Stereochemical Deuterium Labeling as Mechanistic Probe for Differentiating the Singlet- and Triplet-Diradical Spin States in the Rearrangement of the 2-Spiroepoxy-1,3-cyclopentanediyl to Oxetanes

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Substituent effects on the spin multiplicity of diradicals and their reactivity have been a topic of timely current interest.[1,2] We have recently observed that for the 2-spiroepoxy-1,3-diradical **1,3-DR** the singlet ground state is preferred by ∼1 kcal/mol.[3] The latter is conveniently generated by photodenitrogenation of spiroepoxy azoalkane **1**, which unexpectedly led to the oxetane **2** by selective CO-bond cleavage of the epoxide ring.[3] Herein unequivocal stereochemical evidence is presented by means of deuterium-labeling experiments that the oxetane (d_2)-**2** formation in the photodenitrogenation of the azoalkanes *anti*(d_2)- or *syn*(d_2)-**1** depends dramatically on the irradiation conditions (Scheme 1): The direct (singlet) process proceeds with complete retention of the initial azoalkane configuration, the benzophenone-sensitized (triplet) one suffers extensive loss of stereochemical memory. These unprecedented facts are interpreted mechanistically in terms of a singlet nitrogen-free **S-1,3-DR** diradical in the direct photodenitrogenation versus the triplet **T-1,3-DR** in the benzophenone-sensitized one as precursors to the oxetane product **2**.

The direct (344 ± 4 nm) and benzophenone-sensitized (380 ± 4 nm) photodenitrogenation of the *anti*(d_2)-**1** (λ_{max} = 343 nm, ϵ 185) and of the *syn*(d_2)-**1** (λ_{max} = 352 nm, ϵ 85) in C_6D_6 with a 500-W Xenon lamp (a monochromator was used for wavelength selection) led to the oxetane (d_2)-**2** (Scheme 1 and Table 1), for which we have assigned the configurations of all the hydrogen atoms by means of C,H-COSY and NOE measurements (600-MHz in C_6D_6; cf. Supporting Information). The spectral data allowed unequivocally to distinguish between all of the four H_{a-d} hydrogen atoms, as indicated in Figure 1 (spectrum a). The direct irradiation of *anti*(d_2)-**1** (*d* content 88 ± 5%) gave quantitatively the dideuterated oxetane *exo*(d_2)-**2**, whose *d* content was determined directly on the photolysate by ^{1}H NMR (600 MHz) spectroscopy (Table 1, entry 1). As is evident from Figure 1 (spectrum b), only the H_a and H_d positions (*trans* to the CO bond) contain deuterium atoms (90 ± 5% content). Alternatively, the direct irradiation of the *syn*(d_2)-**1** diastereomer (*d* content 88 ± 5%) displayed deuteration (85 ± 5%) only at the H_b and H_c positions [Table 1, entry 2, and Figure 1 (spectrum c)]. Thus, these deuterium distributions unequivocally manifest that the *exo*(d_2)-**2** or *endo*(d_2)-**2** oxetanes are formed stereoselectively [100% retention within the experimental error (± 5%)] in the direct photolysis of the azoalkanes *anti*(d_2)-**1** or *syn*(d_2)-**1**.

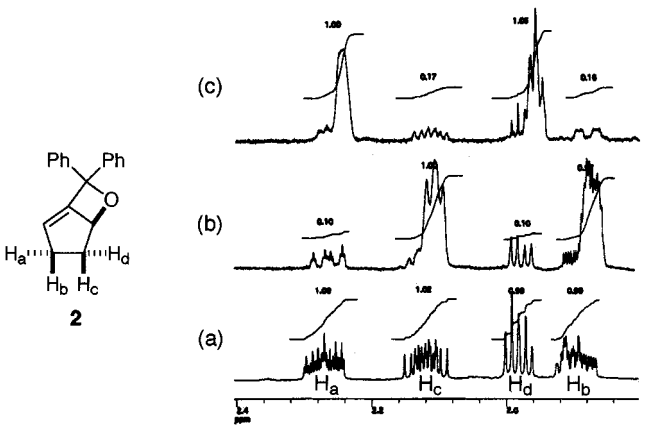
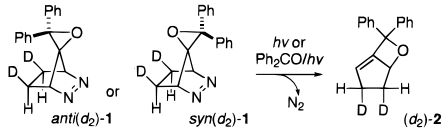


Figure 1. Partial ^{1}H NMR spectra (600 MHz) of the oxetane **2**, formed in the photolysis of (a) nondeuterated azoalkane **1**, (b) *anti*(d_2)-**1**, and (c) *syn*(d_2)-**1**.

Scheme 1



For the benzophenone-sensitized photolysis (380 ± 4 nm), extensively randomized distributions of the deuterium labels were observed at the four H_{a-d} positions (Table 1, entries 3 and 4). In the absence of benzophenone, the oxetane (d_2)-**2** was not observed on irradiation at 380 nm; thus, the oxetane formed in the presence of benzophenone must be derived from the triplet-excited azo chromophore.[4−6] In the sensitized photolysis of *anti*(d_2)-**1** (*d* content 88 ± 5%), the H_a and H_d positions in the oxetane (d_2)-**2** were deuterated only to the extent of 57 ± 5% (64% retention when corrected for the *d* content in **1**),[7] the remainder (25 ± 5%) of the deuteration was found at the H_b and H_c positions (Table 1, entry 3). The sensitized photodenitrogenation of *syn*(d_2)-**1** (*d* content 88 ± 5%) gave similar results (Table 1, entry 4); namely, the extent of retention (%) of configuration in the oxetane (d_2)-**2** was found to be 59%. A control experiment with labeled oxetane *exo*(d_2)-**2** showed that no deuterium scrambling occurred under the benzophenone-sensitized irradiation conditions (380 ± 4 nm). The results clearly signify that the stereochemical course of the oxetane (d_2)-**2** formation depends on the spin state of the n,π*-excited azo chromophore.

The mechanism in Scheme 2 is proposed to account for the spin-state-dependent formation of the oxetane (d_2)-**2**. To simplify the mechanistic discussion, only the photoreaction of the *anti*(d_2)-**1** azoalkane is presented. It is generally accepted that diazenyl diradicals **DZ** are the first intermediates in photodenitrogenation of azoalkanes.[8] In our case, the *anti*(d_2)-**S-DZ** species may be

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(4) Triplet−triplet energy transfer from benzophenone (E_T ∼69 kcal/mol, ref 5) to diazabicyclo[2.2.1]hept-2-ene (DBH) derivatives (E_T ∼60 kcal/mol, ref 6) is an energetically favored process; see, Engel, P. S. *Chem. Rev.* **1980**, *80*, 99.
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(7) Retention (%) = [*d*-content in the H_a or H_d positions/*d* content in (d_2)-**1**] × 100; thus, for complete randomization the retention value (%) would be 50%.
(8) (a) Adams, J. S.; Weisman, R. B.; Engel, P. S. *J. Am. Chem. Soc.* **1990**, *112*, 9115. (b) Adam, W.; Denninger, V.; Finzel, R.; Kita, F.; Platsch, H.; Walter, H.; Zang, G. *J. Am. Chem. Soc.* **1992**, *114*, 5027. (c) Reyes, M. B.; Carpenter, B. K. *J. Am. Chem. Soc.* **1998**, *120*, 1641. (d) Yamamoto, N.; Olivucci, M.; Celani, P.; Bernardi, F.; Robb, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 2391. (e) Diau, E. W.-G.; Abou-Zied, O. K.; Scala, A. A.; Zewail, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 3245.

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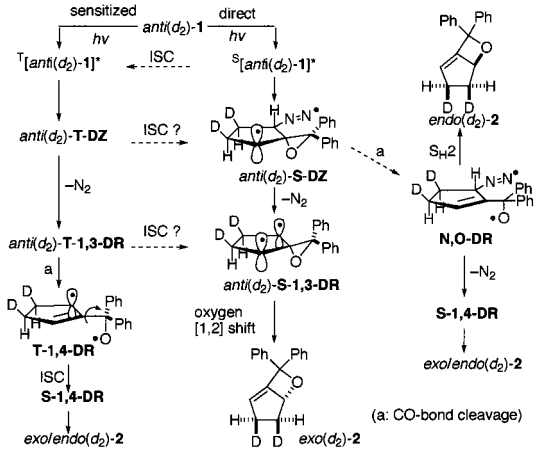
Table 1. Stereoselectivities in the Direct and Benzophenone-Sensitized Photodenitrogenation of the Diastereomerically Deuterium-Labeled *anti*(d_2)- and *syn*(d_2)-Azoalkane **1**[a]

				d content (%) in oxetane (d_2)−**2**[b]					
entry	(d_2)-**1**[c]	irradiation conditions[d]	convn. (%)	H_a	H_b	H_c	H_d	oxetane (d_2)-**2**	retn. (%)[e]
1	*anti*	direct *hν*	73	90	0	0	90	*exo*	100
2	*syn*	direct *hν*	44	0	85	83	0	*endo*	100
3	*anti*	Ph_2CO/*hν*	25	57	24	25	57	*exo*/*endo*	64
4	*syn*	Ph_2CO/*hν*	10	30	50	53	30	*endo*/*exo*	59

[a] At 25 °C, 54 μmol (d_2)-**1** in 0.7 mL of C_6D_6. [b] Deuterium content (%) was determined by ^{1}H NMR (600 MHz) peak areas; error ±5% of the stated value. [c] The deuterium content is 88 ± 5%, the remaining12% is hydrogen. [d] 344 ± 4 nm for the direct irradiation and 380 ± 4 nm for the Ph_2CO-sensitized photolysis were used in the photodenitrogenation (500-W Xenon lamp, focused by a monochromator). [e] Extent of retention (%) of the initial azoalkane configuration in the oxetane (d_2)-**2**; for complete deuterium randomization the value would be 50%.

Scheme 2



also the initial intermediate from the singlet-excited azo chromophore ^{S}[*anti*(d_2)-**1**]*. If epoxide CO bond cleavage of the *anti*(d_2)-**S-DZ** species were faster than denitrogenation, the nitrogen-containing 1,6-diradical **N,O-DR** would result. Subsequent N_2 loss to the nitrogen-free **S-1,4-DR** diradical and closure to the oxetane **2** cannot apply, because in that case an extensively randomized deuterium distribution would be expected. The alternative option of the S_H2 denitrogenation[9] of **N,O-DR** would afford *endo*(d_2)-**2**, which again contradicts the experimental facts, that is, 100% retention in the direct photolysis (Table 1, entries 1 and 2). Consequently, the singlet diazenyl diradical *anti*(d_2)-**S-DZ** expels preferentially N_2 to produce the *anti*(d_2)-**S-1,3-DR** singlet diradical, which by suprafacial oxygen [1,2] shift[10,11] generates the observed *exo*(d_2)-**2** oxetane with complete retention of the initial configuration (stereochemical memory).

In sharp contrast to the singlet pathway (direct irradiation), an extensively randomized distribution of the deuterium atoms was observed in the oxetane (d_2)-**2** for the triplet process (Ph_2CO sensitization) of *anti*(d_2)-**1** and *syn*(d_2)-**1** (Table 1, entries 3 and 4). From the triplet-excited azoalkane ^{T}[*anti*(d_2)-**1**]*, again first the diazenyl diradical *anti*(d_2)-**T-DZ** is generated, which has several options: The most likely one is denitrogenation to the triplet 1,3-diradical *anti*(d_2)-**T-1,3-DR**, subsequent epoxide ring-opening and cyclization would afford the oxetane **2**. Prerequisite for oxetane formation is intersystem crossing (ISC) to the singlet state of the precursor species. If the ISC process of the **T-1,3-DR** to the **S-1,3-DR** were to dominate, retention of the initial configuration would prevail in the oxetane products; however, this is not the case since experimentally extensive randomization was observed in the oxetane (Table 1). Evidently, the *anti*(d_2)-**T-1,3-DR** triplet diradical suffers fast CO-bond cleavage to generate the **T-1,4-DR** diradical. If the latter had enough lifetime to rotate about the CC bond, a 1:1 mixture of *exo* and *endo* oxetanes (d_2)-**2** would result; however, the randomization is not perfect, as judged by the fact that from *anti*(d_2)-**1** 64% and from the *syn*(d_2)-**1** 59% retention have been observed experimentally (Table 1, entries 3 and 4). This indicates some residual stereochemical memory in the triplet-sensitized process, for which the following mechanistic possibilities are feasible: (1) ISC from the triplet diazenyl diradical **T-DZ** to the singlet state **S-DZ** competes with the N_2 extrusion; (2) ISC from the triplet 1,3-diradical **T-1,3-DR** to the singlet state **S-1,3-DR** competes with the CO-bond cleavage; (3) ISC from the triplet 1,4-diradical **T-1,4-DR** to the singlet state **S-1,4-DR** competes with the CC-bond rotation as indicated in structure **T-1,4-DR** (Scheme 2). At this point it is difficult to diagnose these alternatives experimentally.

In summary, our deuterium-labeling study has demonstrated that the stereochemistry of oxetane (d_2)-**2** formation in the photodenitrogenation of diazene (d_2)-**1** depends on the spin state of the intermediary 2-spiroepoxy-1,3-cyclopentanediyl diradical **1,3-DR**. The singlet diradical **S-1,3-DR** is exclusively generated in the direct photolysis and rearranges stereoselectively to the oxetane (d_2)-**2** with complete retention of the initial configuration. Alternatively, in the Ph_2CO-sensitized photodenitrogenation, the triplet diradical **T-1,3-DR** intervenes, which extensively randomizes its deuterium label in the oxetane (d_2)-**2** product through the relatively long-lived triplet 1,4-diradical **T-1,4-DR**.

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Supporting Information Available: Synthetic scheme for the azoalkanes *anti*(d_2)-**1** and *syn*(d_2)-**1**; NOE data for the assignment of H_{a-d} protons (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) The unique CO bond cleavage may be rationalized by a stereoelectronic effect, in which the radical *p* orbitals and the epoxide CO bond are arranged in parallel, as suggested by semiempirical (AM1) calculation (ref 3); see, Giese, B.; Dupuis, J.; Gröninger, K.; Hasskerl, T.; Nix, M.; Witzel, T. In *Substituent Effects in Radical Chemistry*; Viehe, H. G.; Janousek, Z.; Merényi, R., Eds.; NATO Advanced Study Institute Series C189; D. Reidel: Dordrecht, 1986; pp 283−296.

(11) The observed *suprafacial* process (retention of the configuration) is energetically favored, since a highly strained transition state would be expected for the *antarafacial* shift.