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# Relative Reactivities of Three Isomeric Aromatic Biradicals with a 1,4-Biradical Topology Are Controlled by Polar Effects

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## Abstract

Unexpectedly, the 5-dehydroquinoline radical cation was formed in the gas phase from the 5-iodo-8-nitroquinolinium cation upon ion-trap collision-activated dissociation. This reaction involves the cleavage of a nitro group to generate an intermediate monoradical, the 8-dehydro-5-iodoquinolinium cation, followed by rearrangement via abstraction of a hydrogen atom from the protonated nitrogen atom by the radical site. Dissociation of the rearranged radical cation via elimination of an iodine atom generates the 5-dehydroquinoline radical cation. The mechanism was probed by studying isomeric biradicals and via quantum chemical calculations. The 5-dehydroquinoline radical cation showed greater gas-phase reactivity toward dimethyl disulfide, cyclohexane and allyl iodide than the isomeric 5,8-didehydroquinolinium cation, which is more reactive than the isomeric 5,8-didehydroisoquinolinium cation studied previously, all with a 1,4-biradical topology. The reactivity ordering is rationalized by the vertical electron affinities of the radical sites of these biradicals instead of their widely different singlet-triplet splittings.

# Introduction

Aromatic carbon-centered  $\sigma$ -type biradicals are reaction intermediates that are involved in various biochemical<sup>1-3</sup> and chemical processes.<sup>4</sup> para-Benzynes, in particular, have drawn much attention due to their roles as the biologically-active intermediates of some enediyne anticancer drugs.<sup>5-9</sup> However, understanding of the fundamental chemical properties of para-benzynes and the factors that control their reactivity is limited. Therefore, tandem mass spectrometry (MS<sup>n</sup>) has been used in the past to generate such biradicals and related species with a chemically-inert charge site for mass spectrometric manipulation.<sup>10–13</sup> Previously studied *para*-benzynes, including the 2.5didehydropyridinium<sup>12,13</sup> cation and the 5,8-didehydroisoguinolinium cation,<sup>13</sup> showed surprisingly low reactivity. In order to explore this issue further, generation of the 5,8didehydroquinolinium cation from the 5-iodo-8-nitroquinolinium cation precursor via two collision-activated dissociation (CAD) steps was attempted in this study (Scheme 1). However, an entirely unexpected isomer was generated. The identity of this isomer, the rearrangement mechanism leading to its formation, and a comparison of its reactivity to that of the 5,8-didehydroisoquinolinium cation (generated from a different precursor) and the 5,8-didehydroquinolinium cation is described here.



Scheme 1. Attempted generation of the 5,8-didehydroquinolinium cation.

## **Results and Discussion**

#### **Biradical Reactivity**

The charged biradical generated upon two consecutive CAD events in the linear quadrupole ion trap (i.e., upon ion-trap CAD or ITCAD) from **1** (Scheme 1) yielded diagnostic product ions that demonstrated the existence of two radical sites.<sup>14,15</sup> For example, it reacted with dimethyl disulfide predominantly via abstraction of two SCH<sub>3</sub> groups and an HSCH<sub>3</sub> molecule, which is typical for related biradicals.<sup>16,17</sup> Similarly, it generated the expected reaction products upon interactions with allyl iodide and cyclohexane. However, it displayed unusually high reactivity toward all the reagents studied compared to the reactivity previously reported for the 5,8-didehydroisoquinolinium cation.<sup>13</sup> As the previous study used in-source CAD (ISCAD)

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instead of ITCAD to generate the 5,8-didehydroisoquinolinium cation, this biradical was regenerated here from the 5-iodo-8-nitroprecursor 4 (Figure 1) by using ITCAD to make comparison with the unknown biradical more reliable (6; Table 1). Indeed, the unknown biradical has reaction efficiencies of 19%, 4% and 8% for dimethyl disulfide, cyclohexane, and allyl iodide, while the 5,8-didehydroisoquinolinium cation (6) shows much lower efficiencies (1%, 0.1% and 0.2%, respectively; Table 1). This finding suggests that the unknown biradical does not have the expected structure.

In order to explore this result further, the authentic 5,8-didehydroquinolinium cation different precursors, was generated from two 5-nitro-8-iodoand 5.8diiodoquinolinium cations (2 and 3, Figure 1). Similar reactivity observed for the product ion generated from these two different precursors supports the expectation that authentic 5,8-didehydroquinolinum ion (5) had been generated in both cases (Table 1). The 5,8-didehydroquinolinium cation showed lower reactivity than the unknown biradical toward dimethyl disulfide (Figure 2) but greater reactivity than the 5,8didehydroisoquinolinium cation (6, Table 1, for the reaction mass spectra of the radicals with cyclohexane and allyl iodide, see Supporting Information). These reactivity differences suggest that the unknown biradical does not have the structure 5.



Figure 1. Four protonated biradical precursors.



Figure 2. Mass spectra measured after 1000 ms reaction with dimethyl disulfide for the biradicals generated from precursors 1 - 4 (a - d, respectively).

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Table 1. Reactions, Reaction Efficiencies and Primary Product Branching Ratios for Gas-phase Reactions of Dimethyl Disulfide, Cyclohexane and Allyl Iodide With the Biradicals Generated from 1 - 4 Upon ITCAD and their Calculated Vertical Electron Affinities (EA<sub>v</sub>) and Singlet-Triplet Splittings ( $\Delta E_{S-T}$ )

	$\overset{ }{\underset{NO_{2} H}{\overset{N_{+}}{\mapsto}}} \rightarrow ?$	$ \underset{H}{\overset{NO_2}{}} \xrightarrow{\overset{\bullet}{}} \underset{H}{\overset{\bullet}} \underset{H}{} \underset{H}{}$		$\bigcup_{NO_2}^{I} \xrightarrow{N_{H}} \xrightarrow{\bullet} \xrightarrow{\bullet} \xrightarrow{N_{H}}^{I}$
	1	2 5	3 5	4 6
EA <sub>v</sub> (eV) <sup>a</sup>		5.59	5.59	5.15
$\Delta E_{S-T}$ (kcal mol <sup>-1</sup> ) <sup>b</sup>		-3.8	-3.8	-4.8
S	SCH <sub>3</sub> abs. <sup>c</sup> <b>68%</b> 2° SCH <sub>3</sub> abs. <sup>d</sup> HSCH <sub>3</sub> abs. <b>32%</b>	SCH <sub>3</sub> abs. <b>67%</b> 2° SCH <sub>3</sub> abs HSCH <sub>3</sub> abs. <b>33%</b>	SCH <sub>3</sub> abs. <b>70%</b> 2° SCH <sub>3</sub> abs. HSCH <sub>3</sub> abs. <b>30%</b>	SCH <sub>3</sub> abs. <b>58%</b> 2° SCH <sub>3</sub> abs. HSCH <sub>3</sub> abs. <b>42%</b>
	17% URI <sup>e</sup>	92% URI	69% URI	<b>1)</b> 70% URI
	Efficiency = 19%	Efficiency = 4%	Efficiency = 8%	Efficiency = 1%

2 x H abs. Addition	60% 24%	2 x H abs. Addition	69% 21%	2 x H abs. Addition	61% 23%	2 x H abs. Addition	55% 33%
H⁻ abs.	16%	H⁻abs.	10%	H⁻ abs.	16%	H⁻abs.	12%
16% URI Efficiency =	= 4%	97% URI Efficiency =	2%	47% URI Efficiency = 1	1%	95% URI Efficiency =	0.1%
Allyl abs. 2° I abs.	73%	Allyl abs. 2° I abs.	80%	Allyl abs. 2° I abs.	81%	Allyl abs. 2° I abs.	77%
Allyl-H abs. I abs. 2° I abs.	26% 1%	Allyl-H abs. I abs. 2° I abs.	15% 5%	Allyl-H abs. I abs. 2° I abs.	13% 6%	I abs. 2° I abs.	23%
28% URI Efficiency =	= 8%	92% URI Efficiency =	4%	93% URI Efficiency = 5	5%	96% URI Efficiency =	0.2%

<sup>a</sup> All EA<sub>v</sub> values were calculated at the CASPT2/CASSCF(13,12)/cc-pVTZ//CASSCF(12,12)/cc-pVTZ level of theory. <sup>b</sup> Alt 3-7 splittings were calculated at the CASPT2/CASSCF(12,12)/cc-pVTZ/level of theory. Corrected for zero-point vibrational energy differences at 298K by using the UB3LYP/cc-pVTZ frequencies. <sup>c</sup> abs. = abstraction. <sup>d</sup> 2<sup>°</sup> indicates a secondary product and it is listed after the primary product that generated it. <sup>e</sup> URI = unreactive isomer; the CAD processes used to generate these biradicals also yield isomeric enediynes that are unreactive (ref. 13b).

In order to conclusively demonstrate that the unknown biradical does not have structure **5**, the product formed upon abstraction of two SCH<sub>3</sub> groups from dimethyl disulfide was isolated and subjected to ITCAD. The fragmentation behavior was compared to that of the authentic 5,8-dithiomethylquinolinium ion (m/z 222) generated from a synthesized precursor. The fragmentation patterns were found to be distinctly different (Figure 3). This finding unambiguously demonstrates that the unknown biradical does not have structure **5**.



**Figure 3.** ITCAD mass spectra obtained using the same collision energy (20, arbitrary units) for (a) the product ion of m/z 222 formed upon abstraction of two SCH<sub>3</sub> groups from dimethyl disulfide by the biradical generated from 1 and (b) the authentic 5,8-dithiomethylquinolinium cation.

Besides ITCAD, ISCAD was also used to generate the unknown biradical of interest. ISCAD takes place in the medium pressure free-jet expansion region immediately after the MS orifice. In ISCAD, ions are accelerated by an electric field, collide with neutral molecules present (mostly from air), and fragment.<sup>18</sup> This method differs from ITCAD in three important ways. First, the collision gas molecules are larger (mostly molecules from air) for ISCAD than the helium atoms in ITCAD, which results in greater internal energies deposited into the ions upon ISCAD. Second, the ion kinetic energies are greater upon ISCAD than in ITCAD, which again results in greater excitation. For example, earlier studies on para-benzynes and enediynes in the gas phase suggested that ISCAD can be used to homolytically cleave both C-I and C-NO<sub>2</sub> bonds nearly simultaneously,<sup>19</sup> which is not the case for ITCAD. Third, ion activation in ISCAD only involves a few activating collisions while ions undergo a very large number of collisions upon CAD ion traps, each collision depositing only a small amount of internal energy into the ions, until the activation threshold has been reached. This process often leads to rearrangement reactions.<sup>13b</sup> Therefore, ISCAD was used in this study to test whether the formation of the highly reactive, unknown biradical requires several activation steps as in ITCAD or whether it can be generated in just a few steps by using ISCAD. The biradical generated by ISCAD was found to have low reactivity toward dimethyl disulfide, as expected if it had a *para*-benzyne structure (Figure 4). Furthermore, its reaction efficiency was similar to that of **5** (7%; 6% measured for the authentic biradical; Table 1). Similar observations were made for cyclohexane and allyl iodide reagents (see Supporting Information). These findings suggest that a nearly simultaneous cleavage of both C-I and C-NO<sub>2</sub> bonds upon ISCAD of **1** generates the 5,8-didehydroquinolinium cation (**5**) while the several consecutive activation steps utilized in ITCAD yield a rearranged product.



Figure 4. Reaction product mass spectra measured for the unknown biradical generated from 1 by using (a) ITCAD and (b) ISCAD after 1000 ms reaction with dimethyl disulfide.

These results suggest that the formation of the unknown biradical takes place after the first ITCAD event that generates the 8-dehydro-5-iodoquinolinium cation (9) from 1 (Scheme 1). To explore whether 9 is the only precursor which generates this reactive biradical, another monoradical, the 5-dehydro-8-nitroquinolinium cation (10) that was also generated upon the first ITCAD event on precursor 1 (Figure 5a), was isolated and subjected to a second ITCAD to cleave off the nitro group. The reactivity of the so generated biradical toward dimethyl disulfide was found to be similar to that measured for 5 (efficiencies 5% and 6%, respectively) and much lower than that of the unknown biradical (efficiency 19%) generated from 9 (upon elimination of an iodine atom; Figure 6), suggesting that it is the 5,8-didehydroquinolinium cation (5). Interestingly, when precursor 2 (8-iodo-4-nitroquinolinium cation) was employed to generate the biradical in yet a different way, by cleavage of a nitro group from 5-nitro-8-dehydroquinolinium cation could not be generated.



Figure 5. ITCAD mass spectra obtained using the same collision energy (40 arbitrary units) for (a) 1 and (b) 2 (ions of m/z 301). Note that 9 has a higher relative abundance than 10 in (a) because the C-NO<sub>2</sub> bond is easier to break than the C-I bond in a cation.



**Figure 6.** The product ion mass spectra measured for (a) the unknown reactive biradical generated from **9** upon ITCAD and (b) the biradical generated from **10** upon ITCAD, both after reactions with dimethyl disulfide for 1000 ms.

Based on these findings, monoradical cation **9** is the only precursor for the highly reactive, unknown biradical. This may be rationalized by the vicinity of the radical site at C-8 and the protonated nitrogen atom. The reaction mechanism proposed for the formation of the unknown biradical involves a hydrogen atom shift from the protonated nitrogen atom to C-8 in **9** to form the 5-iodoquinoline radical cation upon the second ITCAD event (Scheme 2). After this rearrangement, the iodine atom is lost to generate biradical **7** (Scheme 2).



Scheme 2. Proposed mechanism for the formation of 7 from 1 upon ITCAD.

The proposed isomerization pathway was supported by quantum chemical calculations at the M06-2X/6-311G(d,p) level of theory. The activation enthalpy for the rearrangement via hydrogen atom transfer (Scheme 2) was calculated to be 54.4 kcal mol<sup>-1</sup>, 7.4 kcal mol<sup>-1</sup> lower than the calculated C-I bond dissociation enthalpy. A similar rearrangement cannot occur for **2** because the iodine atom is not cleaved upon the first ITCAD event (Figure 5). On the other hand, the calculated enthalpy changes for homolytic C-I bond cleavages in **3** (Scheme 3) suggest that the first bond cleavage occurs at C-5, not at C-8. Therefore, **9** is not generated and rearrangement does not take place.



Scheme 3. Calculated (M06-2X/6-311G(d,p)) enthalpy changes for two possible iodine atom loss reactions from 3 to generate 5. All values are in kcal mol<sup>-1</sup> and are relative to the protonated radical precursor.

In order to provide more support for the above reaction mechanism, authentic 5dehydroquinoline radical cation (7) was generated (Scheme 4) and its reactivity explored. Comparison of its reactivity to that of the biradical generated from 1 reveals





great similarities (Table 2). In fact, the only significant difference between the reactivity of the unknown biradical and 7 is the observation of 16 - 28% of an unreactive isomer for the unknown biradical but not for 7. The unreactive isomer is likely formed upon ring-opening followed by iodine atom loss upon ITCAD of 9, as shown in Scheme 5 for precursor 11 (and previously reported for the isoquinolinium analog<sup>20</sup>). This is not surprising since there is only a relatively small energy difference (7.4 kcal mol<sup>-1</sup>) between the activation enthalpy for rearrangement (Scheme 2) and the C-I bond dissociation enthalpy for 9, and the energy difference between the activation enthalpy for the ring-opening and the rearrangement should be even smaller (for the isoquinolinium system, the activation enthalpy for ring opening and the C-I bond dissociation enthalpy have been calculated<sup>20</sup> to be 56.8 and 62.2 kcal/mol, respectively).



Scheme 5. Two competing reaction pathways after the first ITCAD event of 3. Top: ring-opening followed by iodine atom loss; bottom: *para*-benzyne (5) formation. Note that the same applies to generation of biradical 6 (ref. 20).



Figure 7. ITCAD mass spectra for the product ion of m/z of 222 generated upon abstraction of two SCH<sub>3</sub> groups from dimethyl disulfide by (a) the unknown biradical generated from 1 and (b) biradical 7.

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Table 2. Reactions, Reaction Efficiencies, and Primary Product Branching Ratios for Gas-Phase Reactions With Dimethyl Disulfide, Cyclohexane and Allyl Iodide for the Unknown Biradical Generated from 1 and for Biradicals 7 and 8 and Their Calculated Vertical Electron Affinities (EA<sub>v</sub>) and Singlet-Triplet Splittings ( $\Delta E_{S-T}$ )

	$\downarrow \\ NO_2 {_{H}} \rightarrow ?$	• • • • • • • •	8
$EA_v$ (eV) $\Delta E_{S-T}$ (kcal mol <sup>-1</sup> )		7.40 <sup>a</sup> -20.3 <sup>c</sup>	8.40 <sup>b</sup>
S S	SCH <sub>3</sub> abs 68% 2° SCH <sub>3</sub> abs HSCH <sub>3</sub> abs 32% 17% URI	$\begin{array}{ccc} SCH_3 \ abs & \mathbf{66\%} \\ 2^\circ SCH_3 \ abs \\ HSCH_3 \ abs & \mathbf{34\%} \end{array}$	e abs 53% H abs 30% SCH <sub>3</sub> abs 17%
	Efficiency = $19\%$ 2 x H abs 60% Addition 24%	Efficiency = $21\%$ 2 x H abs 63% Addition 26%	Efficiency = 28% H abs 100%
	H <sup>-</sup> abs $16\%$ 16% URI	Heation $20\%$ H <sup>-</sup> abs $11\%$	Efficiency - 20/
	Allyl abs $73\%$	Allyl abs $80\%$	Efficiency = $3\%$ I abs 97%
	Allyl-H abs 26% I abs 1% 2° I abs	Allyl-H abs 19% I abs 1% 2° I abs	
	28% URI Efficiency = 8%	Efficiency = 7%	Efficiency = 19%

<sup>&</sup>lt;sup>a</sup> Calculated at the CASPT2/CASSCF(13,12)/cc-pVTZ//CASSCF(12,12)/cc-pVTZ level of theory<sup>.</sup> <sup>b</sup> Calculated at the CASPT2/CASSCF(12,11)/cc-pVTZ//CASSCF(11,11)/cc-pVTZ level of theory. <sup>c</sup> Calculated at the CASPT2/CASSCF(12,12)/cc-pVTZ//CASSCF(12,12)/cc-pVTZ level of theory. Corrected for zero-point vibrational energy differences at 298K by using the UB3LYP/cc-pVTZ frequencies.

Further, the product ion of m/z 222 formed upon abstraction of two SCH<sub>3</sub> groups from dimethyl disulfide by 7 was subjected to ITCAD and the fragmentation behavior was compared to that of the ion of m/z 222 produced from the unknown biradical generated from 1. The fragmentation patterns are similar enough to conclude that the same ion, biradical 7, produced both of them. This finding conclusively identifies the unknown biradical as 7.

The reactivity of the quinoline radical cation (8) was also studied (Table 2). Its reactivity is distinctly different from that of 7. For example, while 7 predominantly abstracts an allyl group from allyl iodide, 8 predominantly abstracts an iodine atom. This finding, as well as the similarity of the reactivity of 7 to that of the two *para*-benzynes discussed above, suggests that the reactions of 7 are initiated by the radical site at C-5 rather than the nitrogen-radical cation site.

The different reactivities of **5**, **6** and **7** are next considered. Based on previous studies, the extent of spin-spin coupling of the unpaired electrons either through-bond, through-space, or a combination of the two, is a major factor that controls the reactivity of most singlet biradicals, such as the ones described here. The extent of spin-spin coupling is reflected by the magnitude of the singlet-triplet (S-T) splitting of the biradical, which is defined as the energy difference between the lowest-energy triplet (excited) electronic state and the singlet (ground) electronic state.<sup>10,21–23</sup> The greater the (calculated) S-T splitting, the lower the reactivity of the singlet biradical. Another important reactivity-controlling factor is the ability of the biradical to polarize the transition state of its reactions, or polar effects, quantified here using the calculated vertical electron affinity (EA<sub>v</sub>) of the radical sites.<sup>24–26</sup> The greater the EA<sub>v</sub>, the more electrophilic the biradical site, and the more reactive the biradical.<sup>13</sup>

All of the EA<sub>v</sub>s and S-T splittings calculated for the biradicals studied here are listed in Tables 1 and 2. While biradicals **5** and **6** have similar S-T splittings (-3.8 kcal mol<sup>-1</sup> vs. –4.8 kcal mol<sup>-1</sup>), the greater EA<sub>v</sub> of **5** (5.59 eV compared to 5.15 eV for **6**) is mainly responsible for the greater reactivity of this biradical. As for biradical **7**, relatively strong spin-spin coupling between the unpaired electrons on the nitrogen atom and on C-5 contributes to the large S-T splitting of this biradical (-20.3 kcal mol<sup>-1</sup>), which hinders radical reactivity. However, this biradical has a very high EA<sub>v</sub> (7.40 eV), which makes it more reactive than the *para*-benzynes **5** and **6**. This is a particularly remarkable example demonstrating that the more important reactivity-controlling factor for biradicals with a 1,4-topology is the vertical electron affinity rather than the S-T splitting, in agreement with previous studies.<sup>13</sup>

#### Conclusions

An unexpected, highly reactive biradical, the 5-dehydroquinoline radical cation, was generated in the gas phase via hydrogen atom transfer in the 8-dehydro-5-

iodoquinolinium cation upon ITCAD followed by a cleavage of the iodine atom in a linear quadrupole ion trap mass spectrometer. The hydrogen atom transfer was found to have a lower activation enthalpy than the homolytic bond dissociation enthalpy of the iodine atom, which explains the formation of the 5-dehydroquinoline radical cation instead of the 5,8-didehydroquinolinium cation. The 5-dehydroquinoline radical cation showed greater reactivity toward the organic reagents studied than two isomeric *para*-benzynes, the 5,8-didehydroquinolinium and –isoquinolinium cations, of which the quinoline-based *para*-benzyne is more reactive. This reactivity ordering is rationalized solely by the vertical electron affinities of the radical sites in these biradicals (EA<sub>v</sub>; 7.40 eV, 5.59, and 5.15 eV, respectively). This finding supports the previous proposal that polar effects predominantly control the reactivities of biradicals with a 1,4-topology,<sup>13</sup> even when they have substantially different singlet-triplet splittings (-20.3 kcal mol<sup>-1</sup>).

#### **Experimental section**

#### **Materials**

The biradical precursors, 5-iodo-8-nitroquinoline, 8-iodo-5-nitroquinoline, 5,8diiodoquinoline, and 5-iodo-8-nitroisoquinoline, as well as 5-iodoquinoline and 8iodoquinoline used to generate monoradicals were synthesized via a Sandmeyer reaction followed by a nitration reaction<sup>27</sup> from 5-aminoquinoline, 8-aminoquinoline and 5-aminoisoquinoline, respectively. The starting materials were purchased from Sigma-Aldrich (St. Louis, MO) and used as received. The model compound 5,8dithiomethylquinoline was synthesized from 2,5-dibromoaniline via Skraup quinoline synthesis followed by an aromatic nucleophilic substitution reaction<sup>28,29</sup> (see Supporting Information for detailed synthetic procedures). The reagents, dimethyl disulfide, allyl iodide and cyclohexane, were purchased from Sigma-Aldrich and used as received.

#### Experiments

All of the gas-phase reactions were studied in a Thermo LTQ linear quadrupole ion trap mass spectrometer (LQIT-MS) coupled with a home-built reagent mixing manifold for reagent introduction. All biradical precursors were dissolved in methanol, injected into the mass spectrometer, and protonated via atmospheric pressure chemical ionization (APCI). Protonated biradicals were generated either by two consecutive collision-activated dissociation (CAD) events in the ion trap (ITCAD, collision energy ranging from 30 to 50, arbitrary units; the monoradical formed in the first ITCAD event was isolated before activating it in the second ITCAD event) and/or in-source CAD (ISCAD, collision energy 60 V), which resulted in homolytic cleavages of the C-I and C-NO<sub>2</sub> bonds. The protonated biradicals were then isolated and allowed to react with dimethyl

disulfide, allyl iodide or cyclohexane in the ion trap for variable reaction times<sup>13</sup> up to 10000 ms. The monoradical precursors 5-iodoquinoline and quinoline were dissolved in  $CS_2$  and ionized via APCI to generate their molecular ions. The 5-iodoquinoline molecular ion was subjected to ITCAD to generate the 5-dehydroquinoline radical cation. The reactivities of the radical cations were studied toward dimethyl disulfide, allyl iodide, and cyclohexane as described above.

Pseudo-first order reaction rate plots were used to determine the reaction efficiencies (defined as the fraction of collisions that lead to reaction) given as  $k_{exp}/k_{coll}$ , where  $k_{exp}$  is the experimentally measured rate constant and  $k_{coll}$  is the collision rate constant calculated using a parameterized trajectory theory.<sup>30</sup> The rate plots were examined carefully, including the fit of the decay of the reactant ion to a single exponential, to rule out the presence of mixtures of isomeric reactive ions. Branching ratios for primary products were also determined. Many of the observed ionic reaction products were isolated and subjected to further ITCAD to obtain structural information.

#### **Computational Methods**

Molecular geometries for all species were optimized at the multiconfigurational selfconsistent field (MCSCF) and density functional (DFT) levels of theory by using either the correlation-consistent polarized valence-triple- $\zeta$  (cc-pVTZ) basis set<sup>31</sup> or the 6-311G(d,p) basis set.<sup>32</sup> The latter basis set was used for calculations in which the chemical species contained at least one iodine atom. The MCSCF calculations were of the complete active space (CASSCF) variety<sup>33</sup> and included (in the active space) the full  $\pi$ -space for each molecule and, for each of the mono- and biradicals, the nonbonding  $\sigma$  orbital(s). The DFT calculations used either (1) the gradient-corrected exchange functional of Becke,<sup>34</sup> which was combined with the gradient-corrected correlation functional of Lee, Yang and Parr<sup>35</sup> (B3LYP), or (2) the M06-2X functional.<sup>36</sup> All DFT geometries were verified to be local minima by computation of analytic vibrational frequencies, and these (unscaled) frequencies were used to compute zeropoint vibrational energies (ZPVE) and 298 K thermal contributions  $(H_{298} - E_0)$  for all DFT calculations for the mono- and biradicals employed an unrestricted species. formalism.

To improve the molecular orbital calculations, dynamic electron correlation was also accounted for by using multi-reference second-order perturbation theory<sup>37,38</sup> (CASPT2) for multi-configurational self-consistent field (MCSCF) reference wave functions; these calculations were carried out for the MCSCF optimized geometries. Some caution must be applied in interpreting the CASPT2 results since this level of theory is known to suffer from a systematic error proportional to the number of unpaired electrons.<sup>39</sup> Thus, the electronic energies are of the CASPT2/CASSCF(m,n)/ccpVTZ//CASSCF(m,n)/cc-pVTZ variety (where m is the number of active electrons and n is the number of active orbitals), and estimates of the thermodynamic quantities,  $E_0$ and H<sub>298</sub>, are derived by adding to these electronic energies ZPVE and the sum of ZPVE and  $(H_{298} - E_0)$ , respectively, where the latter are derived from the DFT (B3LYP) calculations.

In order to compute vertical electron affinities (EA<sub>v</sub>) for the mono- and biradicals, single-point calculations (CASPT2/CASSCF(m,n)/cc-pVTZ), using the CASSCF(m,n)/cc-pVTZ optimized geometry for each radical, were also carried out for the states that are produced when a single electron is added to the nonbonding  $\sigma$  orbital (or one of the two such orbitals) of each molecule.<sup>40</sup> Thus, for the monoradicals, (doublet ground states) these calculations were carried out for (zwitterionic) *singlet* states, whereas for the biradicals (singlet ground states) calculations were carried out for (zwitterionic) *doublet* states.<sup>41</sup>

All CASPT2/MCSCF and DFT calculations were carried out with the MOLCAS 8.0<sup>42</sup> and Gaussian 09<sup>43</sup> electronic structure program suites, respectively.

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#### Keywords

1,4-biradicals, *para*-benzynes, aromatic, gas-phase reactions, quantum chemical calculations, reactivity

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