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Polar Effects Control Hydrogen-Abstraction Reactions of Charged, Substituted Phenyl Radicals

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The rate of hydrogen atom abstraction from tributyltin hydride, benzeneselenol, thiophenol, and tetrahydrofuran was measured in the gas phase for charged phenyl radicals with different neutral substituents at the *meta*- or *ortho*-position. A charged pyridinium substituent (*meta* or *para*) allowed the manipulation of the radicals in the Fourier transform ion cyclotron resonance mass spectrometer that was used to carry out the experiments. All the reaction rates were found to be similarly affected by substituents on the radical: *meta*, H < Br ∼ Cl < CN (most reactive); *ortho*, H < CF_3 ∼ Cl ∼ F. The experimental observations parallel the transition-state energies calculated for hydrogen abstraction from methanol. However, the calculated reaction exothermicities do not correlate with the reactivity trends. Instead, a correlation exists between the reactivity and electron affinity of the radicals. We conclude that the electron-withdrawing substituents studied here lower the reaction barrier by increasing the polarity of the transition state, without an associated increase in reaction exothermicity. The *increase in the electron affinity (ΔEA) of the radical caused by a given substituent provides a sensitive probe for the substituent's barrier-lowering effect* (in the few cases studied in detail, the barrier is lowered by about 10% of ΔEA_v). Another way to lower the barrier involves lowering the ionization energy of the substrate. Indeed, all the radicals follow the reactivity trend of thiophenol > 4-fluorothiophenol > pentafluorothiophenol. This trend reflects the decreasing ionization energies of the three substrates rather than the decreasing reaction exothermicities or increasing homolytic bond-dissociation energies (4-fluorothiophenol > thiophenol > pentafluorothiophenol). Apparently, the polar control overrides the enthalpic control in this case. The results reported for radicals with different distances between the radical site and the charged group suggest that *similar substituent effects are expected for neutral phenyl radicals*, and that the *hydrogen abstraction ability of heteroaromatic radicals is likely to be tunable by pH.*

Introduction

Organic radicals play a crucial role in numerous biological and chemical processes, including the action of some powerful antitumor drugs.[1−6] For example, the naturally occurring enediyne antitumor antibiotics dynemicin and neocarzinostatin are thought to metabolize into aromatic 1,4-σ,σ-biradicals, which are the reactive form of the drugs.[4] The key step in the processes leading to DNA-strand cleavages upon the action of these and other nonhydrolytic DNA cleavers is *hydrogen atom abstraction from a sugar moiety in DNA by the reactive radical formed from the drug.*[3−5] Obviously, detailed knowledge concerning the factors that control the efficiency of the hydrogen atom abstraction reaction would be invaluable for the rational design of pharmaceuticals whose action is based on the nonhydrolytic cleavage of DNA.

Hydrogen atom abstraction reactions of numerous simple radicals (e.g., $^\bullet OH$, $^\bullet H$, $^\bullet CH_3$, $^\bullet Cl$) have been thoroughly examined.[5,7−9] The same applies to substitution reactions of the phenyl radical with simple substrates.[10] However, little is known about reactions of substituted phenyl radicals with complex organic substrates.[11] To the best of our knowledge, only a handful of such studies have appeared thus far. The results are summarized as follows. A reactivity order of *p*-tolyl < phenyl < *p*-bromo < *p*-nitrophenyl radical has been reported for hydrogen abstraction from 19 different hydrogen atom donors, including several hydrocarbons, acetone, methyl acetate, thiophenol, and cyclohexene, as well as toluene and its *p*-fluoro, -nitro, -methyl, and -methoxy derivatives.[11a] Electron-withdrawing *p*-chloro and -nitro substituents were demonstrated to increase phenyl radical's rate of hydrogen abstraction (phenyl < *p*-chloro < *p*-nitro) from acetonitrile,[11b] toluene,[11d] and cyclohexane[11d,f] in solution. An opposite substituent effect (phenyl > *p*-chloro > *p*-nitro) was observed for hydrogen atom abstraction from chloroform. This result was rationalized by the electron-accepting character of this particular substrate.[11d]

The above substituent effects were concluded to arise from the ability of the substituents to polarize the transition state in a favorable manner and thereby decrease its energy. However, the importance of enthalpic effects was not addressed in these studies. Further, only a few substituted radicals have been studied thus far. For example, no data are available for *meta* substituents, which affect the reaction cleanly via inductive and not resonance effects (in contrast to *para* substituents). To be able to predict structure−reactivity relationships for phenyl radicals, it is crucial to obtain more information on the properties of these important reaction intermediates.

We report here a systematic study of substituent effects on the ability of charged phenyl radicals to undergo hydrogen atom abstraction from organic hydrogen atom donors in the gas phase. This research is based on our recent discovery that phenyl radicals with a chemically inert, charged substituent that is remote from the radical site display the same reactions and

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reactivity trends as the corresponding neutral radicals.[12−15] The charged group is essential as it provides a handle for mass spectrometric manipulations,[12−15] such as purification of the reactant radical and analysis of reaction products. Through the addition of neutral substituents to the phenyl ring, these charged radicals can be used to systematically explore the effects of substituents on the radical reactivity.[13,15] In previous studies,[15] we found that the gas-phase reactivities of phenyl radicals (with a pyridinium-charged group) toward iodine abstraction from allyl iodide, thiomethyl abstraction from dimethyl disulfide, and cyano abstraction from *tert*-butyl isocyanide are facilitated by *meta* substituents in the order of $CH_3 \sim H < Br \sim Cl \sim COOH < CN \sim NO_2$. This finding parallels literature reports for substituent effects on bromine and thiomethyl abstraction[11c,11d] by neutral phenyl radicals in solution ($H < p\text{-Cl} < p\text{-NO}_2$). Traditional bond-dissociation energy and/or enthalpy arguments do not adequately explain the above findings. However, they are readily rationalized on the basis of varying abilities of different substituents to stabilize the transition state by increasing its polar character. The above results provide support for the general relevance of the information obtained in our gas-phase studies.

We recently employed the above approach to demonstrate that *fluorine substituents increase reaction rates of phenyl radicals* (with a phosphonium-charged group) *with three hydrogen atom donors*, thiophenol, 1,4-cyclohexadiene, and tetrahydrofuran.[13] The reactivity trend toward these three substrates was found to be the same as that reported[16] for solution, phenol < thiophenol < benzeneselenol. The present study expands this research to include a large number of differently substituted, charged phenyl radicals and several organic hydrogen atom donors. The substituent effects observed for the charged phenyl radicals are also likely to apply to neutral phenyl radicals.

Experimental Section

Some of the experiments were carried out using an Extrel model FTMS 2001 Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR).[12−15] This instrument contains a differentially pumped dual cell aligned within the magnetic field produced by a 3.0 T superconducting magnet operated at ca. 2.8 T. The nominal base pressure was $<10^{-9}$ Torr, maintained by two turbomolecular pumps (330 L/s), each backed with a mechanical pump. The remaining experiments were performed using a Finnigan model FTMS 2001 FT-ICR.[15] The differentially pumped dual cell of this instrument is aligned within the magnetic field produced by a 3.0 T superconducting magnet. The nominal base pressure is $<10^{-9}$ Torr, maintained by two diffusion pumps (800 L/s), each backed with a mechanical pump. In both instruments, the two cells are separated by a common wall (the conductance limit), which contains a 2 mm hole in the center. This plate and the other two trapping plates were kept at +2 V unless otherwise stated.

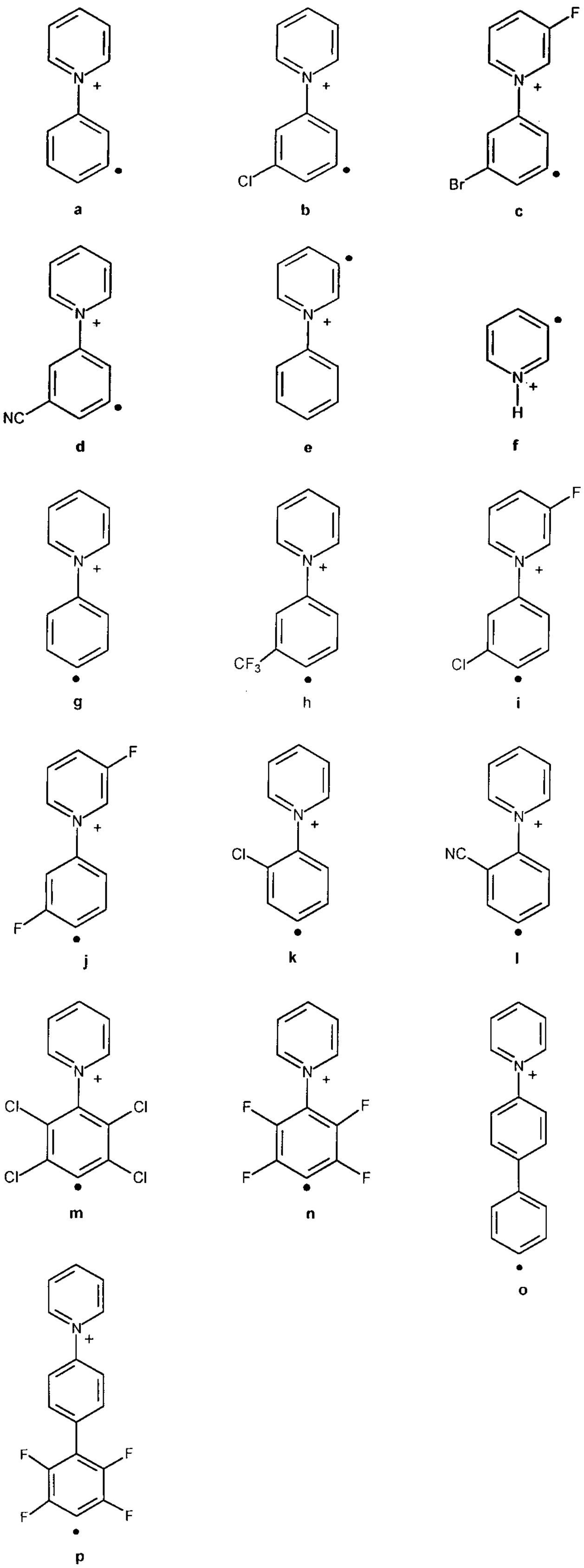
All the radical precursors were obtained commercially, except for 4-chloro-2′,3′,5′,6′-tetrafluoro-4′-iodobiphenyl, the precursor to the radical **p**. A modified Suzuki cross-coupling reaction was used to synthesize this precursor.[17] Under a nitrogen purge, about 2 g (5 mmol) of 1,4-diiodotetrafluorobenzene, 0.8 g (5.25 mmol, 1.05 equiv) of 4-chlorobenzeneboronic acid, and 25 mL of 1-propanol were charged to a 200 mL, three-necked, round-bottomed flask equipped with a magnetic stirring bar, a condenser, and a nitrogen gas inlet. The mixture was stirred at room temperature for 30 min, allowing the solids to dissolve. The resulting solution was treated with ca. 3 mg (0.015 mmol, 0.003 equiv) of palladium acetate, 12 mg (0.045 mmol, 0.009 equiv) of triphenylphosphine, 6 mL of 2 M sodium carbonate (Na_2CO_3) (6 mmol, 1.20 equiv), and 5 mL of deionized water, and heated to reflux under a nitrogen atmosphere. After 45 min at reflux, the heat source was removed and 15 mL of water was added while the mixture was still hot. The nitrogen gas source was removed, and the reaction mixture was stirred and cooled to room temperature while open to the atmosphere overnight. The mixture was diluted with 25 mL of ethyl acetate and transferred into a 200 mL separatory funnel. The two phases were separated, and the aqueous layer was back-extracted with two additional 12 mL portions of ethyl acetate. The combined organic layers were washed with 12 mL of aqueous (aq) 5% sodium bicarbonate ($NaHCO_3$) followed by two washes with 12 mL of a saturated NaCl solution. The organic solution was placed in a 250 mL Erlenmeyer flask with a magnetic stirring bar. To the mixture was added 1.25 g of Darco, and the mixture was stirred at room temperature for 30 min. Then, 2.5 g of sodium sulfate (Na_2SO_4) was added, and the stirring was continued for an additional 30 min. A Büchner funnel was charged with Celite to a depth of 1 cm, and 2.5 g of Florisil was spread evenly on top of the Celite. The above mixture was filtered through this pad of filter aid. The filter cake was rinsed with ethyl acetate, 2 × 10 mL. The filtrate was concentrated under reduced pressure.

Samples were introduced into the instruments by using either a leak valve, a heated solids probe, a set of pulsed valves,[18] or a single-batch inlet system equipped with a variable leak valve. The nominal reagent pressures were measured with two ionization gauges, one located on each side of the dual cell.

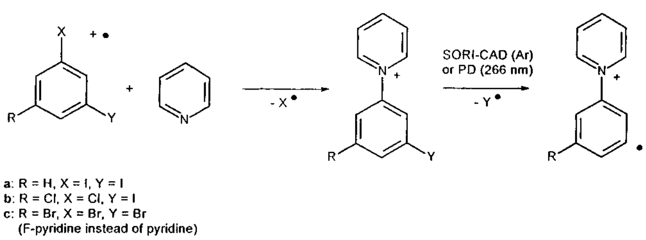
The procedure employed to generate radical **d** has been reported elsewhere.[15] The same applies to the rest of the charged phenyl radicals shown in Scheme 1.[12−16] 1,3-Diiodobenzene was used as the precursor for radical **a**, 1,3-dichloro-5-iodobenzene for **b**, 1,3,5-tribromobenzene for **c**, iodobenzene for **e**, 1,4-diiodobenzene for **g**, 5-bromo-2-iodobenzotrifluoride for **h**, 1-bromo-3-chloro-4-iodobenzene for **i** and **k**, 1-bromo-3-fluoro-4-iodobenzene for **j**, 1-chloro-2-cyano-4-nitrobenzene for **l**, 1,4-dinitrotetrachlorobenzene for **m**, and 1,4-diiodotetrafluorobenzene for **n** (Schemes 2−4). The precursors were introduced at a nominal pressure of 6.0×10^{-8} to 3.0×10^{-7} Torr into one side of the dual cell by using a Varian leak valve or a heated solids probe. Pyridine (3-iodopyridine for **e** and **f**) was added at approximately the same nominal pressure into the same cell through a batch inlet system. The mixture was subjected to electron ionization, which resulted in an intense signal for the substituted benzene radical cation. The ion signal was maximized for each experiment (typically 20 eV of electron energy, 8 μA of emission current, and 30 ms of ionization time). The benzene radical cation was allowed to react with the neutral pyridine present in the cell, leading to the *ipso* substitution[19] of one of the halogen atoms or nitro groups (for radicals **c**, **h**, **i**, and **j**, 3-fluoropyridine was used instead of pyridine to avoid the generation of a product ion with the same mass as that of the reactant ion upon the *ipso* substitution of a bromine atom). Formation of an abundant displacement product occurred in 0.5−5 s. The precursor ion for **f** was generated by protonating 3-iodopyridine with ionized methanol (Scheme 3).

The substituted halo- or nitrobenzene ions, generated in one side of the dual cell as described above, were transferred into the other side by grounding the conductance limit plate for approximately 150 μs, which allowed the ions to pass through the 2 mm hole in the plate. The substituted halo- or nitrobenzene ions were isolated by applying a stored-waveform inverse-

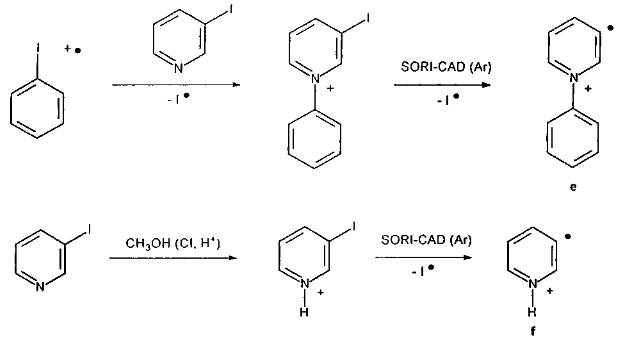
SCHEME 1



SCHEME 2



SCHEME 3

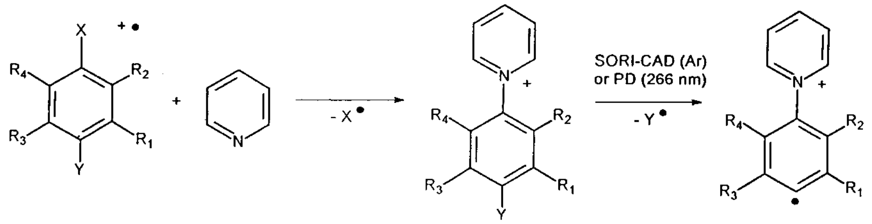


Fourier transform (SWIFT)[20] excitation pulse to the plates of the cell. The desired charged phenyl radicals were generated by homolytic carbon−halogen or carbon−nitro bond cleavage in the substituted benzenes. Photodissociation was used to achieve carbon−bromine bond cleavage,[21] while sustained off-resonance-irradiated collision-activated dissociation[22] (SORI-CAD) was employed to accomplish carbon−iodine and carbon−nitro bond cleavage. SORI-CAD was implemented by introducing argon into the cell via a pulsed valve assembly (the nominal peak pressure in the cell was approximately 1 × 10^{-5} Torr), and collisionally activating the ions with argon for 0.5−1 s at a frequency of 0.5−1 kHz higher than the cyclotron frequency of the ions. Photodissociation involved 5−10 pulses of a 266 nm Nd-YAG laser (10 Hz repetition rate).

The charged phenyl radicals were isolated as described above. They were cooled by allowing them to collide for 1 s with the neutral molecules present in the cell (the reagent to be used in the final stage of the experiment), and by providing time for the emission of IR light. These cooling processes yield ions that are at or near room temperature, as indicated by their inability to undergo endothermic reactions in our experiments. They were allowed to react with a neutral reagent for a variable period of time (typically 0.5−100 s). Detection was carried out using "chirp" excitation (2.7 MHz bandwidth, 3.2 kHz/μs sweep rate). All the spectra are an average of at least 15 transients that were recorded as 64 K data points and subjected to a one-zero fill prior to Fourier transformation.

Primary products were identified on the basis of their fixed relative abundances (branching ratios) at short reaction times. 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 by assuming pseudo-first-order kinetics. The collision rate constant (k_{coll}) was calculated using the parameterized trajectory theory of Su et al.[23] The efficiency of each reaction (i.e., the percent of collisions that result in reaction) is given by $k_{\mathrm{exp}}/k_{\mathrm{coll}} \times 100\%$. The accuracy of the rate constant measurements is estimated to be ±50%, while the precision is usually better than ±10%. The greatest uncertainty arises from the pressure measurement in the cell. The pressure readings of the ion gauges (located remotely 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 correction factor was obtained by measuring rates of reactions assumed to occur at collision rate for the neutral reagent of interest (highly exothermic, barrierless reactions, such as proton transfer and electron transfer).

SCHEME 4



g: R_1-R_4 = H, X = I, Y = I
h: R_1 = CF_3, R_2-R_4 = H, X = Br, Y = I★
i: R_1 = Cl, R_2-R_4 = H, X = Br, Y = I★
j: R_1 = F, R_2-R_4 = H, X = Br, Y = I★
k: R_1,R_3,R_4 = H, R_2 = Cl, X = I, Y = Br
l: R_1,R_3,R_4 = H, R_2 = CN, X = Cl, Y = NO_2
m: R_1, R_2, R_3, R_4 = Cl, X = NO_2, Y = NO_2
n: R_1, R_2, R_3, R_4 = F, X = I, Y = I

★fluoropyridine was used instead of pyridine

TABLE 1: Homolytic Bond-Dissociation Energy (BDE, kcal/mol) and Ionization Energy (IE, eV) Values of the Hydrogen Atom Donors

substrate	BDE	vertical IE[a]
tributyltin hydride	73.7[b]	8.49
benzeneselenol	78[c]	8.07
pentafluorothiophenol	84.9[d]	9.59
4-fluorothiophenol	82.1[d]	8.48
thiophenol	83.3	8.28
tetrahydrofuran	92[e]	9.20

[a] BLYP/LANL2DZ. [b] Ref 27. [c] Ref 28. [d] B3LYP/6-31G(d) + ZPVE; based on isodesmic reaction with thiophenol. [e] Ref 29.

Molecular-orbital calculations based on the density-functional theory were performed using the Gaussian 92 Revision F or Gaussian 98 suite of programs.[25] The geometries of most of the molecules were fully optimized at the B3LYP/6-31G(d) level of theory; B3LYP/LANL2DZ was employed in calculations used to estimate the vertical ionization energies of the hydrogen atom donors (Table 1). Zero-point vibrational energies (ZPVE) were calculated from the B3LYP/6-31G(d) harmonic frequencies and scaled by a factor of 0.9804 to account for the systematic overestimation of the vibrational frequencies made by this density-functional method. In the calculation of the electron affinities, optimization of the molecules was carried out at the B3LYP/6-31+G(d) level of theory. For calculation of vertical thermochemical values, the geometries of the ground state species were directly used in single-point calculations. The force constant matrices obtained for the stationary points were checked for the correct number of negative eigenvalues (zero for equilibrium structures, one for transition states).

Results and Discussion

General Considerations. The energetics of reactions occurring in solution are perturbed by the presence of the solvent (Figure 1). Different degrees of solvation of the reactants, transition state(s), intermediates, and products often have a major influence on the overall potential-energy surface. Therefore, fundamental information on structure−reactivity relationships is better obtained by investigation of reactions that are free of solvent perturbation. This can be accomplished by employing experimental gas-phase techniques. The gas-phase results can be directly modeled by molecular-orbital calculations that also deal with the gas-phase environment.

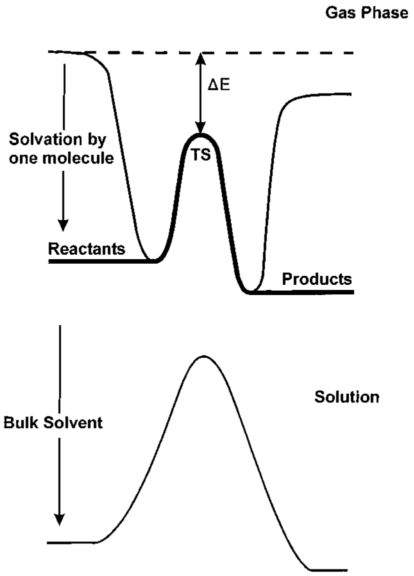
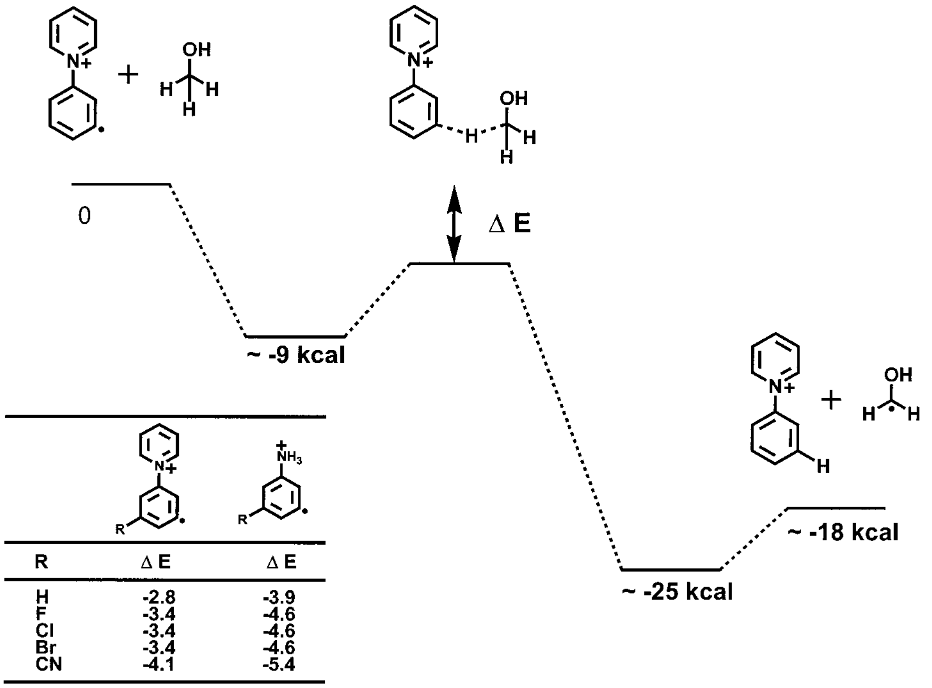


Figure 1. Hypothetical potential-energy surface for a reaction in the gas phase (top), without any solvation effects (middle; line marked with Reactants, TS, and Products), and in solution (bottom).

The present study focuses on gas-phase ion−molecule reactions that take place in high vacuum. These reactions are free from solvent effects, with the exception of the formation of the initial collision complex, i.e., solvation of the reactant ion with the reagent molecule (Figure 1). Ion−dipole and ion-induced dipole forces between the ion and the molecule lower the potential energy of the collision complex.[26] This leads to an increase in the vibrational and rotational energies of the gas-phase reacting system because the total energy of the system is constant and determined by the energy of the isolated reactants. The excess vibrational and rotational energies of the collision complex can be used to overcome barriers on the reaction coordinate but not to drive overall-endothermic reactions.

The ion−molecule reaction rates (or reaction efficiencies, i.e., the percent of collisions yielding a product) are controlled by the difference in energy (ΔE, Figure 1) between the isolated reactants and the transition state corresponding to the reaction bottleneck.[26] *Just like in solution, a decrease in the energy of the transition state leads to a faster gas-phase ion−molecule reaction.* However, endothermic reactions (wherein $\Delta H > 5$ kcal/mol) and reactions with a barrier above the energy of the isolated reactants are not observable under the conditions employed here. In cases wherein the barrier is very low, such that ΔE becomes too large, the reaction is insensitive to barrier-lowering effects because it already occurs at every collision (the reaction efficiency is 100%). This should not be the case for hydrogen atom abstraction reactions, however. Our preliminary



R	ΔE	ΔE
H	-2.8	-3.9
F	-3.4	-4.6
Cl	-3.4	-4.6
Br	-3.4	-4.6
CN	-4.1	-5.4

Figure 2. Major stationary points of the potential-energy surface calculated for abstraction of a hydrogen atom from methanol by the *N*-(3-dehydrophenyl)pyridinium radical (B3LYP/6-31G(d) + ZPVE). Effects of F, Cl, Br, and CN substituents on the energy difference between the transition state and the isolated reactants (Δ*E*) are given for the *N*-(3-dehydrophenyl)pyridinium as well as the 3-dehydroanilinium radical.

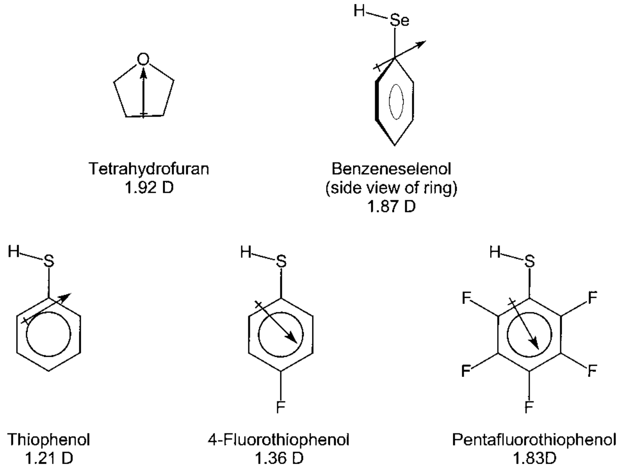


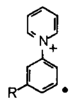
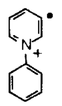
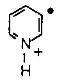
Figure 3. Calculated molecular dipoles (AM1 level) for some hydrogen atom donors.

studies suggest that these reactions are often associated with such substantial energy barriers that they do not occur at the collision rate.[13]

The following pieces of evidence indicate that the reactivity trends reported here for differently substituted, charged phenyl radicals arise from varying transition-state energies for hydrogen atom abstraction, and not from other variables such as those related to collision dynamics. (1) The measured reaction efficiencies reflect the calculated Δ*E* for hydrogen atom abstraction by the differently substituted radicals from a given substrate (B3LYP/6-31G(d) + ZPVE) (Figure 2). (2) The observed substituent-effect trends agree with the limited amount of information available in the literature[11] on the neutral phenyl radical in solution. (3) The same substituent-effect trend was observed for all hydrogen atom donors, independent of their type, magnitude of dipole moment, or orientation of the dipole within the collision complex (Figure 3). The same applies to the size of the radical and the size and location of its substituents (unless they affect the transition-state energy via electronic effects; see below). (4) No correlation was found between the reaction efficiency and the well depth corresponding to the most-stable collision complex. The well depths were calculated to be up to 6.4 and 7.1 kcal/mol for the complexes of thiophenol and pentafluorothiophenol, respectively, with the *N*-(3-dehydrophenyl)pyridinium radical (radical **a**, Scheme 1; many low-energy configurations exist for both collision complexes). About 9 kcal/mol of energy-lowering was calculated for the collision-complex formation between radicals **a**−**d** and methanol. Neither substitution on the radical nor substitution on the neutral substrate was found to affect this collision complex energy. (5) No correlation was found between the reaction efficiency and the specific configurations of the lowest-energy collision complexes. In most cases, calculations involving several different minimum-energy orientations between the ion and molecule revealed energy variations of only <2 kcal/mol. (6) Finally, the collision complex that is formed for one of the radicals studied, the 3-dehydropyridinium radical (**f**, Scheme 1), deserves attention. This complex has a global minimum-energy structure that is substantially lower in energy (by 14 kcal/mol relative to the isolated reactants in the case of thiophenol) than that of the other radicals studied (~6−7 kcal/mol below the energy level of the separated reactants). This especially stable structure involves a hydrogen-bonding interaction between the N−H group in the radical and the sulfur atom of thiophenol. The low energy of this hydrogen-bonded structure might have been expected to hinder radical reactions since this structure does not lead to a radical reaction (the hydrogen atom donor is too far from the reactive radical site). However, the radical **f** reacts slightly faster than its *N*-phenyl analogue, radical **e**, with no hydrogen-bonding ability.

Summary of Results. The charged phenyl radicals chosen for this study are shown in Scheme 1. These radicals carry a chemically inert, positively charged pyridinium group, and are therefore highly electrophilic. Previously, such charged phenyl radicals have been demonstrated to possess chemical properties similar to those of neutral phenyl radicals.[11−15] The radicals were

TABLE 2: Efficiencies[a] and Products[b] Measured for Reactions of the *Meta*-Substituted Charged Radicals a−f with Several Hydrogen Atom Donors

 Radical	Tributyltin hydride	Benzeneselenol	Tetrahydro-furan	Thiophenol	4-Fluorothiophenol	Pentafluoro-thiophenol
R=H **a**	H• Abstraction (100%) Eff= 39%	H• Abstraction (100%) Eff=17%	H• Abstraction (100%) Eff=1%	H• Abstraction (83%) Adduct (17%) Eff=3%	H• Abstraction (93%) Adduct (7%) Eff=2%	H• Abstraction (100%) Eff=0.2%
R=Cl **b**	H• Abstraction (100%) Eff=49%	H• Abstraction (100%) Eff=27%	H• Abstraction (100%) Eff=2%	H• Abstraction (76%) Adduct (24%) Eff=7% (5%)	H• Abstraction (90%) Adduct (10%) Eff=4%	H• Abstraction (100%) Eff=0.5%
R=Br **c**		H• Abstraction (100%) Eff=27%	H• Abstraction (100%) Eff=2%	H• Abstraction (78%) Adduct (22%) Eff=6% (5%)	H• Abstraction (77%) Adduct (23%) Eff=5% (4%)	H• Abstraction (100%) Eff=0.3%
R=CN **d**	H• Abstraction (100%) Eff=71%	H• Abstraction (100%) Eff=38%	H• Abstraction (100%) Eff=6%	H• Abstraction (64%) Adduct (29%) Adduct-H• (7%) Eff= 10% (6%)		H• Abstraction (100%) Eff=1.8%
 **e**	H• Abstraction (100%) Eff=74%	H• Abstraction (83%) SeH• Abstraction (15%) Adduct-H• (2%) Eff= 41% (40%)	H• Abstraction (100%) Eff=21%	H• Abstraction (56%) Adduct-H• (21%) Adduct-SH• (12%) Adduct (11%) Eff=34% (19%)	H• Abstraction (28%) Adduct (25%) Adduct-H• (3%) Adduct-FH• (28%) Adduct-SH• (16%) Eff=22% (6%)	H• Abstraction (49%) Adduct (29%) Adduct-SH•(12%) Adduct-91 (5%) Adduct-FH• (5%) Eff=3% (2%)
 **f**	H• Abstraction (100%) Eff=89%	H• Abstraction (65%) SeH• Abstraction (30%) Adduct-H• (5%) Eff=38% (36%)	H• Abstraction (100%) Eff= 32%	H• Abstraction (47%) Adduct-H• (26%) Adduct-SH• (23%) SH• Abstraction (4%) Eff=42% (21%)	H• Abstraction (20%) Adduct (5%) Adduct-H• (9%) Adduct-FH• (33%) Adduct-SH• (23%) Adduct-F• (10%) Eff=39% (8%)	H• Abstraction (36%) Adduct-SH• (26%) Adduct (22%) Adduct-FH• (16%) Eff=5% (2%)

[a] Reaction efficiency (Eff) = $k_{exp}/k_{coll} \times 100\%$. The value given in parentheses is the hydrogen-atom-abstraction efficiency in those cases where this value deviates from the total reaction efficiency. [b] Relative product abundances are given in parentheses.

synthesized and purified by multistep procedures described earlier in detail (Schemes 2−4).[11−15] They were allowed to react with tributyltin hydride, benzeneselenol, thiophenol, 4-fluorothiophenol, pentafluorothiophenol, and tetrahydrofuran, and some also with phenol (Table 1 shows some physical properties of these reagents[27−30]). The temporal variation of reactant- and product-ion abundances was recorded. The primary products and their branching ratios, together with reaction efficiencies (k_{exp}/k_{coll}), are given in Tables 2 and 6. The data for reactions of **a**−**c** with benzeneselenol and thiophenol have been published previously.[15c] Hydrogen atom abstraction (sometimes in the form of $^{\bullet}$SH and $^{\bullet}$SeH abstraction for thiophenol and benzeneselenol, respectively) is the only reaction observed in most cases. However, a substantial amount of additional products resulting from addition reactions were observed in many of the reactions of thiophenol and 4-fluorothiophenol. In these cases, the efficiency of hydrogen atom abstraction (and SH/SeH abstraction) is given in parentheses next to the total reaction efficiency in Tables 2 and 6. Molecular-orbital calculations were employed to examine the reaction exothermicities, collision-complex and transition-state energies, and polarity of the radicals and substrates (Tables 3−5).

Reaction Efficiencies of Phenyl Radicals with the Charged Substituent in the *Meta*-Position (a−f). The phenyl radicals bearing the pyridinium group as well as a neutral electron-withdrawing substituent in the two *meta*-positions with respect to the radical site (**b**−**f**, Scheme 1) exhibit an enhanced reactivity toward each of the hydrogen atom donors studied compared to that of the "unsubstituted" radical **a**. For example, the radical **a** abstracts a hydrogen atom from tetrahydrofuran at an efficiency of 1% (i.e., 1 out of every 100 collisions leads to a reaction; Table 2), while the cyano-substituted radical **d** undergoes the same reaction at an efficiency of 10% (Table 2). The reactivity of the differently substituted radicals follows the order of R = H < Cl ∼ Br < CN.

In an effort to explore the reactivity of radicals with an even greater electron deficiency than those discussed above, reactions of the *N*-phenyl-3-dehydropyridinium radical **e** and the 3-de-

TABLE 3: Calculated (B3LYP/6-31G(d)) Reaction Enthalpies (kcal/mol) for H$^{\bullet}$ Abstraction from Thiophenol, Benzene, and Methane by Charged Phenyl Radicals aa−dd

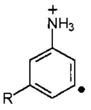
 Radical	Thiophenol	Benzene	Methane
R = H aa	-39.7	-2.7	-8.7
R = Cl bb	-39.8	-2.8	-8.8
R = F bc	-40.0	-3.0	-9.0
R = OH cd	-39.8	-2.8	-8.8
R = CN dd	-40.4	-3.4	

TABLE 4: Calculated (B3LYP/6-31G(d)) Reaction Enthalpies (kcal/mol) for H$^•$ Abstraction from Thiophenol, Benzene, and Methane by Radicals f, ef, and ff

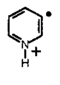
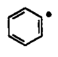
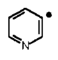
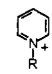
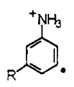
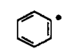
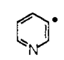
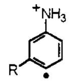
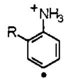
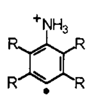
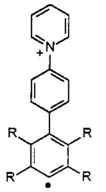
Radical	Thiophenol	Benzene	Methane
 **f**	-43.2	-6.2	-12.2
 **ef**	-37.0	0	-6.0
 **ff**	-37.5	-0.5	-6.5

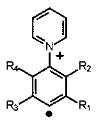
TABLE 5: Calculated (B3LYP/6-31+G(d)) Electron Affinities (eV) for Radicals e, f, aa, bb, cc, dd, ef, ff−nn, o, and p

Radical		Vertical Electron Affinity	Adiabatic Electron Affinity
	R = Phenyl **e**	5.78	
	R = H **f**	6.12	6.53
	R = H **aa**	4.79	5.22
	R = Cl **bb**	5.13	5.55
	R = Br **cc**	5.14	5.52
	R = CN **dd**	5.40	5.82
	**ef**	0.61	1.10
	**ff**	0.98	
	R = H **gg**	4.67	5.10
	R = CF$_3$ **hh**	5.22	
	R = Cl **ii**	5.14	
	R = F **jj**	5.29	
	R = Cl **kk**	4.96	
	R = CN **ll**	5.23	
	R = Cl **mm**	6.19	
	R = F **nn**	6.65	
	R = H **o**	2.04^a	
	R = F **p**	4.93^a	

[a] Calculated at the B3LYP/6-31+G(d)//B3LYP/6-31G(d) level of theory.

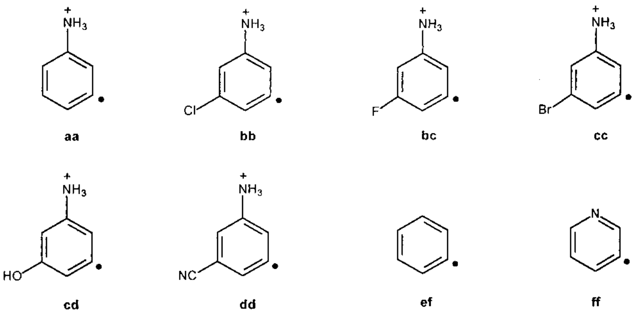
hydropyridinium radical **f** (charge within the same ring that carries the radical site; Scheme 1) were explored. Radical **f** appears to be slightly more reactive than **e**, but both of these radicals react faster than the other radicals studied (Table 2), resulting in a general reactivity order of **a** (R = H) < **b** (Cl) ∼ **c** (Br) < **d** (CN) < **e** ≤ **f**.

TABLE 6: Efficiencies[a] and Products[b] Measured for Reactions of the *o*- and/or *m*-Substituted, Charged Phenyl Radicals g−n with Thiophenol and Tetrahydrofuran

 Radical	Thiophenol	Tetrahydrofuran
g R$_1$-R$_4$ = H	H• Abstraction (79%) Addition (21%) Eff. = 1% (1%)	H• Abstraction (100%) Eff. = 0.3%
h R$_1$ = CF$_3$, R$_2$-R$_4$ = H	H• Abstraction (63%) Addition (37%) Eff. = 4% (2%)	H• Abstraction (100%) Eff. = 4%
i R$_1$ = Cl, R$_2$.R$_4$ = H	H• Abstraction (60%) Addition (40%) Eff. = 8% (5%)	H• Abstraction (100%) Eff. = 3%
j R$_1$ = F, R$_2$.R$_4$ = H	H• Abstraction (38%) Addition (62%) Eff. = 10% (4%)	H• Abstraction (100%) Eff. = 4%
k R$_1$, R$_3$, R$_4$ = H, R$_2$ = Cl	c	H• Abstraction (100%) Eff. = 0.6%
l R$_1$, R$_3$, R$_4$, = H, R$_2$ = CN	H• Abstraction (51%) Addition (49%) Eff. = 5% (3%)	H• Abstraction (100%) Eff. = 2%
m R$_1$-R$_4$ = Cl	c	H• Abstraction (100%) Eff. = 8%
n R$_1$-R$_4$=F	H Abstraction (87%) SH Abstraction (6%) Addition - SH (2%) Addition (5%) Eff. = 45% (42%)	H Abstraction (100%) Eff. = 22%

[a] Reaction efficiency (Eff) = $k_{\mathrm{exp}}/k_{\mathrm{coll}} \times 100\%$. The value given in parentheses is the hydrogen-atom-abstraction efficiency in those cases where this value deviates from the total reaction efficiency. [b] Relative product abundances are given in parentheses. [c] Reaction not examined.

SCHEME 5



Computational Results. *Enthalpic Effects.* The enthalpic driving force for hydrogen abstraction by the differently substituted, charged phenyl radicals was explored computationally (B3LYP/6-31G(d) + ZPVE) by determining the heats of reaction for H$^•$ abstraction from thiophenol, benzene, and methane by the 3-dehydroanilium radical **aa** (a model for the experimentally studied radical **a**) and its *m*-Cl- (**bb**; model for **b**), -F- (**bc**), -OH- (**cd**), and -CN-substituted (**dd**; model for **d**) derivatives (Schemes 1 and 5). All of these reactions are exothermic, and their exothermicities are not sensitive to substitution on the radical (Table 5). The enthalpy change for the abstraction of a hydrogen atom ranges between −39.7 and −40.4 kcal/mol from thiophenol, −2.7 and −3.4 kcal/mol from benzene, and −8.7 and −9.0 kcal/mol from methane (Table 3). As an example, the abstraction of a hydrogen atom from thiophenol is calculated to be exothermic by 39.7 kcal/mol for the 3-dehydroanilinium radical **aa** (R = H) and by 39.8 kcal/mol for the analogous *m*-chloro-substituted radical **bb** (Table

3), a difference of only 0.1 kcal/mol. Similarly, chlorine substitution on the phenyl radical itself changes the exothermicity of hydrogen atom abstraction from thiophenol by only 0.3 kcal/mol (phenyl radical, 34.3 kcal/mol; *m*-chlorophenyl radical, 34.0 kcal/mol).[30] It is concluded that the observed variations in reaction efficiencies toward a given substrate shown by the differently substituted phenyl radicals do not arise from changes in the reaction enthalpy. A similar situation likely applies to the other hydrogen atom donors studied. On the basis of the above results and the relevant bond-dissociation energies reported in Table 1, the exothermicities of hydrogen abstraction by the charged phenyl radicals from tributyltin hydride (most exothermic), benzeneselenol, and tetrahydrofuran (least exothermic) are estimated to be ∼50, ∼45, and ∼24 kcal/mol, respectively, and to vary by <1 kcal/mol for the differently substituted radicals.

Reactions involving the 3-dehydropyridinium radical **f** are calculated to be approximately 3 kcal/mol more exothermic (Table 4) than reactions of the other computationally examined charged radicals (**aa**−**dd**), not a difference large enough to explain the great differences in the efficiencies of the overall highly exothermic reactions studied here. It is especially notable that the exothermicities estimated for radicals **aa**−**dd** are calculated to be only about 3 kcal/mol greater than those involving the neutral phenyl radical **ef** and the neutral 3-dehydropyridine radical **ff** (Table 4; Scheme 1). *Obviously, phenyl radicals' substitution does not have a strong effect on the enthalpy change of exothermic hydrogen atom abstraction reactions even when the substituent is a charged group.*

Polar Effects. Reactions involving radicals that are good electron acceptors or donors are likely to be significantly influenced by the polarization of the transition state, i.e., low-lying ionic "resonance structures" contribute to the electronic structure and thereby lower the energy of the transition state.[8,9,31,32] The phenyl radicals studied here are highly electrophilic[15] due to the electron-withdrawing, positively charged pyridinium group. The hydrogen atom abstraction reactions of these radicals are highly exothermic (Table 3) and thus likely to proceed through an early transition state. Hence, for a reaction of a charged phenyl radical $R^\bullet$ with a reagent X−Y, the ionic resonance structure that most strongly contributes to the transition state has the reactant geometry and can be represented by $[R^-][XY^{+\bullet}]$.[8,9,31,32] This configuration can be stabilized by increasing the electron affinity (EA) of the radical or by decreasing the ionization energy (IE) of the substrate.[31−33] Note that we use the term "electron affinity" for electron-binding energies of the charged phenyl radicals studied here instead of the term "recombination energy" generally employed for radical cations because electron attachment occurs at the radical and not the charge site. Hence, the process chemically resembles the attachment of an electron to a neutral phenyl radical (energetics described by EA) and is quite different from the neutralization of, for example, the benzene radical cation by electron attachment (energetics described by RE).

To examine the influence of substituents on the electron affinities of charged phenyl radicals, the vertical (and a few adiabatic) electron affinities of several model systems (Table 5) were calculated at the B3LYP/6-31+G(d) level of theory (the singlet states of the phenide anions were calculated). This level of theory appears to be suitable for electron-affinity calculations, as the adiabatic electron affinity calculated for the phenyl radical, 1.10 eV, matches the known experimental value.[30] The calculated adiabatic and vertical electron affinities were found to differ by a constant amount, 0.42 ± 0.01 eV (however, for the phenyl radical itself, the difference is 0.49 eV). Therefore, either value can be used to examine trends in the radicals' abilities to accept an electron. We chose to use the vertical electron affinities since they are significantly simpler to calculate, and they also are in better agreement with the models developed to understand polar effects in radical reactions.[9]

Calculations carried out on model radicals, the *meta*-substituted 3-dehydroanilinium radicals **aa** (R = H), **bb** (R = Cl), **cc** (R = Br), and **dd** (R = CN), as well as the 3-dehydropyridinium radical **f**, reveal *an electron-affinity order of* ***aa*** *<* ***bb*** *∼* ***cc*** *<* ***dd*** *<* ***f****, an exact match of the reactivity trend observed for radicals* ***a*−*d*** *and* ***f*** *toward each substrate!* For example, the electron-withdrawing *m*-chlorine substituent (radical **bb**; Scheme 5) increases the electron affinity of the "unsubstituted" radical **aa** by 0.34 eV (from 4.79 to 5.13 eV; Table 5), thus lowering the energy of the ionic electronic configuration of the system. The resulting stabilization of the transition state explains the increased reaction efficiency of the chloro-substituted radical **b** relative to that of the unsubstituted radical **a** toward all the hydrogen atom donors studied. It is interesting to note that the addition of a *p*-chloro substituent to the neutral phenyl radical results in a similar increase in the electron affinity, ∼0.30 eV. The adiabatic electron affinities are 1.11 and 1.41 eV, respectively;[30] the latter value was obtained from known thermochemical data[30,34] by assuming that a homolytic bond-dissociation energy for the *para*-C−H bond in chlorobenzene is the same as in benzene, 113.5 kcal/mol.[35] This finding rationalizes the literature reports on facilitated hydrogen atom abstraction from acetonitrile,[11b] toluene,[11d] and cyclohexane[11d,f] caused by *p*-chloro substitution on the phenyl radical in solution.

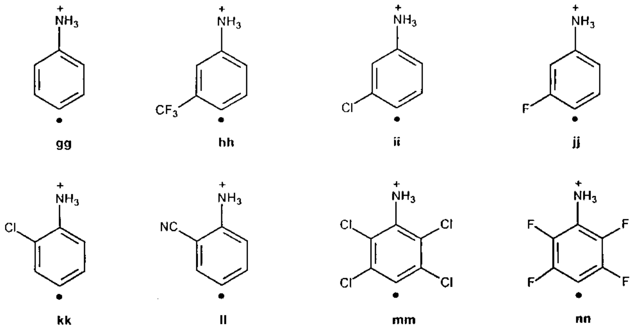
The transition-state energies calculated (B3LYP/6-31G(d)) for hydrogen atom abstraction from methanol (C−H) by the model radicals **aa**, **bb**, **bc**, **cc**, and **dd**, as well as the experimentally studied radicals **a**−**d**, reflect the reactivity trends observed for the differently substituted radicals (**a** < **b** ∼ **c** < **d**; Figure 2). Introduction of a *m*-chloro substituent to the radical **aa** increases the energy gap between the isolated reactants and the transition state (Δ*E*) from −3.9 to −4.6 kcal/mol (by −0.7 kcal/mol). A similar increase was calculated for **a** (0.6 kcal/mol). This stabilization of the transition state by the chloro substituent corresponds to ca. 10% of the associated change in the radical's electron affinity (0.34 eV or 7.8 kcal/mol).

The impact of a positively charged group as a strongly electron-withdrawing substituent is readily apparent upon consideration of the electron affinities of the neutral phenyl radical **ef** and the charged 3-dehydroanilinium radical **aa** (Scheme 5). The vertical electron affinity of **aa** is drastically greater than that of the neutral phenyl radical **ef** (4.79 vs 0.61 eV; Table 5). Hence, the ionic transition-state resonance structure can be expected to be much higher in energy for the neutral radical than for the charged radical and should have less of an effect on the transition-state energy. The analogous finding for the charged 3-dehydropyridinium radical **f** (6.12 eV; Table 5) and its neutral counterpart, the 3-dehydropyridine radical **ff** (0.98 eV), has practical implications. The greater electron affinity of the protonated radical leads to a lower transition-state energy and hence greater reactivity toward hydrogen atom donors. *Thus, the reactivity of dehydropyridine radicals is likely to be subject to pH control.*

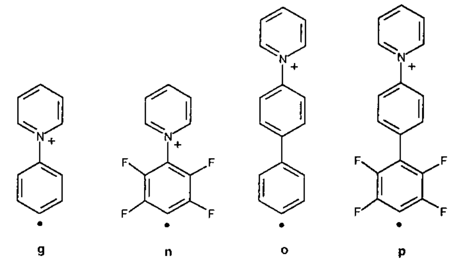
Reaction Efficiencies toward Different Hydrogen Atom Donors. As mentioned above, the hydrogen-abstraction barrier is expected to be lowered by factors that decrease the ionization energy of the substrate.[8,9,31−33] According to the vertical ionization energies listed in Table 1, the reaction efficiencies among the different hydrogen atom donors would be expected to follow the sequence benzeneselenol > thiophenol > tributyltin hydride ≫ tetrahydrofuran. However, the observed reactivity order is tributyltin hydride > benzeneselenol > thiophenol > tetrahydrofuran (Table 2). This order matches the increasing homolytic bond-dissociation energies of the substrates. Although it appears that the reactivity differences toward the different substrates can be rationalized by thermodynamic factors alone, we believe that the situation is not that simple, and that the reactivity order is the result of the combined effects of the reaction exothermicity (favoring tributyltin hydride) and polar effects (less favorable for tributyltin hydride). First, the changes in the bond-dissociation energies do not appear to be large enough to justify the large rate differences (4−5 kcal/mol in two cases). Second, the rates toward the three thiophenols are in disagreement with enthalpic control. *All the radicals studied react fastest with thiophenol and slowest with pentafluorothiophenol (Table 2), although the enthalpy changes for these three reactions are within 1.5 kcal/mol of each other*, and follow the order 4-fluorothiophenol (most exothermic) > thiophenol > pentafluorothiophenol (for the homolytic bond-dissociation energies, see Table 1). This observation is readily explained by the lower ionization energy of thiophenol. In this case, polar effects override the opposing enthalpic effects. The transition-state energies calculated for hydrogen abstraction from thiophenol, 4-fluorothiophenol, and pentafluorothiophenol by the 3-dehydropyridinium radical **f** follow the above reactivity trend ($\Delta E = -8.38$, -7.49, and -3.56 kcal/mol, respectively; B3LYP/6-31G(d) + ZPVE).

Reaction Efficiencies of Phenyl Radicals with the Charged Substituent in the *Para*-Position. The reactions of thiophenol and tetrahydrofuran were examined with several phenyl radicals with the pyridinium group in the *para*-position with respect to the radical site, and additional neutral substituents in the *ortho*- or *meta*-position, or at all positions (**g**−**n**; Table 6). As for the *meta*-substituted phenyl radicals **a**−**d**, the addition of an electron-withdrawing substituent to any position in the charged radical was found to increase the hydrogen atom abstraction efficiency, and the addition of several such substituents has a greater effect than the addition of one (**m** and **n**; Table 6). The reactivity trend for the differently *ortho*-substituted radicals and the tetrahalogenated radicals, **g** (R = H) < **h** (CF_3) ~ **i** (Cl) ~ **j** (F) < **m** (Cl_4) < **n** (F_4), follows the order of the electron affinities calculated for the corresponding model radicals (Table 5). Further, as expected, a chloro substituent in the *ortho*-position (with respect to the radical site; radical **i**) results in a greater reactivity (3% for tetrahydrofuran) than that found with the same substituent at the *meta*-position (**k**; 0.6%), again reflecting the differences in the electron affinities calculated for the model systems **ii** and **kk** (*ortho*, 5.14 eV; *meta*, 4.96 eV). Clearly, the σ-withdrawing ability of this substituent overrides its counterbalancing π-donating ability.

SCHEME 6



SCHEME 7



	Reaction efficiency			
	0.3 %	22 %	0.1 %	5 %
$(C_4H_9)_3SnH$	28 %	92%	17 %	97 %

It also should be noted here that the phenyl radical **a** with a *m*-pyridinium substituent reacts faster than radical **g** with the pyridinium group at the *para*-position (1 vs 0.3% for tetrahydrofuran; Tables 2 and 6), a reflection of the radicals' differing electron affinities (**aa**, 4.79 eV; **gg**, 4.67 eV; Table 5). This observation raised the question of whether or not neutral phenyl radicals are expected to follow the reactivity trends reported here for their charged analogues. To examine this issue, two additional radicals, **o** and **p** (Scheme 7), were generated. These radicals are analogues of the radicals **g** and **n** (tetrafluoro-substituted) but carry an additional phenyl ring that separates the pyridinium charge site from the 4-dehydrophenyl group by several Ångstroms. This separation lowers the vertical electron affinities of the radicals **o** (2.04 eV; Table 5) and **p** (4.93 eV) substantially relative to those of the smaller radicals **g** (4.51 eV) and **n** (6.21 eV, calculated at the B3LYP/6-31+G(d)//B3LYP/6-31G(d) level of theory). However, despite the substantially higher-lying ionic states, the larger radical still displays a strong sensitivity toward the fluoro substituents in the radical bearing the phenyl ring and responds to these substituents in a manner similar to that of their smaller analogues (by a substantial rate enhancement; Scheme 7). Therefore, we predict that neutral phenyl radicals will also show the same reactivity trends, although possibly less pronounced.

Conclusions

The key factor controlling the reactivity of electrophilic, charged phenyl radicals in exothermic hydrogen atom abstraction reactions appears to be the polar character of the reacting system. *For all the hydrogen atom donors studied, the transition-state energy for hydrogen atom abstraction is lowered, and, correspondingly, the hydrogen-abstraction efficiency is increased by increasing the electron deficiency of the phenyl radical. The same result is achieved by decreasing the electron deficiency (or IE) of the hydrogen atom donor. Neutral phenyl radicals are expected to follow the reactivity trends reported here for their charged analogues.* Useful measures for the electron deficiencies of the radical and substrate are provided by the radical's electron affinity (EA) and the substrate's ionization energy (IE). The reactivities of differently substituted, charged radicals were found to follow the same trend for each hydrogen atom donor, and this trend matches the ordering of the calculated transition-state energies as well as the radicals' vertical electron affinities. The reactivity of each radical toward the different hydrogen atom donors appears to be controlled by a mixture of polar and enthalpic effects. However, *the observed reactivity* *trend thiophenol > 4-fluorothiophenol > pentafluorothiophenol matches the increasing vertical ionization energies of the substrates rather than the decreasing reaction exothermicities*. In this particular case, polar effects apparently override enthalpic control. Finally, it should be noted also that while substitution plays a major role in controlling the charged phenyl radical's reactivity via polar effects, it only has a minor or no influence on the enthalpy change of exothermic hydrogen atom abstraction reactions, even when charged as opposed to neutral substituents are involved.

The addition of a *p*-chloro substituent to the neutral phenyl radical results in an increase in the radical's electron affinity similar to that for the charged radicals discussed above. This finding provides the basis for understanding the literature reports that chloro substitution increases hydrogen abstraction rates of the phenyl radical from various hydrogen atom donors in solution.[11] The introduction of a charged group into the phenyl radical raises its electron affinity even more drastically. The magnitude of the increase depends on the distance between the charged group and the radical site. Therefore, *the reactivity of heteroatom-containing phenyl radicals, which can be protonated at the radical-bearing phenyl ring, is predicted to be subject to pH control*. A similar reactivity and pH correlation has been reported[36] for hydrogen atom abstraction reactions involving the closely related 2,5-didehydropyridine biradical, a model of the biradical intermediates formed from enediyne antitumor drugs. This finding was explained by the change in the biradical's singlet−triplet gap caused by protonation. However, our results demonstrate the critical role of polar effects in controlling the reactivity of the closely related monoradical **f**. Therefore, polarization of the transition state is also likely to play a significant if not major role in controlling the hydrogen atom abstraction reactions of the biradical.

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References and Notes

(1) Poutsma, M. *Energy Fuels* **1990**, *4*, 113.

(2) Dean, A. M.; Freund, H.; Green, W. H.; Olmstead, W. N. *Abstracts of Papers*; 208th National Meeting of the American Chemical Society, Washington, DC; American Chemical Society: Washington, DC, 1994.

(3) Bothe, E. G.; Görner, H.; Opitz, J.; Schulter-Frohlinde, D.; Siddiqi, A.; Wala, M. *Photochem. Photobiol.* **1990**, *52*, 949.

(4) (a) Stubbe, J.; Kozarich, J. W. *Chem. Rev.* **1987**, *87*, 1107. (b) Steenken, S. *Chem. Rev.* **1989**, *89*, 503. (c) Meunier, B.; Pratviel, G.; Bernadou, J. *Bull. Soc. Chim. Fr.* **1994**, *131*, 933. (d) Pratviel, G.; Bernadou, J.; Meunier, B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 746. (e) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem.* **1991**, *30*, 1387.

(5) (a) Miaskiewicz, K.; Osman, R. *J. Am. Chem. Soc.* **1994**, *116*, 232. (b) Pardo, L.; Banfelder, J. R.; Osman, R. *J. Am. Chem. Soc.* **1992**, *114*, 2382.

(6) Cerutti, P. A. *Science* **1985**, *227*, 375.

(7) For example, see: Zavitsas, A. A.; Chatgilialoglu, C. *J. Am. Chem. Soc.* **1995**, *117*, 10 645.

(8) Pross, A.; Yamataka, H.; Nagase, S. *J. Phys. Org. Chem.* **1991**, *4*, 135.

(9) (a) Donahue, N. M.; Clarke, J. S.; Anderson, J. G. *J. Phys. Chem. A* **1998**, *102*, 3923. (b) Clarke, J. S.; Krill, J. H.; Donahue, N. M.; Anderson, J. G. *J. Phys. Chem. A* **1998**, *102*, 9847.

(10) (a) Scaiano, J. C.; Stewart, L. C. *J. Am. Chem. Soc.* **1983**, *105*, 3609. (b) Fahr, A.; Stein, S. E. *J. Phys. Chem.* **1988**, *92*, 4951. (c) Kopinke, F.-D.; Zimmermann, G.; Anders, K. *J. Org. Chem.* **1989**, *54*, 3571. (d) Yu, T.; Lin, M. C. *J. Phys. Chem.* **1995**, *99*, 9. (e) Tokmakov, I. V.; Park, J.; Gheyas, S.; Lin, M. C. *J. Phys. Chem. A* **1999**, *103*, 3636. (f) Park, J.; Chakraborty, D.; Bhusari, D. M.; Lin, M. C. *J. Phys. Chem. A* **1999**, *103* (20), 4002. (g) Park, J.; Burova, S.; Rodgers, A. S.; Lin, M. C. *J. Phys. Chem. A* **1999**, *103*, 9036.

(11) (a) Pryor, W. A.; Echols, J. T., Jr.; Smith, K. *J. Am. Chem. Soc.* **1966**, *88*, 1189. (b) Tilset, M.; Parker, V. *Acta Chem. Scand. B* **1982**, *36*, 123. (c) Migita, T.; Nagai, T.; Abe, Y. *Chem. Lett.* **1975**, 543. (d) Migita, T.; Takayama, K.; Abe, Y.; Kosugi, M. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1137. (e) Takayama, K.; Kosugi, M.; Migita, T. *Chem. Lett.* **1973**, 215. (f) Takayama, K.; Kosugi, M.; Migita, T. *Chem. Lett.* **1973**, 193.

(12) Smith, R. L.; Kenttämaa, H. I. *J. Am. Chem. Soc.* **1995**, *117*, 1393.

(13) Li, R.; Smith, R. L.; Kenttämaa, H. I. *J. Am. Chem. Soc.* **1996**, *118*, 5056.

(14) Thoen, K. K.; Smith, R. L.; Nousiainen, J. J.; Nelson, E. D.; Kenttämaa, H. I. *J. Am. Chem. Soc.* **1996**, *118*, 8669.

(15) (a) Tichy, S. E.; Thoen, K. K.; Price, J. M. J.; Ferra, J. J.; Petucci, C.; Kenttämaa, H. I. *J. Org. Chem.* **2001**, *66*, 2726. (b) Heidbrink, J. L.; Thoen, K. K.; Kenttämaa, H. I. *J. Org. Chem.* **2000**, *65* (3), 645. (c) Ramirez-Arizmendi, L. E.; Guler, L.; Ferra, J. J., Jr.; Thoen, K. K.; Kenttämaa, H. I. *Int. J. Mass Spectrom*. In press.

(16) (a) Newcomb, M.; Maneck, M. B.; Glenn, A. G. *J. Am. Chem. Soc.* **1991**, *113*, 949. (b) Newcomb, M.; Varick, T. R.; Ha, C.; Manek, M. B.; Yue, X. *J. Am. Chem. Soc.* **1992**, *114*, 8158. (c) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151.

(17) *Organic Synthesis*; John Wiley & Sons: New York, 1998; Vol. 7, pp 53−60.

(18) Carlin, T. J.; Freiser, B. S. *Anal. Chem.* **1983**, *55*, 571.

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

(20) Chen, L.; Wang, T.-C. L.; Ricca, T. L.; Marshall, A. G. *Anal. Chem.* **1987**, *59*, 449.

(21) Thoen, K. K.; Perez, J.; Ferra, J. J.; Kenttämaa, H. I. *J. Am. Soc. Mass Spectrom.* **1998**, *9*, 1135.

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

(23) Su, T.; Chesnavich, W. J. *J. Chem. Phys.* **1982**, *76*, 5183.

(24) (a) Bartmess, J. E.; Georgiadis, R. M. *Vacuum* **1983**, *33*, 149. (b) Miller, K. J.; Savchik, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 7206.

(25) (a) Frisch, M. J.; Trucks, G. W.; Head-Gorden, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Rahavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *Gaussian 92*; Gaussian, Inc.: Pittsburgh, PA, 1992. (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*; Gaussian, Inc.: Pittsburgh, PA, 1998.

(26) Barfknecht, A. T.; Dodd, J. A.; Salomon, K. E.; Tumas, W.; Brauman, J. I. *Pure Appl. Chem.* **1984**, *56*, 1809.

(27) Lide, D. R. *CRC Handbook of Chemistry and Physics*, 71st ed.; CRC Press: Boca Raton, FL, 1990−1991.

(28) Leeck, D. T.; Chyall, L. J.; Li, R.; Kenttämaa, H. I. *J. Phys. Chem.* **1996**, *100*, 6608.

(29) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.

(30) Mallard, W. G., Linstrom, P. J., Eds. *NIST Chemistry WebBook*, NIST Standard Reference Database Number 69; http://webbook.nist.gov (accessed March 1998).

(31) Pross, A. In *Theoretical and Physical Principles of Organic Reactivity*; John Wiley & Sons: New York, 1995.

(32) (a) In *Free Radicals*; Kochi, J. K., Ed.; John Wiley & Sons: New York, 1973; Vol. 1. (b) Fossey, J.; Lefort, D.; Sorba, J. In *Free Radicals in Organic Chemistry*; John Wiley & Sons: New York, 1995. (c) Tedder, J. M. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 401.

(33) Wong, M. W.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1994**, *116*, 6284.

(34) Wenthold, P. G.; Squires, R. R. *J. Mass Spectrom.* **1995**, *30*, 17.

(35) Davico, G. E.; Bierbaum, V. M.; DePuy, C. H.; Ellison, G. B.; Squires, R. R. *J. Am. Chem. Soc.* **1995**, *117*, 2590.

(36) Horrner, J.; Schottelius, M. J.; Feichtinger, D.; Chen, P. *J. Am. Chem. Soc.* **1998**, *120*, 376.