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Effects of a Hydroxyl Substituent on the Reactivity of the 2,4,6-Tridehydropyridinium Cation, an Aromatic σ,σ,σ -Triradical

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Abstract: The reactivity of 3-hydroxy-2,4,6-tridehydropyridinium cation was found to be drastically different from the reactivity of 2,4,6-tridehydropyridinium cation. While the latter triradical reacts with tetrahydrofuran, dimethyl disulfide and allyl iodide via three consecutive atom or group abstractions, the former triradical exhibits this be-

havior only with tetrahydrofuran. Only a single atom or group abstraction was observed for the 3-hydroxy-2,4,6-tridehydropyridinium cation upon interac-

tion with dimethyl disulfide and allyl iodide. This change in reactivity is caused by the hydroxyl group that strengthens the interactions between the two radical sites adjacent to it, thus reducing their reactivity. This explanation is supported by the observation of similar behavior for related biradicals.

Keywords: FT-ICR • ion–molecule reactions • reactivity • substituent effects • triradicals

Introduction

Aromatic carbon-centered σ,σ,σ -triradicals, reactive intermediates with three formally unpaired electrons, have been the subject of several theoretical studies.^[1–8] However, experimental studies are hindered by the highly reactive nature of these species in solution. Thermochemical measurements on 1,3,5-tridehydrobenzene by Wenthold and co-workers^[9] and matrix isolation and IR detection of 1,2,3-tridehydrobenzene and perfluoro-1,3,5-tridehydrobenzene by Sander and co-workers are among the few experimental studies reported for tridehydroarenes.^[10,11] The first reactivity studies on aromatic carbon-centered σ,σ,σ -triradicals, the 2,4,6-tridehydropyridinium (**7**) and 3,4,5-tridehydropyridinium ions, were reported recently.^[12,13] These triradicals were studied in the gas phase in a Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR). They were found to be highly reactive, but each radical site is not equally reactive. For example, the chemical properties of **7** suggest that this triradical is best described as a *meta*-benzyne of relatively low reactivity with a highly reactive radical site (resonance structure **9** in Figure 1) since its reactivity resembles more closely that of related monoradicals than related biradicals. On the other hand, the reactivity of the isomeric 3,4,5-tridehydro-

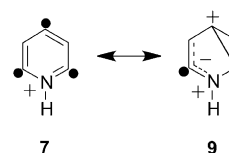


Figure 1. Resonance structures of 2,4,6-tridehydropyridinium ion **7**.

pyridinium cation suggests that this triradical is best described as a highly reactive *ortho*-benzyne with a radical site. Theoretical^[6] and experimental studies^[12,13] suggest that the reactivity of positively charged tridehydroarenes may be at least partially controlled by the coupling between the individual radical sites. Other reactivity controlling parameters have not been reported. While substituent effects have been found to play a major role in controlling the reactivity of aromatic carbon-centered σ,σ -biradicals,^[14] almost nothing is known about substituent effects on triradicals. The only experimental study known to us on a substituted aromatic carbon-centered σ,σ,σ -triradical is that of Sander and co-workers on the detection of the perfluoro-1,3,5-tridehydrobenzene by IR spectroscopy. Their computational results suggest that the ground electronic state of this triradical is not affected by substitution of the three hydrogen atoms with three fluorine atoms.^[10] In contrast, recent computational studies by Nash et al.^[6] suggest that incorporation of an NH^+ group into the aromatic ring of tridehydrobenzenes may affect both the electronic ground state and the doublet-quartet splitting of these species. These effects depend on the position of the NH^+ group with respect to the three radical sites.

In order to gain insights into substituent effects on the chemical properties of triradicals, we have carried out a reactivity study on a substituted carbon-centered aromatic σ,σ,σ -triradical, the 3-hydroxy-2,4,6-tridehydropyridinium

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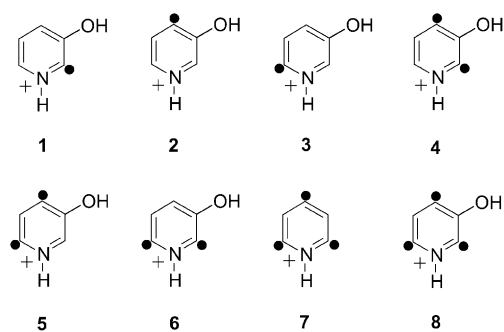


Figure 2. Studied radicals.

cation (**8**) (Figure 2). The gas-phase reactions of this triradical are compared to those of the previously reported 2,4,6-tridehydropyridinium cation (**7**), three related and previously unreported σ,σ -biradicals, 3-hydroxy-2,4-didehydropyridinium cation (**4**), 5-hydroxy-2,4-didehydropyridinium cation (**5**) and 3-hydroxy-2,6-didehydropyridinium cation (**6**), and three previously reported σ -monoradicals,^[15] 3-hydroxy-2-dehydropyridinium cation (**1**), 3-hydroxy-4-dehydropyridinium cation (**2**) and 5-hydroxy-2-dehydropyridinium cation (**3**) (Figure 2).

Results and Discussion

The hydroxyl-substituted triradical **8** (calculated to have a doublet electronic ground state; D–Q gap: $-39.2 \text{ kcal mol}^{-1}$; RHF-UCCSD(T)/cc-pVTZ//UBW91/cc-pVDZ) was found to behave drastically differently from its unsubstituted analog, triradical **7** (Table 1). While **7** reacts^[12] by three consecutive atom or group abstractions with several reagents, such as tetrahydrofuran (H-atom abstractions), allyl iodide (I-atom abstractions), and dimethyl disulfide (SCH_3 abstractions), **8** undergoes only one such reaction with all these reagents, with the exception of tetrahydrofuran. This reactivity most closely resembles that observed for related monoradicals,^[17] including the hydroxyl-substituted monoradicals **1**, **2**, and **3**.^[15] The only observation indicating the presence of more than one radical site in **8** is the abstraction of three hydrogen atoms from tetrahydrofuran (THF). To rationalize these findings, the reactivities of **1–8** are discussed in detail below.





The reactivity of the hydroxyl-substituted monoradicals (**1**, **2**, and **3**) is straightforward. They rapidly abstract a H atom from THF, HCN and CN groups from *tert*-butyl isocyanide, an I atom from allyl iodide and a SCH_3 group from dimethyl disulfide, as expected (Table 1).^[17] All these reactions have been reported for related monoradicals with no hydroxyl substituent.^[12,13] Monoradical **1** is slightly more reactive than **2** and **3** toward allyl iodide, and reacts with similar efficiencies with dimethyl disulfide and *tert*-butyl isocyanide (Table 1). This behavior can be rationalized by the electrophilic nature of these monoradicals. For electrophilic monoradicals, an increase in the electron affinity (EA) at the radical site leads to more polar, and hence lower-energy,

transition states, thus enhancing their reactivity.^[18] Therefore, the greater vertical electron affinity^[19] (EA) calculated for the radical site of **1** (**1**: 6.97 eV; **2**: 6.28 eV; **3**: 6.54 eV; Table 1) explains its greater reactivity toward allyl iodide compared to **2** and **3**. Since the reactions of dimethyl disulfide and *tert*-butyl isocyanide occur near or at the collision rate (efficiency = 100 %), it is not surprising that significant differences were not observed for the efficiencies of the isomeric monoradicals.^[17] The finding that monoradical **2** reacts faster with tetrahydrofuran than **3**, in spite of its lower EA, is rationalized by the ability of **2** to form a stabilizing hydrogen bonding interaction between the hydroxy-substituent and THF in the transition state for H-atom abstraction. This ability has been earlier demonstrated to facilitate radicals' H-atom abstraction rates from THF.^[20] On the other hand, **1** is expected to react faster than **2** and **3** due to its greater EA and the ability to form a stabilizing hydrogen bond (either involving the NH proton or the OH proton) in the transition state. However, for yet an unknown reason, **1** reacts slower than **2** or **3**.

The hydroxyl-substituted singlet biradical **5** undergoes mostly the same reactions as the monoradicals discussed above, together with some additional reactions (Table 1). For example, it abstracts two H atoms from a THF molecule (as well as hydride and CH_2O , along with some other minor pathways), two iodine atoms (as well as an allyl group) from allyl iodide molecules and two SCH_3 groups (as well as CH_3SS) from dimethyl disulfide molecules.^[14,20,23] However, compared to the hydroxyl-substituted monoradicals, biradical **5** is generally less reactive. Theoretical and experimental studies on aromatic σ,σ -biradicals with singlet ground states suggest that their reactivities are affected by their S–T gaps, EAs, and also, in the case of *meta*-benzynes, dehydrocarbon atom separations.^[14,21–23] The lower reactivity of **5**, when compared to the monoradicals, can be understood based on the relatively strong coupling between the radical sites in **5** (reflected by a large S–T gap; Table 1). This stabilizing interaction is partially lost in the transition states of radical reactions, which hinders these reactions.^[21] When the reactivity of **5** is compared to that of the analogous unsubstituted biradical (the 2,4-didehydropyridinium cation), which has the same S–T gap but a greater EA (6.46 eV vs. 5.74 eV for **5**), **5** is found to react faster with all reagents except THF.^[12] The greater reactivity of **5** can be explained by its greater dehydrocarbon atom separation (1.99 Å vs. 1.50 Å for the unsubstituted analog; UBLYP/cc-pVDZ//UBLYP/cc-pVDZ), which has been shown previously to have an effect on the reactivity of *meta*-benzyne type biradicals.^[14] A greater dehydrocarbon atom separation was observed to lead to greater radical-type reactivity.

In contrast to biradical **5**, the isomeric biradical **4** (EA = 6.43 eV; Table 1), with the hydroxyl-substituent between the two radical sites, is unreactive toward THF, allyl iodide and dimethyl disulfide, and reacts at a substantially lower efficiency with *tert*-butyl isocyanide. This biradical has a much greater EA than **5** (6.43 eV vs. 5.74 eV; Table 1), but also a significantly larger S–T gap (-35.8 vs. $-19.9 \text{ kcal mol}^{-1}$;

Table 1. Reaction efficiencies^[a] and product branching ratios for reactions^[b] of radicals **1–5**, **7**, and **8** with various reagents, and relevant S–T or D–Q gaps and EAs.^[c]

	1		2		3		4		5		7		8		
Gap ^[d]	–		–		–		–35.8		–19.9		–30.9		–39.2		
EA ^[e]	6.97		6.28		6.54		6.43 ^[f]		5.74		7.01		6.86		
	H abs	95 %	H abs	100 %	H abs	100 %	n.r.		2 H abs	28 %	H ⁺ trns	39 %	H abs	86 %	
	H ⁺ trns	5 %							H [–] abs	24 %	2 H abs	25 %	2 H abs	14 %	
									CH ₂ O abs	10 %	2°H abs		2°H abs		
									H ₂ O abs	8 %	2°CH ₂ abs				
									C ₂ H ₄ O abs	8 %	2°C ₂ H ₃ abs				
									H ⁺ trns	8 %	H [–] abs	17 %			
									C ₃ H ₃ abs	7 %	H ₂ O abs	16 %			
									C ₃ H ₃ abs	4 %	2°H abs				
									C ₄ H ₄ abs	2 %	H abs	3 %			
									C ₃ H ₅ O abs	1 %					
	eff = 59 %		eff = 81 %		eff = 68 %		eff = 0 %		eff = 28 % ^[g]		eff = 74 %		eff = 41 %		
	I abs	89 %	I abs	92 %	I abs	85 %	n.r.		I abs	54 %	I abs	76 %	I abs	91 %	
	C ₃ H ₅ abs	11 %	C ₃ H ₅ abs	7 %	C ₃ H ₅ abs	13 %			2°H abs		2°C ₃ H ₅ abs		C ₃ H ₅ abs	9 %	
			H abs	1 %	H abs	2 %			2°C ₃ H ₅ abs		2°C ₃ H ₅ abs				
									2°I abs		3°I abs				
									C ₃ H ₅ abs	29 %	2°I abs				
									2°C ₃ H ₅ abs		3°C ₃ H ₅ abs				
									2°I abs		3°I abs				
									CH + I abs	8 %	CH ₂ abs	13 %			
									2°C ₃ H ₅ abs		C ₃ H ₅ abs	6 %			
									C ₃ H ₄ abs	7 %	C ₃ H ₄ abs	5 %			
	eff = 94 %		eff = 65 %		eff = 75 %		eff = 0 %		eff = 37 % ^[h]		eff = 58 %		eff = 69 %		
	SCH ₃ abs	100 %	SCH ₃ abs	100 %	SCH ₃ abs	99 %	n.r.		SCH ₃ abs	73 %	SCH ₃ abs	100 %	SCH ₃ abs	72 %	
					SSCH ₃ abs	1 %			2°SCH ₃ abs		2°SCH ₃ abs		e [–] trns	28 %	
									SSCH ₃ abs	22 %	3°SCH ₃ abs				
									2°SCH ₃ abs		2°HSCH ₃ abs				
									SCH ₂ abs	3 %	2°SSCH ₃ abs				
									HSCH ₃ abs	2 %					
		eff = 89 %		eff = 85 %		eff = 90 %		eff = 0 %		eff = 67 % ^[i]		eff = 72 %		eff = 85 %	
	CN abs	68 %	CN abs	52 %	CN abs	83 %	HCN abs	80 %	CN [–] abs	61 %	CN [–] abs	95 %			
	2°C ₄ H ₈ abs		HCN abs	48 %	2°C ₄ H ₈ abs		2°HCN abs		HCN abs	39 %	HCN abs	5 %	CN [–] abs	89 %	
	H ⁺ trns	17 %	2°HCN abs		H ⁺ trns	12 %	2°C ₄ H ₈ abs		2°C ₄ H ₈ abs				HCN abs	6 %	
	HCN abs	15 %	2°C ₄ H ₈ abs		HCN abs	5 %	2°add						CN abs	5 %	
	2°C ₄ H ₈ abs		2°add		2°C ₄ H ₈ abs		CN [–] abs	20 %							
	eff = 98 %	eff = 97 %	eff = 100 %		eff = 33 %		eff = 97 %		eff = 98 %		eff = 85 %				







[a] Reaction efficiency = $k_{\text{reaction}}/k_{\text{collision}} \times 100$ (eff = efficiency). [b] abs = abstraction, add = addition, n.r. = no reaction, trns = transfer; secondary and tertiary products are indicated as 2° and 3°, respectively, and listed under the primary/secondary products that produce them. [c] Ref. [16]. [d] S–T or D–Q gap (kcal mol^{–1}); calculated at the RHF-UCCSD(T)/cc-pVTZ//UBPW91/cc-pVDZ level of theory. [e] In eV; calculated at the UBLYP/aug-cc-pVDZ//UBLYP/cc-pVDZ level of theory. [f] Calculated at the UBLYP/aug-cc-pVDZ//MCSCF(8,8)/cc-pVDZ level of theory. [g] 11 % unreactive isomer (UI). [h] 8 % UI. [i] 9 % UI.

Table 1), approaching that of *ortho*-benzynes, which do not undergo radical reactions. The large S–T gap may partially or completely counteract the reactivity enhancing effect of a greater EA, thus explaining the low reactivity. However, besides lower reactivity, biradical **4** also displays somewhat different reactivity from the isomeric biradical **5** and the related monoradicals. Instead of the expected CN-group abstraction from *tert*-butyl isocyanide, **4** undergoes predominant HCN abstraction. This was also observed for a related *ortho*-benzyne (Table 2). These findings suggest that non-radical reactions dominate for **4**. A rationale for this behavior comes from the consideration of the most stable ionic resonance structure (**11**; Figure 3) for **4** (such as **9** shown

above for **7**, Figure 1). The ionic resonance structure **11** illustrates how the hydroxyl-group between the two radical sites stabilizes the cyclopropenium cation moiety via delocalization of the charge to the oxygen atom. This should lead to a smaller dehydrocarbon atom separation for **4** than **5** (and the unsubstituted analog discussed above), and hence, based on earlier studies, lower radical reactivity.^[14]

The third isomeric hydroxyl-substituted biradical, **6**, behaves yet differently. This biradical appears to mostly undergo non-radical reactions, typical for *ortho*-benzynes,^[13] and the presence of an unreactive isomer was also observed (Table 2). These findings suggest that during or after generation of **6**, rearrangement to at least two different isomers

Table 2. Reaction efficiencies^[a] and product branching ratios for reactions^[b] of two hydroxy-substituted didehydropyridinium cations with various reagents.

Reagent	Expected biradical structure			
				
	H ₂ O abs	51 %	H ₂ O abs	51 %
	CH ₂ O abs	25 %	CH ₂ O abs	33 %
	H ⁺ trns	11 %	H ⁺ abs	8 %
	H ⁻ abs	9 %	H ⁺ trns	7 %
	2 H abs	4 %	2 H abs	1 %
	eff = 78 % ^[c]		eff = 99 %	
	C ₃ H ₄ abs	82 %	C ₃ H ₄ abs	78 %
	add	8 %	I abs	11 %
	HI abs	5 %	C ₃ H ₅ abs	6 %
	C ₃ H ₅ abs	5 %	HI abs	3 %
			add	2 %
	eff = 64 % ^[d]		eff = 57 %	
	HSCH ₃ abs	45 %	SCH ₃ abs	47 %
	SCH ₃ abs	30 %	HSCH ₃ abs	44 %
	2°SCH ₃ abs		SCH ₂ abs	9 %
	SCH ₂ abs	25 %		
	eff = 100 % ^[e]		eff = 91 %	
	CN ⁻ abs	60 %	CN ⁻ abs	59 %
	HCN abs	40 %	HCN abs	41 %
	2°C ₄ H ₈ abs		2°C ₄ H ₈ abs	
	eff = 54 %		eff = 100 %	

[a] Reaction efficiencies are reported as $k_{\text{reaction}}/k_{\text{collision}} \times 100\%$ (eff = efficiency). The reaction efficiency is the percentage of collisions leading to a reaction. [b] abs = abstraction, add = addition, trns = transfer; secondary products are indicated as 2°, and are listed under the primary products that produce them. [c] 39 % unreactive isomer (UI). [d] 53 % UI. [e] 59 % UI.

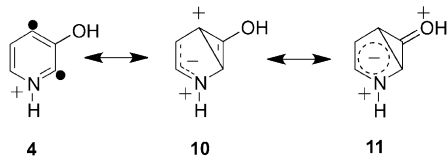


Figure 3. Resonance structures of 3-hydroxy-2,4-didehydropyridinium ion 4.

takes place. One of the isomers of **6** is entirely unreactive, and has a yet unknown structure. The other one is likely the *ortho*-benzyl **12** that reacts with THF and dimethyl disulfide similarly as **6**. However, **12** displays iodide-ion abstraction from allyl iodide, which was not observed for **6**. Further, the reaction efficiencies of **6** and **12** toward *tert*-butyl isocyanide are very different (Table 2). The formation of these isomers is under investigation. However, it should be noted here that when attempting to generate the analog of **6** with no hydroxyl-substituent, a mixture of isomers is also formed.^[15]

The reactivity of the hydroxyl-substituted triradical **8** differs drastically from that of the isomeric hydroxyl-substituted biradicals **6** (likely a mixture of **12** and something else;

see above) and **4** (where the hydroxyl-group between the radical sites drastically lowers radical reactivity). Its reactivity more closely resembles that of the monoradicals **1–3**, biradical **5** and triradical **7**, all of which display radical reactivity. However, while biradical **5** and triradical **7** undergo two or three consecutive atom or group abstractions, respectively, triradical **8** displays only one I-atom abstraction from allyl iodide and one SCH₃-group abstraction from dimethyl disulfide (Table 1). Hence, with the exception of THF, no secondary reactions were observed. These results indicate that only one of the radical sites of **8** is reactive toward most reagents. This finding can be rationalized in the same way as the lack of reactivity of biradical **4** with the hydroxyl-substituent in the 3-position. The hydroxyl-substituent between the radical sites decreases the dehydrocarbon atom separation and thus reduces radical reactivity. However, due to the third radical site at the 6-position, **8** still remains highly reactive. The resonance structure **14** shown below illustrates the situation. This favorable resonance structure leads to a smaller dehydrocarbon atom separation between C2 and C4 for **8** than **7**, and lowers the radical reactivity of these two sites (Figure 4).^[14]

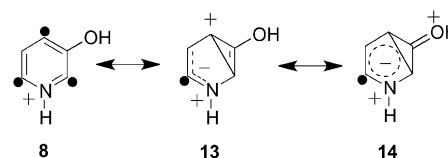


Figure 4. Resonance structures of 3-hydroxy-2,4,6-tridehydropyridinium ion 8.

The reactivity of **8** toward THF differs from its reactivity toward allyl iodide, dimethyl disulfide and *tert*-butyl isocyanide. A single H-atom abstraction from a THF molecule was observed for **8** as the main reaction, which is consistent with the observations made for other neutral reagents. However, in addition to this reaction, also abstraction of two H atoms followed by a single H-atom abstraction were observed. The latter reactions lend support for the presence of three radical sites in **8**. Based on the analysis of the reactivities of biradicals **4**, **5** and **6**, the single H-atom abstraction occurs at carbon 6 in the triradical, yielding biradical **4** that is unreactive toward THF. The two H-atom abstractions from THF likely occurs at carbons 4 and 6 to produce monoradical **1**, which then abstracts a H atom from another THF molecule.

Conclusion

Substitution has been demonstrated to strongly affect the reactivity of a carbon-centered aromatic σ,σ,σ -triradical. The placement of a hydroxyl group between two of the three radical sites in the 2,4,6-tridehydropyridinium cation inactivates the radical sites adjacent to the substituent. This is rationalized by the ability of the hydroxyl group to stabilize

the cyclopropenium moiety of an ionic resonance structure, which results in a reduced dehydrocarbon atom separation for these two radical sites. Hence, this triradical is best described as a reactive monoradical with a chemically inert *meta*-benzynes moiety, while the unsubstituted analog acts as a true triradical with three reactive radical sites.

Experimental Section

The precursor of monoradical **1**, 3-hydroxy-2-iodopyridine, was purchased from Sigma Aldrich Co. The precursors of the monoradicals **2** and **3** were synthesized using literature methods.^[24] The monoradicals **1**, **2** and **3** were generated in the FT-ICR by using methods described previously.^[15] The precursors of the biradicals **4**, **5**, and **6** and the triradicals **7** and **8** were synthesized using literature methods.^[15,24] The bi- and triradicals were generated in an FT-ICR using methods described previously.^[12,15] Sustained off-resonance irradiation, collision-activated dissociation (SORI-CAD) was used to cleave C–I bonds in the protonated precursors.^[25] The radicals were isolated and allowed to react with reagents for varying periods of time, as described previously.^[15,23] The structures of all the radical species were confirmed by using earlier reported structurally diagnostic reactions.^[17] All molecular orbital calculations were carried out with the Gaussian 98^[26] and Molpro^[27] electronic structure program suites.

Acknowledgements

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