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Hydrogen atom abstraction and addition reactions of charged phenyl radicals with aromatic substrates in the gas phase

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Abstract

In order to investigate competition between radical substitution and addition reactions, the gas-phase reactivity of phenyl radicals bearing a chemically inert, positively charged group and a neutral substituent (CH_3, Cl, or Br), both at a meta position with respect to the radical site, was examined toward several aromatic substrates in a dual-cell Fourier transform ion cyclotron resonance mass spectrometer. The radicals undergo hydrogen atom abstraction from the substituent and/or addition to the phenyl ring of benzeneselenol, thiophenol, benzaldehyde, toluene, aniline, and phenol. The presence of an electron-withdrawing substituent Cl or Br on the phenyl ring of the radical slightly increases the rates for both hydrogen atom abstraction and addition due to favorable polarization of the reactions' transition states. The observation of a stable ion-molecule addition product in most reactions was unexpected since in a low-pressure gas-phase environment, adducts are typically unable to release their excess energy before dissociation to products or back to reactants. However, the addition products discussed here are low in energy [addition is exothermic by 24–30 kcal/mol; B3LYP/6-31G**d**+ZPVE] and hence are long lived enough to become stabilized by infrared emission. The extent to which the charged radicals are able to abstract a hydrogen atom from the aromatic substrate and form stable products via addition to the aromatic ring was found to vary greatly. The outcome of this competition can be rationalized by reaction exothermicities only in extreme cases, i.e. for benzeneselenol and thiophenol, that predominantly react by hydrogen atom abstraction due to their especially weak heteroatom-hydrogen bonds and aniline that undergoes almost exclusive addition due to particularly stable resonance-stabilized addition products. For the other substrates, competition between the two reaction pathways is controlled by a complex interplay of polar effects that affects the energies of both transition states but to different extents. (Int J Mass Spectrom 210/211 (2001) 511–520) © 2001 Elsevier Science B.V.

1. Introduction

Many important chemical and biological processes involve hydrogen atom abstraction and addition reactions between aromatic σ-radicals and DNA [1–7]. For example, antiviral therapies are being developed based on DNA cleavage via hydrogen atom abstraction by aromatic radicals [8]. The keen current interest in hydrogen atom abstraction reactions of aromatic biradicals arises from the desire to better understand and utilize the high DNA-degrading ability of the biradical intermediates generated from the enediyne antitumor antibiotics in biological systems [4]. Further, damage of DNA caused by phenyl radicals is the

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Dedicated to Professor Nico Nibbering on the occasion of his retirement.

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origin of the biological activity of some compounds, such as the tumor promoter action of benzoyl peroxide that is widely used in preparation of plastics, in food industry as a bleaching agent, and for acne treatment. Phenyl radicals damage DNA predominantly by adding to a nucleobase but also by abstracting a hydrogen atom from the sugar moiety of DNA [7].

Although the reactions of the phenyl radical with simple molecules have been thoroughly explored [9,10], the factors that control competition between hydrogen atom abstraction and addition are poorly understood [3–5,8,11]. This is especially true for the complex situation of substituted phenyl radicals reacting with polyfunctional substrates, such as nucleobases and nucleotides. We are aware of only one study that specifically focuses on the competition between hydrogen atom abstraction and addition [10(f)]. The results of this study suggest that both addition and hydrogen abstraction reactions are facilitated by electronegative substituents on the phenyl radical. However, the reaction rates were measured relative to chlorine atom abstraction which also may be affected by polar effects; hence, it is difficult to make unambiguous conclusions based on this study. Further, substituted phenyl radicals were found to add to carbon–carbon double bonds much faster than they undergo hydrogen atom abstraction [10(f)]. The preference for addition is almost irrespective of the substitution in the radical. This result may suggest that the nature and magnitude of polar influences of substituents on a radical are similar for hydrogen abstraction and addition reactions. Finally, studies on homolytic arylation by para-nitro-, chloro-, methyl-, and methoxy-substituted phenyl radicals in solution has led to the conclusion that the ortho- and para-positions of substituted benzenes are more reactive toward radical attack than the meta positions, irrespective of the polar nature of the attacking radical [10(h)].

In our previous research, we have employed Fourier-transform ion cyclotron resonance mass spectrometry to examine gas-phase reactions of substituted phenyl radicals that also carry a chemically inert, positively charged group [12–14]. This approach allows us to perform kinetic reactivity studies on radicals under clean conditions, with only the radical and the desired substrate present. The results obtained for simple organic hydrogen atom donors demonstrated that the addition of electron-withdrawing substituents (Br, Cl, F, CN, CF_3) to the phenyl radical enhances its hydrogen atom abstraction ability via polarization of the transition state [12]. The same conclusion was found to apply to iodine abstraction from allyl iodide [13], thiomethyl abstraction from dimethyldisulfide [14], and cyano abstraction from tert-butylisocyanide [14]. The present study expands the current knowledge by exploring substituent effects on the competition between addition and hydrogen abstraction reactivity of phenyl radicals toward aromatic substrates. The information obtained is hoped to shed light into the factors that control addition vs. hydrogen abstraction reactivity of aromatic radicals toward nucleobases in DNA.

2. Experimental

All samples were commercially available and used as received. Their purity was verified by using mass spectrometry. The experiments were performed using both an Extrel and a Finnigan Model 2001 Fourier-transform ion cyclotron resonance mass spectrometer. These instruments contain a differentially pumped dual cell aligned within the magnetic field produced by a 3.0 T superconducting magnet. The nominal base pressure was $<10^{-9}$ Torr, as maintained by two turbomolecular pumps (330 L/s; Extrel model) or two diffusion pumps (800 L/s; Finnigan model), each backed with a mechanical pump. The two cells of both instruments are separated by a wall (the conductance limit) containing a 2 mm hole in the center. All the trapping plates were maintained at $+2$ V unless otherwise stated.

Samples were introduced into the instruments by using leak valves, heated solids probes, pulsed valves [15], or batch inlet systems equipped with variable leak valve. The nominal reagent pressures ($1.0–3.0\times10^{-7}$ Torr) were measured with two ionization gauges located on each side of the dual cell.

The charged phenyl radicals were generated by

using procedures reported earlier [12–14,16,17]. The halogenated neutral precursors (3,5-dibromotoluene for **a**, 1,3-diiodobenzene for **b**, 1,3-dichloro-5-iodobenzene for **c**, and 3,5-dibromonitrobenzene for **d** were introduced at a nominal pressure of about 1×10^{-7} Torr into one side of the dual cell by using the solids probe or the Varian leak valve. Pyridine or 3-fluoropyridine was added into the same cell through a batch inlet system at a nominal pressure of approximately 1×10^{-7} Torr. The mixture was subjected to electron ionization (~25 eV electron energy, 5 μA emission current, 30–50 ms ionization time) which produced an intense signal for the halobenzene radical cation. This species was allowed to react with a nucleophile (pyridine or 3-fluoropyridine) for approximately 2 s, which lead to ipso substitution of a halogen atom [18].

The substituted halobenzene ions were transferred into the other side of the dual cell by grounding the conductance limit plate for approximately 180 μs. The transferred ions were cooled for one second by giving them time to undergo infrared (IR) emission and to collide with the neutral molecules present in this cell (the aromatic substrates to be used in the final step of the experiment). The substituted halobenzene ions were then isolated by ejecting unwanted ions via the application of a stored-waveform inverse Fourier transform [19] excitation pulse to the plates of the cell. After isolation, the carbon–iodo and carbon–nitro bonds were cleaved by using sustained off-resonance irradiated collision-activated dissociation [20] (SORI-CAD) to generate **b**, **c**, and **d**, whereas the carbon–bromo bond was homolytically cleaved by photolysis[21] to yield **a**. SORI-CAD was achieved by kinetically activating the ions for about one second via an rf-pulse at 1.0 kHz greater frequency than the cyclotron frequency of the ions, and allowing them to undergo collisions with argon introduced into the cell via a pulsed valve assembly (the nominal peak pressure in the cell was about 1×10^{-5} Torr). The charged phenyl radicals were cooled by providing 400 ms time delay for IR emission, and by allowing collisions with the neutral molecules present in the cell. Photolysis was accomplished by using a Continuum Minilite 10 Nd-yttrium-aluminum-garnet laser operated at the fourth harmonic (266 nm, 1.5 mJ/pulse). The laser was triggered (4 ns pulse width) approximately 3–4 times (100 ms delay between each laser pulse was required by the laser electronics) [21]. The product ions were cooled by allowing them to undergo IR emission for one second, and to collide with argon introduced into the cell via a pulsed valve assembly after the last laser pulse.

The charged phenyl radicals were isolated, as described previously, and allowed to react with a neutral reagent for a variable period of time (typically 0.5–45 s). The product ions were excited for detection by applying an excitation sweep of 124 $V_{p\text{-}p}$ amplitude, 2.7 MHz bandwidth, and 3.2 kHz/μs sweep rate. All the spectra are the average of at least 15 transients, which were recorded as 64k data points and subjected to one zero fill prior to Fourier transformation. Each reaction spectrum was background corrected by using a previously described procedure [12,17,22].

Primary products were identified based on their fixed relative abundances (branching ratios) at short reaction times. By assuming pseudo first-order kinetics, the second-order rate constant of each reaction (k_{exp}) was obtained from a semilogarithmic plot of the relative abundance of the reactant ion versus time. A parameterized trajectory theory [23] was employed to calculate the collision rate constant (k_{coll}). The reaction efficiencies are given by k_{exp}/k_{coll}. The accuracy of the rate constant measurements is estimated to be $\pm$50% whereas the precision is better than $\pm$10%. The greatest uncertainty arises from pressure measurement in the cell. The pressure readings of the ion gauges (located remote from the cell) were corrected for the sensitivity of the ion gauges toward each neutral reagent [24] and for the pressure gradient between the cell and the ion gauge. The latter correction factor was obtained for each neutral reagent by measuring rates of exothermic electron and proton transfer reactions assumed to occur at collision rate.

The Gaussian 98 Revision A.7 suite of programs [25] was employed to perform molecular orbital calculations based on density functional theory. For determination of the reaction exothermicities, the geometries of all species were fully optimized using the B3LYP/6-31G**d** basis set. The relative energies

Table 1
Efficiencies[a] and products (relative abundance given in parenthesis) measured for the reactions of charged phenyl radicals **a–d** with aromatic substrates

R =	Benzeneselenol	Thiophenol	Benzaldehyde	Toluene	Aniline	Phenol
a CH_3	H• Abstraction (100%) eff = 19%	H• Abstraction (85%) Adduct (15%) eff = 3%	H• Abstraction (35%) Adduct (65%) eff = 3%	H• Abstraction (15%) Adduct - H• (8%) Adduct (77%) eff = 1%	Adduct - H• (13%) Adduct (87%) eff = 4%	(not examined)
b H	H• Abstraction (100%) eff = 17%	H• Abstraction (83%) Adduct (17%) eff = 3%	H• Abstraction (29%) Adduct (71%) eff = 4%	H• Abstraction (15%) Adduct - H• (14%) Adduct - CH_3• (5%) Adduct (66%) eff = 1%	H• Abstraction (2%) Adduct - H• (26%) Adduct (72%) eff = 6%	Adduct - H• (13%) Adduct - OH• (1%) Adduct (86%) eff = 1%
c Cl	H• Abstraction (100%) eff = 27%	H• Abstraction (74%) Adduct (26%) eff = 7%	H• Abstraction (29%) Adduct (71%) eff = 6%	H• Abstraction (12%) Adduct - H• (13%) Adduct - CH_3• (4%) Adduct (71%) eff = 4%	H• Abstraction (2%) Adduct - H• (31%) Adduct (67%) eff = 15%	Adduct - H• (11%) Adduct - OH• (3%) Adduct (86%) eff = 3%
d Br	H• Abstraction (100%) eff = 27%	H• Abstraction (75%) Adduct (25%) eff = 6%	H• Abstraction (26%) Adduct (74%) eff = 7%	H• Abstraction (11%) Adduct - H• (13%) Adduct - CH_3• (5%) Adduct (71%) eff = 4%	H• Abstraction (3%) Adduct - H• (31%) Adduct (66%) eff = 16%	Adduct - H• (10%) Adduct - OH• (3%) Adduct (87%) eff = 4%

[a] $eff = k_{exp}/k_{coll}$ (second-order reaction rate constant/collision rate constant)

obtained from these calculations were corrected by adding the zero point vibrational energy estimated at the same level of theory. The vertical electron affinities for the charged phenyl radicals were obtained by using the B3LYP/6-31+G**d** basis set (the geometries of the radicals were optimized and their structures used in single-point calculations of their reduced forms). Vertical instead of adiabatic electron affinities were calculated because of the simplicity of the calculation. Both values follow the same trends for the radicals studied here [13].

3. Results and Discussion

A multistep synthetic procedure described in detail elsewhere [12–14,16,17] was employed to generate the charged phenyl radicals **a**–**d**[N-(3-dehydro-5-methylphenyl)-3-fluoropyridinium **a**, N-(3-dehydrophenyl)pyridinium **b**, N-(3-chloro-5-dehydrophenyl)-pyridinium **c**, and N-(3-bromo-5-dehydrophenyl)pyridinium radical **d**]. The 3-fluoropyridinium charged group was employed instead of pyridinium in radical because pyridine has the same mass as ^{79}Br, the fragment being lost when the radical site is generated. Location of the substituents in the metaposition with respect to the radical site allows the study of the substituents' inductive effects without interfering resonance influences. All the radicals studied carry a remote, chemically inert charged group, and they have been demonstrated to possess chemical properties similar to those of the neutral phenyl radical [12–14,16,17]. Hence, radicals of this type can be thought of as phenyl radicals that carry a handle for mass spectrometric manipulation, i.e. the charged group allows the radical to be isolated, detected, and studied inside a mass spectrometer [9–14,16,17].

The charged phenyl radicals **a**–**d** were allowed to react with benzeneselenol, thiophenol, benzaldehyde, toluene, aniline, and phenol, and the temporal variation of reactant and product ion abundances was recorded. The reaction products and the second-order reaction rate constants are listed in Table 1. Hydrogen atom abstraction and/or addition reactions were observed for each of the reagents examined.

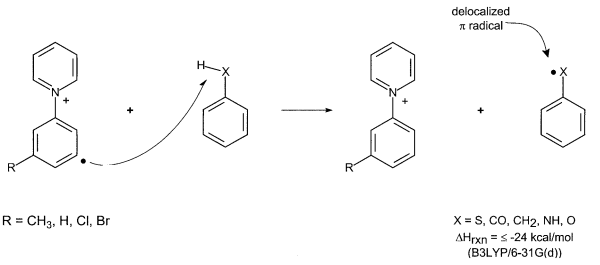
Table 2
Exothermicities (ΔBDE; kcal/mol) for hydrogen atom abstraction from aromatic substrates[a] by the charged phenyl radicals **a–d** [B3LYP/6-31G(d)+ZPVE; calculated using an isodesmic reaction with benzene] and by the neutral phenyl radical; and the radicals' hydrogen atom affinities (HA; experimental for the phenyl radical;[b] for others, calculated using an isodesmic reaction with benzene)

R =	Radical HA	Thiophenol SH	Benzaldehyde CHO	Toluene CH_3	Aniline NH_2	Phenol OH
a CH_3	115.4	-37.5	-26.0	-27.3	-23.8	-26.8
b H	115.7	-37.8	-26.3	-27.6	-24.1	-27.1
c Cl	115.8	-37.8	-26.4	-27.7	-24.2	-27.2
d Br	115.6	-37.7	-26.2	-27.5	-24.0	-27.0
	113.5[b]	-35.6	-24.1	-25.4	-21.9	-24.9

[a] The calculated BDE:s are: thiophenol: 77.95 kcal/mol; benzaldehyde: 89.41 kcal/mol; toluene: 88.12 kcal/mol; aniline: 91.56 kcal/mol; phenol: 88.62 kcal/mol.
[b] Reference 26.

3.1. Hydrogen atom abstraction reactions

Most of the aromatic substrates studied donate a hydrogen atom to the charged phenyl radicals. The likely origin of the donated hydrogen is the substituent due to the weakness of the bonds to the heavy atom bound directly to the aromatic ring. This was verified for aniline by examination of the reaction of d_5-ring-labeled aniline with the radical **c**; exclusive hydrogen atom transfer was observed in these experiments. The hydrogen atom abstraction reactions studied here are calculated to be very exothermic [$\Delta H_{rxn} \leq$-23 kcal/mol for all of the reagents studied; B3LYP/6-31G**d** + ZPVE; Table 2] due to the high degree of delocalization of the resulting radical (Scheme 1). However, the competing addition reactions are also highly exothermic (see discussion below). The extent to which hydrogen atom abstraction is able to compete with addition was found to be related to the X–H bond dissociation energy (Table 3) only in extreme cases. Specifically, hydrogen atom abstraction is the dominant reaction only for benzeneselenol (100%; Table 1) and thiophenol (75–85%), whose X–H bond dissociation energies (BDE) are the lowest among the substrates studied (78 kcal/mol [28] and 83 kcal/mol [30], respectively; Table 3). For the rest of the substrates (BDE≥87 kcal/mol[30]), addition predominates, with products arising from addition corresponding to 65–100% of the total product ion distribution. None of the charged phenyl radicals is able to abstract a hydrogen atom from benzene (BDE=113.5 kcal/mol [26]). For this substrate, addition predominates, and is occasionally accompanied by fragmentation.



Scheme 1.

As opposed to the predominant radical addition observed for phenol and toluene (Table 1), previous gas-phase studies revealed predominant hydrogen atom abstraction upon reaction of the phenyl radical

Table 3
Homolytic bond dissociation energies (BDE, kcal/mol), ionization energies (IE, eV), and dipole moments (D) of aromatic substrates, and adiabatic ionization energies (IE, eV) for the neutral radicals arising from hydrogen atom abstraction from each substrate

Substrate	BDE	Adiabatic IE[a]	Vertical IE	Dipole
Benzeneselenol	78[b]	7.7	8.07[c]	1.54[d]
Thiophenol	83[e]	8.3	8.49[a]	1.2[f]
Benzaldehyde	87[g]	9.5	~9.72[a]	2.93[f]
Toluene	88[g]	8.83	~8.89[a]	0.25[f]
Aniline	88[g]	7.72	~8.05[a]	1.55[f]
Phenol	87[g]	8.49	~8.66[a]	1.23[f]

[a] See 27, [b] See 28, [c] B3LYP/LANL2DZ, [d] PM3, [e] See 29, [f] AM1, [g] See 30.

Table 4
Estimated reaction enthalpies and TS energies (given as ΔE, the energy difference between the isolated reactants and the transition state; in kcal/mol) for hydrogen atom abstraction from the substituent and addition to the benzene ring of the aromatic substrates by the charged phenyl radical **b** [R=H; B3LYP/6-31G(d) + ZPVE]; as a comparison, some data are also presented for the phenyl radical; note that the more negative is the value ΔE, the lower is the TS energy

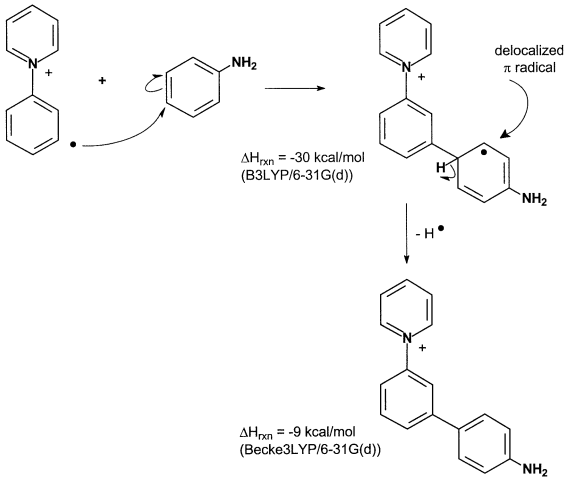
Substrate	Radical b ΔH_{rxn} for H· abstraction	ΔE	ΔH_{rxn} for para-addition	ΔE[a]	ΔH_{rxn} for ortho-addition	ΔE[b]	Phenyl radical ΔH_{rxn} for H· abstraction	ΔH_{rxn} for para-addition[a]
Thiophenol	−37.8	−2.0	−25.2	−1.1	−26.0	−2.1	−35.6	
Benzaldehyde	−26.3	−7.3	−24.3	1.1	−29.5	−4.0	−24.1	
Toluene	−27.6	−2.0	−24.8	−1.2	−24.5	−1.6	−25.4	−20.0
Aniline	−24.1	−5.1	−30.2[c]	−5.6	−28.4	−5.1	−21.9	−20.4
Phenol	−27.1	−2.4	−25.0	−2.6	−27.1	−3.7	−24.9	

[a] Para-addition, [b] Ortho-addition, [c] Radical **c** (R = Cl); −31.2 kcal/mol.

with these two reagents [9(b),31]. The difference between these two sets of results may have its origins in the different reaction conditions employed; the high temperatures (700 K) used in the earlier experiments should disfavor the reversible addition pathway [9(b),31,32]. Further, molecular orbital calculations performed at the B3LYP/6-31G**d** level of theory (Table 4) revealed that the adducts formed upon reaction of the charged phenyl radical **b** with all substrates are more stable by at least 5 kcal/mol than those formed for the neutral phenyl radical (for aniline, the energy difference is ∼10 kcal/mol).

3.2. Addition reactions

The chemical nature of the stable adducts observed in our experiments can be either covalent or electrostatically bound. In order to test the latter possibility, reactions of the even-electron N-phenylpyridinium ion were examined with several of the aromatic substrates. Although this even-electron ion should be able to form electrostatic adducts with the aromatic reagents just as easily as the phenyl radicals, no adduct formation was observed. It is concluded that the adduct formation observed in our experiments requires the presence of a radical site, and that this reaction likely involves addition of the radical to the aromatic ring of the substrate (Scheme 2). Our data further demonstrate that the functional groups of the aromatic substrates (-SeH, -SH, -CHO, $-CH_3$, $-NH_2$ and -OH) are not necessary for a stable adduct to be observed, since the reaction of benzene with the N-(3-dehydrophenyl)pyridinium ion **b** and the N-(3-chloro-5-dehydrophenyl)pyridinium ion **c** produces an abundant adduct, perhaps via a mechanism analogous to that shown in Scheme 2.



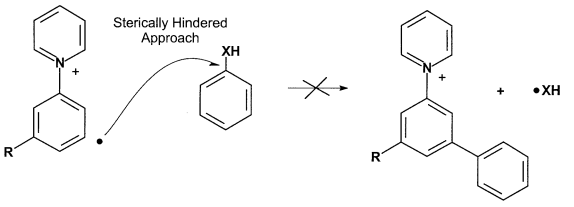
Scheme 2.

The addition of a phenyl radical to the phenyl ring of an aromatic substrate yields an arylcyclohexadienyl radical, i.e. a delocalized π-radical is formed from a localized σ-radical. This process is calculated to be highly exothermic for the radicals studied here, being 24–30 kcal/mol exothermic for the addition reactions of the radical **b** (Scheme 2; Table 4; addition to the

ortho- and para-positions differ little in exothermicity). In contrast, addition of the phenyl radical to the para-position of aniline and toluene is exothermic by 20.4 and 20.0 kcal/mol, respectively; substantially less than the reactions of the charged radicals (30.2 and 24.8 kcal/mol, respectively).

In spite of the high exothermicity of addition, the observation of an abundant adduct for nearly every reaction examined here (the adduct accounts for ≥65% of the product distribution for benzaldehyde, toluene, aniline, and phenol; Table 1) was unexpected because adducts are infrequently observed at low pressures in the gas phase. This is attributed to the lack of a solvent, which can serve as a "heat sink" into which the excess energy can be released that is gained by the system upon formation of a bond. In the gas-phase environment, adducts are stabilized via collisional cooling or by emission of IR photons [33]. In our experiments, collisional cooling is not a factor due to the low pressures employed [33–36] ($\leq 3\times10^{-7}$ Torr; at this pressure, an ion will encounter a neutral molecule approximately only three times per second). Therefore, the stable adducts formed upon reactions of the aromatic substrates with the charged phenyl radicals must be the result of cooling via IR emission. This can be rationalized by the large size and many internal degrees of freedom of the systems studied (≥96) that increase the lifetime of the initially formed, internally hot adduct. Radiative stabilization has been reported to be an efficient process for systems with only half as many degrees of freedom (~50) [36,37]. Covalent bonding and delocalization of the radical site into the aromatic ring of the substrates further increases the lifetime of the adduct. Nonaromatic hydrogen atom donors, such as tetrahydrofuran and tributyltin hydride, do not form stable adducts with the charged phenyl radicals [12(b)]. The same applies to methyl mercaptan (CH_3SH) and methanol (CH_3OH), the nonaromatic analogs of thiophenol and phenol.

In some cases, minor products arising from fragmentation of the adduct were observed. For aniline, toluene, and phenol, the predominant fragmentation pathway is elimination of a hydrogen



Scheme 3.

atom from the aromatic ring of the adduct to regain the aromaticity in the ring (Table 1). These results agree with literature results reported for high pressure and high-temperature conditions [9(b)]. The loss of the functional group of the substrate (i.e. amino, mercapto, formyl, methyl, or hydroxyl radical) is estimated to be more exothermic [by 7 kcal/mol for aniline at the B3LYP/6-31G(d) + ZPVE level of theory] than the loss of a hydrogen atom from the adduct. However, this reaction was only observed for toluene and phenol, and even then as a very minor reaction channel. It is concluded that steric hindrance likely prevents ipso-addition of the radicals to the aromatic substrates (Scheme 3).

3.3. Radical substituent effects

The presence of a meta-methyl-, chloro- or bromo-substituent in the charged phenyl radicals was found to have only a minor effect on the product branching ratios in their reactions with the aromatic substrates (Table 1). However, compared to the charged phenyl radical **b** with no such substituents, the presence of an electron-withdrawing chloro- or bromo-substituent was found to slightly increase the overall reaction efficiencies. For example, the N-(3-dehydrophenyl)pyridinium ion **b** reacts with toluene at an efficiency of 1% (one out of 100 collisions lead to a product), whereas the N-(-3-chloro-5-dehydrophenyl) pyridinium ion **c** reacts four times faster (eff.=4%; Table 1). Small rate enhancements were also observed for the remaining substrates, i.e. an increase by approximately a factor of two was observed for benzeneselenol, thiophenol, benzaldehyde, aniline, and phenol. The chloro- and bromo-substituents have essentially the same effect on the overall reaction

efficiencies, whereas the methyl substituent has little or no effect (Table 1).

The reaction efficiencies for addition and hydrogen atom abstraction are obtained by multiplying the corresponding product branching ratios by the overall reaction efficiency (Table 1). The charged radical **b** abstracts a hydrogen atom from toluene at an efficiency of 0.15%, whereas radicals **c** and **d** do so three times faster (0.48% and 0.44%, respectively). A slightly greater rate enhancement was observed for the addition pathway. The efficiency of addition for radicals **c** and **d** (3.52% and 3.56%, respectively) is approximately a factor of four greater than for radical **b** (0.85%). A similar pattern was observed for the other substrates. For example, hydrogen atom abstraction from thiophenol is faster for **c** and **d** by a factor of two and addition by a factor of ~3.5, as compared to **b**. These results demonstrate that both pathways are sensitive to the radicals' substituents, and suggest that addition may be more sensitive to substituent effects than substitution.

Molecular orbital calculations performed at the B3LYP/6-31G(d)+ZPVE level of theory revealed that the reaction exothermicities for hydrogen atom abstraction and addition are not affected by substitution on the charged phenyl radicals. For example, abstraction of a hydrogen atom from toluene by radicals **a**–**d** was estimated to be exothermic by 27.3–27.7 kcal/mol. Para-addition to aniline is exothermic by 30.2 kcal/mol for radical **b** and 31.2 kcal/mol for radical **c** (Table 4). These findings demonstrate that the observed substituent effects are not due to variations in reaction exothermicities. Instead, their likely origin is changes in the polar character, and thereby energy, of the transition states. The energies of the relevant charge-transfer transition state resonance structures can be lowered by increasing the electron affinity of the radical (energy released upon attachment of an electron at the radical site) [38–43]. Indeed, molecular orbital calculations carried out at the B3LYP/6-31+G(d) level of theory reveal that the vertical electron affinities (EA_V) of the radicals **a** and **b** are lower than those of the radicals **c** and **d** (4.78, 4.86, 5.11, and 5.12 eV, respectively). Therefore, the observed substituent effects are concluded to arise from different extents of polarization of the transition state for both the hydrogen abstraction and addition pathways. Analogous results have been reported for substitution reactions of charged radicals with allyl iodide [13], dimethyl disulfide [14], and other hydrogen atom donors [12(b)]. However, this is the first such report for gas-phase addition reactions.

3.4. Reactivity toward different substrates

The radical **b** was chosen as the test case to learn more about the factors that control the phenyl radicals' reactivity toward each of the aromatic substrates. The overall reactivity (overall reaction efficiency; Table 1) toward the different substrates does not vary much, with the exception of benzeneselenol that transfers a hydrogen atom to all the radicals at a very high efficiency (due to its low BDE and low ionization energy). In contrast, the competition between the hydrogen atom abstraction and addition channels varies significantly among the substrates studied. These findings are rationalized based on the transition state energies calculated for the hydrogen abstraction and addition reactions for radical **b**. These transition state energies are given in Table 4 as the energy difference between the separated reactants and the transition state (ΔE); the greater the numerical value of ΔE, the lower the transition state energy.

The transition state energies calculated for addition reactions of the radical **b** appear to correlate with the measured reaction efficiencies. The numerical value of ΔE increases, and hence transition state energy decreases, in the order thiophenol (ΔE=-2.1 kcal/mol) ~toluene (ΔE=-1.6 kcal/mol) >phenol (ΔE=-3.7 kcal/mol) >benzaldehyde (ΔE=-4.0 kcal/mol) >aniline (ΔE=-5.6 kcal/mol), whereas the addition efficiency increases in the same order (0.5%; 0.9%; 1.0%; 2.8%; 5.9%; respectively; the stable adduct as well as its fragmentation products are included in these values obtained from Table 1). This is a remarkable finding, as it suggests that the rate of formation of the stable adduct and its fragmentation products is controlled by the magnitude of the chemical barrier to addition, rather than, for example, rate of emission of IR light of the different collision complexes.

The efficiency of hydrogen atom abstraction by **b**

from the different substrates (Table 1) follows the order benzeneselenol (17%) > thiophenol (2.5%) benzaldehyde (1.2%) >toluene (0.2%) >aniline (0.1%) >phenol (0%). This order does not match with changes in the transition state energies for hydrogen abstraction. The ΔE values vary randomly from −2.0 kcal/mol (highest TS energy) calculated for thiophenol and toluene to −7.3 kcal/mol (lowest TS energy) calculated for benzaldehyde. However, the observed reactivities can be rationalized by considering competition between the two reaction channels. Addition is the intrinsically faster reaction because many different molecular orientations lead to a feasible transition state (only the lowest TS energies are listed in Table 4). Therefore, addition can be expected to dominate the reactivity when the barriers for hydrogen abstraction and addition are of equal magnitude, and even in some cases where the hydrogen abstraction TS lies lower in energy. The ratio of the transition state energies (given as ΔΔE) for hydrogen abstraction and addition (lowest-energy TS) follow the order benzaldehyde (1.8) >toluene (1.3) >aniline (0.9) >phenol (0.6). This order matches the observed reactivity trend for hydrogen abstraction from the different substrates. Thiophenol (ratio 1.0; most efficient hydrogen atom donor) is the only substrate that fails to fit into the previous correlation.

4. Conclusions

Hydrogen atom abstraction and/or addition reactions were observed upon reaction of the aromatic substrates benzeneselenol, thiophenol, benzaldehyde, toluene, aniline, and phenol with four differently substituted, charged phenyl radicals. Thermodynamic control was found to be of minor importance in determining competition between the two reaction channels, except in the extreme cases of benzeneselenol and thiophenol, two very efficient hydrogen atom donors due to their weak homolytic bond dissociation energies and relatively low ionization energies. For the other systems, the addition reactivity was found to correlate with the transition state energy for addition. However, the competitiveness of hydrogen atom abstraction appears to be determined by the relative energies of hydrogen abstraction and addition transition states rather than their absolute values. The addition is the intrinsically faster reaction due to many different molecular orientations that lead to a feasible transition state.

A stable covalently bound adduct accounted for a major portion of the reaction products in most cases. This finding was somewhat unexpected because adducts formed in a low-pressure gas-phase environment typically undergo fragmentation to form products or dissociation back to reactants before they can be stabilized via emission of photons. For the systems studied, adduct formation is facilitated by its high exothermicity. The low potential energy and the large number of internal degrees of freedom of the initially formed hot adduct expand its lifetime enough for efficient cooling by emission of IR light.

The efficiency of both hydrogen atom abstraction and addition was found to increase upon addition of the electron-withdrawing bromo- and chloro-substituents to the meta position in the phenyl radicals, in agreement with the tentative conclusion made earlier based on relative rate measurements in solution [10(f)]. The addition reaction appears to be more sensitive to substituent effects than hydrogen abstraction. The rate enhancements are rationalized by enhanced polarization of the transition state for both hydrogen atom abstraction and addition. Hence, the overall reactivity of phenyl radicals toward aromatic substrates can be enhanced through the placement of electron-withdrawing substituents on the radical's phenyl ring.

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