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Mechanism of an Alcohol-Trapping Reaction in the Direct and Benzophenone-Sensitized Photodenitrogenation of a Spiroepoxy-Substituted Azoalkane: Solvent Effects and Stereochemical Deuterium Labeling

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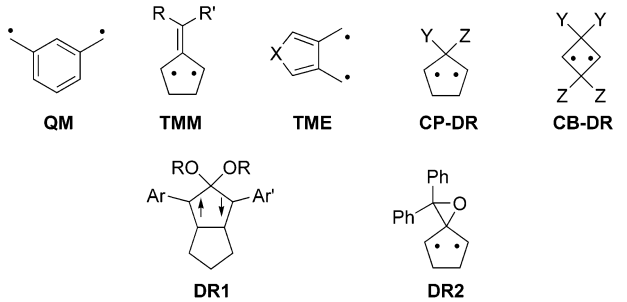
The spin-state-dependent reactivity, singlet versus triplet, of the 2-spiroepoxy-1,3-cyclopentane-1,3-diyl **DR2** has been assessed through alcohol-trapping reactions for which the effect of solvent acidity on the product distribution of the alcohol trapping products **2** versus **3** + **4** and stereochemical deuterium-labeling studies have been performed. The proposed mechanism for the solvent effect on the product ratio (**2**/**3** + **4**) reveals the importance of the hydrogen-bonded intermediates **I1** and **I2** in the trapping reactions; the stereochemical deuterium-labeling results clarify the dipole structure trapped by the alcohol. The dipoles **DP1** and **DP2**, in which the configuration between the epoxide oxygen and the deuterium atoms is retained, are inferred for the direct photodenitrogenation reactions (singlet state), whereas for the benzophenone-sensitized photoreactions (triplet state), after ISC, the ring-opened dipole **DP3** is implied as the intermediate that is trapped by the alcohol.

Introduction

Singlet−triplet energy gaps and spin-state-dependent reactivity have attracted considerable attention in diradical chemistry; these mechanistic features must be clarified to understand the behavior of the reactive intermediates.[1] In this regard, considerable effort has been expended on non-Kekulé molecules, such as **QM**,[2] **TMM**,[3] **TME**,[4] whose investigation has provided important knowledge on the ground-state spin-multiplicity and the reactivity of these species.



For localized diradicals, experimental work on the singlet-state chemistry has come quite late due to their high reactivity (short-lived intermediates),[5] compared to the triplet-state chemistry.[6] Borden[7] and our group[8,9] have proposed that the kinetically stabilized 1,3-diradicals are good candidates for the investigation of the singlet state. We have found that alkoxy groups (Y, Z = OR) place the singlet state below the triplet state in cyclopentane-1,3-diyls **CP-DR**[8] and cyclobutane-1,3-diyls **CB-DR**[9] with considerable energy gaps, $\Delta E_{ST} = E_S - E_T = -6$ to -12 kcal/mol, as reported for the singlet ground state of the 2,2-difluoro-1,3-cyclopentanediyl (Y, Z = F in **CP-DR**).[7] This made possible the examination of singlet state chemistry. Actually, the kinetically stabilized 2,2-dialkoxy-1,3-diarycyclopentane-1,3-diyl **DR1** has a lifetime of microseconds, which is the longest lived singlet diradical reported to date for localized carbon-centered diradicals. This has allowed the investigation of the chemistry of its singlet state, which revealed characteristic differences compared to its triplet state.[8b,c]

We have also reported the spin-state-dependent reactivity of the 2-spiroepoxy-1,3-cyclopentanediyl **DR2**[10] in the photodenitrogenation of the deuterated azoalkanes

† Osaka University.

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(1) (a) In *Diradicals*; Borden, W. T., Ed.; Wiley: New York, 1982. (b) In *Kinetics and Spectroscopy of Carbenes and Biradicals*; Platz, M. S., Ed.; Plenum Press: New York, 1990.

(2) (a) Migirdicyan, E.; Baudet, J. *J. Am. Chem. Soc.* **1975**, *97*, 7400−7404. (b) Rule, M.; Matlin, A. R.; Seeger, D. E.; Hilinski, E. F.; Doughterty, D. A.; Berson, J. A. *Tetrahedron* **1982**, *38*, 787−798. (c) Wright, B. B.; Platz, M. S. *J. Am. Chem. Soc.* **1983**, *105*, 628−630. (d) Goodman, J.; Berson, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 5409−5424. (e) Biewer, M. C.; Biehn, C. R.; Platz, M. S.; Després, A.; Migirdicyan, E. *J. Am. Chem. Soc.* **1991,** *113*, 616−620. (f) Haider, K. W.; Migirdicyan, E.; Soundrarajan, N.; Despres, A. *J. Am. Chem. Soc.* **1990**, *112*, 733−738. (g) Hrovat, D. A.; Murcko, M. A.; Lahti, P. M.; Borden, W. T. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1037−1044. (h) Bushby, R. J.; Gooding, D. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1069−1075.

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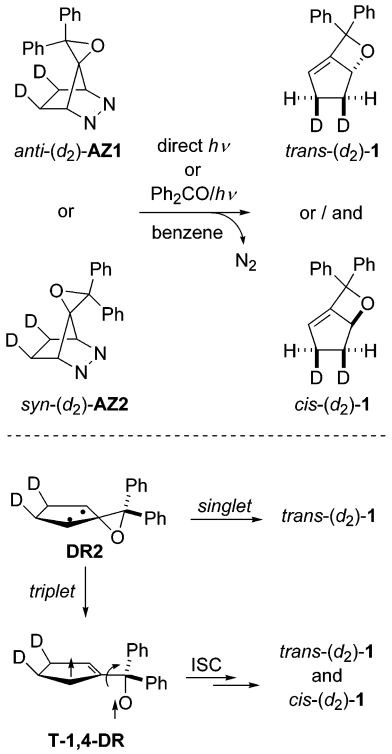
anti-(d_2)-**AZ1** and *syn*-(d_2)-**AZ2**. Thus, in an aprotic solvent (benzene), the singlet diradical generated upon direct irradiation (λ_{exc} = 330 nm) of the azo chromophore gave stereoselectively the oxetane, i.e., *trans*-(d_2)-**1** from *anti*-(d_2)-**AZ1** and *cis*-(d_2)-**1** from *syn*-(d_2)-**AZ2** (Scheme 1), by concerted rearrangement of the 2-spiroepoxy 1,3-diradical **DR2**. In contrast, nonselective formation of the oxetanes *trans*- and *cis*-(d_2)-**1** was observed from the triplet state generated by benzophenone sensitization (λ_{exc} = 370 nm) through stepwise migration in the intermediary triplet 1,4-diradical **T-1,4-DR** (Scheme 1). In methanol, a spin-state-dependent product distribution was also found in the formation of the MeOH adducts **2a** and **3a** (Scheme 2).[8a] Whereas the direct photodenitrogenation (singlet state) gave a 25/75 mixture of the MeOH adduct **2a** and its regioisomer **3a** (the latter derived from the methanolysis of the oxetane **1**), for the benzophenone-sensitized reaction (triplet state) the yield of adduct **2a** decreased; i.e., the ratio **2a**/**3a** (= **1**) was 10/90.

What dipoles are being trapped by methanol? Is the structure of the dipole in the direct irradiation different from that in the sensitized photodenitrogenation? The answers to these questions would clarify the mechanism of the spin-state-dependent reactivity. The possible structures of the dipoles **DP1**−**3** are shown in Scheme 3, in which **DP1** and **DP2** are the resonance forms of the singlet state of the diradical **DR2**. Such mesomeric forms have been proposed for singlet diradicals by Salem,[11] Borden,[12] and our group.[8c]

In the present study, we have investigated first the solvent effect on the product distribution, i.e., **2** vs **3** + **4** (= **1**), to elucidate the mechanism for the formation of the trapping product **2**. We have selected 2,2,2-trifluoroethanol (TFE, pK_a[13] = 12.4, N_T[14] = −3.93) and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP, pK_a[13] = 9.2, N_T[14] = −5.26) as solvents, which are more acidic (pK_a) and less nucleophilic (N_T) than methanol (MeOH, pK_a =15.5, N_T =0.17). For such alcoholic solvents, we had already determined the thermal reactivity of the oxetane **1**.[15] Thus, the TFE-induced reaction of oxetane **1** gave a 2:1 mixture of **3b** (R = CH_2CF_3) and *cis*-**4b** (R = CH_2CF_3) in high yield (total > 85%); the adduct *cis*-**4c** [R = $CH(CF_3)_2$] was observed exclusively in the HFIP-induced reaction (Scheme 2).[15] Presently, we have performed the deuterium-labeling study for the dipole-trapping reactions by using

SCHEME 1. Stereoselectivity (Singlet versus Triplet) of the Oxetane (d_2)-1 Formed in the Photodenitrogenation of the Deuterated Azoalkanes *anti*-(d_2)-AZ1 and *syn*-(d_2)-AZ2



(3) (a) Dowd, P. *J. Am. Chem. Soc.* **1966**, *88*, 2587−2589. (b) Gold, A. *J. Am. Chem. Soc.* **1969**, *91*, 4961−4962. (c) Borden, W. T.; Davidson, E. R. *Acc. Chem. Res.* **1981**, *14*, 69−76. (d) Dixon, D. A.; Dunning, T. H.; Eades, R. A.; Kleier, D. A. *J. Am. Chem. Soc.* **1981,** *103*, 2878−2880. (e) Kelly, D. F.; Rentzepis, O. M.; Mazur, M. R.; Berson, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 3764−3766. (f) Bushby, R. J. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1211−1215. (g) Adam, W.; Finzel, R. *J. Am. Chem. Soc.* **1992**, *114*, 4563−4568. (h) Hirano, T.; Kumagai, T.; Miyashi, T.; Akiyama, K.; Ikegami, Y. *J. Org. Chem.* **1992**, *57*, 876−882. (i) irano, T.; Kumagai, T.; Miyashi, T.; Akiyama, K.; Ikegami, Y. *J. Org. Chem.* **1991**, *56*, 1907−1914. (j) Little, R. D.; Brown, L. M.; Masjedizadeh, M. R. *J. Am. Chem. Soc.* **1992**, *114*, 3071−3075. (k) Duncan, R. D.; Corwin, L. R.; Davis, J. H.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 2350−2358. (l) Berson, J. A.; Bushby, R. J.; McBride, J. M.; Tremelling, M. *J. Am. Chem. Soc.* **197,0**, *93*, 1544−1546. (m) Paul, G. C.; Gajewski, J. J. *J. Org. Chem.* **1996**, *61*, 1399−1404. (n) Cramer, C. J. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1007−1013. (o) Hill, B. T.; Squires, R. R. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1027−1035. (p) Sorensen, T. S.; Sun, F. J. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1053−61. (q) Snyder, G. J.; Dougherty, D. A. *J. Am. Chem. Soc.* **1985**, *107*, 1774−1775.

(4) (a) Du, P.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1986**, *108*, 8086−8087. (b) Berson, J. A. *Acc. Chem. Res.* **1997**, *30*, 238−244. (c) Clifford, E. P.; Wenthold, P. G.; Lineberger, W. C.; Ellison, G. B.; Wang, C. X.; Grabowski, J. J.; Vila, F.; Jordan, K. D. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1015−1022. (d) Matsuda, K.; Iwamura, H. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1023−1026.

(5) (a) Recently, Bertrand and co-workers isolated a singlet boron-centered 1,3-diradical: Scheschkewitz, D.; Amii, H.; Gornitzka, H.; Schoeller, W. W.; Bourissou, D.; Bertrand, G. *Science* **2002**, *295*, 1880−1881. (b) Wentrup, C. *Science* **2002**, *295*, 1846−1847. (c) Adam, W.; Platsch, H.; Wirz, J. *J. Am. Chem. Soc.* **1989**, *111*, 6896−6898.

(6) (a) Buchwalter, S. L.; Closs, G. L. *J. Am. Chem. Soc.* **1975**, *97*, 3857−3858. (b) Buchwalter, S. L.; Closs, G. L. *J. Am. Chem. Soc.* **1979**, *101*, 4688−4693. (c) Conrad, M. P.; Pitzer, R. M.; Schaefer, H. F., III. *J. Am. Chem. Soc.* **1979**, *101*, 2245−2246. (d) Goldberg, A. H.; Dougherty, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 284−290. (e) Dougherty, D. A. *Acc. Chem. Res.* **1991**, *24*, 88−94. (f) Scaiano, J. C. *Tetrahedron* **1982**, *38*, 819−824. (g) Kita, F.; Adam, W.; Jordan, P.; Nau, W. M.; Wirz, J. *J. Am. Chem. Soc.* **1999**, *121*, 9265−9275. (h) Adam, W.; Grabowski, S.; Wilson, R. M. *Acc. Chem. Res.* **1990**, *23*, 165−172. (i) Griesbeck, A. G.; Mauder, H.; Stadtmüller, S. *Acc. Chem. Res.* **1994**, *27*, 70−75.

(7) (a) Xu, J. D.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1994**, *116*, 5425−5427. (b) Getty, S. J.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1994**, *116*, 1521−1527. (c) Adam, W.; Borden, W. T.; Burda, C.; Foster, H.; Heidenfelder, T.; Heubes, M.; Hrovat, D. A.; Kita, F.; Lewis, S. B.; Scheutzow, D.; Wirz, J. *J. Am. Chem. Soc.* **1998**, *120*, 593−594.

(8) (a) Abe, M.; Adam, W.; Nau, W. M. *J. Am. Chem. Soc.* **1998**, *120*, 11304−11310. (b) Abe, M.; Adam, W.; Heidenfelder, T.; Nau, W. M.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 2019−2026. (c) Abe, M.; Adam, W.; Hara, M.; Hattori, M.; Majima, T.; Nojima, M.; Tachibana, K.; Tojo, S. *J. Am. Chem. Soc.* **2002**, *124*, 6540−6541.

(9) Abe, M.; Ishihara, C.; Nojima, M. *J. Org. Chem.*, in press.

(10) Abe, M.; Adam, W.; Ino, Y. Nojima, M. *J. Am. Chem. Soc.* **2000**, *122*, 6508−6509.

(11) Salem, L.; Rowland, C. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 92−111.

(12) (a) Borden, W. T. *Chem. Commun.* **1998**, 1919−1925. (b) Getty, S. J.; Hrovat, D. A.; Xu, J. D.; Barker, S. A.; Borden, W. T. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 1689−1701.

(13) (a) DeTar, D. F. *J. Am. Chem. Soc.* **1982**, *104*, 7205−7212.

(14) Kevill, D. N.; Andersen, S. W. *J. Org. Chem.* **1991**, *56*, 1845−1850.

(15) Abe, M.; Minamoto, T.; Ino, Y. Kawakami, T.; Nojima, M. *Tetrahedron* **2002**, *58*, 7043−7047.

SCHEME 2. Reactivity of the 2-Spiroepoxy 1,3-Diradical DR2 and of the Oxetane 1 in Aprotic (Benzene) and Protic (Methanol) Solvents

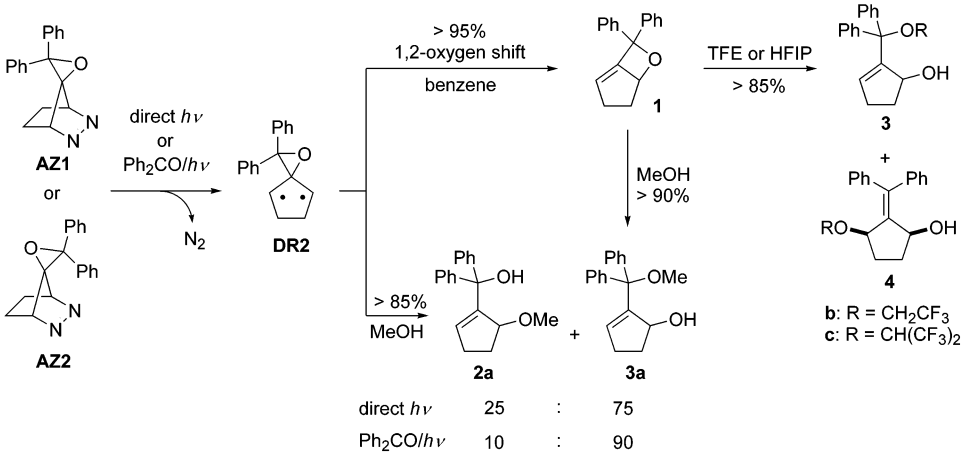
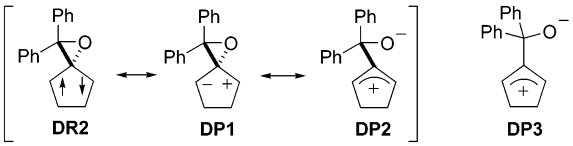


TABLE 1. Solvent Effects on the Product Ratio of ROH Adducts in the Photodenitrogenation of the Spiroepoxy-Substituted Azoalkanes AZ1 and AZ2[a]

								product ratios (%)[f]			
entry	AZ	ROH	pK_a[b]	N_T[c]	$h\nu$	convn[d] (%)	**2**−**4**[e] (%)	**2**	**3**	**4**	**2**/(**3** + **4**) (= **1**)
1	**AZ1**	MeOH	15.5	0.17	direct $h\nu$, 340 nm	>97	90	26	74	*g*	26/74
2	**AZ1**	MeOH (2.5 M)			direct $h\nu$, 340 nm	>97	90	13	87	*g*	13/87
3	**AZ1**	MeOH (1.0 M)			direct $h\nu$, 340 nm	>97	91	7	93	*g*	7/93
4	**AZ2**	MeOH			direct $h\nu$, 340 nm	89	91	29	71	*g*	29/71
5	**AZ1**	MeOH			$Ph_2CO/h\nu$, 380 nm	>97	88	9	91	*g*	9/91
6	**AZ1**	MeOH (2.5 M)			$Ph_2CO/h\nu$, 380 nm	>97	93	4	96	*g*	4/96
7	**AZ2**	MeOH			$Ph_2CO/h\nu$, 380 nm	>97	88	6	94	*g*	6/94
8	**AZ1**	TFE (2.5 M)	12.4	−3.93	direct $h\nu$, 330 nm	45	93	28	49	23	28/72
9	**AZ2**	TFE (2.5 M)			direct $h\nu$, 330 nm	44	88	25	45	30	25/75
10	**AZ1**	TFE (2.5 M)			$Ph_2CO/h\nu$, 380 nm	>97	89	16	57	27	16/84
11	**AZ1**	HFIP (2.5 M)	9.2	−5.26	direct $h\nu$, 330 nm	12	89	49	*g*	51	49/51
12	**AZ1**	HFIP (2.5 M)			$Ph_2CO/h\nu$, 380 nm	>97	87	32	*g*	68	32/68

[a] A solution of azoalkane **AZ1** or **AZ2** (70 mg, 0.05 M) in ROH/benzene (5 mL) was degassed and irradiated by using a 500-W Xenon lamp, focused with a monochromator (± 5 nm) at ca. 20 °C. **AZ1:** λ_{max} 344 nm (ϵ 230) in benzene; λ_{max} 340 nm (ϵ 96) in MeOH; λ_{max} 328 nm (ϵ 81) in TFE; λ_{max} 320 nm (ϵ 55) in HFIP. **AZ2**: λ_{max} 352 nm (ϵ 90) in benzene; λ_{max} 338 nm (ϵ 37) in MeOH; λ_{max} 333 nm (ϵ 49) in TFE; λ_{max} 329 nm (ϵ 30) in HFIP. [b] The pK_a values were taken from ref 13. [c] N_T: nucleophilicity of ROH (ref 14). [d] The conversions (%) were calculated from the recovered azoalkane **AZ1** or **AZ2** after irradiation for 28 h; the value >97 means that the azoalkane was not observed after irradiation. [e] The total yield (%) of isolated materials. [f] The product ratios were determined by ^{1}H NMR (270 or 600 MHz) peak areas, error ± 3% of the stated values, and normalized to 100%. [g] The product was not detected in the NMR analysis.

SCHEME 3. Dipolar Structures DP1−3 as Possible Precursors in the Formation of the MeOH Adduct 2a



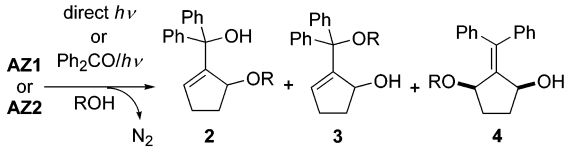
the selectively *exo*-deuterated azoalkanes *anti*-(d_2)-**AZ1** and *syn*-(d_2)-**AZ2**. The experimental results reported herein have provided valuable mechanistic information on the dipole structures involved in the alcohol-trapping reactions.

Results

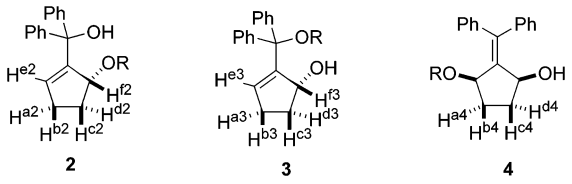
Solvent Effects. The azoalkane **AZ1** or **AZ2** (λ_{max} = 320−340 nm, depends on the solvent) was photochemically denitrogenated in the protic solvent (ROH) by means of a 500-W Xenon lamp, focused with a monochromator at ca. 20 °C for 28 h (Scheme 4, Table 1).

In pure MeOH, as observed previously, the product ratios **2a/3a (= 1)** were independent of the configuration

SCHEME 4. Photodenitrogenation of the Spiroepoxy-Substituted Azoalkanes AZ1 and AZ2 in Protic Solvents (ROH)



of the azoalkane **AZ1, AZ2** (entries 1, 4, 5, 7), but depended on the irradiation conditions (entries 1, 4, 5, and 7), i.e., direct (λ_{exc} = 340 nm) versus benzophenone-sensitized photodenitrogenation (λ_{exc} = 380 nm).[8a] A control experiment (λ_{exc} = 340 nm) showed that the presence of the triplet quencher piperylene (0.1 M) did not affect the conversion of the azoalkane nor the product ratios. Thus, the direct photodenitrogenation proceeds from the singlet-excited azo chromophore to generate the singlet diradical **S-DR2**. Another control experiment (λ_{exc} = 380 nm, 28 h, conversion <5%) established that without benzophenone (Ph_2CO) no photodenitrogenation occurred at this wavelength; thus, triplet sensitization by Ph_2CO affords the triplet diradical **T-DR2**.



a: R = Me, **b**: R = CH_2CF_3, **c**: R = $CH(CF_3)_2$

	NOE2 (%)	
	H^{f2}-H^{c2}	H^{f2}-H^{b2}
2a	3.1	1.1
2b	5.0	1.4
2c	4.2	1.0

	NOE3 (%)	
	H^{f3}-H^{c3}	H^{f3}-H^{b3}
3a	3.2	1.1
3b	3.1	0.9
3c	3.5	1.2

FIGURE 1. NOE data (%), NOE2 and NOE3, measured for the compounds **2** and **3**.

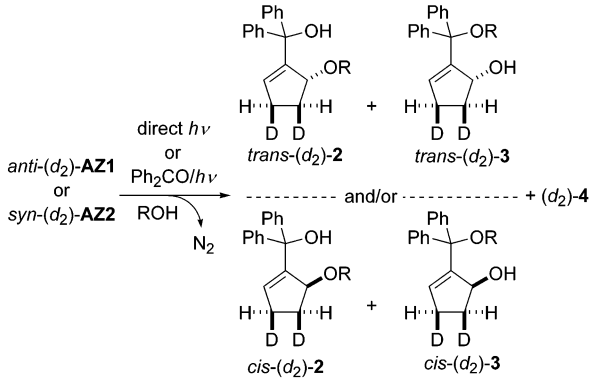
The product ratio of the MeOH adducts **2a** and **3a** significantly depends on the MeOH concentration; in particular, the product yield of **2a** decreased as the concentration of MeOH was lowered (entries 1−3, 5, 6). To gain more mechanistic information on the dipole-trapping mechanism, the photodenitrogenation was performed in the more acidic and less nucleophilic solvents trifluoroethanol (TFE) and hexafluoro-2-propanol (HFIP). Under the direct irradiation conditions (entries 8, 9, and 11), the conversions (%) of the azoalkane decreased with increasing acidity of the solvent. In contrast, no solvent effect was observed on the photodenitrogenation (conversion >97%) for the triplet-sensitized reactions (entries 10 and 12). The solvent effects on the azoalkane conversion may be readily explained by the well-known quenching of the singlet-excited azoalkanes by protic solvents.[16]

Mechanistically informative, the formation of the dipole trapping product **2**, i.e., the product ratio **2**/(**3** + **4**), increased with increasing acidity (pK_a) and decreasing nucleophilicity (N_T) of the solvent, irrespective of the irradiation conditions (for direct photolysis, compare entries 2, 8, and 11; for Ph_2CO-sensitized photolysis, compare entries 6, 10, and 12). Form these results it is evident that protonation of the oxygen atom plays an important role in the dipole-trapping reactions (cf. Scheme 7); however, the question arises which of the dipoles **DP1**, **DP2**, and/or **DP3** are being trapped by ROH? For this purpose, stereochemical deuterium-labeling studies were conducted, which are subsequently described.

Deuterium-Labeling Studies. To determine the deuterated positions and their deuterium content (%) in the ROH-trapping products **2**−**4**, a reliable assignment of all of the chemical shifts of the aliphatic hydrogen atoms in the five-membered rings of the ROH adducts **2**, **3**, and **4** was required (Figure 1).

Unfortunately, the chemical shifts of the hydrogen atoms H^{a4}, H^{b4}, H^{c4}, and H^{d4} in **4b**,**c** were not sufficiently separated for assignment and determination of the peak areas even in the 600-MHz NMR measurements; thus, the stereochemical deuterium-tracer experiments were not considered for the trapping product **4**. However, the

SCHEME 5 . Stereochemical Deuterium-Labeling Studies for the Formation of ROH Adducts 2 and 3 in the Photodenitrogenation of *anti*-(d_2)-AZ1 or *syn*-(d_2)-AZ2



hydrogen atoms H^{a-d} of the adducts **2** and **3** were sufficiently separated to assign definitively the chemical shifts and the peak areas. The chemical shifts for all of the hydrogen atoms were determined by using a combination of CH−COSY and NOE measurements (600-MHz NMR analyses). From the two-dimensional correlations between the ^{13}C and the ^1H NMR spectral data, the chemical shifts of H^e and H^f were reliably assigned for both products **2** and **3**. Furthermore, additional correlations allowed us to assess the chemical shifts of the pair of the hydrogen atoms H^a−H^b and H^c−H^d, which are attached to the same carbon atom. To distinguish the two hydrogen atoms, NOE measurements (NOE2, NOE3) were performed on the products **2** and **3** (Figure 1). The clear-cut NOE data (%) of H^f with H^b and H^c made it possible to determine the specific chemical shifts of these products. The assignments for **2a** and **3a** are shown in the partial ^1H NMR spectra (Figures 2a and 3a).

The assignments for products **2b**, **3b**, and **2c** are given in the Supporting Information (Figures S1−3). These unequivocal assignments of the chemical shifts allowed to determine reliably the positions of the deuterium atoms and their deuterium content (%).

The stereochemical deuterium-labeling studies were performed by using the exo-selectively deuterated azoalkane *anti*-(d_2)-**AZ1** and *syn*-(d_2)-**AZ2**, in which the *d* content was 72 ± 3% (Scheme 5, Figures 2 and 3, and Figures S1−3 (Supporting Information)). The deuterated positions in the ROH adducts **2** and **3** and their *d* content (%) were determined by ^1H NMR (600 MHz) peak areas (Figures 2, 3 and Figures S1−3 (Supporting Information), Table 2).

For the direct irradiation of *anti*-(d_2)-**AZ1** in MeOH (entry 1), as is evident from Figures 2b and 3b, a high degree of deuterium content (retention > 88%), was observed for H^{b2a} and H^{c2a} in **2a** (R = Me) and for H^{b3a} and H^{c3a} in **3a** (R = Me), which are both trans-configured relative to the OR (OH) group in the cyclopentene ring. Thus, *trans*-(d_2)-**2a** and *trans*-(d_2)-**3a** were selectively formed from *anti*-(d_2)-**AZ1**. The retention (%) of the configuration in *trans*-(d_2)-**2a** was found to be slightly lower than that in *trans*-(d_2)-**3a** derived from the oxetane *trans*-(d_2)-**1.** A similar product selectivity was observed for the direct photodenitrogenation of *syn*-(d_2)-**AZ2** (entry 2, Figures 2c and 3c), namely, *cis*-(d_2)-**2a** and *cis*-(d_2)-**3a** were selectively formed. In contrast, for the Ph_2CO-

(16) (a) Mirbach, M. J.; Liu, K.-C.; Mirbach, M. F.; Cherry, W. R.; Turro, N. J.; Engel, P. S. *J. Am. Chem. Soc.* **1997**, *119*, 5550−5555. (b) Adam, W.; Moorthy, J. N.; Nau, W. M.; Scaiano, J. C. *J. Am. Chem. Soc.* **1997**, *119*, 5550−5555.

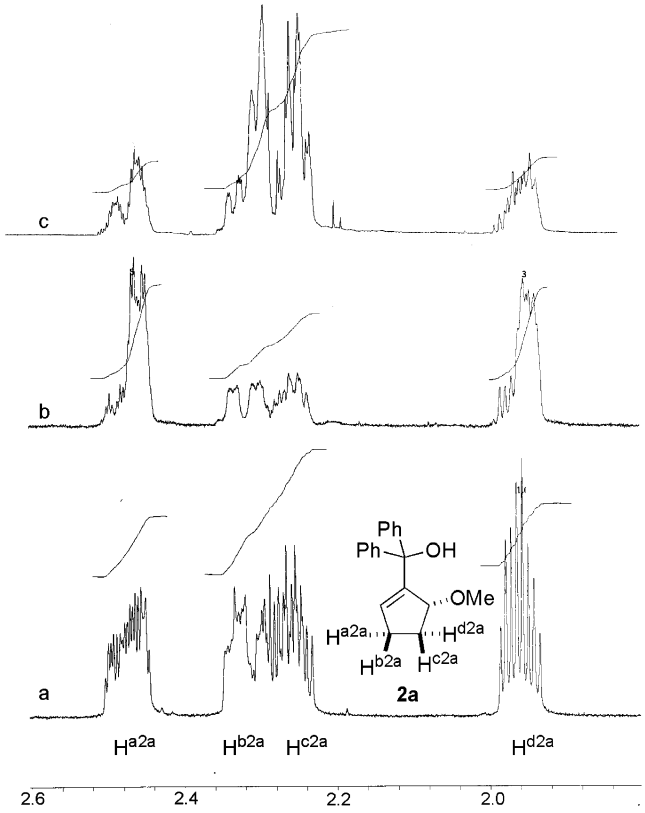


FIGURE 2. Partial ^{1}H NMR spectra (600 MHz) of the MeOH adduct **2a**, formed in the photolysis of (a) nondeuterated azoalkane **AZ1**, (b) *anti*-(d_2)-**AZ1**, and (c) *syn*-(d_2)-**AZ2**.

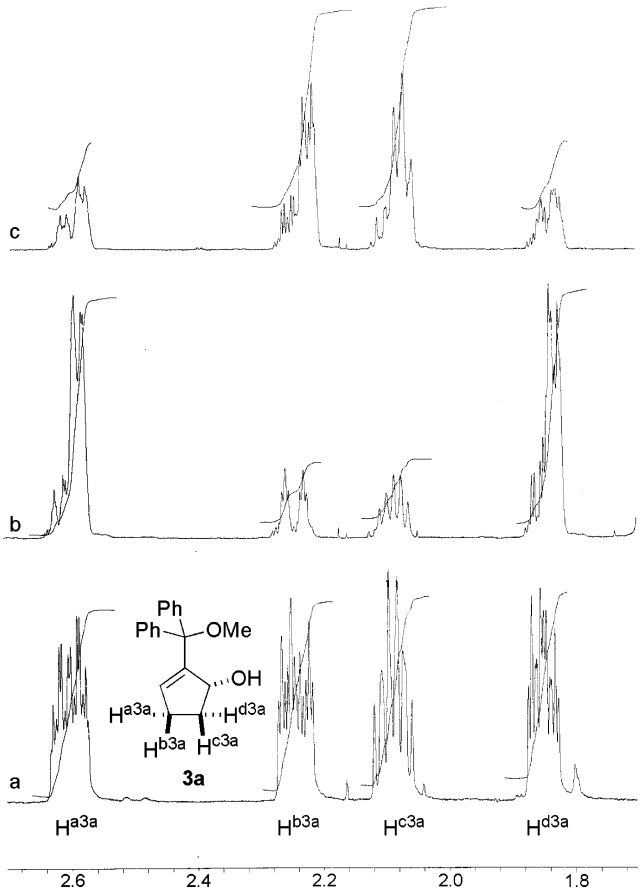


FIGURE 3. Partial ^{1}H NMR spectra (600 MHz) of the MeOH adducts **3a**, formed in the photolysis of (a) nondeuterated azoalkane **AZ1**, (b) *anti*-(d_2)-**AZ1**, and (c) *Syn*-(d_2)-**AZ2**.

sensitized irradiation (entries 3 and 4), an unselective formation of (d_2)-**2a** and (d_2)-**3a** was assessed from the NMR-spectral analysis. Control experiments for *trans*-(d_2)-**2a** (*d*-content: H^{a2a} = 4%, H^{b2a} 64%, H^{c2a} 66%, H^{d2a} 4%) and *trans*-(d_2)-**3a** (*d*-content: H^{a3a} 0%, H^{b3a} 74%, H^{c3a} 73%, H^{d3a} 1%) in the presence of Ph_2CO (λ_{exc} = 380 nm, 20 h in MeOH) did not produce a change of the deuterated positions and the deuterium content (%). Thus, the *d* contents (%) observed in the Ph_2CO-sensitized photodenitrogenation of the azoalkanes (entries 3, 4, 6, and 8) indicate the original configuration of the primary photoproducts **2** and **3**.

In the TFE and HFIP solvents (entries 5−8, Figures S1−3 (Supporting Information)), the randomization of the *d* content (%) was much more significant than that observed in MeOH. For example, the extent of retention (%) of the configuration decreased with increasing acidity (decreasing nucleophilicity) of the solvent under the direct irradiation conditions; i.e., for product **2** it is 88% in MeOH (entry 1), 78% in TFE (entry 5), and 70% in HFIP (entry 7), while for product **3** it is 100% in MeOH (entry 1) and 86% in TFE (entry 5). For the Ph_2CO-sensitized irradiation, almost complete loss of stereoselectivity was observed, since the extent of retention was ca. 50% (entries 6 and 8). It should be noted that the extent of retention of the configuration in the ROH-adduct **3b** (R = CH_2CF_3), formed in the direct irradiation, was not 100% as observed for the methanol case, although the adduct was derived from the oxetane **1**. A control experiment of the TFE-induced decomposition of the pure *trans*-(d_2)-**1** afforded the *trans*-(d_2)-**3b** with complete retention of configuration (Scheme 6). Furthermore, the stereoselective formation of the oxetane was also observed in the polar solvent DMSO. The results strongly suggest that the oxetane (d_2)-**1** is produced in low stereoselectivity in the protic trifluoroethanol, which reflects on the low extent of retention (86%) of the configuration of (d_2)-**3b** (Table 2, entry 5).

Discussion

The mechanism in Scheme 7 is proposed to account for the spin-state-dependent dipole-trapping reactions. To simplify the mechanistic discussion, only the photodenitrogenation of the *anti*-(d_2)-**AZ1** azoalkane is depicted.

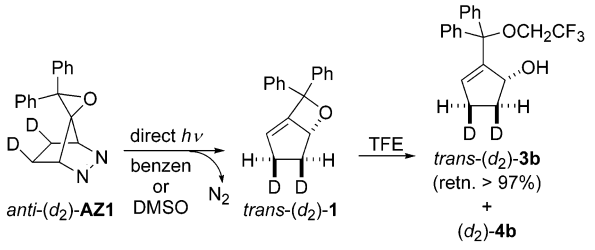
On direct irradiation of the azo chromophore, denitrogenation affords the trans-configured singlet 1,3 diradical *t*-(d_2)-**S-DR2**, which is stabilized by dipolar mesomeric structures *t*-(d_2)-**DP1** and *t*-(d_2)-**DP2**. The oxygen 1,2-shift and protonation by ROH occurs competitively to give the oxetane *trans*-(d_2)-**1** and the protonated intermediate **I1**, as inferred from the effects of the methanol concentration and the solvent acidity on the product distributions (Table 1). Subsequent ROH-induced solvolysis of the oxetane **1** leads to the adducts **3** and/or **4** with complete retention of configuration. Rotation around the C1−C2 bond in the **I1** species is hindered, such that rapid attack of the methoxy group (R = Me) from the side of

TABLE 2. Stereoselectivities in the Direct and Benzophenone-Sensitized Photodenitrogenation of the Diastereomerically Deuterium-Labeled *anti*-(d_2)-AZ1 and *ayn*-(d_2)-AZ2[a]

				d content (%) in ROH adduct[c]									retn (%)[d]	
entry	(d_2)-**AZ**[b]	ROH	hν		H^{a2}	H^{b2}	H^{c2}	H^{d2}		H^{a3}	H^{b3}	H^{c3}	H^{d3}	**2**	**3**
1	anti	MeOH	direct	**2a**	4	65	66	4	**3a**	0	74	73	1	88	100
2	syn	MeOH	direct	**2a**	66	6	6	66	**3a**	72	2	0	73	89	100
3	anti	MeOH	sens.	**2a**	29	47	48	27	**3a**	24	51	52	24	63	69
4	syn	MeOH	sens.	**2a**	45	30	32	44	**3a**	28	47	48	26	61	63
5	anti	TFE	direct	**2b**	14	58	58	14	**3b**	9	64	64	7	78	86
6	anti	TFE	sens.	**2b**	33	42	42	33	**3b**	27	47	47	28	57	63
7	anti	HFIP	direct	**2c**	20	52	52	20	-	-	-	-	-	70	-
8	anti	HFIP	sens.	**2c**	36	39	39	36	-	-	-	-	-	53	-

[a] Solutions of azoalkane *anti*-(d_2)-**AZ1** or *syn*-(d_2)-**AZ2** (70.0 mg, 0.05 M) in ROH/benzene (5 mL) were degassed and irradiated by a 500-W xenon lamp, focused with a monochromator, at ca. 20 °C. [b] The deuterium content is 72 ± 3%. [c] Deuterium content (%) was determined by ^{1}H NMR (600 MHz) peak areas; error ± 3% of the stated value. [d] Extent of retention (%) of the initial azoalkane configuration in the deuterated ROH adducts; for complete deuterium randomization, the value would be 50%.

SCHEME 6. Retention of Configuration (>97%) in the TFE-Induced Decomposition of Oxetane *trans*-(d_2)-1



the oxygen affords the trans-configured adduct *trans*-(d_2)-**2a** in high extent of retention of the configuration (ca. 90%).

As for the trapping reactions in more acidic solvents, protonation is facilitated, which enhances the formation of the intermediates **I1** and **I2** and increases the yields of adduct **2**. The deuterium-labeling studies clearly disclose that the rotation around the C1−C2 bond in **I2** competes with alkoxy attack and the degree of retention (stereochemical memory) is diminished. This loss of stereochemical memory is most pronounced in the adduct **3b** (R = CH_2CF_3) and clearly supports the formation of the oxetane **1** through the intermediate **I2** in the TFE reaction (entry 5 in Table 2). The lower solvent nucleophilicity (MeOH, N_T = 0.7; TFE, N_T = −3.93) accounts for these experimental facts.

In the Ph_2CO-sensitized photodenitrogenation, the triplet 1,3-diradical *t*-(d_2)-**T-DR2** transforms rapidly to the ring-opened triplet 1,4-diradical (d_2)-**T-1,4-DR**. The fast ring-opening reaction has already been inferred from quantum-chemical calculation (UB3LYP/6-31G*), in which the energy barrier for the ring-opening was found to be nearly zero for the triplet state (no energy minimum) and ca. 1 kcal/mol for the singlet state (energy minimum).[8a] Thus, the singlet state of the diradical **S-DR2** is sufficiently long-lived to interact with the alcohol. The C1−C2 bond rotation in the triplet 1,4-diradical (d_2)-**T-1,4-DR** would compete with the intersystem-crossing (ISC) process to lose stereochemical control and the resulting the singlet 1,4 diradical (d_2)-**S-1,4-DR** should rapidly cyclize to the oxetane **1** in low stereoselectivity. The *trans*/*cis*-(d_2)-**DP3** dipole is the likely structure for the formation of the *trans*/*cis*-(d_2)-**2** adduct.

As shown in the deuterium contents of the Ph_2CO-sensitized reaction, the configuration of the starting azoalkane is not completely lost in the primary photoproducts **2** and **3**, since the extent of retention is ca. 60% in MeOH, 57% in TFE, and 53% in HFIP. There are two possibilities to account for these facts: ISC of the triplet 1,3-diradical *t*-(d_2)-**T-DR2** to its singlet state competes with the ring opening to the triplet 1,4-diradical (d_2)-**T-1,4-DR**; however, this possibility is unlikely because for localized cyclopentane-1,3-diyls, a rather low ISC rate constant (k_{ISC}) has been reported, namely around 10^6 s^{-1}.[5g] The relatively slow ISC process may be rationalized in terms of a small spin−orbit coupling (SOC) constant for the parallel orientation of the two singly occupied p orbitals (Scheme 8).[5h,i,17] In contrast, for ring-opening of oxiranylcarbinyl monoradicals a rate constant of $k_r > 10^{10}$ s^{-1} has been reported.[18] In our diradical case, as stated previously, the energy barrier of the epoxide ring has been calculated to be zero kcal/mol; thus, the ring-opening rate constant for the diradical should be larger than for the corresponding monoradical, namely $k_o > 10^{10}$ s^{-1}. Consequently, this comparison of rate constants suggest that the ISC process is much slower than the ring-opening reaction, i.e., $k_o \gg k_{ISC}$ (Scheme 8).

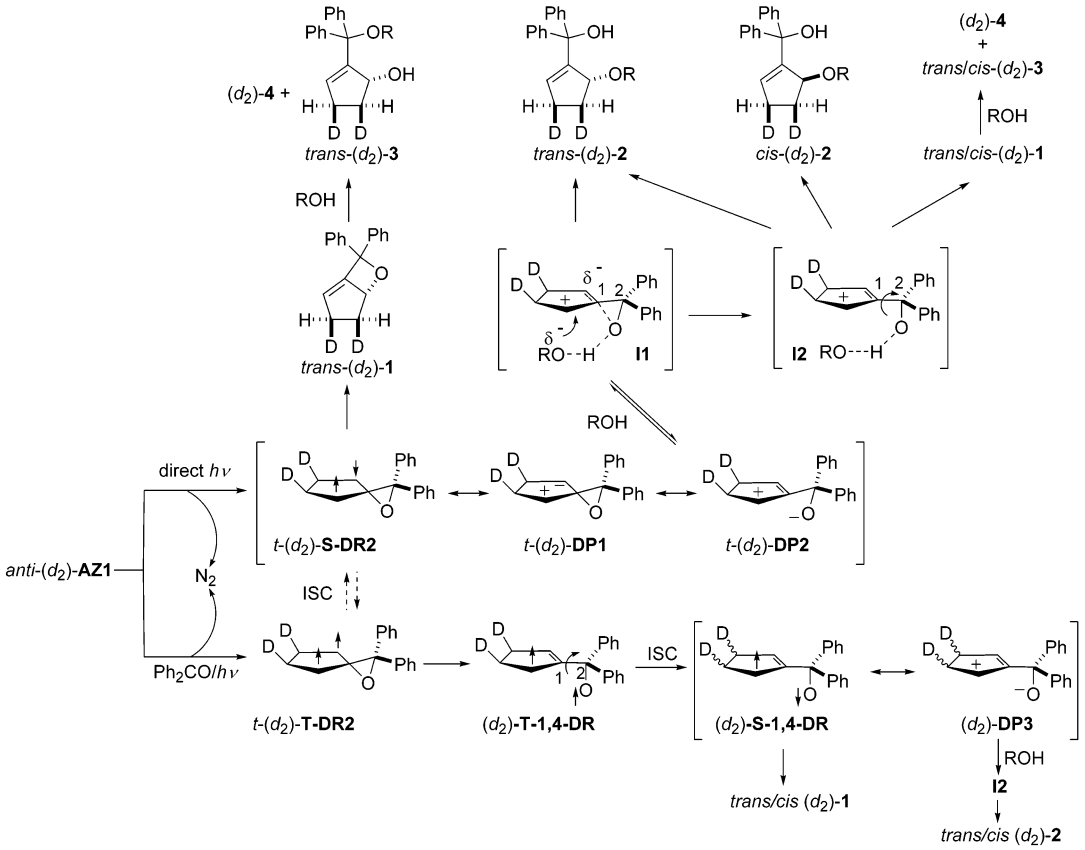
The back-reaction of **T-1,4-DR** to **T-DR2** could also be possible; however, within our experimental error limits, not even traces of the regioisomeric oxetane **5** could be observed from the thermodynamically more stable **T-1,4-DR′** in the Ph_2CO-sensitized irradiation. This implies that the back reaction is much slower than the ISC process to the singlet 1,4 diradical **S-1,4-DR**, i.e., $k_{ISC'} \gg k_{-0}$.

Alternatively, the retention of the configuration observed in the triplet state may result from competition of dipole trapping with C1−C2 bond rotation (Scheme 7). This seems to be the more likely reason, since the extent of the stereoselectivity loss increases as the nucleophilicity (N_T) of the solvent decreases; the extent of retention is 63% in MeOH, 57% in TFE, and 53% in HFIP.

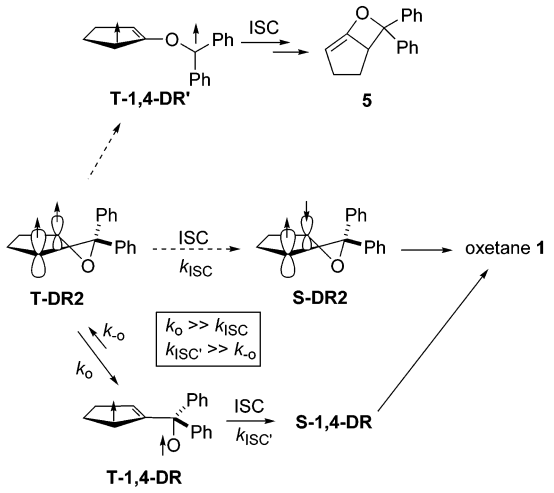
(17) (a) Carlacci, L.; Doubleday, C., Jr.; Furlani, T. R.; King, H. F.; Mclver, J. W., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 5323−5329. (b) Kutateladze, A. G. *J. Am. Chem. Soc.* **2001**, *123*, 9279−9282. (c) Michl, J.; Havlas, Z. *Pure Appl. Chem.* **1997**, *69*, 785−789. (d) Havlas, Z.; Downing, J. W.; Michl, J. *J. Phys. Chem. A* **1998**, *102*, 5681−5689.

(18) (a) Amaudrut, J.; Wiest, O. *Org. Lett.* **2000**, *2*, 1251−1254. (b) Ziegler, F. E.; Peterson, A. K. *J. Org. Chem.* **1995**, *60*, 2666−2667. (c) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091−2115. (d) Krosley, K. W.; Gleicher, G. J. *J. Phys. Org. Chem.* **1993**, *6*, 228−232. (e) Dickinson, J. M.; Murphy, J. A.; Patterson, C. W.; Eooster, N. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1179−1184. (f) A.-Kaloustian, S.; Agosta, W. C. *J. Org. Chem.* **1983**, *48*, 1718−1725. (g) Stogryn, E. L.; Gianni, M. H. *Tetrahedron Lett.* **1970**, *34*, 3025−3028.

SCHEME 7. Mechanism for the Dipole-Trapping Reactions in the Photodenitrogenation of *anti*-(d_2)-AZ1



SCHEME 8. Possible Pathways from the Triplet 1,3-Diradical T-DR2



Expectedly, a lower nucleophilicity of ROH would decrease the rate of the trapping reaction.

In summary, we have investigated the spin-state-dependent behavior of 2-spiroepoxy-1,3-diyl **DR2** in protic solvents (ROH). The detailed mechanistic studies (solvent effect and deuterium labeling) clarifies the spin-state-dependent mechanism for the formation of the dipole-trapping product **2**. In the singlet-state chemistry (direct irradiation), 1,3- and 1,4-dipoles **DP1**−**3** are proposed to be trapped by ROH. In contrast, the 1,4-dipole **DP3** is the only intermediate that is trapped in the triplet-state chemistry (Ph_2CO-sensitized irradiation).

Experimental Section

The nondeuterated and exo-deuterated azoalkanes **AZ1** and **AZ2** were prepared according to the method described previously.[8a,10] The *d* content (%) of **AZ1** and **AZ2** prepared in this study was 72% ± 3%. The structures of the ROH adducts **2a, 3a**−**c**, and **4b**−**c** have been characterized in the previous work.[8a,15] For a complete and reliable assignment of all the hydrogen atoms of the adducts **2** and **3**, CH−COSY and NOE measurements (600 MHz in $CDCl_3$) were performed.

General Procedure for the Direct Photodenitrogenation. A solution of the azoalkane **AZ1** or **AZ2** (70.0 mg, 0.05 M) in ROH/benzene or ROH (5 mL) was degassed and irradiated by means of a 500-W Xenon lamp, focused with a monochromator, at room temperature (ca. 20 °C); λ_{exc} = 340 ± 5 nm. After 28-h irradiation, the solvent was removed by using a rotary evaporator (ca. 100 mmHg). The residue was analyzed by ^{1}H NMR (270 or 600 MHz) spectroscopy to determine the product ratio of the ROH adducts. The errors were within ±3% of the stated values. The ROH adducts were separated by flash chromatography on silica gel; mass balances were >85% for each experiment. The deuterium contents (%) for the pure products were determined by ^{1}H NMR (600 MHz) peak areas. The standard deviations were within ±3% of the stated values, averaged for five runs.

General Procedure for the Ph_2CO-Sensitized Photodenitrogenation. The triplet-sensitized denitrogenation was performed in the presence of Ph_2CO (0.1 M) at λ_{exc} = 380 nm by means of a 500-W xenon lamp, focused by a monochromator. The other reaction conditions were the same as for the direct irradiation. The procedures of the isolation of the products and the spectroscopic analysis were similar to the method described for the direct irradiation.

The spectral data for the new compounds **2b** (R = CH_2CF_3) and **2c** (R = $CH(CF_3)_2$) are as follows:

1-(1′,1′-Diphenylhydroxymethyl)-5-(2′,2′,2′-trifluoroethoxy)-1-cyclopentene (2b): viscous oil; FTIR (liquid film)

3523, 3058, 2932, 1448, 1276, 1163, 1112 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.93−1.99 (m, 1 H), 2.26−2.31 (m, 1 H), 2.32−2.36 (m, 1 H), 2,46−2.53 (m, 1 H), 3.56 (qd, J = 8.6, 12.0 Hz, 1 H), 3.70 (qd, J = 8.5 and 12.0 Hz, 1 H), 4.38 (br s, 1 H), 4.69−4.73 (m, 1 H), 5.49−5.51 (m, 1 H), 7.20−7.53 (m, 10 H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 29.7(t). 30.2(t), 66.3 (tq, O*C*H_2-CF_3, J_{CF} = 33.0 Hz), 79.1 (d), 88.5 (s), 123.5 (q, CF_3, J_{CF} = 269.2 Hz), 126.9 (2 × d), 127.2 (4 × d), 127.6 (2 × d), 128.1 (2 × d), 136.7 (d), 144.9 (s), 145.1 (s), 146.6 (s). Anal. Calcd for $C_{20}H_{19}F_3O_2$: C, 68.96; H, 5.50. Found: C, 69.15; H, 5.71.

1-(1′,1′-Diphenylhydroxymethyl)-5-(1′,1′,1′,3′,3′,3′-hexafluoro-2-propoxy)-1-cyclopentene (2c): viscous oil; FTIR (liquid film) 3566, 3060, 3026, 1368, 1285, 1220, 1194, 1134 cm^{-1} ;^1H NMR (600 MHz, $CDCl_3$) δ 2.05−2.10 (m, 1 H), 2.23−2.29 (m, 1 H), 2.31−2.38 (m, 1 H), 2.53−2.59 (m, 1 H), 3.76 (br s, 1 H), 4.03 (sept, J = 5.7 Hz, 1 H), 4.97−4.99 (m, 1 H), 5.57−5.59 (m, 1 H), 7.22−7.47 (m, 10 H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 29.5 (t), 30.3 (t), 74.1 (d, O*C*H$(CF_3)_2$, J_{CF} = 33.0 Hz), 78.9 (d), 90.5 (s), 123.2 (2 × q, CF_3 J_{CF} = 266.5 Hz), 126.8 (2 × d), 127.0 (2 × d), 127.2 (2 × d), 127.7 (2 × d), 128.1 (2 × d), 138.4 (d), 144.5 (s), 145.0 (s), 146.5 (s). Anal. Calcd for $C_{21}H_{18}F_6O_2$: C, 60.58; H, 4.36. Found: C, 60.33; H, 4.56.

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Supporting Information Available: Partial ^1H NMR spectra for compounds **2b**, **3b**, and **2c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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