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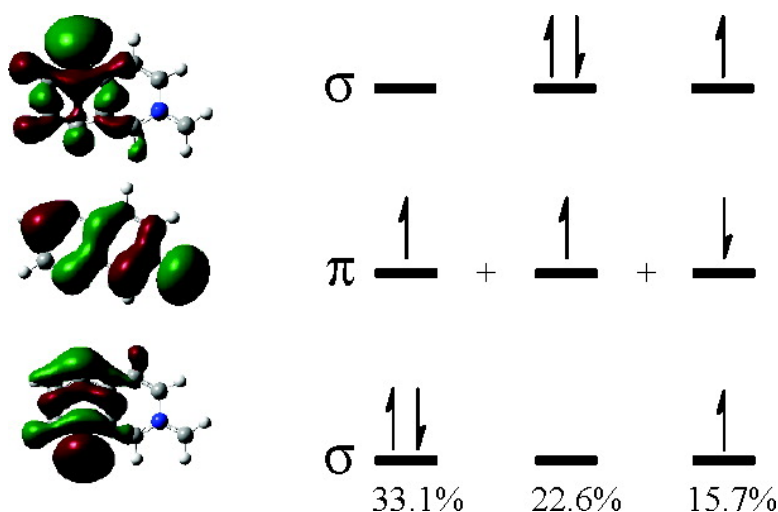
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Reactivity of the *N*-Methylene-5,8-didehydroisoquinolinium Triradical Ion

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Triradicals contain three electrons in three orbitals that are similar in energy.[1] As a result, these species have several low-lying electronic states. This characteristic makes triradicals fascinating species to study. However, most prior studies of organic triradicals have been computational in nature because of the difficulty in studying such highly reactive species experimentally.[2–6] π,π,π-Polyarylmethyl and calixarene triradicals have been characterized via ESR, NMR, and UV–vis spectroscopy and cyclic voltammetry by Rajca and Rajca.[7–9] Magnetic field effects on the decay kinetics of π,π,π-triradicals have been examined by Hayashi and co-workers using UV–vis spectroscopy.[10] Roffia and co-workers have investigated substituted fullerene π,π,π-triradicals via ESR and cyclic voltammetry.[11] Finally, Wenthold et al. have carried out thermochemical measurements on 1,3,5-tridehydrobenzene (σ,σ,σ-triradical), 5-dehydro-1,3-quinodimethane (σ,π,π-triradical), and 1,3,5-trimethylenebenzene (π,π,π-triradical).[12–15]

The chemical properties of organic triradicals appear to be unexplored, in contrast to organic biradicals.[16–19] We report here a kinetic reactivity study on an organic triradical, the positively charged σ,σ,π-triradical *N*-methylene-5,8-didehydroisoquinolinium ion (**a**). The gas-phase reactivity of this triradical is compared to that of a related, previously unreported σ,π-biradical, *N*-methylene-5-dehydroisoquinolinium ion (**b**), and π-monoradical, *N*-methyleneisoquinolinium ion (**e**), as well as a previously studied σ,σ-biradical, *N*-methyl-5,8-didehydroisoquinolinium[20] ion (**c**), and a σ-monoradical, *N*-methyl-5-dehydroisoquinolinium ion (**d**).[17,20] The positive charge in these molecules acts merely as an electron-withdrawing substituent, as demonstrated earlier for mono- and biradicals.[17–20]

Triradical **a** was synthesized in a dual-cell Fourier transform ion cyclotron resonance mass spectrometer[17–19] (FT-ICR) by using the procedure shown in Scheme 1. Biradical **b** was generated by transfer of $CH_2^{+\bullet}$ from the 4-dehydrobutanoyl cation to the nitrogen atom of 5-nitroisoquinoline (analogous reaction as shown in Scheme 1) followed by sustained off-resonance irradiated collision-activated dissociation[21] (SORI-CAD) to cleave the nitro group. Biradical **c** and monoradical **d** were generated by previously described methods.[17,20] Monoradical **e** was generated by transfer of $CH_2^{+\bullet}$ from the 4-dehydrobutanoyl cation to the nitrogen atom of isoquinoline. Radicals **a**–**e** were transferred into a clean cell, isolated, and allowed to react with reagents for varying periods of time to determine second-order reaction rate constants (k_{exp}) and reaction efficiencies ($k_{exp}/k_{collision}$), as described previously.[17–20,22] The structures of the new triradical, **a**, and biradical, **b**, were confirmed using structurally diagnostic reactions described previously.[17–19]

A general comparison of the reactivity of triradical **a** and the biradicals **b** and **c** (Table 1) reveals a somewhat surprising result: the triradical is not more reactive than the biradicals despite its three radical sites. In fact, the triradical is substantially *less reactive*

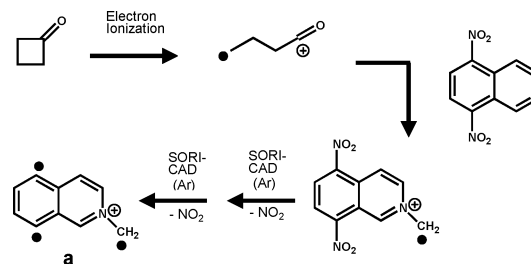† Current address: Kos Pharmaceuticals, Inc., 1 Cedar Brook Drive, Cranbury, NJ 08512.

Scheme 1

Table 1. Reaction Efficiencies[a] and Product Branching Ratios[b]

	allyl iodide	THF	N C (tert-butyl isocyanide)	S–S (dimethyl disulfide)
a	No reaction	No reaction	HCN abs 1.00 (2°) CN abs (2°) $CH_2^{+\bullet}$ trans Eff= 41%	SCH3 abs 0.87 (2°) SCH3 abs H abs 0.04 2H abs 0.09 Eff=14%
b	I abs 1.00 Eff=24%	H abs 0.73 2xH abs 0.27 Eff=9%	CN abs 0.51 (2°)$CH_2^{+\bullet}$ trans HCN abs 0.49 Eff=71%	SCH3 abs 1.00 Eff=19%
c	I abs 0.83 Adduct 0.17 Eff=0.3%	No reaction	CN abs 0.15 (2°) CN abs HCN abs 0.85 (2°) HCN abs (2°) Addition Eff=40%	SCH3 abs 1.00 (2°) SCH3 abs Eff=6%
d	I abs 0.98 Allyl abs 0.02 Eff=29%	H abs 1.00 Eff=7%	CN abs 1.00 Eff=67%	SCH3 abs 1.00 Eff=26%
e	I abs 0.67 Allyl abs 0.33 Eff=0.16%	H abs 1.00 Eff=very slow	HCN abs 0.68 (2°) Adduct (2°) m/z 185[c] $CH_2^{+\bullet}$ trans 0.32 Eff=2%	No reaction

[a] Reaction efficiencies (Eff) are reported as $k_{reaction}/k_{collision} \times 100\%$. [b] abs = abstraction, tran = transfer; secondary products are noted as (2°) and are listed under the primary product that produces them. [c] Unknown secondary product.

than the σ,π-biradical **b**. However, it displays reactivity similar to that of the σ,σ-biradical **c**. For example, the triradical is unreactive toward tetrahydrofuran (THF), just like **c**, and reacts with *tert*-butyl isocyanide at the same efficiency as **c**. On the other hand, **b** reacts with THF, *tert*-butyl isocyanide, and allyl iodide at a higher efficiency than **a** and **c**. To rationalize these observations, the reactivity of related monoradicals was also examined.

A comparison of the reactivity of the σ- and π-monoradicals **d** and **e** provides information on the characteristic reactivity of each radical type (Table 1). The π-radical site is clearly the less reactive moiety (due to spin delocalization), as evidenced by very low efficiencies measured for **e** in reactions with THF, *tert*-butyl isocyanide, and allyl iodide, and the lack of reactivity toward dimethyl disulfide. The analogous σ-monoradical **d** is substantially more reactive. This radical undergoes H-atom abstraction from THF, CN-abstraction from *tert*-butyl isocyanide, and I-atom abstraction from allyl iodide at drastically greater efficiencies, and it also abstracts CH_3S from dimethyl disulfide at a high efficiency.

When the σ- and π-radical moieties are present in the same molecule, the reactivity is dominated by the σ-radical site, as revealed by the reactivity of the σ,π-biradical **b**. Biradical **b** reacts at a similar efficiency as the σ-monoradical **d** with THF (9 vs 7%), *tert*-butyl isocyanide (71 vs 67%), dimethyl disulfide (19 vs 26%), and allyl iodide (24 vs 29%). The π-radical site contributes after reactions have quenched the σ-radical site. This takes place either via reactions with the neutral radical products formed at the σ-radical site before the collision complex dissociates or via secondary reactions after dissociation of the collision complex. For example, after the σ-radical site in **b** has abstracted CN from *tert*-butyl isocyanide, the collision complex either directly dissociates to the CN-abstraction product and *tert*-butyl radical (51% of the time) or the *tert*-butyl radical reacts with the π-radical site by H-atom transfer (before dissociation) to yield isobutene and an HCN-abstraction product (49%). The CN-abstraction product still contains an unreacted π-radical site, which undergoes a secondary reaction by transfer of $CH_2^{+\bullet}$ to another *tert*-butyl isocyanide molecule. This behavior has also been observed for other charged carbon-centered radicals.[23−31] The $CH_2^{+\bullet}$ transfer reaction is facilitated by electron-withdrawing substituents in the remote phenyl ring of the radical. For example, while the π-monoradical **e** undergoes the reaction at about 1% efficiency (in competition with HCN-abstraction), the 5-nitro derivative of **e** reacts at 46% efficiency and the 5,8-dinitro derivative reacts at collision rate (100% efficiency). Similar observations were made for CH_3S-abstraction from dimethyl disulfide and I-atom abstraction from allyl iodide. The π-monoradical **e** is unreactive toward dimethyl disulfide and reacts only very slowly with allyl iodide, while the 5-nitro and 5,8-dinitro derivatives of **e** react with both reagents at substantially higher efficiencies.

In contrast to the minor influence of addition of a π-radical site (**b**) to the σ-monoradical (**d**), an additional σ-radical site in **d** has a substantial influence on its reactivity. Although the σ,σ-biradical **c** displays reactivity at both radical sites (e.g., consecutive abstraction of two I-atoms from allyl iodide and two CH_3S groups from dimethyl disulfide), it is substantially less reactive than the σ-monoradical **d**. This finding does not come as a surprise since biradical **c** is predicted to be a ground-state singlet (S−T gap = −5.0 kcal/mol; CASPT2/cc-pVDZ//MCSCF/cc-pVDZ). The (stabilizing) coupling of the formally unpaired electrons is known to hinder radical reactions.[17−20,32] Hence, the greater reactivity of the σ,π-biradical **b** compared to that of **c** is explained by the smaller S−T gap of **b** (−1.4 kcal/mol).

The σ,σ,π-triradical **a** is calculated to have a doublet ground state ($^2A''$; Figure 1) and a doublet-quartet gap of −4.5 kcal/mol. The triradical contains two weakly interacting orthogonal radical systems—σ,σ-biradical and π-monoradical moieties. Neither one of these moieties is highly reactive; however, a comparison of the reactivities of the σ,σ-biradical **c** and the π-radical **e** (Table 1) suggests that **c** is generally the more reactive of the two. Hence, it is not surprising that the reactivity of the σ,σ,π-triradical **a** closely
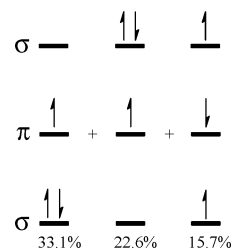
Figure 1. Principal ground-state electron configurations for triradical **a** (CASPT2/cc-pVDZ//MCSCF/cc-pVDZ level of theory).

resembles that of the σ,σ-biradical **c**, as mentioned above. The π-radical site in triradical **a** reacts only after reactions have taken place at the more reactive σ-radical sites, just like for the σ,π-biradical **b**. For example, the HCN-abstraction product of **a** (as the CN-abstraction product of **b**) transfers $CH_2^{+\bullet}$ to *tert*-butyl isocyanide (Table 1). In conclusion, addition of a π-radical site to the σ,σ-biradical **c** or a σ-radical site to the σ,π-biradical **b** does not enhance their reactivity.

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