Simultaneous Observation of Triplet and Singlet Cyclopentane-1,3-diyil 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, $k_{ISC} \approx 3 \times 10^6 \text{ s}^{-1}$, for cyclopentane-1,3-diyil diradicals was unequivocally determined by the simultaneous observation of the decay process of the triplet diradical ($\lambda_{obs} = 320 \text{ nm}$) and the growth process of the corresponding singlet diradical ($\lambda_{obs} = 560 \text{ nm}$). The two spin states were directly observed using a long-lived singlet 2,2-dimethoxy-1,3-diphenylcyclopentane-1,3-diyl diradical.

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Introduction

Diradicals are key intermediates in processes involving homolytic bond cleavage and bond formation reactions (Scheme 1a).\cite{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 $<3 \text{ Å}$.\cite{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.\cite{3,4}

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 ($k_{ISC} \approx 10^6 \text{ s}^{-1}$) of a 1,3-diradical DR1 from the decay process of the triplet state ($\lambda_{max} \approx 320 \text{ nm}$) (Scheme 1b).\cite{5} 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 $\pi$-single bond character, e.g. DR2 ($\lambda_{max} \approx 560 \text{ nm}$), by the photodenitrogenation of the precursor azoalkane AZ2 ($\lambda_{max} = 68 \text{ L mol}^{-1} \text{ cm}^{-1}$ in acetonitrile).\cite{5a-d} The singlet diradical decays with a rate constant $k_{CP}$ of $3.03 \times 10^6 \text{ s}^{-1}$, i.e. lifetime $\approx 330 \text{ ns}$, to afford the ring-closed compound CP2 (Scheme 1c).

Herein, we report the simultaneous observation of the decay process of triplet diradical DR3 ($\approx 320 \text{ nm}$) and the growth of singlet diradical DR3 ($\approx 560 \text{ nm}$) in the denitrogenation of triplet-sensitized azoalkane precursor AZ3 (Scheme 2); in AZ3, the benzophenone unit (triplet energy ($E_T = 69 \text{ kcal mol}^{-1}$) (1 kcal mol$^{-1} = 4.186 \text{ kJ mol}^{-1}$), $\epsilon_{320} = 108 \text{ L mol}^{-1} \text{ cm}^{-1}$ in acetonitrile) is attached to the meta position of the phenyl ring for the triplet sensitization of the azo-chromophore ($E_T = 62 \text{ kcal mol}^{-1}$).\cite{5} We hypothesize that meta-substitution can prevent the direct growth of 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 $\pi$-dimethylation of 3 was performed by Tiecco’s method to obtain 4 (Scheme 3). The synthesis of pyrazole 5 followed by the Diels–Alder reaction of 5 with cyclopentadiene afforded azoalkane 6.\cite{9} Benzoylation using a Weinreb amide 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\textsuperscript{DR2} by the photodenitrogenation of azoalkane precursor AZ2.

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

Scheme 3. Synthesis of AZ3. Conditions: (a) NaH, THF, 0°C; (b) Ph\textsubscript{2}Se\textsubscript{2}, (NH\textsubscript{4})\textsubscript{2}S\textsubscript{2}O\textsubscript{8}, MeOH; (c) N\textsubscript{2}H\textsubscript{2} H\textsubscript{2}O, CHCl\textsubscript{3}; (d) cyclopentadiene, CF\textsubscript{3}CO\textsubscript{2}H, CH\textsubscript{2}Cl\textsubscript{2}, 0°C; (e) n-BuLi, N-methoxy-N-methylbenzamide, THF, –78°C; (f) H\textsubscript{2}, Pd/C, EtOAc; (g) high-pressure Hg lamp, benzene.
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 \(\text{N}_2\) 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 (\(\lambda_{\text{exc}}\) 355 nm), planar singlet diradical \(\text{DR2}\) was immediately observed at \(\sim560\) nm; however, it decayed with a lifetime (\(\tau\)) of 330 ns (\(k_{\text{cp}}=3.03 \times 10^6\) 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 \(\text{DR3}\) was also observed in the same region with a \(\lambda_{\text{max}}\) of \(\sim560\) nm (Fig. 2a). In contrast to the flash photolysis of AZ2, the growth of \(\text{DR3}\) was observed until \(\sim100\) ns after laser excitation (Fig. 2b). From the double-exponential fit of the data on the time profile of \(\text{DR3}\), the decay rate constant (k\(_{\text{d}}\)) of \(\text{DR3}\) and the growth rate constant (k\(_{\text{g}}\)) were determined to be \(2.02 \times 10^6\) and \(3.24 \times 10^7\) 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 \(\text{TR3}\), 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 \(3.44 \times 10^7\) s\(^{-1}\), which is consistent with the growth rate constant of \(\text{DR3}\). The species observed at 320 nm was assigned to triplet diradical \(\text{TR3}\), because the absorption band is observed at a position typical for the triplet state of 1,3-diphenylpropane-1,3-diyd diradicals,\(^{(12)}\) e.g. \(\text{DR1}\); \(\lambda_{\text{max}}\) \(\sim320\) nm.\(^{(3)}\) Time-dependent density functional theory (DFT) calculation at the UB3LYP/6–31G+(d, p) level of theory suggests that triplet diradical \(\text{TR3}\) has an absorption at 354 nm. The residue at 320 nm is due to the formation of product CP3.

The intramolecular energy transfer from the triplet benzo-phenone 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 \(\sim5 \times 10^9\) s\(^{-1}\). The rapid decay

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**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 \(\mu\)s in the laser flash photolysis (LFP) of AZ2 in acetonitrile at 293 K.

**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 \(\mu\)s 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 $k_g = 3.49 \pm 0.10 \times 10^7$ 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.

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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Temperature [K]</th>
<th>Rate constant$^\text{a}$ [s$^{-1}$] at 320 nm</th>
<th>Rate constant$^\text{a}$ [s$^{-1}$] at 560 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AZ3</td>
<td>293</td>
<td>$k_{d,320} \times 10^{-7}$</td>
<td>$k_{g,560} \times 10^{-7}$</td>
</tr>
<tr>
<td>2</td>
<td>CP3</td>
<td>293</td>
<td>$3.44 \pm 0.08$</td>
<td>$3.24 \pm 0.23$</td>
</tr>
<tr>
<td>3</td>
<td>AZ3</td>
<td>243</td>
<td>$3.49 \pm 0.06$</td>
<td>$3.24 \pm 0.17$</td>
</tr>
<tr>
<td>4</td>
<td>CP3</td>
<td>243</td>
<td>$3.49 \pm 0.10$</td>
<td>$3.33 \pm 0.23$</td>
</tr>
</tbody>
</table>

$^\text{a}$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.
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 $3.49 \pm 0.06 \times 10^7 \text{s}^{-1}$ with single-exponential fitting, which is also consistent with the value of $k_{\text{obs}} = 3.44 \pm 0.08 \times 10^7 \text{s}^{-1}$ 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 $^3\text{DR3}$ to $^1\text{DR3}$ and not to the denitrogenation of $^3\text{AZ3}^*$, which includes the bond-breaking process.

The assignment of ISC, i.e. the simultaneous detection of the decay process of $^3\text{DR3}$ (320 nm) and the growth process of $^1\text{DR3}$ (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.\[1,4\] In fact, the temperature effect on the rate constant of the growth at 560 nm ($k_{\text{g,560}}$) and the decay at 320 nm ($k_{\text{d,320}}$) 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 ($k_{\text{d,560}}$) of $^1\text{DR3}$, i.e. C–C bond formation process, was significantly affected by temperature. The small temperature effects on $k_{\text{d,320}}$ and $k_{\text{g,560}}$ 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, $k_{\text{ISC}} \sim 3.24 \times 10^7 \text{s}^{-1}$, for 2,2-dimethoxycyclopentane-1,3-diradical DR3 was significantly higher than that\[1,4\] for 2,2-dimethylcyclopentane-1,3-diradical DR1 by two orders of magnitude, $k_{\text{ISC}} \sim 3.69 \times 10^5 \text{s}^{-1}$. 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-diyli diradicals.\[4\] A large SOC in diradicals enhances the rate constant of ISC, because the transmission factor of SOC, $A_{\text{SOC}}$, is proportional to the square of $C_\ast$, which represents the coefficient of the wave function of the singlet diradicals in the ground state,\[2,4\] as shown in Eqn 1.

$$A_{\text{SOC}} \propto C_\ast^2 \quad (1)$$

The coefficient $C_\ast$ is expressed in Eqn 2,\[2,4\] where $\gamma_{\text{AB}}$ denotes the covalent perturbation, and $K_{\text{AB}}$ denotes the coulomb integral function.

$$C_\ast \approx \gamma_{\text{AB}}^{2} K_{\text{AB}} \quad (2)$$

$\gamma_{\text{AB}}$ corresponds to the energy gap between the two nonbonding molecular orbitals (NBMOs) that are occupied by the two electrons for the corresponding 1,3-diradical fragment (Fig. 5). The low-lying C–O $\sigma^*$ orbital is stabilized by hyperconjugation with the symmetric NBMO(s) while the C–C $\sigma^*$ orbital is too high-lying to interact (Fig. 5); thus, $\gamma_{\text{AB}}$ in $X = \text{OMe}$ becomes larger than that in $X = \text{Me}$, 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.

![Fig. 5. Effect of substituent on the energy gap between the two nonbonding molecular orbitals (NBMOs) in cyclopentane-1,3-diyl diradicals.](image-url)
as light source, Unisoku-MD200 monochromator and a photo-multiplier. The temperature was controlled with a CoolSpec 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 \(\text{H}_{2}\text{O-DO}_{2}\) (1:1 by volume) solution. The details of the measurement system have been described elsewhere.\(^{[58,15]}\)

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 acetonophene 2 (4.12 g, 33.4 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 1M hydrochloric acid (20 mL) with stirring. The organic layer was extracted with ethyl acetate (3 \(\times\) 10 mL) and dried over sodium sulfate. After evaporation of the solvent under vacuum, the residue was purified by silica gel column chromatography (hexane/\(\text{EtOAc}\) 8:1, v/v) to give the crude product as a red liquid. The crude was not stable on silica.

Hydrazine monohydrate (0.83 g, 16.5 mmol) was added to the solution of compound 4 (\(\approx 10\) g, crude) in chloroform (70 mL) with stirring under an \(\text{N}_2\) 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 \(\times\) 10 mL) and dried over sodium sulfate. After evaporation of the solvent under vacuum, the residue was purified by silica gel column chromatography (hexane/\(\text{EtOAc}\) 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. \(\text{v}_{\text{max}}\) (KBr/cm\(^{-1}\)) \(3071, 2943, 2832, 1553, 1443, 1318, \delta_h\) (400 MHz, CDC\(_13\)) 8.42 (s, 1H, ArH), 8.26 (d, \(J\) 8.0, 1H, ArH), 8.20 (d, \(J\) 7.8, 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, \(\text{OCH}_3\)). \(\delta_c\) (100 MHz, CDC\(_13\)) 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 \(\text{C}_{17}\text{H}_{16}\text{O}_{2}\text{N}_{2}\text{Br Na}\) [M \(+\) H\(^+\)] \(359.04076).

(3R,4R,4aS,7aR)-1-(3-Bromophenyl)-8,8-dimethoxy-4-phenyl-4a,5,7a-tetrahydro-1H-1,4-methanocyclopenta[d]pyridazin 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 \(\text{N}_2\) 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 \(\times\) 10 mL) and dried over magnesium sulfate. After evaporation of the solvent under vacuum, the residue was purified by chromato-
$^{1}H$ and $^{13}C$ NMR spectra of the compounds synthesized in this study are available on the Journal’s website.

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Reference

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