

A General Method for the Synthesis of Charged Phenyl Radicals in the Gas Phase

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Abstract: A new and generally applicable approach for the gas-phase synthesis of charged phenyl radicals is described. Reaction of nucleophiles with the radical cations of dihalobenzenes in a Fourier transform ion cyclotron resonance mass spectrometer leads to *ipso*-substitution of a halogen atom. Collisional activation of the resulting ion induces loss of the remaining halogen atom to yield a phenyl radical with a charged substituent. This method was used to generate a series of novel charged phenyl radicals that were purified by ejecting unwanted ions from the cell, and verified to be stable and to have spatially separated charge and radical sites. The reactivity of these charged radicals closely resembles that of the neutral phenyl radical. For example, the radicals abstract an iodine atom from allyl iodide and a thiomethyl radical from dimethyl disulfide, and the rates of these reactions are enhanced by additional electron-withdrawing substituents.

Introduction

Distonic ions, species with spatially separated charge and radical sites,¹ have received a lot of attention recently.^{2,3} Distonic ions that have an unreactive charge site and a reactive radical site are especially interesting from the point of view of their radical-type reactivity.³ These charged radicals may provide a useful tool for the examination of the reactions of gas-phase radicals since the charge site allows for mass spectrometric manipulation of the reactive radical. The charged radical $(\text{CH}_3)_2\text{S}^+-\text{CH}_2^\bullet$ has been considered as a possible example of such a distonic ion. This species has a relatively inert, coordinatively saturated sulfonium charge site and a radical site largely localized on the methylene carbon.³ However, the charge site participates in certain reactions, and it also influences the reactivity of the adjacent radical site through a strong electron-withdrawing effect.^{4,5} In an attempt to study the influence of an *inert* as well as *remote* charge site on the reactions of carbon-centered radicals, reactions of distonic acylium ions with up to three heavy atoms between the charge and radical sites have been examined (*e.g.*, $^+\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}^+$).⁶ However, the flexible skeleton of these species allows a neutral reagent to interact with the charge and radical sites simultaneously. Indeed, acylium distonic ions react with many

neutral reagents by charge catalyzed mechanisms wherein the first step involves the formation of a covalent bond between the neutral reagent and the charge site of the ion.^{6a}

In order to avoid the aforementioned complications in the study of radical reactions of charged, carbon-centered radicals, we have attempted⁷ to generate distonic ions wherein the charge and radical sites are separated by a rigid molecular framework. The first species of this type, the 4-dehydroanilinium ion, was found to isomerize to ionized aniline upon collisions with bases.^{7,8} However, a variety of stable, charged phenyl radicals can be generated by using the general approach described herein.

Experimental Section

The experiments were performed using an Extrel Model 2001 Fourier-transform ion cyclotron resonance mass spectrometer (FT-ICR) equipped with a 1280 computer system.^{3,5-7} This instrument contains a differentially pumped dual cell that is aligned collinearly with the magnetic field produced by a 3.0-T superconducting magnet operated at 2.2–2.8 T. The base pressure in the instrument is $<10^{-9}$ Torr which is maintained by two Balzers turbomolecular pumps, each backed by an Alcatel mechanical pump. The two cells are separated by a common wall (the conductance limit plate) which contains a 2-mm hole in the center. This plate and the other two trapping plates perpendicular to the magnetic field were kept at +2 V unless otherwise noted.

Samples were introduced into the FT-ICR by using a heated solids probe, a Varian leak valve, or an Extrel FT/MS heated batch inlet equipped with a variable leak valve. Unless otherwise noted, the nominal reagent pressure in both sides of the dual cell was about 1×10^{-7} Torr, as measured by ionization gauges located on each side of the cell. The ionization conditions were optimized for each experiment (see below).

The dihalobenzenes (diiodo- or bromiodobenzene) were introduced at a nominal pressure of 3×10^{-7} Torr into one side of the dual cell by using the solids probe. The appropriate nucleophile was added at a nominal pressure of 1×10^{-7} Torr into the same cell through the heated batch inlet system. The mixture of the dihalobenzene and the nucleophile was subjected to electron ionization (20-eV electron energy, 8- μA filament current, 30-ms ionization time) which resulted in an intense signal for the dihalobenzene radical cations. All other ions

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(1) (a) Yates, B. F.; Bouma, W. J.; Radom, L. *J. Am. Chem. Soc.* **1984**, *106*, 5805. (b) Yates, B. F.; Bouma, W. J.; Radom, L. *Tetrahedron* **1986**, *42*, 6225. (c) Hammerum, S. *Mass Spectrom. Rev.* **1988**, *7*, 123.

(2) See, for example: (a) Goldberg, N.; Iraqi, M.; Schwarz, H. *Chem. Ber.* **1993**, *126*, 2353. (b) Yu, S. J.; Holliman, C. L.; Rempel, D. L.; Gross, M. L. *J. Am. Chem. Soc.* **1993**, *115*, 9676. (c) de Koster, C. G.; van Houte, J. J.; van Thuijl, J. *Int. J. Mass Spectrom. Ion Processes* **1993**, *123*, 59. (d) Mourgues, P.; Audier, H. E.; Hammerum, S. *Rapid Commun. Mass Spectrom.* **1994**, *8*, 53. (e) Radom, L. *Int. J. Mass Spectrom. Ion Processes* **1992**, *118/119*, 339. (f) Kenttämää, H. I. *Org. Mass Spectrom.* **1994**, *29*, 1.

(3) (a) Smith, R. L.; Chyall, L. J.; Stirk, K. M.; Kenttämää, H. I. *Org. Mass Spectrom.* **1993**, *28*, 1623. (b) van Amsterdam, M. W.; Zappey, H. W.; Ingemann, S.; Nibbering, N. M. M. *Org. Mass Spectrom.* **1993**, *28*, 30. (c) van Amsterdam, M. W.; Stancke, P. O.; Ingemann, S.; Nibbering, N. M. M. *Org. Mass Spectrom.* **1993**, *28*, 919.

(4) See, for example: (a) Boyd, R. J.; Glover, J. N.; Pincock, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 5152. (b) Bordwell, F. G.; Zhang, X.-M.; Alnajjar, M. *J. Am. Chem. Soc.* **1992**, *114*, 7623.

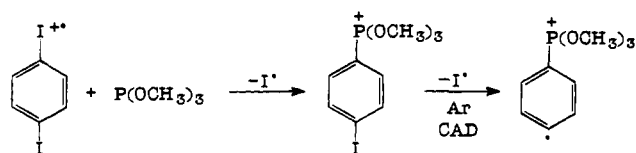
(5) Chyall, L. J.; Byrd, H. C. M.; Kenttämää, H. I., *J. Am. Chem. Soc.*, **1994**, *116*, 10767.

(6) (a) Stirk, K. M.; Smith, R. L.; Orłowski, J. C.; Kenttämää, H. I. *Rapid Commun. Mass Spectrom.* **1993**, *7*, 392. (b) Smith, R. L.; Chyall, L. J.; Chou, P. K.; Kenttämää, H. I. *J. Am. Chem. Soc.* **1994**, *116*, 781.

(7) Chyall, L. J.; Kenttämää, H. I. *J. Am. Chem. Soc.* **1994**, *116*, 3135.

(8) Chyall, L. J.; Kenttämää, H. I., *J. Mass Spectrom.*, in press.

Scheme 1



were ejected out of the cell by applying a stored-waveform inverse Fourier-transform excitation pulse (SWIFT) to the excitation plates of the cell. The isolated ions were then allowed to react with the neutral nucleophile. Depending on the system, formation of an abundant halogen displacement product required 500 ms to 5 s.

The substituted halobenzene ions generated in the above experiment were transferred into the other side of the dual cell by grounding the conductance limit for approximately 150 μ s which causes the ions to pass through the 2-mm hole in the center of this plate. The transferred ions were cooled by allowing them to collide for 1 s with the neutral molecules present in this cell (the reagent to be used in the final stage of the experiment; see below). The substituted halobenzene ions were then isolated by ejecting all other ions from the cell by using the SWIFT method, as described above. After isolation, argon was introduced into the cell via a pulsed valve assembly (peak nominal pressure of argon was 6×10^{-5} Torr), and the ions were collisionally activated with argon for 1 s by employing the sustained off-resonance irradiation (SORI) technique⁹ at a frequency 0.5–0.85 kHz higher than the cyclotron frequency of the ions. The ions were then given a 1-s delay to kinetically cool through collisions with the neutral atoms and molecules present in the cell. This method led to predominant cleavage of the remaining carbon–halogen bond to yield a charged phenyl radical.

The charged radical was isolated by ejecting all the other ions from the cell, as described above. The isolated ions were allowed to undergo reactions with the neutral reagent present in the cell for a variable period of time (typically 1–25 s). After the reaction, the ions present in the cell were excited for detection by using the SWIFT excitation method (0.5-cm final radius for all ions). All the spectra are the average of 50 transients and were recorded as 32 k data sets and subjected to one zero fill before Fourier transformation.

The reaction rate constants (*k*) were determined from a decay of the relative abundance of the reactant ion as a function of time and an estimated pressure of the neutral reagent. For the pressure measurements, the ion gauges were calibrated for their sensitivity^{10b} toward each neutral reagent and for the pressure gradient between the dual cell and the ion gauge, as described earlier.^{3,5–7} The collision rates (*k*_{coll}) were calculated using the parameterized trajectory theory.^{10a}

Energy-resolved collision-activated dissociation (CAD) experiments were performed by on-resonance excitation of the isolated ions. For these experiments, the charged phenyl radical was synthesized by the SORI technique⁹ as described above but by using a static argon pressure of 1×10^{-7} Torr instead of pulsing argon into the cell. This resulted in a smaller number of collisions of the ion with argon during CAD as is desirable for ion structure determination. The product ions were detected in the usual manner.

Results and Discussion

The radical cations of certain dihalobenzenes are known¹¹ to react with ammonia via *ipso*-substitution of a halogen atom. This approach was utilized to generate differently substituted charged iodobenzenes in one side of the dual cell of a Fourier-transform ion cyclotron resonance mass spectrometer. Diiodo- or bromiodobenzene was ionized by electron impact, and the resulting abundant radical cation was allowed to react with a nucleophile (see Scheme 1 and Figure 1 for trimethyl phosphite). Bromine replacement occurs in preference to iodine replacement

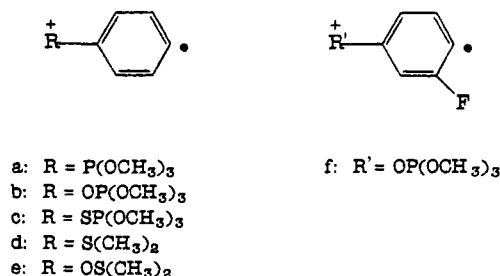
(9) Gauthier, J. W.; Trautman, T. R.; Jacobson, D. B. *Anal. Chim. Acta* **1991**, *246*, 211.

(10) (a) Su, T.; Chesnavich, W. J. *J. Chem. Phys.* **1982**, *76*, 5183. (b) Bartmess, J. E.; Georgiadis, R. M. *Vacuum* **1983**, *33*, 149.

(11) (a) Thölmán, D.; Grützmacher, H.-F. *J. Am. Chem. Soc.* **1991**, *113*, 3281. (b) Thölmán, D.; Grützmacher, H.-F. *Org. Mass Spectrom.* **1989**, *24*, 439.

for the bromiodobenzenes studied. The resulting even-electron iodobenzene ion was transferred into the other side of the dual cell, collisionally cooled, and isolated (Figure 1d). Collision-activated dissociation⁹ of the ion results in the predominant loss of the iodine atom (Scheme 1, Figure 1e), yielding an abundant charged phenyl radical.

The procedure described above was used to generate the charged radicals expected to have the *para*-substituted structures shown below (a–f), as well as selected *meta*-isomers (for a, b, and d). The structures were verified by using ion–molecule



reactions and collision-activated dissociation. The observation of CH₃S⁺ abstraction from dimethyl disulfide (Figure 1g) and CH₃Se⁺ abstraction from dimethyl diselenide as the exclusive reaction channel provides strong support for the proposed structures for the charged radicals since only species with spatially separated charge and radical sites are known to undergo these reactions.^{12,13} For example, a conventional isomer of d, ionized *p*-tolyl methyl sulfide, was found to be unreactive toward dimethyl disulfide. Further evidence in support of the expected structures was obtained from collisional activation experiments. When the charged radical e derived from dimethyl sulfoxide was accelerated and allowed to collide with argon, it decomposed by a predominant methyl radical loss. This behavior is analogous to that observed for protonated dimethyl sulfoxide under the same conditions (predominant methyl radical loss), and indicates that both of these ions have the dimethyl sulfonium charge site. The charged radical expected to have the structure d also dissociates via the same process.

Ab initio molecular orbital calculations carried out at the ROHF/4-31G* level of theory¹⁴ for the charged radical d indicate that the charge site is localized on the sulfur atom (approximately +0.8 e). The odd spin density is localized on the carbon atom *para* to the charge site (1.2 e); the value calculated for the phenyl radical is about 1.1 e). Thus, the charged phenyl radical can be expected to show radical-type reactivity similar to that of the phenyl radical. Indeed, all the charged radicals were found to undergo reactions common^{15,16} for the phenyl radical, including CH₃S⁺, H⁺, and I⁺ abstraction reactions.

In solution, electron-withdrawing substituents enhance the reactivity of phenyl radicals toward many reagents. For

(12) Stirk, K. M.; Orłowski, J. C.; Leeck, D. T.; Kenttämaa, H. I. *J. Am. Chem. Soc.* **1992**, *114*, 8604.

(13) (a) Beasley, B. J.; Smith, R. L.; Chyall, L. J.; Leeck, D. T.; Chou, P. K.; Kenttämaa, H. I. In *Proceedings of the 42nd Annual Conference on Mass Spectrometry and Allied Topics*, American Society for Mass Spectrometry, Chicago, 1994. (b) Beasley, B. J.; Smith, R. L.; Kenttämaa, H. I. *J. Mass Spectrom.*, in press.

(14) (a) Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. Gaussian, Inc.: Pittsburgh, PA, 1990. (b) Pople, J. A.; Nesbet, R. K. *J. Chem. Phys.* **1954**, *22*, 571. (c) Pople, J. A.; Raghavachari, K.; Frisch, M. J.; Binkley, J. S.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1983**, *105*, 6389.

(15) Migita, T.; Takayama, K.; Abe, K.; Kosugi, M. *J. Chem. Soc., Perkin Trans. 2* **1979**, *8*, 1137.

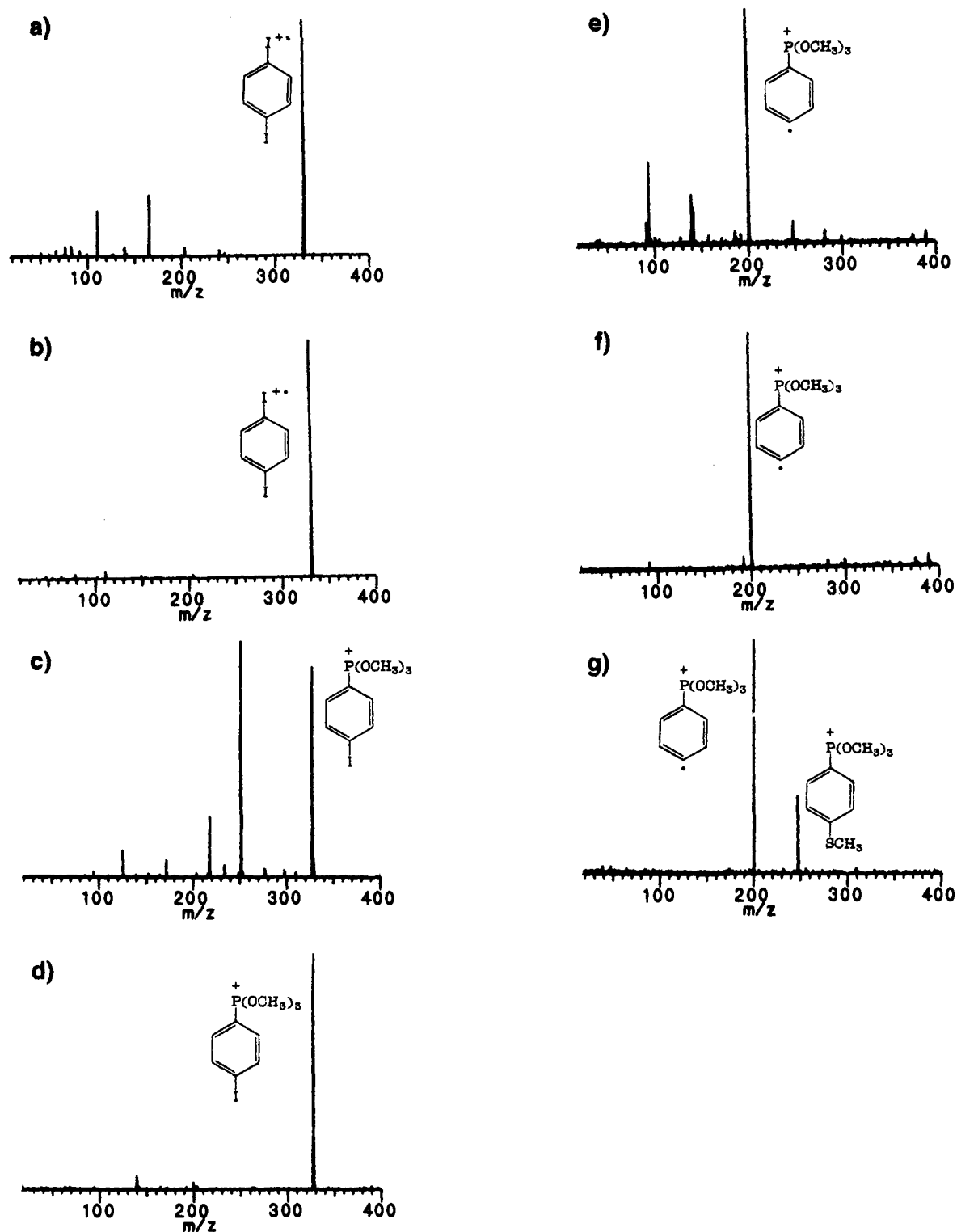


Figure 1. (a) Electron ionization of 1,4-diiodobenzene, (b) isolation of the molecular ion (m/z 330), and (c) reaction with trimethyl phosphite yield the 4-iodophenyltrimethoxyphosphonium cation of m/z 327. Another abundant product ion, likely to be the iodotrimethoxyphosphonium cation ($(\text{CH}_3\text{O})_3\text{P}^+-\text{I}$), is also formed. (d) Isolation and (e) collision-activated dissociation of the ion of m/z 327 result in an abundant charged radical, the 4-dehydrophenyltrimethoxyphosphonium cation (m/z 200). (f, g) Reaction of the isolated charged radical for 5 s with dimethyl disulfide at 1.2×10^{-7} Torr occurs by exclusive thiomethyl abstraction.

example, $\text{CH}_3\text{S}^\bullet$ abstraction occurs approximately three times as fast for $p\text{-O}_2\text{NC}_6\text{H}_4^\bullet$ as for $\text{C}_6\text{H}_5^\bullet$.¹⁵ Similar observations

(16) (a) Pryor, W. A.; Platt, P. K. *J. Am. Chem. Soc.* **1963**, *85*, 1496. (b) Pryor, W. A.; Guard, H. *J. Am. Chem. Soc.* **1964**, *86*, 1150. (c) Pryor, W. A.; Smith, K. *J. Am. Chem. Soc.* **1970**, *92*, 2731. (d) Danen, W. C. In *Methods in Free-Radical Chemistry*; Huyser, E. S., Ed.; Marcel Dekker: New York, 1974; Chapter 1. (e) Poutsma, M. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. II, Chapter 13.

were made for the gaseous, charged phenyl radicals. Radicals with the charge site adjacent to the ring react more efficiently with dimethyl disulfide (e.g., the reaction efficiencies¹⁰ or k/k_{coll} are 6% and 7% for **a** and **d**, respectively) than the radicals with the charge site separated from the ring by one heavy atom (e.g., reaction efficiency is 1% for **b** and **c**). A similar rate enhancement was also observed for the abstraction of an iodine

atom from allyl iodide (this is the exclusive reaction pathway; the reaction efficiencies are 31% and 20% for **a** and **d**, respectively, and 14% and 16% for **b** and **c**, respectively). Further, the *meta*-isomer of the charged radical **b** abstracts $\text{CH}_3\text{S}^\bullet$ from dimethyl disulfide and an iodine atom from allyl iodide faster (efficiencies 3% and 24%, respectively) than the *para*-isomer (efficiencies 1% and 14%, respectively). The enhanced reactivity in each case is attributed to the stronger electron-withdrawing ability of the charged substituent closer to the radical site. Additional electron-withdrawing substituents on the ring have a similar effect: the reaction efficiencies of the fluorine-substituted charged radical **f** (23% for thiomethyl abstraction; 34% for iodine atom abstraction) are significantly greater than those of the analogous charged radical **b** without a fluorine atom (1% for thiomethyl abstraction; 14% for iodine abstraction).

Conclusions

Ipso-substitution of a halogen atom by a nucleophile in the radical cations of diiodo- and bromiodobenzenes, followed by collision-activated cleavage of the remaining halogen atom,

provides a novel general approach for the gas-phase synthesis of stable charged phenyl radicals. This method was used to generate several new species with different types of inert charge sites located on the *meta*- and *para*-positions with respect to the σ -radical site. The chemical properties of these charged radicals resemble those of the neutral phenyl radical. The reaction efficiencies were found to be greater when the charge site is closer to the reactive radical site. A similar effect is observed when additional electron-withdrawing substituents are added to the phenyl ring. A detailed study of the substituent effects on the chemical properties of isolated, charged phenyl radicals is ongoing in our laboratory.

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