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Aust. J. Chem. **2015**, *68*, 1700–1706
http://dx.doi.org/10.1071/CH15062

Full Paper

Simultaneous Observation of Triplet and Singlet Cyclopentane-1,3-diyl Diradicals in the Intersystem Crossing Process

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Intersystem crossing is an important chemical process. In this study, the rate constant of intersystem crossing, $k_{\mathrm{ISC}} \sim 3 \times 10^7\,\mathrm{s}^{-1}$, for cyclopentane-1,3-diyl diradicals was unequivocally determined by the simultaneous observation of the decay process of the triplet diradical ($\lambda_{\mathrm{obs}} = 320$ nm) and the growth process of the corresponding singlet diradical ($\lambda_{\mathrm{obs}} = 560$ nm). The two spin states were directly observed using a long-lived singlet 2,2-dimethoxy-1,3-diphenylcyclopentane-1,3-diyl diradical.

Manuscript received: 5 February 2015.
Manuscript accepted: 1 March 2015.
Published online: 1 April 2015.

Introduction

Diradicals are key intermediates in processes involving homolytic bond cleavage and bond formation reactions (Scheme 1a).[1] Intersystem crossing (ISC) between two spin states – singlet and triplet – is important for understanding the chemistry of homolytic reactions, although in principle, the spin-flip process is forbidden. However, spin–orbit coupling (SOC) permits ISC for diradicals with short two-spin distances of <3 Å.[2] For example, the appropriate geometry of two p orbitals, which accelerate ISC by the SOC mechanism from triplet to singlet, plays an important role in determining the stereoselectivity of radical–radical coupling reactions.[3]

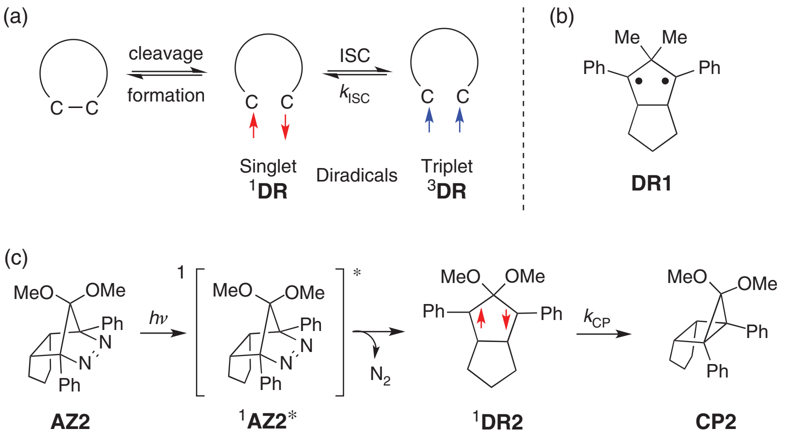
Thus far, ISC rate constants (k_{ISC}) have been experimentally determined by the detection of the decay process of long-lived triplet diradicals, because in general, the lifetime of singlet diradicals is too short to be observed by conventional spectroscopic analysis. For instance, Adam and coworkers determined the ISC rate constant ($k_{\mathrm{ISC}} \sim 10^5\,\mathrm{s}^{-1}$) of a 1,3-diradical **DR1** from the decay process of the triplet state ($\lambda_{\max} \sim 320$ nm) (Scheme 1b).[4] As the corresponding singlet state was short-lived, its growth was not observed. If the growth process of the singlet state can be simultaneously observed along with the decay process of the triplet state, k_{ISC} thus obtained would be significantly more reliable. Recently, we succeeded in generating long-lived singlet diradicals with π-single bond character, e.g. ^{1}**DR2** ($\lambda_{\max} \sim 560$ nm), by the photodenitrogenation of the precursor azoalkane **AZ2** ($\varepsilon_{355} = 68\,\mathrm{L\,mol^{-1}\,cm^{-1}}$ in acetonitrile).[5a–d] The singlet diradical decays with a rate constant k_{CP} of $3.03 \times 10^6\,\mathrm{s}^{-1}$, i.e. lifetime ~330 ns, to afford the ring-closed compound **CP2** (Scheme 1c).

Herein, we report the simultaneous observation of the decay process of triplet diradical ^{3}**DR3** (~320 nm) and the growth of singlet diradical ^{1}**DR3** (~560 nm) in the denitrogenation of triplet-sensitized azoalkane precursor **AZ3** (Scheme 2); in **AZ3**, the benzophenone unit (triplet energy (E_{T}) = 69 kcal mol^{-1}[6] (1 kcal mol^{-1} = 4.186 kJ mol^{-1}), $\varepsilon_{355} = 108\,\mathrm{L\,mol^{-1}\,cm^{-1}}$ in acetonitrile) is attached to the meta position of the phenyl ring for the triplet sensitization of the azo-chromophore (E_{T} = 62 kcal mol^{-1}).[7] We hypothesize that meta-substitution can prevent the direct growth of ^{1}**DR3** by the conjugation of the corresponding ketyl radical of the singlet excited state. Intramolecular sensitization was utilized for the clear observation of ISC from the triplet to the singlet diradical, because the intermolecular triplet sensitization of **AZ2** with benzophenone was highly dependent on the **AZ2** concentration.

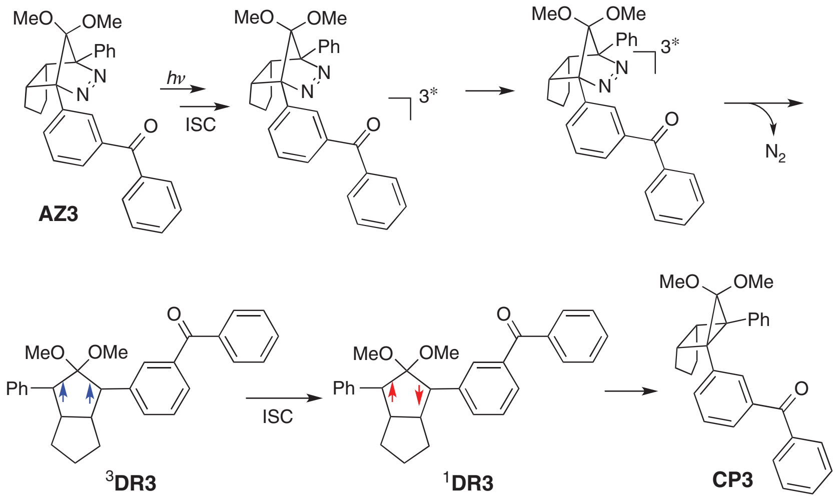
Results

Synthesis and Photodenitrogenation of *AZ3*

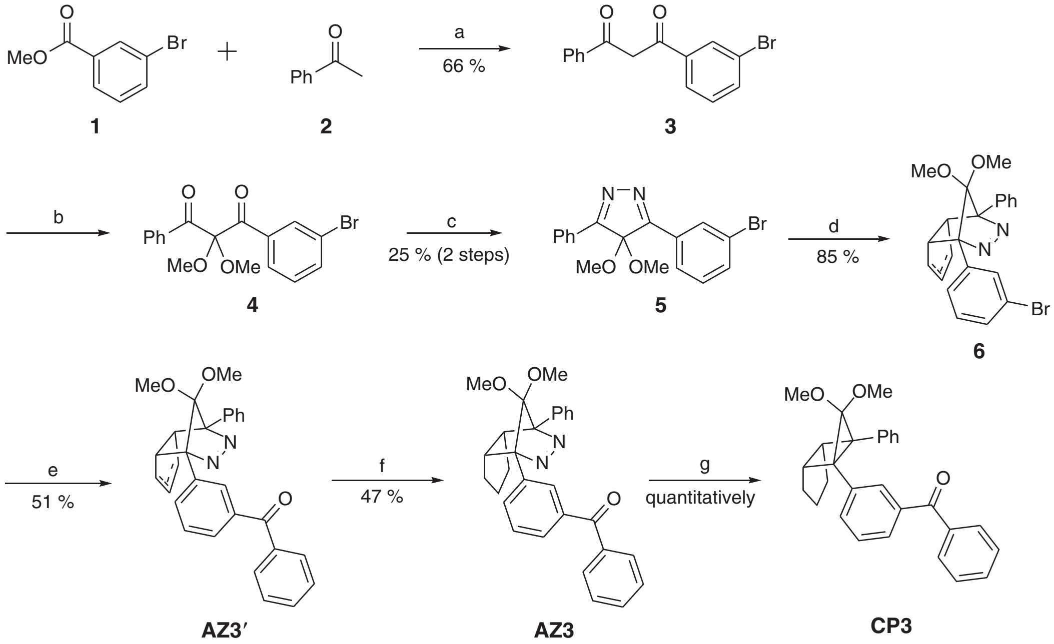
The synthesis of precursor azoalkane **AZ3** and its photochemical reaction are shown in Scheme 3. The α-dimethoxylation of **3**[8] was performed by Tiecco's method to obtain **4**.[9] The synthesis of pyrazole **5** followed by the Diels–Alder reaction of **5** with cyclopentadiene afforded azoalkane **6**.[10] Benzoylation using a Weinreb amide[11] produced **AZ3′**, followed by hydrogenation to yield precursor **AZ3**. The photo-irradiation of



Scheme 1. (a) Intersystem crossing (ISC) in diradicals; (b) structure of **DR1**; and (c) generation of ^{1}**DR2** by the photodenitrogenation of azoalkane precursor **AZ2**.



Scheme 2. Generation of triplet diradical ^{3}**DR3** and its ISC (intersystem crossing) to ^{1}**DR3** in the photochemical denitrogenation of **AZ3** in this study.



Scheme 3. Synthesis of **AZ3**. Conditions: (a) NaH, THF, 0°C; (b) Ph_2Se_2, $(NH_4)_2S_2O_8$, MeOH; (c) N_2H_2 H_2O, $CHCl_3$; (d) cyclopentadiene, CF_3CO_2H, CH_2Cl_2, 0°C; (e) *n*-BuLi, *N*-methoxy-*N*-methylbenzamide, THF, −78°C; (f) H_2, Pd/C, EtOAc; (g) high-pressure Hg lamp, benzene.

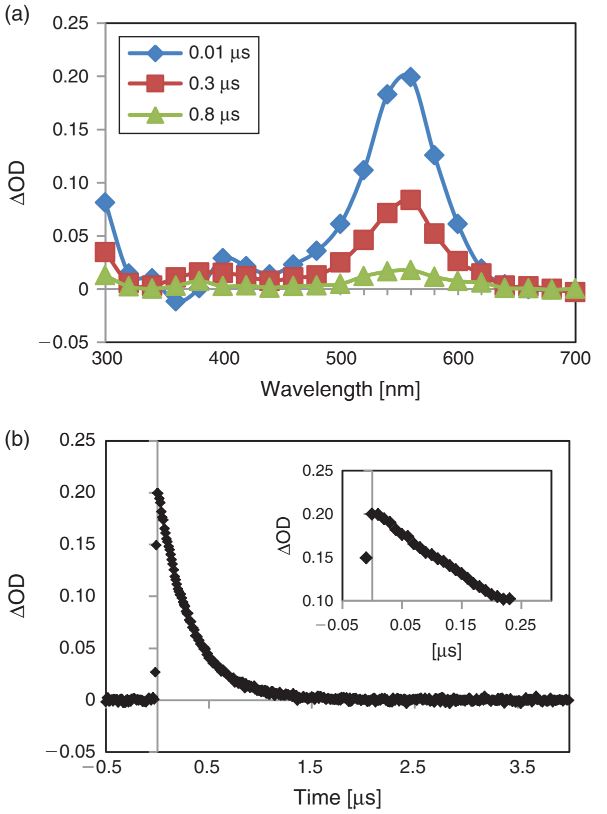


Fig. 1. (a) Transient absorption spectra of **AZ2**; (b) absorbance change observed at 560 nm; and (inset) the absorbance change in the range of −0.05 to 0.30 µs in the laser flash photolysis (LFP) of **AZ2** in acetonitrile at 293 K.

AZ3 using a high-pressure Hg lamp through a Pyrex filter (>290 nm) quantitatively formed the denitrogenated compound **CP3** in a deoxygenated benzene solution by bubbling N_2 through it for 15 min.[3c]

Transient Absorption Spectroscopy of ***AZ2*** *and* ***AZ3***

The transient absorption spectrum observed in the photolysis of **AZ2** in acetonitrile at 293 K is shown in Fig. 1. On applying a 4–6-ns pulse from a Nd-YAG laser (λ_{exc} 355 nm), planar singlet diradical ^{1}**DR2** was immediately observed at ~560 nm; however, it decayed with a lifetime (τ) of 330 ns ($k_{\text{CP}} = 3.03 \times 10^6\ \text{s}^{-1}$) at 293 K (Fig. 1b) to yield the ring-closed product **CP2**. In the photolysis of **AZ3**, the transient absorption of singlet diradical ^{1}**DR3** was also observed in the same region with a $\lambda_{\max}$ of ~560 nm (Fig. 2a). In contrast to the flash photolysis of **AZ2**, the growth of ^{1}**DR3** was observed until ~100 ns after laser excitation (Fig. 2b). From the double-exponential fit of the data on the time profile of ^{1}**DR3**, the decay rate constant (k_{d}) of ^{1}**DR3** and the growth rate constant (k_{g}) were determined to be 2.02×10^6 and $3.24 \times 10^7\ \text{s}^{-1}$ at 293 K respectively (Table 1, entry 1).

The decay process corresponds to the formation of the ring-closed compound **CP3**, because **CP3** is quantitatively isolated from the photolysis reaction. The growth process was assigned to the ISC from triplet state ^{3}**DR3**, generated by the elimination of molecular nitrogen from the triplet excited state of **AZ3**. In fact, a decay species was observed at 320 nm with a rate constant of $3.44 \times 10^7\ \text{s}^{-1}$, which is consistent with the growth rate constant of ^{1}**DR3**. The species observed at 320 nm was assigned to triplet diradical ^{3}**DR3**, because the absorption band is observed at a position typical for the triplet state of 1,3-diphenylpropane-1,3-diyl diradicals,[12] e.g. ^{3}**DR1**; $\lambda_{\max}$ ~320 nm.[4] Time-dependent density functional theory (DFT) calculation at the UB3LYP/6–31G+(d, p) level of theory suggests that triplet diradical ^{3}**DR3** has an absorption at 354 nm. The residue at 320 nm is due to the formation of product **CP3**.

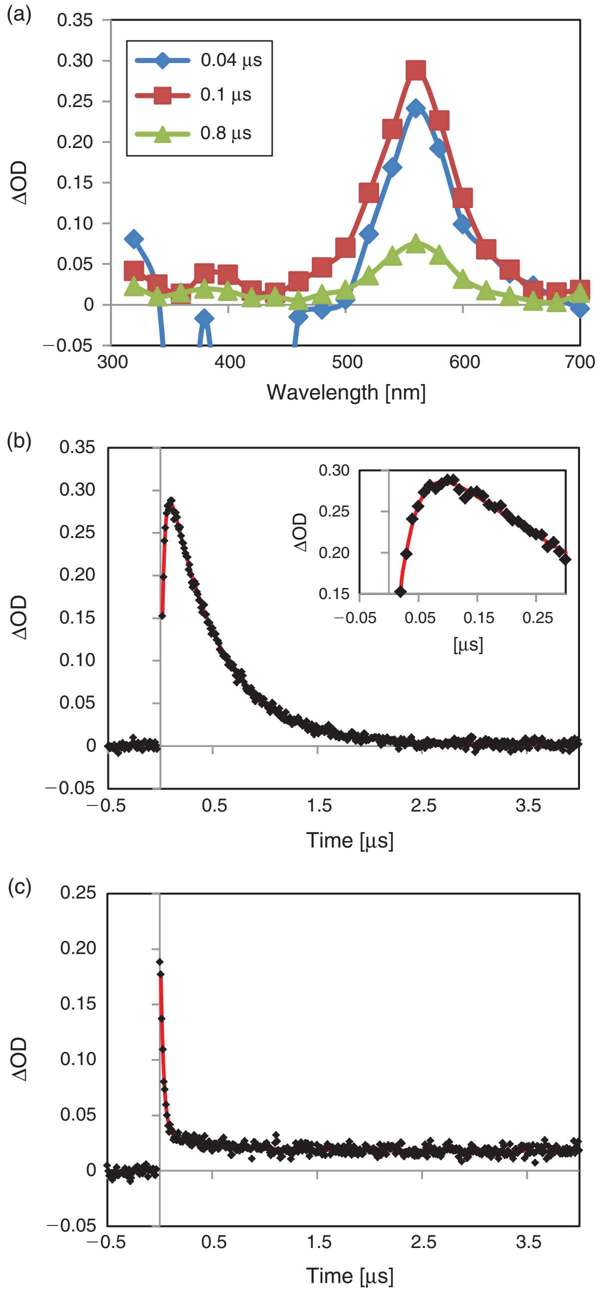


Fig. 2. (a) Transient absorption spectra of **AZ3**; (b, c) absorbance changes observed at 560 and 320 nm respectively; and (inset) the absorbance change in the range of −0.05 to 0.30 µs in acetonitrile at 293 K. The negative absorptions in (a) are caused by the emission signal.

The intramolecular energy transfer from the triplet benzophenone moiety ($\lambda_{\text{T-T}} = 530$ nm)[13] to the azo-chromophore was visualized by picosecond time-resolved transient absorption measurements of the photolysis of **AZ3** in acetonitrile (Fig. 3). The kinetic trace at 530 nm indicated a fast decay process with a rate constant of ~$5 \times 10^{10}\ \text{s}^{-1}$. The rapid decay

Table 1. Time-resolved absorption spectroscopic data for laser flash photolysis (LFP) experiments of AZ3 and CP3

Entry	Substrate	Temperature [K]	Rate constant^A [s^{-1}]		
			at 320 nm	at 560 nm	
			$k_{d,320} \times 10^{-7}$	$k_{g,560} \times 10^{-7}$	$k_{d,560} \times 10^{-6}$
1	**AZ3**	293	3.44 ± 0.08	3.24 ± 0.23	2.02 ± 0.01
2	**CP3**	293	3.49 ± 0.06	3.24 ± 0.17	2.01 ± 0.01
3	**AZ3**	243	3.49 ± 0.10	3.33 ± 0.23	0.086 ± 0.003
4	**CP3**	243	3.04 ± 0.15	3.04 ± 0.16	0.091 ± 0.005

^{A}Mean value and standard error after three measurements under a nitrogen atmosphere.

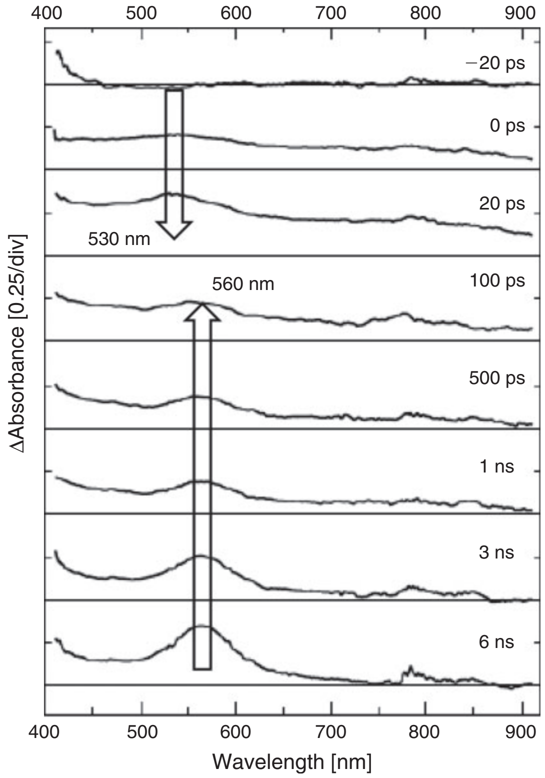


Fig. 3. Transient absorption spectra of **AZ3** by picosecond time-resolved transient absorption measurements in acetonitrile.

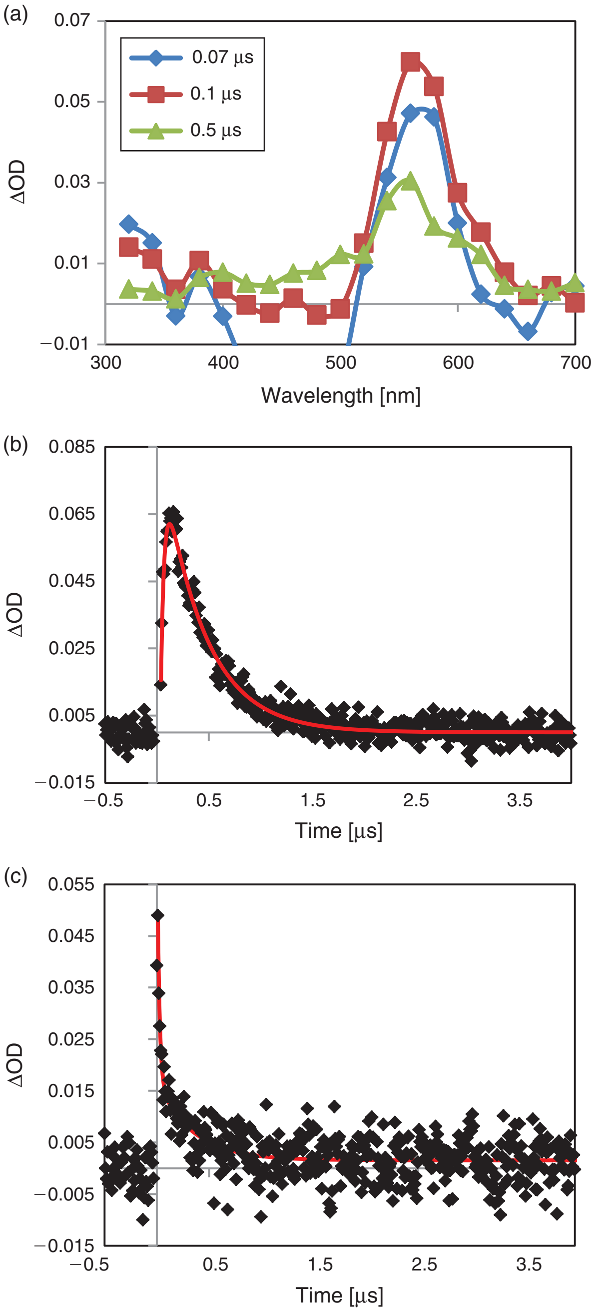


Fig. 4. (a) Transient absorption spectra of **CP3**; and (b, c) absorbance changes observed at 560 and 320 nm respectively in acetonitrile at 293 K. The negative absorptions in (a) are caused by the emission signal.

process at 530 nm corresponds to the energy transfer from the triplet-excited benzophenone to the diazene unit, which generates triplet diradical ^{3}**DR3**, followed by ISC to singlet diradical ^{1}**DR3**. In fact, the growth process of the 560-nm species was observed by time-resolved spectroscopic analysis (Fig. 3).

*Transient Absorption Spectroscopy of **CP3***

To confirm the observation of ISC, i.e. the simultaneous detection of the decay process of ^{3}**DR3** at 320 nm and the growth process of ^{1}**DR3** at 560 nm in the laser flash photolysis (LFP) of **AZ3**, the time-resolved transient absorption spectroscopic analysis of the corresponding ring-closed compound **CP3** was investigated in acetonitrile under similar LFP conditions (Fig. 4). Similar time profiles of the transients at 320 and 560 nm were observed in the LFP of **CP3** at 293 K. Thus, the growth process with $k_g \approx 3.24 \pm 0.7 \times 10^7\,s^{-1}$ and the decay process with $k_d \approx 2.01 \pm 0.01 \times 10^6\,s^{-1}$ were detected at 560 nm (Fig. 4b); both their rate constants at 560 nm were in good agreement with those observed in the LFP of **AZ3** (entries 1 and 2, Table 1). The decay rate constant of the species observed at 320 nm was found to be $3.49 \pm 0.06 \times 10^7\,s^{-1}$ with single-exponential fitting, which is also consistent with the value of $k_d = 3.44 \pm 0.08 \times 10^7\,s^{-1}$ observed in the LFP of **AZ3** (entries 1 and 2 respectively). Similar transient absorption spectroscopic behaviour suggested that the decay process at 320 nm corresponds to ISC from ^{3}**DR3** to ^{1}**DR3** and not to the denitrogenation of ^{3}**AZ3***, which includes the bond-breaking process.

The assignment of ISC, i.e. the simultaneous detection of the decay process of ^{3}**DR3** (320 nm) and the growth process of ^{1}**DR3** (560 nm), was confirmed by the temperature effect on the rate constants. The temperature effect on the spin-flip process, i.e. ISC, is known to be small, although the rate constants of bond breaking and bond formation are supposed to be significantly affected by temperature.[14] In fact, the temperature effect on the rate constant of the growth at 560 nm ($k_{g,560}$) and the decay at 320 nm ($k_{d,320}$) was observed to be marginal in the temperature range from 293 to 243 K (compare entries 1 and 2 with entries 3 and 4; Table 1), although the decay rate constant ($k_{d,560}$) of ^{1}**DR3**, i.e. C–C bond formation process, was significantly affected by temperature. The small temperature effects on $k_{d,320}$ and $k_{g,560}$ strongly suggested that the time profiles of the decay at 320 nm and the growth at 560 nm originate from ISC from the triplet to the singlet in 1,3-diradical **DR3**.

Discussion

The ISC rate constant determined in the present study, $k_{ISC} \sim 3.24 \times 10^7\,s^{-1}$, for 2,2-dimethoxycyclopentane-1,3-diradical **DR3** was significantly higher than that[4] for 2,2-dimethylcyclopentane-1,3-diradical **DR1** by two orders of magnitude, $k_{ISC} \sim 3.69 \times 10^5\,s^{-1}$. The question arises as to why ISC in **DR3** is significantly faster than that in **DR1**. Adam and coworkers have discussed the effect of substituents on the ISC rate constants for cyclopentane-1,3-diyl diradicals.[4] A large SOC in diradicals enhances the rate constant of ISC, because the transmission factor of SOC, A_{SOC}, is proportional to the square of C_+, which represents the coefficient of the wave function of the singlet diradicals in the ground state,[2,4] as shown in Eqn 1.

$$A_{SOC} \propto C_+^2 \tag{1}$$

The coefficient C_+ is expressed in Eqn 2,[2,4] where γ_{AB} denotes the covalent perturbation, and K'_{AB} denotes the coulomb integral function.

$$C_+ \approx \frac{\gamma_{AB}}{2K'_{AB}} \tag{2}$$

γ_{AB} corresponds to the energy gap between the two non-bonding molecular orbitals (NBMOs) that are occupied by the two electrons for the corresponding 1,3-diradical fragment (Fig. 5). The low-lying C–O σ* orbital is stabilized by hyperconjugation with the symmetric NBMO(s) while the C–C σ* orbital is too high-lying to interact (Fig. 5); thus, γ_{AB} in X = OMe becomes larger than that in X = Me, indicating that ISC in **DR3** with the singlet ground state is significantly faster than that in **DR1** with the triplet ground state.

Conclusions

In summary, we attempted to directly observe ISC by the simultaneous detection of triplet and singlet diradicals. Nanosecond time-resolved transient absorption measurements by LFP of azoalkane **AZ3** permitted the simultaneous detection of the growth process of singlet diradical ^{1}**DR3** ($\lambda_{obs} = 560$ nm) and the decay process of triplet diradical ^{3}**DR3** ($\lambda_{obs} = 320$ nm), because ^{1}**DR3** is a long-lived singlet diradical. Kinetic analyses of the processes revealed that the rate constant of the growth process (observed at 560 nm) was consistent with that of the decay process (observed at 320 nm). The observation of a similar transient absorption at 320 nm in the photolysis for the corresponding ring-closed product **CP3** indicated that the absorbance originates from triplet diradical ^{3}**DR3**. The observation of ISC was strongly supported by the small temperature effect on both the decay rate constant at 320 nm ($k_{d,320}$) and the growth rate constant at 560 nm ($k_{g,560}$). This is the first report on the simultaneous observation of both the triplet and singlet states in localized diradicals.

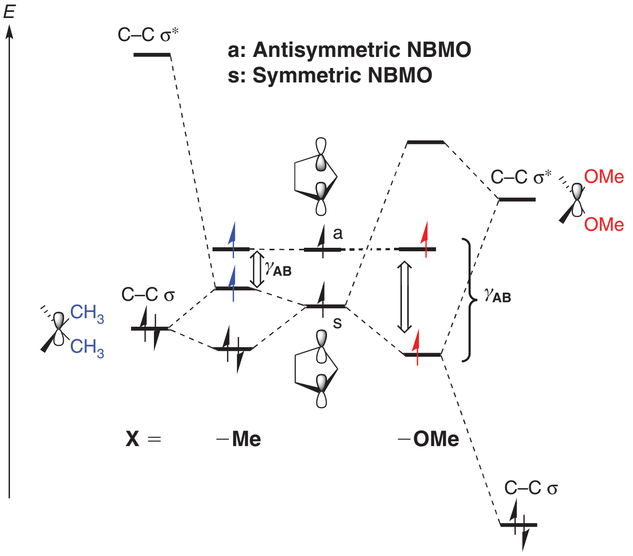


Fig. 5. Effect of substituent on the energy gap between the two non-bonding molecular orbitals (NBMOs) in cyclopentane-1,3-diyl diradicals.

Experimental

General Chemical Procedures

All reagents and solvents were purchased from commercial sources and were used without further purification. Silica gel (60N, spherical, neutral, 63–210-μm) was purchased from Kanto Chemical Co., Inc. to use in silica gel column chromatography. ^{1}H and ^{13}C NMR spectra were measured on a Bruker Ascend™ 400 spectrometer. ^{1}H and ^{13}C NMR chemical shifts are given in parts per million (ppm) relative to internal $CDCl_3$ or C_6D_6. IR spectra were recorded on a PerkinElmer Spectrum One Fourier-transform (FT)-IR spectrometer. UV-vis spectra were recorded on a Jasco V-630 spectrophotometer. Mass-spectrometric data were measured with a mass spectrometric Thermo Fisher Scientific LTQ Orbitrap XL.

Laser Flash Photolysis Measurements

Spectral grade acetonitrile was purchased from Wako and used without further purification. All samples were purged with nitrogen gas or argon gas for 15 min to remove oxygen before measurement. The concentration of samples was adjusted to an optical density of 0.1–0.2 at the excitation wavelength (355 nm). The excitation source for the LFP system was an Nd-YAG laser that produces a 4–6-ns pulse of up to 7 mJ at 355 nm. The monitoring system consisted of a 150-W xenon lamp as light source, Unisoku-MD200 monochromator and a photomultiplier. The temperature was controlled with a CoolSpeck USP-203 (Unisoku). The excitation source for the picosecond–nanosecond LFP system was a mode-locked Nd-YAG laser (Continuum PY61C-10, full-width half-maximum (fwhm) = 17 ps, 10 Hz). The third harmonic (355 nm, 3-mJ pulse^{-1}) was used to excite a sample in solution contained in a 1-cm quartz cell. Picosecond transient absorption spectra in a delay time range of −20–6000 ps were obtained using a picosecond white continuum, which was produced by focussing the fundamental laser pulse into a flowing H_2O/D_2O (1 : 1 by volume) solution. The details of the measurement system have been described elsewhere.[5d,15] For picosecond transient absorption measurements, the absorbance at 355 nm of the sample solutions was adjusted to ~0.8.

*Preparation of Azoalkane **AZ3** and Ring-Closed Compound **CP3***

*(3-Bromophenyl)-3-phenylpropane-1,3-dione **3***

Sodium hydride (2.26 g, 60 %, 56.6 mmol) was suspended in THF (35 mL) at 0°C under an N_2 atmosphere. A solution of methyl 3-bromobenzoate **1** (7.43 g, 34.6 mmol) in THF (10 mL) was added with stirring. After 15 min, a solution of acetophenone **2** (4.12 g, 34.3 mmol) in THF (10 mL) was slowly added to the reaction mixture, and then the mixture was stirred at room temperature (rt) for 2 h. The reaction mixture was poured into cracked ice containing 1 M hydrochloric acid (20 mL) with stirring. The organic layer was extracted with ethyl acetate (3 × 10 mL) and dried over sodium sulfate. After evaporation of the solvent under vacuum, the residue was purified by silica gel column chromatography (hexane/EtOAc 8 : 1 v/v) and recrystallization with ethanol afforded compound **3** (6.95 g, 22.9 mmol, 66 %) as a yellow solid; mp 66–68°C. ν_{max} (KBr)/cm^{-1} 1599, 1517, 1456, 1225, 759. δ_H (400 MHz, $CDCl_3$) 8.11 (s, 1H, ArH), 8.00 (d, *J* 7.2, 2H, ArH), 7.91 (d, *J* 8.0, 1H, ArH), 7.68 (d, *J* 8.0, 1H, ArH), 7.58 (t, *J* 7.2, 1H, ArH), 7.50 (t, *J* 7.8, 2H, ArH), 7.37 (t, *J* 7.8, 1H, ArH), 6.81 (s, 1H, C*H*). δ_C (100 MHz, $CDCl_3$) 186.25, 184.19, 137.73, 135.36, 132.89, 130.39, 130.32, 128.91, 127.40, 125.84, 123.09, 93.43. *m*/*z* (high-resolution electrospray ionization mass spectrometry (HRMS-ESI)) 324.98361; calc. for $C_{15}H_{11}BrO_2Na$ [M + Na$^+$] 324.98346.

*1-(3-Bromophenyl)-2,2-dimethoxy-3-phenylpropane-1,3-dione **4***

A mixture of compound **3** (6.95 g, 22.9 mmol), diphenyl diselenide (3.50 g, 11.2 mmol), and ammonium peroxodisulfate (10.4 g, 45.6 mmol) was refluxed in methanol (100 mL) with stirring under an N_2 atmosphere for 1 h. Then water was added to the mixture until the ammonium peroxodisulfate had dissolved. The organic layer was extracted with chloroform (3 × 10 mL) and dried over sodium sulfate. Evaporation of the solvent under vacuum gave the crude product as a red liquid. The crude was directly used in the next step because compound **4** was not stable on silica.

*4,4-Dimethoxy-5-phenyl-4*H*-pyrazole **5***

Hydrazine monohydrate (0.83 g, 16.5 mmol) was added to the solution of compound **4** (~10 g, crude) in chloroform (70 mL) with stirring under an N_2 atmosphere and the mixture was allowed to stand for 1.5 h. Hydrochloric acid (1 M) was added and the mixture was stirred for 10 min. The organic layer was extracted with chloroform (3 × 10 mL) and dried over sodium sulfate. After evaporation of the solvent under vacuum, the residue was purified by silica gel column chromatography (hexane/EtOAc 4 : 1 v/v) to afford compound **5** (2.09 g, 5.83 mmol, 25 % in two steps) as a yellow solid; mp 126–128°C. ν_{max} (KBr)/cm^{-1} 3071, 2949, 2931, 2832, 1553, 1443, 1118. δ_H (400 MHz, $CDCl_3$) 8.42 (s, 1H, ArH), 8.26 (d, *J* 8.0, ArH), 8.20 (d, *J* 8.0, 1H, ArH), 7.69 (d, *J* 8.0, 1H, ArH), 7.58 (t, *J* 7.3, 1H, ArH), 7.52 (t, *J* 7.6, 2H, ArH), 7.39 (t, *J* 8.0, 1H, ArH), 3.07 (s, 6H, OCH_3). δ_C (100 MHz, $CDCl_3$) 166.98, 165.66, 135.21, 132.61, 130.56, 130.40, 129.53, 129.07, 127.81, 127.46, 126.22, 123.17, 117.18, 52.05. *m*/*z* (HRMS-ESI) 359.03983; calc. for $C_{17}H_{16}O_2N_2Br$ [M + H$^+$] 359. 03897.

*(1*R*,4*R*,4a*S*,7a*R*)-1-(3-Bromophenyl)-8,8-dimethoxy-4-phenyl-4,4a,5,7a-tetrahydro-1*H*-1,4-methanocyclopenta[*d*]pyridazine **6***

Cyclopentadiene (7.07 g, 0.11 mol) was added to a solution of compound **5** (2.09 g, 5.82 mmol) in dry dichloromethane (50 mL) in a flask covered with aluminium foil under an N_2 atmosphere at 0°C with stirring. Then a solution of trifluoroacetic acid (0.13 mg, 1.18 mmol) in dichloromethane (10 mL) was added at the same temperature. The reaction mixture was allowed to stand for 1 h, and then a saturated aqueous solution of sodium bicarbonate was added until the solution was neutralized. The organic layer was extracted with dichloromethane (3 × 10 mL) and dried over magnesium sulfate. After evaporation of the solvent under vacuum, the residue was purified by silica gel column chromatography (hexane/EtOAc 8 : 1, v/v) to afford compound **6** (2.10 g, 4.95 mmol, 85 %) as a white solid. The product was a mixture of two isomers; mp 154–156°C. ν_{max} (KBr)/cm^{-1} 3067, 2946, 2920, 2842, 1596, 1563, 1477, 1183, 1102. δ_H (400 MHz, C_6D_6) 8.40, 8.26 (s, 1H, ArH), 8.07, 8.01 (d, *J* 7.2, 1H, ArH), 7.93, 7.86 (d, *J* 7.2, 2H, ArH), 7.33–7.26 (m, 3H, ArH), 7.19 (t, *J* 7.2, 1H, ArH), 6.92–6.90 (m, 1H, ArH), 5.44–5.33 (m, 2H,CH), 3.95–3.82 (m, 1H, CH), 3.39–3.24 (m, 1H, CH), 2.59 (s, 3H, OCH_3), 2.43 (s, 3H, OCH_2), 2.28–1.97 (m, 2H, CH_2). δ_C (100 MHz, $CDCl_3$) 136.65, 138.48, 135.79, 135.62, 134.57, 134.13, 131.63, 131.07, 130.92, 130.89, 129.90, 129.84, 128.65, 128.35, 128.32, 128.06, 127.89, 127.14, 126.42, 126.12, 122.63, 122.57, 118.12, 94.56, 93.63, 57.34, 56.76, 52.06, 52.05, 51.77, 51.75, 42.46, 41.97, 32.17, 32.06. *m*/*z* (HRMS-ESI) 447.06812; calc. for $C_{22}H_{21}O_2N_2BrNa$ [M + Na$^+$] 447.06786.

*(3-((1*R*,4*R*,4a*S*,7a**R**)-8,8-Dimethoxy-4-phenyl-4,4a,5,7a-tetrahydro-1*H*-1,4-methanocyclopenta[*d*]pyridazin-1-yl)phenyl)(phenyl)methanone **AZ3′***

A flask was dried by heating under reduced pressure before compound **6** was introduced into it. Under an N_2 atmosphere, a solution of compound **6** (2.10 g, 4.95 mmol) in dry THF (45 ml) was cooled to −78°C with acetone/liquid nitrogen. A solution of *n*-butyl lithium in hexane (3.7 mL, 5.92 mmol) was added slowly with stirring, followed by immediate addition of a solution of *N*-methoxy-*N*-methylbenzamide (0.81 g, 4.93 mmol) in THF (5 mL). The reaction mixture was allowed to stand for 1 h and then water was added to the flask. The organic layer was extracted with diethyl ether (3 × 10 mL), washed with brine and dried over magnesium sulfate. After evaporation of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, hexane/EtOAc 4 : 1 v/v) to afford **AZ3′** (1.15 g, 2.55 mmol, 51 %) as a white solid. The product was a mixture of two isomers; mp 178–182°C. ν_{max} (KBr)/cm^{-1} 2946, 1654, 1184, 719. δ_H (400 MHz,

C_6D_6) 8.66, 8.51 (s, 1H, ArH), 8.32–8.00 (m, 3H, ArH), 7.85–7.78 (m, 3H, ArH), 7.31–7.03 (m, 7H, ArH), 5.49–5.33 (m, 2H, CH), 3.98–3.91 (m, 1H, CH), 3.45–3.31 (m, 1H, CH), 2.63 (s, 3H, OCH_3), 2.48 (s, 3H, OCH_3), 2.31–2.26 (m, 1H, CH_2), 2.07–2.03 (m, 1H, CH_2). δ_C (100 MHz, $CDCl_3$) 196.80, 196.78, 137.95, 137.84, 137.69, 136.50, 136.12, 135.94, 134.90, 134.35, 133.27, 132.72, 132.42, 130.53, 130.35, 130.31, 129.98, 129.83, 129.76, 128.70, 128.62, 128.59, 128.47, 128.27, 128.11, 127.95, 126.80, 126.32, 118.47, 94.58, 94.42, 92.89, 92.66, 57.87, 56.66, 52.27, 52.03, 52.01, 42.95, 41.89, 32.42, 32.32. *m*/*z* (HRMS-ESI) 473.18341; calc. for $C_{29}H_{26}O_3N_2Na$ [$M + Na^+$] 473.18356.

*(3-((1*R*,4*R*,4a*S*,7a*R*)-8,8-Dimethoxy-4-phenyl-4,4a,5,6,7,7a-hexahydro-1*H*-1,4-methanocyclopenta[*d*]pyridazin-1-yl)phenyl)(phenyl)methanone* ***AZ3***

In a flask covered with aluminium foil, **AZ3′** (0.46 g, 1.01 mmol) and Pd/C (0.10 g) were suspended in ethyl acetate (70 mL) under an N_2 atmosphere. After an H_2 purge, the solution was stirred for a day. After filtration over Celite and evaporation of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, hexane/EtOAc 4 : 1, v/v) to afford **AZ3** (0.21 g, 0.47 mmol, 47 %) as a white solid; mp 134–138°C. ν_{max} (KBr)/cm^{-1} 2964, 2943, 1662, 1183, 700. δ_H (400 MHz, C_6D_6) 8.59 (s, 1H, ArH), 8.26 (d, *J* 7.5, 1H, ArH), 8.09 (d, *J* 7.2, 2H, ArH), 7.84 (d, *J* 7.1, 2H, ArH), 7.79 (d, *J* 7.6, 1H, ArH), 7.31–7.03 (m, 7H, ArH), 3.33–3.24 (m, 2H, CH), 2.63 (s, 3H, OCH_3), 2.47 (s, 3H, OCH_3), 1.66–1.19 (m, 6H, CH_2). δ_C (100 MHz, $CDCl_3$) 197.17, 138.10, 138.02, 137.31, 136.72, 133.29, 133.01, 130.66, 130.55, 130.10, 128.94, 128.84, 128.75, 128.70, 128.36, 119.65, 94.92, 94.74, 52.46, 52.17, 49.74, 48.63, 28.33, 26.16, 26.04. *m*/*z* (HRMS-ESI) 475.19940; calc. for $C_{29}H_{28}O_3N_2Na$ [$M + Na^+$] 475.19921.

*(3-((1*S*,2*R*,4*S*,5*S*)-3,3-Dimethoxy-4-phenyltricyclo[3.3.0.0^{2,4}]octan-2-yl)phenyl)(phenyl)methanone* ***CP3***

In a test tube, a solution of **AZ3** (29.3 mg, 64.7 μmol) in dry benzene (5 mL) was purged with nitrogen gas for 10 min. Then the solution was exposed to light from a 300-W high-pressure Hg lamp for 2 h. After evaporation of the solvent under vacuum, the residue was purified by silica gel column chromatography (hexane/EtOAc 4 : 1 v/v) to afford **CP3** (26.0 mg, 61.2 μmol, 95 %) as a white solid; mp 40–43°C. ν_{max} (KBr)/cm^{-1} 3084, 2943, 1662. δ_H (400 MHz, C_6D_6) 8.06 (s, 1H, ArH), 7.79 (d, *J* 7.0, 2H, ArH), 7.69 (d, *J* 7.9, 1H, ArH), 7.46 (d, *J* 8.0, 1H, ArH), 7.28 (d, *J* 7.0, 2H, ArH), 7.13–7.00 (m, 7H, ArH), 3.41 (s, 3H, OCH_3), 2.94–2.84 (m, 2H, CH), 2.76 (s, 3H, OCH_3), 1.82–2.80 (m, 3H, CH_2), 1.47–1.34 (m, 3H, CH_2). δ_C (100 MHz, $CDCl_3$) 197.20, 138.05, 137.52, 135.65, 134.77, 134.36, 132.80, 132.19, 130.51, 130.23, 128.64, 128.29, 128.25, 126.65, 98.59, 54.86, 52.97, 48.17, 47.25, 41.63, 41.48, 28.43, 28.34, 25.26. *m*/*z* (HRMS-ESI) 447.19287; calc. for $C_{29}H_{26}O_3Na$ [$M + Na^+$] 447.19307.

Supplementary Material

^1H and ^{13}C NMR spectra of the compounds synthesized in this study are available on the Journal's website.

Acknowledgements

NMR and MS measurements were performed at N-BARD, Hiroshima University. This study was supported by a Grant-in-Aid for Science Research on Innovative Areas 'Stimuli-responsive Chemical Species' (nos. 24109008 and 24109002a) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

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