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## Reactivity of the 4,5-Didehydroisoquinolinium Cation

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**Abstract:** The chemical properties of a 1,8-didehydronaphthalene derivative, the 4,5-didehydroisoquinolinium cation, were examined in the gas phase in a dual-cell Fourier-transform ion cyclotron resonance (FT-ICR) mass spectrometer. This is an interesting biradical because it has two radical sites in close proximity, yet their coupling is very weak. In fact, the biradical is calculated to have approximately degener-

ate singlet and triplet states. This biradical was found to exclusively undergo radical reactions, as opposed to other related biradicals with nearby radical sites. The first bond formation occurs

**Keywords:** biradicals • didehydronaphthalene • FT-ICR • ion-molecule reactions • reactive intermediates

at the radical site in the 4-position, followed by that in the 5-position. The proximity of the radical sites leads to reactions that have not been observed for related mono- or biradicals. Interestingly, some *ortho*-benzynes have been found to yield similar products. Since *ortho*-benzynes do not react via radical mechanisms, these products must be especially favorable thermodynamically.

### Introduction

Didehydroarenes and their derivatives are reaction intermediates that have been known for more than 60 years.<sup>[1]</sup> Two decades of studies have identified the crucial role of didehydroarenes in the biological action of certain antitumor antibiotics, which has led to a renewed interest in the properties of these aromatic carbon-centered  $\sigma,\sigma$ -biradicals.<sup>[2]</sup> However, condensed-phase studies of organic biradicals are challenging due to the difficulty in generating them cleanly in solution. In fact, condensed-phase studies have led to an in-depth understanding of the chemical behavior of only one of the didehydroarenes, 1,2-didehydrobenzene (*ortho*-benzyne) and its derivatives.<sup>[1]</sup> Many of the issues that complicate the studies of highly reactive species in condensed phases are less problematic in the gas phase. One way to study reaction intermediates in the gas phase involves the well-known distonic ion approach<sup>[3]</sup> wherein a chemically inert charged group is attached to the reactive intermediate of interest so that it can be manipulated in a mass spectrom-

eter. Previous studies carried out by using this approach have demonstrated that the reactivity of charged 1,2-didehydroarenes in the gas phase is analogous to that reported for their neutral analogs in solution.<sup>[4]</sup> A comparison of the reactivity<sup>[3a,b,5]</sup> of charged 1,2-didehydroarenes to that of 1,3-didehydroarenes in the gas phase has revealed drastic differences that partially reflect the differences in their singlet-triplet gaps ( $\Delta E_{ST}$ ). The magnitude of  $\Delta E_{ST}$  for singlet biradicals is thought to affect their ability to undergo radical reactions due to the requirement for partial uncoupling of the biradical electrons in the transition state.<sup>[6]</sup> Consequently, a higher  $\Delta E_{ST}$  is expected to lead to higher barriers and slower radical reactions. Indeed, 1,2-didehydroarenes (with large  $\Delta E_{ST}$ ) have been found to react like activated alkynes and rapidly undergo nucleophilic or electrophilic addition reactions rather than radical reactions.<sup>[4,5b]</sup> However, gaseous 1,3-didehydroarenes (often with just slightly lower  $\Delta E_{ST}$  than 1,2-didehydroarenes) have been demonstrated to undergo both radical and nonradical reactions, depending on their dehydrocarbon atom separation.<sup>[5a]</sup> A greater dehydrocarbon atom separation facilitates radical reactions for 1,3-didehydroarenes. Didehydroarenes with more than one heavy atom between the dehydrocarbon atoms (and lower  $\Delta E_{ST}$ ), such as the 4,6-didehydroisoquinolinium cation, have been demonstrated to react exclusively via radical mechanisms.<sup>[7]</sup>

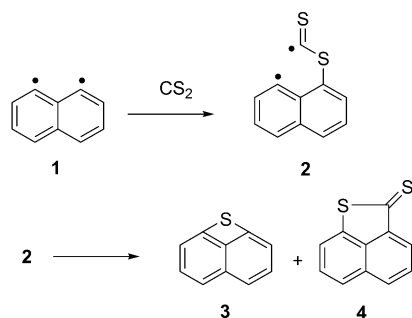
The 1,8-didehydronaphthalene (**1**) has been a focus of attention for some time. Based on the computational studies of Squires and Cramer,<sup>[8]</sup> the 1,8-isomer is an especially interesting 1,3-didehydroarene since the lowest lying singlet and triplet states are calculated to be nearly degenerate ( $\Delta E_{ST} = -0.9 \text{ kcal mol}^{-1}$ ) due to the parallel orientation of the formally singly occupied nonbonding molecular orbitals.

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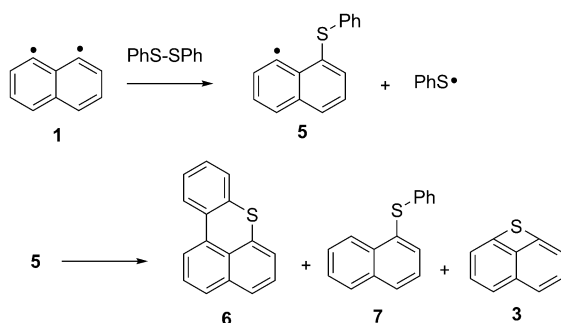
This didehydroarene represents a rare case wherein the coupling between the biradical electrons is very weak even though the radical sites are spatially close. These characteristics should result in interesting chemical properties. Previous experimental work on this biradical in solution by Rees and Storr<sup>[9]</sup> revealed that it abstracts two hydrogen atoms from cyclohexane and undergoes 1,2-addition to benzene and to olefins. Later, Nakayama et al.<sup>[10]</sup> examined the reaction of **1** with carbon disulfide (Scheme 1) since aryl radicals



Scheme 1. Reaction of biradical **1** with carbon disulfide.

were known to add to this reagent.<sup>[11]</sup> Indeed, **1** was found to add to a sulfur atom to yield several products. Two of these products, the naphtho[1,8-*bc*]thiete (**3**) and the naphtho[1,8-*bc*]thiophen-2-thione (**4**), provided evidence for the formation of a 1,5-biradical intermediate (**2**).

Following this work, de Luca et al.<sup>[12]</sup> examined the reaction of **1** with diphenyl disulfide (Scheme 2) and identified benzo[*kl*]thioxanthene (**6**), 1-naphthylphenylsulfide (**7**) and naphtho[1,8-*bc*]thiete (**3**) as the final products. All these products were thought to be formed via a radical intermediate (**5**) produced by the attack of **1** on the sulfur atom of the diphenyl disulfide.



Scheme 2. Reaction of biradical **1** with diphenyl disulfide.

Herein, we report a kinetic reactivity study on a positively charged analog of 1,8-didehydronaphthalene, the 4,5-didehydroisoquinolinium cation (**8**) (Figure 1). Its reactivity is compared to that of two related monoradicals (4-dehydroisoquinolinium cation<sup>[7]</sup> **9** and 5-dehydroisoquinolinium cation<sup>[7]</sup> **10**) (Figure 1) and two isomeric biradicals, the unre-

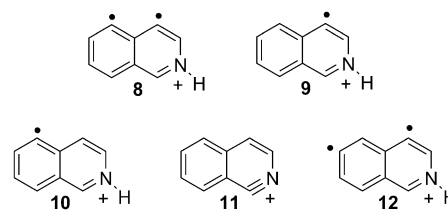


Figure 1. The dehydro- and didehydroisoquinolinium cations studied.

ported 1-isoquinolyl cation **11** and the previously reported 4,6-didehydroisoquinolinium cation<sup>[7]</sup> **12** (Table 1, Figure 1). The 4,5-didehydroisoquinolinium cation (**8**) is calculated to have nearly degenerate low-lying singlet and triplet states ( $\Delta E_{ST} = -0.6 \text{ kcal mol}^{-1}$ ).





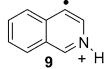
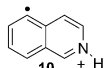
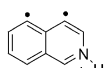
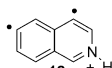
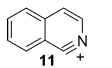
## Results and Discussion

The five positively charged radicals (**8–12**) studied in the gas phase in an FT-ICR mass spectrometer are shown in Figure 1. Their reactivity toward four reagents was investigated. The biradical of interest, **8**, was found to yield similar product ions as the two related monoradicals (**9** and **10** in Table 1), but also many additional product ions not observed for these monoradicals. The latter products represent a combination of most of the product ions observed for biradicals **11** and **12**, in addition to some novel product ions. This finding was unexpected due to the structural differences between these three biradicals and the drastically different reactivities of **11** (a 1,2-didehydroarene with a large  $\Delta E_{ST}$  of  $-29.0 \text{ kcal mol}^{-1}$  calculated<sup>[13]</sup> at the RHF-UCCSD(T)/cc-pVTZ//UBPW91/cc-pVDZ level of theory) and **12** (a 1,4-didehydroarene with a small calculated  $\Delta E_{ST}$ ;  $-0.7 \text{ kcal mol}^{-1}$ ).

Both monoradicals **9** and **10** react predominantly by abstraction of a hydrogen atom from tetrahydrofuran (THF), an iodine atom from allyl iodide (AI), a  $\text{SCH}_3$  group from dimethyl disulfide (DMDS), and CN and HCN groups from *tert*-butyl isocyanide (*t*BuNC), as expected<sup>[3a,5b]</sup> (Table 1). Monoradical **9** is more reactive than monoradical **10**. This can be explained by its higher electrophilicity,<sup>[14]</sup> which can be quantified by using the calculated vertical electron affinity (EA; the energy released upon attachment of an electron to a radical site). The vertical EAs of **9** and **10** are calculated to be 5.72 eV and 5.04 eV, respectively.<sup>[14a,15]</sup>

Biradical **12**, which has two carbon atoms between the radical sites, yields reaction products analogous to those obtained for the related monoradical **9** and the unrelated monoradical **10**. For example, **12** reacts by the abstraction of one (or two) hydrogen atoms from THF, two  $\text{SCH}_3$  groups from DMDS, two CN groups from *t*BuNC, and two iodine atoms from AI. These reactions indicate that **12** reacts via typical radical pathways. However, the addition of a second radical site to monoradical **9** to generate biradical **12** results in a decrease in the reactivity, in spite of an increase in the EA. Biradical **12** likely reacts from both the singlet ground

Table 1. Reaction efficiencies<sup>[a]</sup> and product branching ratios<sup>[b]</sup> for reactions of radicals **8–12** with various reagents.

				
 <b>9</b> EA <sup>[d]</sup> = 5.72 eV	H abs <sup>[c]</sup> 100% Efficiency = 39%	I abs 94% C <sub>3</sub> H <sub>5</sub> (allyl) abs 6% Efficiency = 71%	SCH <sub>3</sub> abs 100% Efficiency = 73%	CN abs 96% HCN abs 4% Efficiency = 84%
 <b>10</b> EA = 5.04 eV	H abs 100% Efficiency = 8%	I abs 98% C <sub>3</sub> H <sub>5</sub> abs 2% Efficiency = 36%	SCH <sub>3</sub> abs 100% Efficiency = 48%	CN abs 94% HCN abs 6% Efficiency = 63%
 <b>8</b> EA = 5.93 eV ΔE <sub>ST</sub> <sup>[e]</sup> = −0.6 kcal mol <sup>−1</sup>	2 × H abs 40% H abs 14% (2°) H abs CH <sub>2</sub> O abs 25% H <sub>2</sub> O abs 6% C <sub>2</sub> H <sub>4</sub> abs 6% H <sup>−</sup> abs 5% C <sub>3</sub> H <sub>3</sub> abs 2% C <sub>2</sub> H <sub>4</sub> O abs 1% C <sub>3</sub> H <sub>6</sub> abs 1% Efficiency = 27% <sup>[f]</sup>	I abs 58% (2°) I abs (2°) C <sub>3</sub> H <sub>5</sub> abs C <sub>3</sub> H <sub>4</sub> (allene) abs 42% Efficiency = 42% <sup>[g]</sup>	SCH <sub>3</sub> abs 51% (2°) SCH <sub>3</sub> abs SCH <sub>2</sub> abs 31% HSCH <sub>3</sub> abs 18% Efficiency = 62% <sup>[h]</sup>	HCN abs 70% CN abs 30% (2°) CN abs (2°) HCN abs (2°) addition Efficiency = 55% <sup>[i]</sup>
 <b>12</b> EA = 5.99 eV ΔE <sub>ST</sub> <sup>[e]</sup> = −0.8 kcal mol <sup>−1</sup>	H abs 100% (2°) H abs Efficiency = 26%	I abs 92% (2°) I abs (2°) C <sub>3</sub> H <sub>5</sub> abs C <sub>3</sub> H <sub>3</sub> abs 8% Efficiency = 57%	SCH <sub>3</sub> abs 100% (2°) SCH <sub>3</sub> abs Efficiency = 59%	CN abs 88% (2°) CN abs (2°) HCN abs HCN abs 12% Efficiency = 94%
 <b>11</b> EA = 6.35 eV ΔE <sub>ST</sub> = −29.0 kcal mol <sup>−1</sup>	CH <sub>2</sub> O abs 61% H <sub>2</sub> O abs 39% Efficiency = 88%	addition 72% C <sub>3</sub> H <sub>4</sub> abs 21% C <sub>3</sub> H <sub>5</sub> abs 6% Efficiency = 60% <sup>[j]</sup>	HSCH <sub>3</sub> abs 92% (2°) SCH <sub>2</sub> abs SCH <sub>2</sub> abs 8% Efficiency = 54% <sup>[k]</sup>	HCN abs 83% (2°) C <sub>4</sub> H <sub>8</sub> abs C <sub>4</sub> H <sub>9</sub> abs 17% (2°) H <sup>+</sup> transfer Efficiency <sup>[l]</sup> = 106%

[a] Reaction efficiencies are reported as  $k_{\text{reaction}}/k_{\text{collision}} \times 100$ . [b] Primary products' branching ratios; secondary products are noted as (2°) and are listed under the primary products that produce them. [c] abs = abstraction. [d] Calculated vertical electron affinities (EA) for **8**, **9**, **10**, and **12** from reference [14]. [e] ΔE<sub>ST</sub> calculated at the CASPT2/cc-pVDZ//MCSCF(12,12)/cc-pVDZ level of theory; reference [14b]. Note that a negative value means that the singlet state lies energetically below the triplet state. [f] From non-linear curve fit (least squares non-linear fit of the pseudo-first-order plot), 25% of the reactant ion population is unreactive. [g] Same as [f] but 47%. [h] Same as [f] but 43%. [i] Same as [f] but 13%. [j] Same as [f] but 6%. [k] Same as [f] but 9%. [l] The absolute values of the measured efficiencies are estimated to be accurate only within ±50%, but the precision is much better (±10%).

state and the lowest-energy triplet state. The interaction (albeit weak) between the two biradical electrons in the singlet state of **12** may explain the reduced reactivity compared to **9**. However, **12** reacts at higher efficiencies than monoradical **10**, likely due to its much higher EA (5.99 eV; Table 1) than that of **10** (5.04 eV).<sup>[14,15]</sup>

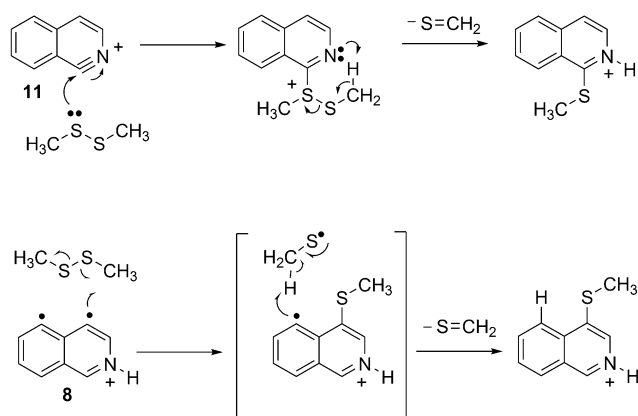
Biradical **12**, with a calculated ΔE<sub>ST</sub> of −0.8 kcal mol<sup>−1</sup> (Table 1), is an excellent biradical to compare with **8** (calculated<sup>[14,15]</sup> EA 5.93 eV and ΔE<sub>ST</sub> of −0.6 kcal mol<sup>−1</sup>) due to their similar EA and ΔE<sub>ST</sub>, and because **12** is thought to react entirely via radical pathways.<sup>[7]</sup> Most of the reactions of **12** were observed for **8** (e.g., two consecutive hydrogen atom abstractions from THF, two consecutive iodine atom abstractions from AI, two consecutive SCH<sub>3</sub> group abstractions from DMDS, and two consecutive CN group abstractions from *t*BuNC), thus indicating that **8** also reacts via radical mechanisms. However, a number of reactions were ob-

served for **8** that were not observed for **12** (e.g., CH<sub>2</sub>O abstraction from THF, H<sub>2</sub>C=C=CH<sub>2</sub> abstraction from AI, and SCH<sub>2</sub> abstraction from DMDS), suggesting that the close proximity of the two radical sites in **8** makes alternative reaction pathways possible. In spite of these additional reaction pathways, the reaction efficiencies of **8** and **12** are generally similar. This finding suggests, as discussed above for **12**, that **8** reacts from both the singlet ground state and the lowest-energy triplet state. To better understand the effects of two radical sites in close proximity, the reactivity of biradical **11** was examined.

Biradical **11**, where the radical sites are on adjacent carbon and nitrogen atoms, reacts faster than biradicals **8** and **12** with almost all the reagents studied (Table 1), and its reaction products differ drastically from those observed for **12**. This is likely due to the large ΔE<sub>ST</sub> for **11** (Table 1). The strong through-space interaction between the formally un-

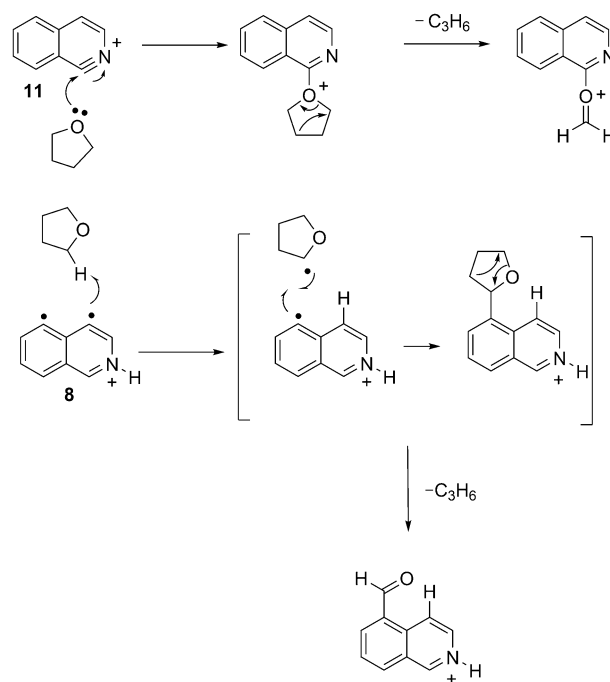
paired electrons on adjacent carbon and nitrogen atoms in **11** prevents radical reactions.<sup>[4b,6]</sup> Instead, **11** behaves like an activated electrophilic alkyne and readily undergoes nonradical addition reactions, as observed in previous studies.<sup>[16]</sup> The main reactions of **11** with THF (CH<sub>2</sub>O abstraction (49 %) and H<sub>2</sub>O abstraction (36 %)), AI (addition (72 %)), DMDS (HSCH<sub>3</sub> abstraction (92 %)), and *t*BuNC (HCN abstraction (90 %)), are thought to occur via nonradical mechanisms and hence do not require uncoupling of the biradical electrons in the transition state.<sup>[16]</sup> Therefore, they are not expected to be dependent on the magnitude of  $\Delta E_{ST}$ .

Comparison of the reactivity of biradical **8** to that of biradicals **11** and **12** and monoradicals **9** and **10** reveals that almost all the product ions formed for **8**, but not for **9**, **10**, or **12**, are also formed for biradical **11**. The dominant abstraction of HCN from *t*BuNC, as well as the abstraction of CH<sub>2</sub>O from THF, SCH<sub>2</sub> and HSCH<sub>3</sub> from DMDS, and H<sub>2</sub>C=C=CH<sub>2</sub> from AI, were observed for both **8** and **11** but not for **9**, **10**, or **12** (Table 1). Although **8** most likely only undergoes radical reactions, as opposed to **11** which does not, the close proximity of the two radical centers in both **8** and **11** is likely the reason for the coincidental formation of similar products (albeit via different mechanisms). The two radical sites of **8**, due to their proximity, can undergo multiple radical reactions with a reagent molecule before the collision complex of the reaction products dissociates. An example is the HSCH<sub>3</sub> abstraction by **8** (and **11**) from DMDS, which can occur by at least two different mechanisms (Scheme 3), radical and nonradical. The nonradical mecha-



Scheme 3. Proposed mechanisms for the abstraction of HSCH<sub>3</sub> by **11** and **8**. Brackets indicate a reaction within an intermediate collision complex.

nism probably involves nucleophilic addition of DMDS to the most electron-deficient carbon atom in **11**, which is likely followed by proton transfer and elimination of CH<sub>2</sub>S (Scheme 3). On the other hand, biradical **8** most likely abstracts a CH<sub>3</sub>S group from DMDS (via the same mechanism as monoradicals), which is followed by hydrogen atom abstraction from the departing CH<sub>3</sub>S radical by the second radical site, leading to elimination of CH<sub>2</sub>S.

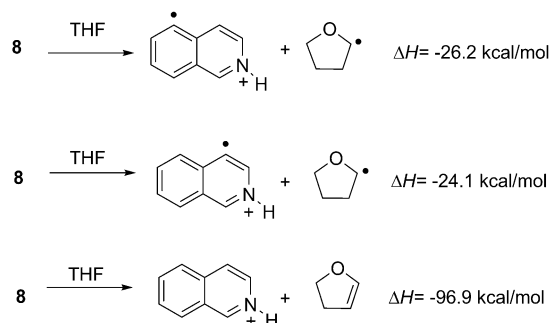


Scheme 4. Proposed mechanisms for the abstraction of CH<sub>2</sub>O by **11** and **8**. Brackets indicate a reaction within an intermediate collision complex.

Similar behavior is expected for CH<sub>2</sub>O abstraction by **8** and **11** from THF (Scheme 4). Support for the mechanism proposed for **8** was obtained by isolating the CH<sub>2</sub>O abstraction product (*m/z* 158) and subjecting it to collisionally-activated dissociation (CAD). It was found to yield a major fragment ion (*m/z* 130) by loss of CO. Protonated isoquinoline-5-carboxaldehyde (*m/z* 158) also yields a major fragment ion of *m/z* 130. On the other hand, the product ion formed from **11** loses CH<sub>2</sub>O upon CAD.

Further insights into the reactivity of **8** were obtained from the observation that it abstracts two hydrogen atoms simultaneously or nearly simultaneously from a single THF molecule. This reactivity was not observed for either **12**, which abstracts two hydrogen atoms in a consecutive manner and from two different THF molecules (as a primary and a secondary reaction; Table 1), or **11**, which does not abstract hydrogen atoms. These results suggest that the abstraction of the two hydrogen atoms by **8** from one THF molecule occurs via a radical mechanism and is facilitated by the closeness of the two radical sites.

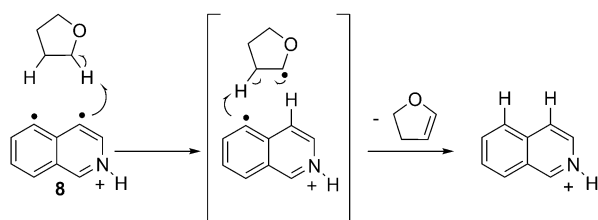
Computational studies were performed to examine the enthalpy changes for the reactions of **9**, **10**, and **8** with THF (calculated at the UMPW1K/6-31+G(d,p)//UMPW1K/6-31+G(d,p) level of theory). The results indicate that the abstraction of a hydrogen atom from the  $\alpha$ -carbon of THF is slightly more exothermic for **9** than for **10** (−25.2 kcal mol<sup>−1</sup> and −23.1 kcal mol<sup>−1</sup>, respectively), as expected. Hydrogen atom abstraction from THF by the C4 radical site in **8** is thermodynamically more favorable by about 2 kcal mol<sup>−1</sup> than by the C5 radical site (Scheme 5). The abstraction of two hydrogen atoms from a single THF molecule is calculat-



Scheme 5. Calculated enthalpies for reaction of **8** with THF.

ed to be highly favorable (Scheme 5), consistent with the experimental result that the abstraction of two hydrogen atoms from one THF molecule is the predominant reaction.

Transition-state calculations (at the UMPW1K/6-31+G-(d,p)//UMPW1K/6-31G+(d,p) level of theory) carried out for **8** failed to locate a transition state for a concerted double hydrogen atom abstraction. Although this is not conclusive, we propose a stepwise (Scheme 6) rather than a con-



Scheme 6. Proposed mechanism for the nearly simultaneous abstraction of two hydrogen atoms from THF by **8**. Brackets indicate a reaction within an intermediate collision complex.

certed mechanism for this reaction. Instead, transition states were found for hydrogen atom abstraction by the C4 radical site (Figure 2) and by the C5 radical site (not shown) in **8**. The activation enthalpies were calculated to be  $-7.0 \text{ kcal mol}^{-1}$  and  $-4.0 \text{ kcal mol}^{-1}$ , respectively (for the  $\alpha$ -carbon of THF). These results suggest that abstraction of the first hydrogen atom by the C4 radical site is not only thermodynamically but also kinetically more favorable than by the C5 radical site. The activation enthalpy for hydrogen atom abstraction from THF by monoradical **9** ( $-6.3 \text{ kcal mol}^{-1}$ ) was found to be lower by about  $3 \text{ kcal mol}^{-1}$  than that for **10** ( $-3.2 \text{ kcal mol}^{-1}$ ), a result that is in agreement with the observed relative reaction efficiencies of these monoradicals, and explained by the higher EA of **9**.

In contrast, the activation enthalpies calculated for biradical **8** ( $-7.0 \text{ kcal mol}^{-1}$ ) and the more reactive monoradical **9** ( $-6.3 \text{ kcal mol}^{-1}$ ) are not in agreement with the substantially lower hydrogen atom abstraction efficiency (4%) of the biradical from THF. However, the many competing reaction pathways for the biradical prevent a direct comparison of hydrogen atom abstraction efficiencies in this case.

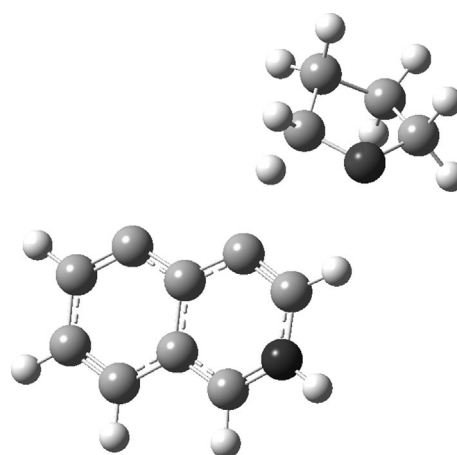
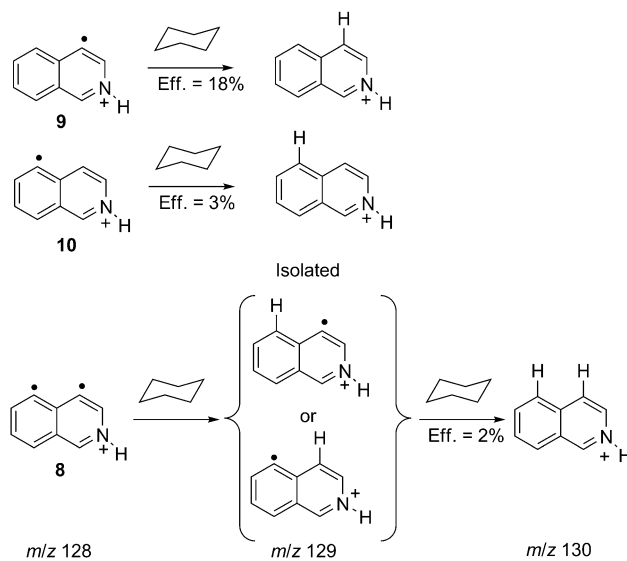


Figure 2. Transition state calculated for hydrogen atom abstraction from THF by the C4 radical site in **8**.

To gain additional insight into the hydrogen atom abstraction reactions of **8**, another hydrogen atom donor, cyclohexane, was examined. In a previous study,<sup>[16]</sup> mono- and biradicals were found to react with cyclohexane solely by one and/or two hydrogen atom abstractions. Biradical **8** reacts with cyclohexane by addition (19%), and by one (35%) as well as two (46%) hydrogen atom abstractions (Scheme 7; reaction efficiency = 18%). To determine the site of the first (and hence also second) hydrogen atom abstraction, the product of this reaction was isolated and allowed to react with cyclohexane (Scheme 7) to determine the efficiency of the second hydrogen atom abstraction, which was measured to be 2%. This efficiency is comparable to the efficiency of hydrogen atom abstraction by monoradical **10** (3%) and quite different from that of monoradical **9** (18%; Scheme 7). This result demonstrates that the second hydro-



Scheme 7. Reactivity of monoradicals **9** and **10** and biradical **8** toward cyclohexane.

gen atom is abstracted by the radical site at C5 after abstraction of the first hydrogen atom by the radical site at C4 of **8** (in agreement with the transition-state calculations discussed above). Hence, the reactions of **8** with THF, DMDS, and AI are also likely initiated by atom or group abstraction by the radical site at C4.

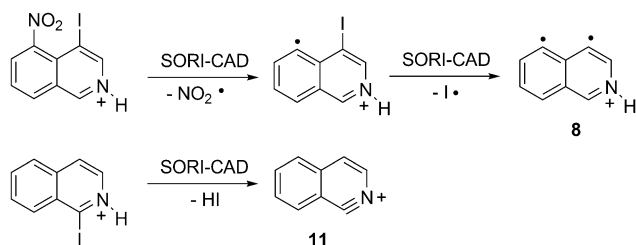
The CN group differs from the above groups in being highly electron withdrawing. Thus, CN abstraction from *t*BuNC may take place at C5 in **8**, which is less electron deficient than C4. However, based on the observation that monoradical **9** reacts more efficiently with this reagent than **10**, it is concluded that the first CN abstraction likely occurs at radical site C4 in **8** (Table 1).

## Conclusion

Examination of the gas-phase reactions of biradical **8** with THF, AI, DMDS, and *t*BuNC indicates that this biradical reacts solely by radical pathways, and that the products formed in these reactions are similar to those of related monoradicals **9** and **10** and biradical **12**. The abstraction of two hydrogen atoms from a single THF molecule is calculated to be quite favorable, consistent with the experimental results. The experimental and theoretical studies indicate that the first bond formation occurs at C4, followed by C5. The proximity of the two radical sites in **8** also leads to radical reactions that were not observed for the monoradicals **9** and **10** or biradical **12**. Reactions similar to those observed for **8** were also observed for **11** although the reactions of **11** involve nonradical mechanisms.

## Experimental Section

All experiments were carried out in a Finnigan FTMS 2001 dual-cell FT-ICR mass spectrometer. The mono- and biradicals **8–12** (Table 1) were generated by using previously reported methods.<sup>[5b,17]</sup> The ionized precursors were then transferred from one cell into the other, followed by sustained off-resonance irradiated collision-activated dissociation<sup>[18]</sup> (SORI-CAD) to homolytically cleave C–I and/or C–NO<sub>2</sub> bonds of the protonated precursors (for an example, see Scheme 8). The (bi)radicals **8–12** were isolated and allowed to react with tetrahydrofuran (THF), allyl iodide (AI), dimethyl disulfide (DMDS) and *tert*-butyl isocyanide (*t*BuNC) for varying periods of time. The second-order reaction rate constants ( $k_{\text{exp}}$ ) and reaction efficiencies ( $k_{\text{reaction}}/k_{\text{coll}}$ ) were determined as described in



Scheme 8. Generation of biradical **8** from protonated 4-iodo-5-nitroisoquinoline and biradical **11** from protonated 1-iodoisoquinoline by SORI-CAD.

the literature.<sup>[3b,19]</sup> The absolute values are estimated to be accurate only within  $\pm 50\%$ , but the relative values are much more accurate ( $\pm 10\%$ ). The product branching ratios were determined by dividing the abundance of each primary reaction product ion by the sum of all primary reaction product abundances. Isoquinoline-5-carboxaldehyde and the precursor for monoradical **10**, 5-nitroisoquinoline, were purchased from Sigma–Aldrich and used without further purification. The precursor for monoradical **9**, 4-iodoisoquinoline, was synthesized by a known method.<sup>[20]</sup> The precursor for biradical **8**, 4-iodo-5-nitroisoquinoline, was synthesized for the first time by using the reaction conditions described by Grubbs et al.<sup>[21]</sup> for 4-iodoisoquinoline. The structure was verified by x-ray crystallography. The precursors for biradical **12**, 4,6-dinitroisoquinoline,<sup>[22]</sup> and biradical **11**, 1-iodoisoquinoline,<sup>[23]</sup> were synthesized by known methods.

Molecular orbital calculations were carried out with the Gaussian 03<sup>[24]</sup> and Molpro<sup>[25]</sup> electronic structure program suites.

**Supporting Information:** (1) Cartesian coordinates, electronic and zero-point vibrational energies, 298 K thermal contributions and derived enthalpies. (2) Synthesis procedure for 4-iodo-5-nitroisoquinoline and its X-ray structure. (3) Full references [24] and [25].

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