+</sup> and  $72.5 \text{ kcal mol}^{-1}$  for **TS4**<sup>+</sup> at the CASMP2//CASSCF(6,5)/6-31G(d) level of theory.<sup>11</sup> The DFT calculations capably reproduced the high-level computations. During the optimization of the transition state for **TS3**<sup>+</sup> (entry 8), the ring-flip of the dihedral angle of C–N–N–C was observed to finally give the same structure of **TS4**<sup>+</sup>. The energetic preference of **TS4**<sup>+</sup> over **TS3**<sup>+</sup> was rationalized by the parallel alignment of the radical p orbital with the breaking bond of 4 (see the structure of  ${}^3\text{AZ}^{+*}$  in Scheme 3). Thus, the stereoelectronic effect plays an important role in controlling the reactivity of the triplet state of AZ (X = H). In fact, the bond distance of 4 ( $155.4 \text{ pm}$ ) was calculated to be slightly longer than that of the bond 3 ( $154.2 \text{ pm}$ ) in  ${}^3\text{AZ}^{+*}$ .

Similar computational studies were performed for the potential energy surface of the triplet state of AZc (X =  $-\text{O}(\text{CH}_2)_2\text{O}-$ ) and AZd (X =  $-\text{O}(\text{CH}_2)_3\text{O}-$ ) at the same level of theory (Scheme 3, entries 10–20 for  ${}^3\text{AZc}^*$  and entries 21–31 for  ${}^3\text{AZd}^*$ ). As mentioned before, the two equilibrium structures  ${}^3\text{AZc,d}^{+*}$  (entries 10 and 21,  $\Delta E_{\text{rel}} = 60.4 \text{ kcal mol}^{-1}$  for  ${}^3\text{AZc}^{+*}$  and  $61.0 \text{ kcal mol}^{-1}$  for  ${}^3\text{AZd}^{+*}$ ) and  ${}^3\text{AZc,d}^{-*}$  (entries 11 and 22,  $\Delta E_{\text{rel}} = 60.3 \text{ kcal mol}^{-1}$  for  ${}^3\text{AZc}^{-*}$  and  $61.6 \text{ kcal mol}^{-1}$  for  ${}^3\text{AZd}^{-*}$ ) were found for the triplet states of AZc,d at the UM06-2X/cc-PVDZ level of theory. As expected, the substituent X effect at the remote position of the azo chromophore was found to be quite small on the triplet energy. The two triplet states were connected to one another via the transition state **TSc** (entry 12, X =  $-\text{O}(\text{CH}_2)_2\text{O}-$ ,  $\Delta E_{\text{rel}} = 61.4 \text{ kcal mol}^{-1}$ ,  $\nu = {}^{\text{im}}229 \text{ cm}^{-1}$ ) and **TSd** (entry 23, X =  $-\text{O}(\text{CH}_2)_3\text{O}-$ ,  $\Delta E_{\text{rel}} = 62.1 \text{ kcal mol}^{-1}$ ,  $\nu = {}^{\text{im}}200 \text{ cm}^{-1}$ ). Thus, the activation energies for the ring-flip processes were found to be  $\sim 1 \text{ kcal mol}^{-1}$ ,  $\Delta \Delta E_{\text{rel}} = 1.1 \text{ kcal mol}^{-1}$  for **TSc**, and  $\Delta \Delta E_{\text{rel}} = 1.1 \text{ kcal mol}^{-1}$  for **TSd**. The small

Table 2. Energies for the Potential Energy Surfaces of Azoalkanes AZ, AZc, and AZd

entry	AZ	X	$\theta^a$ (deg)	$\Delta E_{\text{rel}}^b$ (kcal mol <sup>-1</sup> )	$\Delta\Delta E_{\text{rel}}^c$ (kcal mol <sup>-1</sup> )	dipole moment <sup>c</sup> (debye)	$\nu^d$ (cm <sup>-1</sup> )
1	<sup>3</sup> AZ*	H	–	~62 (experimental value)	–	–	–
2	<sup>3</sup> AZ <sup>+</sup> * ( <sup>3</sup> AZ <sup>-</sup> *)		+28.1	56.9 (UB3LYP/cc-PVDZ)		2.9	none
3	<sup>3</sup> AZ <sup>+</sup> *		+28.2	62.6 (UM06-2X/cc-PVDZ)	0	3.0	none
4	<sup>3</sup> AZ <sup>+</sup> *		+28.4	62.6 (UM06-2X/aug-cc-PVDZ)		3.3	none
5	<sup>3</sup> AZ <sup>+</sup> *		+28.1	63.7 (UCCSD/cc-PVDZ//UB3LYP/cc-PVDZ)		3.5	none
6 <sup>e</sup>	TS1 <sup>+</sup>			70.3	7.7	3.2	<sup>im</sup> 676
7 <sup>e</sup>	TS2 <sup>+</sup>			73.5	10.9	3.1	<sup>im</sup> 769
8 <sup>e</sup>	TS3 <sup>+</sup>			<i>f</i>		<i>f</i>	<i>f</i>
9 <sup>e</sup>	TS4 <sup>+</sup>			82.9	20.3	3.2	<sup>im</sup> 717
10 <sup>e</sup>	<sup>3</sup> AZc <sup>+</sup> *	–O(CH <sub>2</sub> ) <sub>2</sub> O–	+26.2	60.4	0.1	4.2	none
11 <sup>e</sup>	<sup>3</sup> AZc <sup>-</sup> *		–26.3	60.3	0	4.2	none
12 <sup>e</sup>	TSc			61.4	1.1	4.2	<sup>im</sup> 229
13 <sup>e</sup>	TS1c <sup>+</sup>			70.3 (73.3) <sup>g</sup> (73.3) <sup>h</sup>	10.0	4.0	<sup>im</sup> 711
14 <sup>e</sup>	TS2c <sup>+</sup>			73.4	13.1	3.8	<sup>im</sup> 788
15 <sup>e</sup>	TS3c <sup>+</sup>			<i>i</i>		<i>i</i>	<i>i</i>
16 <sup>e</sup>	TS4c <sup>+</sup>			73.2 (76.2) <sup>g</sup> (73.7) <sup>h</sup>	12.9	5.2	<sup>im</sup> 461
17 <sup>e</sup>	TS1c <sup>-</sup>			73.2	12.9	3.9	<sup>im</sup> 793
18 <sup>e</sup>	TS2c <sup>-</sup>			70.4	10.1	4.1	<sup>im</sup> 712
19 <sup>e</sup>	TS3c <sup>-</sup>			73.8	13.5	5.3	<sup>im</sup> 465
20 <sup>e</sup>	TS4c <sup>-</sup>			<i>j</i>		<i>j</i>	<i>j</i>
21 <sup>e</sup>	<sup>3</sup> AZd <sup>+</sup> *	–O(CH <sub>2</sub> ) <sub>3</sub> O–	+26.1	61.0	0	4.1	none
22 <sup>e</sup>	<sup>3</sup> AZd <sup>-</sup> *		–24.2	61.6	0.6	4.1	none
23 <sup>e</sup>	TSd			62.1	1.1	4.1	<sup>im</sup> 200
24 <sup>e</sup>	TS1d <sup>+</sup>			70.5 (73.8) <sup>g</sup> (74.3) <sup>h</sup>	9.5	4.0	<sup>im</sup> 707
25 <sup>e</sup>	TS2d <sup>+</sup>			73.8	12.8	3.9	<sup>im</sup> 811
26 <sup>e</sup>	TS3d <sup>+</sup>			<i>k</i>		<i>k</i>	<i>k</i>
27 <sup>e</sup>	TS4d <sup>+</sup>			72.8 (75.8) <sup>g</sup> (74.5) <sup>h</sup>	11.8	5.1	<sup>im</sup> 492
28 <sup>e</sup>	TS1d <sup>-</sup>			74.6	13.6	3.9	<sup>im</sup> 806
29 <sup>e</sup>	TS2d <sup>-</sup>			70.6	10.6	4.1	<sup>im</sup> 716
30 <sup>e</sup>	TS3d <sup>-</sup>			79.1	18.1	4.8	<sup>im</sup> 590
31 <sup>e</sup>	TS4d <sup>-</sup>			<i>l</i>		<i>l</i>	<i>l</i>

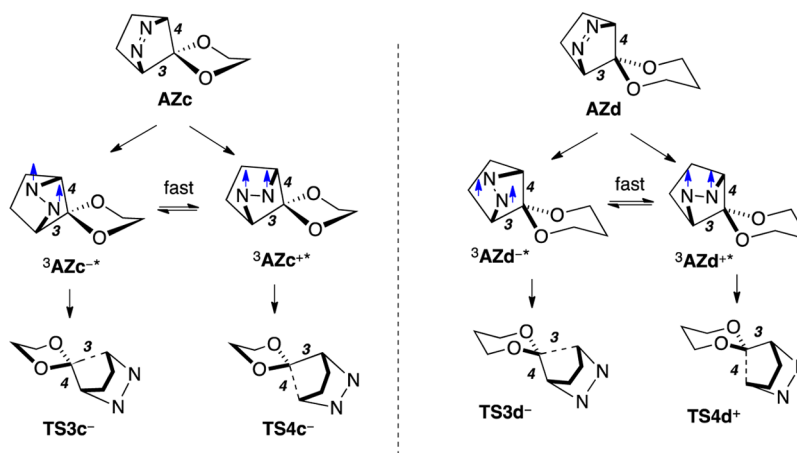
<sup>a</sup>Dihedral angle of C–N–N–C. <sup>b</sup>Energies are relative to the energy of the singlet ground state of AZ, AZc, and AZd, after the zero-point energy correction. <sup>c</sup>Calculated dipole moment for the structures. <sup>d</sup>Imaginary frequency for the transition states. <sup>e</sup>At the UM06-2X/cc-PVDZ level of theory. <sup>f</sup>The structure TS4<sup>+</sup> was obtained after the optimization. <sup>g</sup>Values were obtained before the zero-point energy corrections. <sup>h</sup>Single-point energies of the optimized structures were calculated in methanol using IPCM method. <sup>i</sup>The structure TS4c<sup>+</sup> was obtained after the optimization. <sup>j</sup>The structure TS3c<sup>-</sup> was obtained after the optimization. <sup>k</sup>The structure TS4d<sup>+</sup> was obtained after the optimization. <sup>l</sup>The structure TS3d<sup>-</sup> was obtained after the optimization.

activation energies suggest that the equilibrium between the two conformers was expected to be very fast at ambient temperature (Scheme 3).

The energies of the transition states of TS1c,d<sup>+</sup> (entries 13 and 24,  $\Delta E_{\text{rel}} = 70.3$  kcal mol<sup>-1</sup> for TS1c<sup>+</sup> and 70.5 kcal mol<sup>-1</sup> for TS1d<sup>+</sup>) and TS2c,d<sup>+</sup> (entries 14 and 25,  $\Delta E_{\text{rel}} = 73.4$  kcal mol<sup>-1</sup> for TS2c<sup>+</sup> and 73.8 kcal mol<sup>-1</sup> for TS2d<sup>+</sup>) for the  $\alpha$  C–N bond-cleavage reaction were found to be nearly identical to those of the parent <sup>3</sup>AZ<sup>+</sup>\* (comparing entries 6 and 7 with 13, 14 and 24, 25). The activation energies for the  $\alpha$  C–N bond-cleavage process ( $\Delta\Delta E_{\text{rel}} = 10.0$  kcal mol<sup>-1</sup> for <sup>3</sup>AZc\* and 9.5 kcal mol<sup>-1</sup> for <sup>3</sup>AZd\*) were found to be slightly higher than that of <sup>3</sup>AZ\* ( $\Delta\Delta E_{\text{rel}} = 7.7$  kcal mol<sup>-1</sup>). The energies of TS1c,d<sup>-</sup> were found to be nearly the same as those calculated for TS2c,d<sup>+</sup>; compare entries 17, 28 with 14, 25. Also, the energies of TS2c,d<sup>-</sup> were calculated to be nearly the same as those calculated for TS1c,d<sup>+</sup>; compare entries 18, 29 with 13, 24. The results are quite reasonable because the two conformers possess the enantiomer relationship with each other in the 2,3-diazabicyclo[2.2.1]-

heptane moiety. Thus, no significant substituent (X) effect was calculated for the energy barrier of the denitrogenation reaction.

However, the transition state energies of the  $\beta$  C–C bond-cleavage reactions through TS4c<sup>+</sup> (X = –O(CH<sub>2</sub>)<sub>2</sub>O–,  $\Delta E_{\text{rel}} = 73.2$  kcal mol<sup>-1</sup>,  $\nu^{\text{im}} 461$  cm<sup>-1</sup>, entry 16) and TS4d<sup>+</sup> (X = –O(CH<sub>2</sub>)<sub>3</sub>O–,  $\Delta E_{\text{rel}} = 72.8$  kcal mol<sup>-1</sup>,  $\nu^{\text{im}} 492$  cm<sup>-1</sup>, entry 27) were calculated to be significantly lower than that of TS4<sup>+</sup> by ca. 10 kcal mol<sup>-1</sup> ( $\Delta E_{\text{rel}} = 82.9$  kcal mol<sup>-1</sup>, entry 9). The energy barrier of the  $\beta$  C–C bond cleavage reaction in <sup>3</sup>AZc<sup>+</sup>\* was found to be  $\Delta\Delta E_{\text{rel}} = 12.9$  kcal mol<sup>-1</sup>, which was higher than that of <sup>3</sup>AZd<sup>+</sup>\* ( $\Delta\Delta E_{\text{rel}} = 11.8$  kcal mol<sup>-1</sup>). The computational results provided important information about the substituent (X) effect on the formation of the  $\beta$  C–C bond-cleavage product in the triplet-sensitized reaction of AZc,d. The IRC calculations revealed that the  $\beta$  C–C bond-cleavage reactions produced the hydrazonyl diradical HRc,d. The optimization of TS3c<sup>+</sup> and TS3d<sup>+</sup> led to the structures TS4c<sup>+</sup> and TS4d<sup>+</sup> (entries 15 and 26), as found for TS3<sup>+</sup> (entry 8). Similarly, the transition states TS3c,d<sup>-</sup> were obtained during the optimization of the transition states of TS4c,d<sup>-</sup> (entries 19, 20 and 30, 31).

Table 3. NBO Analyses in AZc,d, <sup>3</sup>AZc,d\*, and TS4c,d

entry	X	$\Delta E_S^a$ (kcal mol <sup>-1</sup> )				$d_3^b$	$d_4^c$
		$n_O \rightarrow \sigma_3^*$	$n_O \rightarrow \sigma_4^*$				
1	AZc	-O(CH <sub>2</sub> ) <sub>2</sub> O-	7.7	8.4	153.3	154.4	
2	<sup>3</sup> AZc <sup>+*</sup>		3.6	4.3	154.3	157.8	
3	TS4c <sup>+</sup>		1.7	5.8	151.0	212.1	
4	<sup>3</sup> AZc <sup>-*</sup>		4.4	3.6	156.5	155.2	
5	TS3c <sup>-</sup>		6.0	0.32	211.5	150.6	
6	AZd	-O(CH <sub>2</sub> ) <sub>3</sub> O-	<0.25	9.5	153.0	155.5	
7	<sup>3</sup> AZd <sup>+*</sup>		<0.25	5.5	154.1	159.2	
8	TS4d <sup>+</sup>		<0.25	5.8	151.0	211.5	
9	<sup>3</sup> AZd <sup>-*</sup>		<0.25	4.7	155.9	156.7	
10	TS3d <sup>-</sup>		0.25	4.8	209.5	152.4	

<sup>a</sup>NBO delocalization energy. <sup>b</sup>Bond distance of the bond 3. <sup>c</sup>Bond distance of the bond 4.

The notable substituent X effect that lowered the  $\beta$  C–C bond-cleavage reaction can be rationalized nicely in terms of a stereoelectronic effect derived from orbital overlap of non-bonding orbitals on oxygen atoms with the  $\beta$  C–C bond 4 being broken, that is, anomeric effect;<sup>21</sup> see the structures of TS4c<sup>+</sup> and TS4d<sup>+</sup> in Scheme 3. Thus, TS4c,d<sup>+</sup> are energetically stabilized by the electron delocalization of the lone pair electrons to the  $\sigma^*$  orbital of the breaking C–C bond 4,  $\sigma_4^*$ . A similar anomeric effect was observed in the hydrogen atom abstraction reaction on tetrahydropyranyl ether by the triplet excited state of benzophenone.<sup>22</sup> The stereoelectronic effect was also proved by the comparison of the bond distance of 3 and 4 in <sup>3</sup>AZc,d<sup>+\*</sup>. Thus, the bond 4 distances in <sup>3</sup>AZc<sup>+\*</sup> and <sup>3</sup>AZd<sup>+\*</sup> were found to be 157.8 and 159.2 pm, which are longer than the bond 3 distances of 154.3 and 154.1 pm, respectively. The difference of the bond distances in <sup>3</sup>AZd<sup>+\*</sup>, 5.1 pm, was found to be larger than that in <sup>3</sup>AZc<sup>+\*</sup> for which the bond difference was calculated to be 3.5 pm. As mentioned above, the energy barrier of the bond 4 cleavage in <sup>3</sup>AZd<sup>+</sup>,  $\Delta\Delta E_{\text{rel}} = 72.8$  (TS4d<sup>+</sup>) – 61.0 (<sup>3</sup>AZd<sup>+</sup>) = 11.8 kcal mol<sup>-1</sup>, was found to be smaller than that in <sup>3</sup>AZc<sup>+</sup>,  $\Delta\Delta E_{\text{rel}} = 12.8$  kcal mol<sup>-1</sup>. The substituent effect on the bond distance and the energy barrier of the bond-breaking process is quite reasonable because the nonbonding orbital on oxygen atoms in the dioxolane moiety is not perfectly oriented to the bond being broken in <sup>3</sup>AZc<sup>+\*</sup>. Thus, the stereoelectronic effect of the dioxolane ring is smaller than that of the dioxane ring because the 1,3-dioxolane ring is more planar than the 1,3-dioxane ring. Indeed, as mentioned above, McClelland et al. reported that the hydrolysis rate constant of ortho esters containing 1,3-dioxane was faster than that of ortho esters containing 1,3-dioxolane because of the anomeric effect.<sup>16</sup>

As expected, the energy of the transition state TS3d<sup>-</sup> for the  $\beta$  C–C bond cleavage (Scheme 3, entry 30 in Table 2,  $\Delta E_{\text{rel}} = 79.1$  kcal mol<sup>-1</sup>), in which the cleavage of the equatorial C–C bond 3 occurred, was found to be much larger than that of TS4d<sup>+</sup> (entry 27 in Table 2,  $\Delta E_{\text{rel}} = 72.8$  kcal mol<sup>-1</sup>). However, the energy of TS3c<sup>-</sup> (entry 19,  $\Delta E_{\text{rel}} = 73.8$  kcal mol<sup>-1</sup>,  $\nu^{\text{OH}}$  465 cm<sup>-1</sup>) was calculated to be nearly the same energy as that of TS4c<sup>+</sup> (entry 16). The results are quite reasonable because the electron delocalization of lone pair electrons on oxygen atoms of the dioxolane ring can participate equally in stabilizing energetically the two transition states of the bond 3 cleavage and the bond 4 cleavage. The nonbonding orbitals on oxygen atoms of the dioxane ring are difficult to participate in the energetic stabilization of the equatorial bond-breaking process. Such electron delocalization is structurally quite difficult for the dimethoxy acetal system (X = OMe) with the gauche–gauche conformation of the acetal moiety.<sup>21c</sup> The importance of the stereoelectronic effect<sup>21</sup> was confirmed by the natural bond orbital (NBO) analyses<sup>23</sup> in the structures AZc,d, <sup>3</sup>AZc,d\*, and TS4c,d, which will be discussed in detail below (Table 3).

As mentioned in the experimental studies on the reactivity of the triplet state of AZa–d (Table 1 and Scheme 2), the chemical yield of the  $\beta$  C–C bond-breaking products CC' (X = –O(CH<sub>2</sub>)<sub>3</sub>O–) and CC'' (X = –O(CH<sub>2</sub>)<sub>2</sub>O–) was found to increase with the increase of the solvent polarity, for example, benzene ( $E_{\text{T}}^{\text{N}} = 0.111$ ) < DMSO ( $E_{\text{T}}^{\text{N}} = 0.444$ ) ~ CH<sub>3</sub>CN ( $E_{\text{T}}^{\text{N}} = 0.460$ ) < MeOH ( $E_{\text{T}}^{\text{N}} = 0.762$ ). To clarify the solvent effect on the product distribution, the dipole moment of the computed structures in the reaction of <sup>3</sup>AZ\*, <sup>3</sup>AZc\*, and <sup>3</sup>AZd\* was carefully considered (Table 2). The dipole moment (~3.0 debye) of the transition states for the  $\beta$  C–C bond-breaking

reaction of AZ ( $X = H$ ) was calculated to be nearly the same as the dipole moments of the transition state for the  $\alpha$  C–N bond-cleavage reaction (entries 6, 7, and 9). However, the dipole moment ( $\sim 5$  debye) of the transition states for the  $\beta$  C–C bond-breaking reaction of **AZc,d** was found to be larger than that of the transition states for the  $\alpha$  C–N bond cleavage,  $\sim 4.0$  (compare entries 13, 14, 24, 25 with 16, 27 and entries 17, 18, 28, 29 with 19, 30). The calculated dipole moments suggest that the transition states of the  $\beta$  C–C bond-breaking reaction of **AZc,d** are more stabilized in polar solvents than that of the  $\alpha$  C–N bond cleavage. Indeed, the energies of the transition states **TS4c<sup>+</sup>** and **TS4d<sup>+</sup>** were calculated to be 73.7 and 74.5 kcal mol<sup>-1</sup>, respectively, in methanol, which were significantly smaller than that in the gas phase values of 76.2 and 75.8 kcal mol<sup>-1</sup>, respectively (entries 16 and 27). The solvent effect was computed using a static isodensity surface polarized continuum model (IPCM)<sup>24</sup> for describing the solvent effect. The energies of  $\Delta E_{\text{rel}} = 76.2$  and 75.8 kcal mol<sup>-1</sup> in parentheses are the relative values to **AZc** and **AZd** before correcting the zero-point vibrational energies. However, the solvent stabilization energy estimated using IPCM method can be only computed as single-point energy for the optimized structures in gas phase. The vibrational analyses are not available for the calculations. The significant solvent effect was not calculated for the  $\alpha$  C–N bond-cleavage reactions of <sup>3</sup>**AZc\*** and <sup>3</sup>**AZd\*** (entries 13 and 24). Thus, the transition state energies of the  $\beta$  C–C bond-cleavage process of <sup>3</sup>**AZc** and <sup>3</sup>**AZd** were found to be nearly the same as those of the  $\alpha$  C–N bond-cleavage process in polar solvents. The computation results may explain the experimental observation of the selective formation of  $\beta$  C–C bond-cleavage products in polar solvents.

**NBO Analyses in AZc,d, <sup>3</sup>AZc,d\*, and TS4c,d.** As mentioned above, the transition state energies of **TS4c<sup>+</sup>** (73.2 kcal mol<sup>-1</sup>) and **TS3c<sup>-</sup>** (73.8 kcal mol<sup>-1</sup>) were calculated to be nearly the same, although the energy of **TS4d<sup>+</sup>** (72.8 kcal mol<sup>-1</sup>) is significantly smaller than the value of **TS3d<sup>-</sup>** (79.1 kcal mol<sup>-1</sup>). The anomeric effect nicely explained the substituent effect on the energy difference (Scheme 3). In order to understand the stereoelectronic effect quantitatively, NBO analysis was conducted for **AZc,d**, <sup>3</sup>**AZc,d\***, and **TS4c,d**.

The results of the NBO analyses are summarized in Table 3. In the ground state of dioxolane-substituted azoalkane **AZc** ( $X = -O(CH_2)_2O-$ , entry 1), the electron delocalization of the lone pair electrons to the  $\sigma^*$  orbitals of 3 and 4,  $\sigma^*_3$  and  $\sigma^*_4$ , were found to be effective (entry 1). Thus, the similar orbital interaction energies ( $\Delta E_s$ ) for the  $n_O \rightarrow \sigma^*_3$  and  $n_O \rightarrow \sigma^*_4$  were calculated to be 7.7 and 8.4 kcal mol<sup>-1</sup>, respectively, at the M06-2X/cc-PVDZ level of theory. Thus, the bond distances of 3 and 4,  $d_3$  and  $d_4$ , were found to be nearly the same. The equal electron delocalization to the two  $\sigma^*$  orbitals is reasonable because of the nearly planar structure of the dioxolane ring. The dihedral angle of O–C–O–C in the dioxolane ring was found to be  $\sim 3^\circ$  in **AZc**. The similar electron delocalizations to  $\sigma^*_3$  and  $\sigma^*_4$  were found also in the triplet states <sup>3</sup>**AZc<sup>+</sup>\*** (entry 2) and <sup>3</sup>**AZc<sup>-</sup>\*** (entry 4). The effective electron delocalization to the breaking bond 4,  $n_O \rightarrow \sigma^*_4$ , was computed in **TS4c<sup>+</sup>** (5.8 kcal mol<sup>-1</sup>, entry 3). Similarly, in **TS3c<sup>-</sup>**, the effective electron delocalization to the breaking  $\sigma^*_3$ ,  $n_O \rightarrow \sigma^*_3$ , was found (6.0 kcal mol<sup>-1</sup>, entry 5). Thus, both transition states **TS4c<sup>+</sup>** and **TS3c<sup>-</sup>** are expected to be significantly stabilized in energy. Indeed, the substituent effect was found in our computations (entries 16 and 19 in Table 2).

In contrast to the electron delocalization feature in **AZc**, the electron delocalization of the lone pair electrons was found only

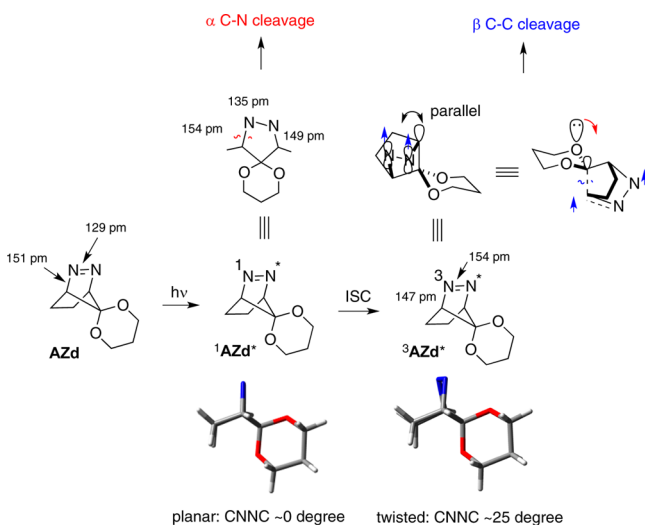
in one of the two  $\sigma^*$  bonds in the dioxane-substituted azoalkane **AZd** (entries 6, 7, and 9). Thus, the effective electron delocalization was found in the  $\sigma^*$  orbital of the axial bond 4,  $n_O \rightarrow \sigma^*_4$ . The bond 4 was calculated to be longer than the bond 3 in **AZd**, <sup>3</sup>**AZd<sup>+</sup>**, and <sup>3</sup>**AZd<sup>-</sup>**. In contrast to the effective electron delocalization in the two breaking  $\sigma$  bonds in <sup>3</sup>**AZc\***, a significant stereoelectronic effect on the electron delocalization was found in the fixed chair conformation of the dioxane-substituted azoalkane <sup>3</sup>**AZd\***. Thus, in **TS4d<sup>+</sup>**, the effective electron delocalization was found in the breaking axial bond 4 (5.8 kcal mol<sup>-1</sup>, entry 8). However, the weak electron delocalization in the breaking equatorial bond 3 was found in the transition state structure of **TS3d<sup>-</sup>** (0.25 kcal mol<sup>-1</sup>, entry 10). The NBO analyses clarify the reason for the large energy difference between **TS4d<sup>+</sup>** and **TS3d<sup>-</sup>** (entries 27 and 30 in Table 2).

As mentioned above, the dipole moment of the  $\beta$  C–C bond-cleavage process was found to be larger than that of the  $\alpha$  C–N bond-cleavage process. The large dipole moment is expected from the zwitterionic character of the C(+) and C(–)–N=N in the transition state of the  $\beta$  C–C bond-cleavage process. Indeed, the positive NPA charge on the acetal carbon was calculated to increase from 0.22 to 0.65 during the bond 4 cleavage process. The negative NPA charge in the azo moiety was found to also increase from  $-0.25$  to  $-0.53$ . Thus, the large dipole moment may be derived from the zwitterionic character of the transition state in the  $\beta$  C–C bond-breaking process.

**Computational Studies on Singlet Excited State of AZd.** As mentioned in the Experimental Section, the notable substituent effect of the 1,3-dioxane group on the product distribution was observed only in the triplet-sensitized reaction (Table 1 and Scheme 2). The computational studies mentioned above revealed that the stereoelectronic effect, so-called anomeric effect, played an important role in lowering the transition state energy of the  $\beta$  C–C bond-breaking reaction of **AZd** (Tables 2 and 3 and Scheme 3). The substituent effect, however, was not detected under the direct irradiation conditions, that is, in the singlet excited state chemistry of the azoalkanes. The question quickly arose, why was the  $\beta$  C–C bond-cleavage product **CC'** not obtained in the reaction of the singlet excited state of **AZd**, that is, <sup>1</sup>**AZd\***? To understand the experimental result, the structural feature of the singlet excited state of the model azoalkane **AZd** was computed with the complete active space self-consistent field (CASSCF) level of theory and a 3-21G basis set. In order to describe the singlet excited state of the azo chromophore, the four orbitals ( $\pi$  and  $\pi^*$  and two n orbitals) were chosen as the active space for 6 electrons in the  $\pi$  orbital and the two n orbitals (Scheme 4). The singlet excited state of <sup>1</sup>**AZd\*** with one short and one long C–N bond (i.e., 149 and 154 pm) was optimized at the (6/4)CASSCF/3-21G level of theory. The C–N–N–C dihedral angle ( $\theta$ ) was nearly  $0^\circ$ . Thus, the singlet excited state ( $S_1$ ) possesses a  $n, \pi^*$  character of the azo chromophore. Olivucci and Robb reported the quite similar structure for the singlet excited state of the parent DBH **AZ**. The  $\alpha$  C–N bond cleavage was reported to be only the reaction path from the  $n, \pi^*$  singlet excited. The structural feature of one short and one long C–N bond in the singlet excited state of **AZd** explains the selective cleavage of the  $\alpha$  C–N bond from the singlet excited state. The triplet state of **AZd** was also optimized at the same level of theory. The twisted structure (CNNC  $\sim 25^\circ$ ) of the azo chromophore was similar to the structure calculated by the DFT method. Thus, the twisted conformation of the triplet excited state involve the  $\pi, \pi^*$  character of the azo chromophore.



Scheme 4



## SUMMARY

In summary, the azo compounds **AZ5a–d** offered a unique opportunity to see the substituent X effect at the remote position of the azo chromophore on the reactivity of the triplet excited state of bicyclic azoalkanes. Under the direct photolysis conditions, the efficient denitrogenation reactions ( $\alpha$  C–N bond cleavage,  $\phi_{N_2} \sim 0.90$ ) were observed for all DBH derivatives to quantitatively afford the corresponding ring-closed compounds **CN**. An unusual  $\beta$  C–C bond-cleavage reaction was found in the  $\text{Ph}_2\text{CO}$ -sensitized irradiation of DBH derivatives with cyclic ketal substituents at the methano bridge carbon of C(7). The formation of the  $\beta$  C–C bond-cleavage product increased with the increase of solvent polarity. Computational studies on the model DBH derivatives were done at the CASSCF(6/4)/3-21G level of theory for the singlet excited state and at the UB3LYP/cc-PVDZ and UM06-2x/cc-PVDZ level of theory for the triplet state. A nearly planar and asymmetric structure of the azo chromophore was found for the singlet excited state. A twisted structure of the azo chromophore was calculated for the triplet state. The notable substituent effect of the cyclic ketal group on the reactivity of the triplet state of DBH derivatives was rationalized by the stereoelectronic effect on lowering the transition state energy of the  $\beta$  C–C bond-cleavage reaction.

## EXPERIMENTAL SECTION

**General Procedure for the Direct or Sensitized Photo-reactions of DBH Derivatives AZ5a–d.** For direct photoreactions: A solution of DBH derivatives in benzene was degassed by  $\text{N}_2$  bubbling for 10 min. The solution was irradiated with a high-pressure Hg lamp (HALoS EH8500 C/S 60) through a Pyrex filter ( $>290$  nm) at room temperature for 6 h. The solvent was evaporated under reduced pressure.

For sensitized photoreactions: A solution of DBH derivatives and 10.0 equiv of benzophenone in benzene (0.50 mL) was degassed by  $\text{N}_2$  bubbling for 10 min. The solution was irradiated through a filter ( $>370$  nm) at room temperature for 12 h. The solvent was evaporated under reduced pressure.

The product yields and product ratios were determined based on the  $^1\text{H}$  NMR (500 MHz) peak areas; error  $\pm 3\%$ . Triphenylmethane ( $\text{Ph}_3\text{CH}$ ) was used as an internal standard. Azoalkanes **AZ5a**,<sup>25</sup> **AZ5b**,<sup>12c</sup> and **AZ5c**,<sup>12b</sup> and the denitrogenation products **CNa**,<sup>25</sup> **CNb**,<sup>12c</sup> and **CN'**,<sup>12b</sup> are known compounds. The spectroscopic data for the known compounds are listed in the literature. The spectroscopic

data for the new compounds **AZ5d**, **CNd**, **CN'**, **CC'**, and **CC''** are listed below.

**endo-2,3-Diaza-10,10-propylenedioxy-1,4-diphenyltricyclo-[5.2.1.0<sup>5,9</sup>]dec-2-ene (AZ5d):** colorless solid (from MeOH);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91–7.92 (m, 4H), 7.46–7.49 (m, 4H), 7.39–7.43 (m, 2H), 3.61–3.64 (m, 4H), 3.29 (t,  $J = 6.1$  Hz, 2H), 1.61–1.68 (m, 2H), 1.47–1.56 (m, 3H), 1.37–1.43 (m, 1H), 1.30 (tt,  $J = 6.2, 6.1$  Hz, 2H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  136.1 (s), 128.3 (d), 127.9 (d), 118.1 (s), 95.1 (s), 61.4 (t), 60.3 (t), 47.5 (d), 28.0 (t), 25.5 (t), 23.6 (t). Anal. Calcd for  $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_2$ : C, 76.64; H, 6.71; N, 7.77. Found: C, 76.51; H, 6.70; N, 7.82; IR [ $\text{cm}^{-1}$ ] (KBr)  $\nu$  3057, 1603, 1496, 1446; UV [nm] (benzene)  $\lambda_{\text{max}}$  364; mp = 144 °C.

**2,4-Diphenyl-3,3-propylenedioxytricyclo[3.3.0<sup>1,5</sup>.0<sup>2,4</sup>]octane (CNd):** colorless solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28–7.31 (m, 4H), 7.20–7.24 (m, 6H), 4.04 (t,  $J = 5.3$  Hz, 2H), 3.21 (t,  $J = 5.5$  Hz, 2H), 2.86 (d,  $J = 6.7$  Hz, 2H), 1.79–1.87 (m, 3H), 1.74 (tt,  $J = 5.5, 5.3$  Hz, 2H), 1.63–1.68 (m, 1H), 1.49–1.56 (m, 2H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  135.1 (s), 129.5 (d), 127.8 (d), 125.9 (d), 95.4 (s), 65.8 (d), 64.3 (d), 46.9 (d), 40.8 (d), 27.8 (t), 26.1 (t), 24.8 (t); HRMS (EI(+)) calcd for  $\text{C}_{23}\text{H}_{24}\text{O}_2$  332.1777, found 332.1769; IR [ $\text{cm}^{-1}$ ] (KBr)  $\nu$  3052, 2961, 2949, 2861, 1600, 1495; mp 117–118 °C.

**trans-2,4-Diphenyl-3-(2'-hydroxyethoxy)-4-methoxybicyclo-[3.3.0]oct-2-ene (CN'')**: pale yellow liquid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27–7.67 (m, 10H), 3.88–4.00 (m, 1H), 3.64–3.69 (m, 2H), 3.52–3.54 (m, 2H), 3.41 (s, 3H), 2.74–2.81 (m, 1H), 1.92–1.98 (m, 1H), 1.72–1.80 (m, 1H), 1.18–1.38 (m, 4H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  142.6 (s), 135.7 (s), 128.8 (2xd), 128.4 (2xd), 128.4 (s), 128.0 (2xd), 127.5 (2xd), 127.3 (d), 127.0 (d), 93.6 (s), 71.9 (s), 61.9 (t), 50.1 (q), 49.0 (d), 46.8 (d), 31.6 (t), 31.1 (t), 25.9 (t); HRMS (EI) calcd for  $\text{C}_{23}\text{H}_{26}\text{O}_3$  350.1882, found 350.1868; IR [ $\text{cm}^{-1}$ ] (NaCl)  $\nu$  3402, 2949, 2866, 1866.

**(1R)-3-Hydroxypropyl-1,4-diphenyl-2,4a,5,6,7,7a-hexahydro-1H-cyclopenta[d]pyridazine-1-carboxylate (CC')**: colorless solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66–7.68 (m, 2H), 7.46–7.48 (m, 2H), 7.29–7.40 (m, 6H), 6.46–6.47 (m, 1H), 4.26–4.31 (m, 1H), 4.06–4.11 (m, 1H), 3.48–3.53 (m, 1H), 3.41–3.45 (m, 1H), 3.34–3.39 (m, 1H), 3.23–3.29 (m, 1H), 2.14–2.21 (m, 1H), 1.87 (br, 1H), 1.59–1.75 (m, 3H), 1.36–1.52 (m, 3H), 1.20–1.27 (m, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  174.4 (s), 153.7 (s), 139.2 (s), 137.0 (s), 128.8 (d), 128.4 (d), 128.3 (d), 128.0 (d), 125.7 (d), 124.7 (d), 67.2 (s), 62.9 (t), 59.1 (t), 45.3 (d), 35.7 (d), 33.1 (t), 31.4 (t), 28.7 (t), 25.2 (t). Anal. Calcd for  $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_3$ : C, 72.99; H, 6.92; N, 7.40. Found: C, 73.04; H, 7.08; N, 7.27.

**(1S,4aS,7aR)-1-(2-Methoxy-1,3-dioxolan-2-yl)-1,4-diphenyl-2,4a,5,6,7,7a-hexahydro-1H-cyclopenta[d]pyridazine (CC'')**: colorless solid;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57–7.64 (m, 4H), 7.24–7.35 (m, 6H), 6.22 (br s, 1H, NH), 3.91–4.10 (m, 3H), 3.60–3.66 (m, 1H), 3.49–3.54 (m, 1H), 3.26 (s, 3H), 3.13–3.24 (m, 1H), 1.96–2.03 (m, 1H), 1.56–1.65 (m, 1H), 1.26–1.39 (m, 4H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  147.9 (s), 138.5 (s), 127.9 (2xd), 127.3 (2xd), 127.1 (d), 126.9 (2xd), 126.6 (d), 125.9 (2xd), 125.7 (s), 66.8 (2xt), 62.3 (s), 48.8 (q), 41.1 (d), 35.4 (d), 31.2 (t), 30.0 (t), 22.8 (t); HRMS (EI) calcd for  $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_3$ : 378.1943, found 378.1933. Anal. Calcd for  $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_3$ : C, 72.99; H, 6.92; N, 7.40. Found: C, 72.80; H, 6.85; N, 7.30; mp 160–161 °C.

**Computational Method.** Geometry optimizations were carried out at the B3LYP<sup>26</sup> or M06-2X<sup>27</sup> level of theory with the cc-PVDZ<sup>28</sup> or aug-cc-PVDZ<sup>29</sup> basis set. The broken-symmetry (BS) method<sup>30</sup> (initial guess  $\langle S^2 \rangle = 1.00$ ) was used for the singlet diradicals. CCSD<sup>31</sup> energy was used for the UB3LYP-optimized geometry. The triplet state of diradicals was calculated with the unrestricted method (initial guess  $\langle S^2 \rangle = 2.00$ ). CASSCF<sup>32</sup> method with the 3-21G<sup>33</sup> basis set was used for the optimization for the singlet excited state of **AZd**.

## ASSOCIATED CONTENT

### Supporting Information

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of new compounds and optimized geometry obtained by quantum chemical calculations. This



material is available free of charge via the Internet at <http://pubs.acs.org>.

## AUTHOR INFORMATION

### Corresponding Author

\*E-mail: [mabe@hiroshima-u.ac.jp](mailto:mabe@hiroshima-u.ac.jp).

### Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

NMR and MS measurements were performed at N-BARD, Hiroshima University. This work was supported by the Grant-in-Aid for Scientific Research on Innovative Areas "Stimuli-responsive Chemical Species" (No 24109008),  $\pi$ -Space (No 21108516), the Scientific Research (No. 19350021), Tokuyama Science Foundation, and Mazda Foundation.

## REFERENCES

- (1) (a) Adam, W.; Diederling, M.; Trofimov, A. *J. Phys. Org. Chem.* **2004**, *17*, 643. (b) Sinicropi, A.; Page, C. S.; Adam, W.; Olivucci, M. *J. Am. Chem. Soc.* **2003**, *125*, 10947. (c) Little, D. R. *Chem. Rev.* **1996**, *96*, 93. (d) Berson, J. A. *Acc. Chem. Res.* **1991**, *24*, 215. (e) Engel, P. S. *Chem. Rev.* **1980**, *80*, 99.
- (2) (a) Shinkai, S.; Ogawa, T.; Nakaji, T.; Kusano, Y.; Nanabe, O. *Tetrahedron Lett.* **1979**, *20*, 4569. (b) Siewertsen, R.; Neumann, H.; Buchheim-Stern, B.; Herges, R.; Naether, C.; Renth, F.; Temps, F. *J. Am. Chem. Soc.* **2009**, *131*, 15594. (c) Beharry, A. A.; Woolley, G. A. *Chem. Soc. Rev.* **2011**, *40*, 4422. (d) Venkataramani, S.; Jana, U.; Dommaschk, M.; Soennichsen, F. D.; Tuzcek, F.; Herges, R. *Science* **2011**, *331*, 445.
- (3) (a) Solomon, B. S.; Thomas, T. F.; Steel, C. J. *Am. Chem. Soc.* **1968**, *90*, 2249. (b) Rau, H. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 224. (c) Samanta, S.; Qin, C.; Lough, A. J.; Woolley, G. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 6452.
- (4) (a) Reyes, M. B.; Carpenter, B. K. *J. Am. Chem. Soc.* **2000**, *122*, 10163. (b) Hamaguchi, M.; Nakaishi, M.; Nagai, T.; Nakamura, T.; Abe, M. *J. Am. Chem. Soc.* **2007**, *129*, 12981. (c) Ishihara, C.; Abe, M. *Aust. J. Chem.* **2010**, *63*, 1615. (d) Yagi, S.; Hiraga, Y.; Abe, M. *J. Phys. Org. Chem.* **2011**, *24*, 894. (e) Abe, M.; Iwakura, I.; Yabushita, A.; Yagi, S.; Liu, J.; Okamura, K.; Kobayashi, T. *Chem. Phys. Lett.* **2012**, *527*, 79.
- (5) Franck-Neumann, M.; Martina, D.; Dietrich-Buchecker, C. *Tetrahedron Lett.* **1975**, *15*, 1763.
- (6) Turro, N. J.; Renner, C. A.; Waddell, W. H.; Katz, T. J. *J. Am. Chem. Soc.* **1976**, *98*, 4320.
- (7) Adam, W.; Lucchi, O. D. *J. Am. Chem. Soc.* **1980**, *102*, 2109.
- (8) Chang, M. H.; Dougherty, D. A. *J. Am. Chem. Soc.* **1982**, *104*, 2333.
- (9) Adam, W.; Gillaspay, W. D.; Peters, E.-M.; Peters, K.; Rosenthal, R. J.; Schnering, H. G. *J. Org. Chem.* **1985**, *50*, 580.
- (10) (a) Adam, W.; Nau, W. M.; Sendelbach, J. *J. Am. Chem. Soc.* **1994**, *116*, 7049. (b) Adam, W.; Fragale, G.; Klapstein, D.; Nau, W. M.; Wirz, J. *J. Am. Chem. Soc.* **1995**, *117*, 12578. (c) Adam, W.; Moorthy, J. N.; Nau, W. M.; Scaiano, J. C. *J. Am. Chem. Soc.* **1997**, *119*, 5550.
- (11) Yamamoto, N.; Olivucchi, M.; Celani, P.; Bernardi, F.; Robb, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 2391.
- (12) (a) Abe, M.; Hattori, M.; Takegami, A.; Masuyama, A.; Hayashi, T.; Seki, S.; Tagawa, S. *J. Am. Chem. Soc.* **2006**, *128*, 8008. (b) Abe, M.; Adam, W.; Borden, W. T.; Hattori, M.; Hrovat, D. A.; Nojima, M.; Nozaki, K.; Wirz, J. *J. Am. Chem. Soc.* **2004**, *126*, 574. (c) Abe, M.; Adam, W.; Hara, M.; Hattori, M.; Majima, T.; Nojima, M.; Tachibana, K.; Tojo, S. *J. Am. Chem. Soc.* **2002**, *124*, 6540.
- (13) Clark, W. D. K.; Steel, C. J. *Am. Chem. Soc.* **1971**, *93*, 6347.
- (14) A similar solvent effect was observed for AZ4 in ref 10.
- (15) Recharadt, C. *Chem. Rev.* **1994**, *94*, 2319.
- (16) McClelland, R. A.; Gedge, S.; Bohnnek, J. *J. Org. Chem.* **1981**, *46*, 886.
- (17) Abe, M.; Adam, W.; Heidenfelder, T.; Nau, W. M.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 2019.
- (18) Abe, M.; Ye, J.; Mishima, M. *Chem. Soc. Rev.* **2012**, *41*, 3808.
- (19) Frisch, M. J.; et al. *Gaussian 09*, revision B.01, Gaussian Inc.: Wallingford, CT, 2009.
- (20) Roberson, M. J.; Simons, J. *J. Phys. Chem. A* **1997**, *101*, 2379.
- (21) (a) Edward, J. T. *Chem. Ind.* **1955**, 1102. (b) Kabayama, M.; Petterson, D. *Can. J. Chem.* **1958**, *36*, 563. (c) Salzner, U.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1993**, *115*, 10231. (d) Salzner, U.; Schleyer, P. v. R. *J. Org. Chem.* **1994**, *59*, 2138. (e) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer Verlag: Berlin, 1983. (f) *The Anomeric Effect*; Thatcher, G. R. J, Ed.; ACS Symposium Series 539, 1993.
- (22) Hayday, K.; McKelvey, R. D. *J. Org. Chem.* **1976**, *41*, 2222.
- (23) (a) Reed, A. E.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 1736. (b) Carpenter, J. E.; Weinhold, F. *J. Mol. Struct.* **1988**, *169*, 41. (c) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.
- (24) Foresman, J. B.; Keith, T. A.; Wiberg, K. B.; Snoonian, J.; Frisch, M. J. *J. Phys. Chem.* **1996**, *100*, 16098.
- (25) Adam, W.; Froehlich, L.; Nau, W. M.; Korth, H.-G.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1339.
- (26) (a) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
- (27) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215.
- (28) Dunning, T. H. *J. Phys. Chem.* **1989**, *90*, 1007.
- (29) (a) Kendall, R. A.; Dunning, T. H., Jr.; Harrison, R. H. *J. Chem. Phys.* **1992**, *96*, 6796. (b) Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1993**, *98*, 1358.
- (30) Yamaguchi, K.; Jensen, F.; Dorigo, A.; Houk, K. N. *Chem. Phys. Lett.* **1988**, *149*, 537.
- (31) (a) Cizek, T. In *Advance in Chemical Physics*; Hariharan, P. C., Ed.; Wiley Interscience: New York, 1969; Vol. 14, p 35. (b) Purvis, G. D., III; Bartlett, R. J. *J. Chem. Phys.* **1982**, *76*, 1910. (c) Scuseria, G. E.; Janssen, C. L.; Schaefer, H. F., III. *J. Chem. Phys.* **1988**, *89*, 7382. (d) Scuseria, G. E.; Schaefer, H. F., III. *J. Chem. Phys.* **1989**, *90*, 3700.
- (32) Eade, R. H. E.; Robb, M. A. *Chem. Phys. Lett.* **1981**, *83*, 362.
- (33) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939.