SUBSTITUENT EFFECTS ON THE ACIDITY OF WEAK ACIDS. 4. ANILINIUM IONS

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Dedicated to Professor Otto Exner on the occasion of his 80th birthday.

The gas phase acidity of anilinium ions has been calculated at a number of theoretical levels from B3LYP/6-311++G** to MP2 and CCSD/6-311++G(2dp,2pd). The highest level calculations find anilinium ion and *p*-protonated aniline to have essentially the same energy, in agreement with experimental studies. They also give a proton affinity for aniline that is in very good agreement with the experimental value. The B3LYP and MP2 calculations are less successful, with B3LYP favoring *p*-protonation and MP2 favoring N-protonation for aniline. Despite this difficulty, the calculated effect of substituents on the proton affinities of *p*-substituted anilines that undergo N-protonation agreed well with the experimental data. The effect of substituents on the anilinium ions and on the anilines were examined separately using a series of group transfer reaction.
Keywords: Gas phase acidity; Substituent effects; Ab initio calculations; Ammonium salts; Protonation; Isodesmic reactions.

Substituent effects on aromatic systems have been of interest to organic chemists for many years. We and others have made detailed computational studies of substituent effects on bicyclo[2.2.2]octane-1-carboxylic acids[1], benzoic acids[2] and phenols[3]. We now continue this examination by studying the effect of substituents on the acidity of anilinium ions. They differ from the other compounds in that the acid has a positive charge and the conjugate base is neutral. In our study of the other acids, it was found that large basis sets along with correction for electron correlation were necessary in order to reproduce the experimental gas phase acidities.

RESULTS AND DISCUSSION

Site of Protonation and the Acidity of Anilinium Ion

Anilinium ion has been the subject of both experimental[4] and computational studies[5]. The experimental data suggest that N-protonated and *p*-protonated forms have similar energies with N-protonation being kinetically favored. The proton affinity of aniline has been determined[6] to be 210.9 kcal/mol. Calculations at different levels of theory disagree as to which protonated form has the lower energy.

We have attempted to obtain further information by carrying out CCSD(T) calculations for aniline and anilinium ion using 6-311+G*, 6-311++G** and 6-311++G(2df,2pd) and the MP2/6-311+G* calculated geometries. CCSD is generally recognized as being among the best of the single reference structure theoretical methods[7], and the basis set should be large enough to give satisfactory results The inclusion of the triples correction provides an additional level of accuracy. The calculations are summarized in Table I.

TABLE I
CCSD(T) calculations for aniline and anilinium ion
a. Total energies

Compound	CCSD(T) 6-311+G*	CCSD(T) 6-311++G**	CCSD(T) 6-311++G(2df,2pd)	H_{corr}[a]
Aniline	–286.84464	–286.90251	–286.96808	0.12353
$ArNH_3^+$	–287.19378	–287.25370	–287.31792	0.13880
p-Protonated	–287.18932	–287.25000	–287.31527	0.13629

b. Relative enthalpies at 25 °C, kcal/mol

Compound	H_{rel} 6-311+G*	H_{rel} 6-311++G**	H_{rel} 6-311++G(2df,2pd)
$ArNH_3^+$	0.0	0.0	0.0
p-Protonated	1.2	0.7	0.1
Aniline[b]	211.0	212.3	211.4

[a] Zero-point energy and enthalpy correction to 25 °C calculated using the B3LYP/6-311+G* vibrational frequencies. [b] The values are the proton affinities of aniline and include the 1.5 kcal/mol translational enthalpy of the proton.

The CCSD(T) results indicate that there is little difference in energy between the two protonated species, and is in agreement with the experimental result. The proton affinity may be derived from the calculated energies of aniline, anilinium ion and a proton. The calculated value, 211.4 kcal/mol, is in very good agreement with the experimental value.

Site of Protonation of p-Substituted Anilines

Experimental studies suggest that in the gas phase *p*-nitroaniline and *p*-formylaniline are preferentially protonated at an oxygen of the substituent[4]. In this way they are similar to amides that are protonated at oxygen rather than nitrogen[8]. Recent calculations suggest that *p*-cyanoaniline is also protonated at the cyano group rather than at nitrogen[9]. We have carried out calculations for protonation at various positions of aniline in order to gain further information on the preferred site of protonation.

The anilinium ions were initially studied at the B3LYP/6-311+G* level including a calculation of the vibrational frequencies. This is a good theoretical level for an initial study since it is efficient with respect to computer resources. However, in our previous studies, MP2 was found to give more satisfactory calculated acidities than B3LYP. Therefore it was followed by MP2 geometry optimizations using 6-311+G*, followed by 6-311++G** and 6-311++G(2df,2pd) calculations using the former geometries.

The total energies of the anilinium ions are shown in Table II, part a, and the relative enthalpies corrected for the differences in zero-point energy and the change in enthalpy on going from 0 to 298 K are given in Table II, part b. In the case of X = CHO, NO_2 and CN, *p*-protonation refers to protonation at the substituent, and in the other cases it is protonation at the carbon to which the substituent is attached.

It should first be noted that there is a fairly large difference between the results of the B3LYP and MP2 calculations, and that the MP2 calculations at the several basis sets give quite good agreement for X = Me, NH_2, OH, F, Cl and CF_3. There is also agreement among the MP2 calculations for N- and *o*-protonation for X = CHO, CN and NO_2. Any deficiency in these MP2 calculations therefore is inherent in the method and is not a basis set effect. When the proton was attached to the substituent, however, the MP2 calculations find that the reaction becomes significantly more exothermic as the size of the basis set is increased.

Despite the effect of basis set size, it can be seen that the proton is preferentially attached to the substituent when X = NO_2, CHO and CN. With *p*-nitroaniline, protonation at an oxygen of the nitro group is favored at the

TABLE II
Calculated energies of anilinium ions
a. Total energies[a]

X	Position	B3LYP			MP2 6-311+G*	MP2 6-311++G**	MP2 (2df,2pd)
		6-311+G*	ZPE	Hc			
H	NH$_2$	−288.01944	82.60	0.138799	−287.10699	−287.16405	−287.33406
H	*para*	−288.02020	81.17	0.136290	−287.09395	−287.15191	−287.32200
H	*ortho*	−288.01326	81.05	0.136249	−287.08644	−287.14439	−287.31403
Me	NH$_2$	−327.34823	99.65	0.167941	−326.29561	−326.36748	−326.56292
Me	*para*	−327.34382	99.03	0.166172	−326.27978	−326.35270	−326.54723
Me	*ortho*	−327.34281	98.30	0.165320	−326.27583	−326.34860	−326.54376
NH$_2$	NH$_2$	−343.40064	92.65	0.156629	−342.33430	−342.40247	−342.60622
NH$_2$	*para*	−343.37315	91.81	0.154771	−342.29808	−342.36801	−342.56992
NH$_2$	*ortho*	−343.38840	91.20	0.154036	−342.31018	−342.37938	−342.58188
OH	NH$_2$	−363.26331	85.17	0.143994	−362.18270	−362.24654	−362.45799
OH	*para*	−363.24191	83.74	0.141793	−362.15055	−362.21574	−362.42474
OH	*ortho*	−363.25024	83.15	0.141047	−362.15618	−362.22123	−362.43170
F	NH$_2$	−387.28299	77.39	0.131298	−386.18540	−386.23523	−386.45212
F	*para*	−387.26672	76.43	0.129444	−386.15759	−386.20863	−386.42368
F	*ortho*	−387.27253	75.85	0.128738	−386.16098	−386.21170	−386.42825
Cl	NH$_2$	−747.63724	76.49	0.130228	−746.16797	−746.21805	−746.43492
Cl	*para*	−747.62777	75.69	0.128634	−746.14587	−746.19736	−746.41298
Cl	*ortho*	−747.62818	74.96	0.127686	−746.14458	−746.19559	−746.41195
CF$_3$	NH$_2$	−625.15804	85.34	0.146751	−623.56155	−623.61126	−623.94498
CF$_3$	*para*	−625.15380	84.39	0.144777	−623.54698	−623.59758	−623.93136
CF$_3$	*ortho*	−625.15012	83.84	0.144230	−623.54014	−623.59067	−623.92430
CHO	NH$_2$	−401.36704	88.17	0.149745	−400.17978	−400.23676	−400.46409
CHO	*para*[b]	−401.39014	88.13	0.149151	−400.18478	−400.24962	−400.48169
CHO	*ortho*	−401.35856	86.54	0.147069	−400.15677	−400.21461	−400.44088
CN	NH$_2$	−380.27127	81.57	0.138964	−379.13773	−379.18720	−379.40037
CN	*para*[b]	−380.28529	79.83	0.136001	−379.13069	−379.18424	−379.40273
CN	*ortho*	−380.26191	80.04	0.136411	−379.11372	−379.16400	−379.37690
NO$_2$	NH$_2$	−492.56524	83.90	0.143407	−491.20418	−491.25358	−491.52825
NO$_2$	*para*[b]	−492.58454	83.01	0.141696	−491.20492	−491.26188	−491.54075
NO$_2$	*ortho*	−492.55656	82.32	0.140803	−491.18026	−491.23060	−491.50483

TABLE II
(*Continued*)
b. Energy changes, kcal/mol, relative to N-protonation

X	Position	H_{rel}, 298 K			
		B3LYP 6-311+G*	MP2 6-311+G*	MP2 6-311++G**	MP2 6-311++G(2df,2pd)
H	NH_2	0.0	0.0	0.0	0.0
H	*para*	−2.1	6.6	6.0	6.0
H	*ortho*	2.3	11.3	10.7	11.0
Me	NH_2	0.0	0.0	0.0	0.0
Me	*para*	1.7	8.8	8.2	8.7
Me	*ortho*	1.8	10.8	10.2	10.4
NH_2	NH_2	0.0	0.0	0.0	0.0
NH_2	*para*	16.1	21.6	20.5	21.6
NH_2	*ortho*	6.1	13.5	12.9	13.6
OH	NH_2	0.0	0.0	0.0	0.0
OH	*para*	12.0	18.8	17.9	19.5
OH	*ortho*	6.4	14.8	14.0	14.6
F	NH_2	0.0	0.0	0.0	0.0
F	*para*	9.0	16.3	15.5	16.7
F	*ortho*	5.0	13.7	13.2	13.4
Cl	NH_2	0.0	0.0	0.0	0.0
Cl	*para*	4.9	12.9	12.0	12.8
Cl	*ortho*	4.1	13.1	12.5	12.8
CF_3	NH_2	0.0	0.0	0.0	0.0
CF_3	*para*	1.4	7.9	7.3	7.3
CF_3	*ortho*	2.8	11.9	11.3	11.4
CHO	NH_2	0.0	0.0	0.0	0.0
CHO	*para*	−14.9	−3.5	−8.4	−11.4
CHO	*ortho*	3.6	12.8	12.2	12.9
CN	NH_2	0.0	0.0	0.0	0.0
CN	*para*	−10.7	2.6	0.0	−3.3
CN	*ortho*	4.3	13.5	13.0	13.1
NO_2	NH_2	0.0	0.0	0.0	0.0
NO_2	*para*	−13.2	−1.5	−6.3	−8.9
NO_2	*ortho*	3.8	13.4	12.8	13.1

[a] Energies are given in Hartrees, except for zero-point energies (ZPE) and the enthalpy correction to 25 °C including the ZPE (Hc), that are given in kcal/mol. [b] Here, *p*-protonation refers to protonation at the substituent group.

largest MP2 level over the NH_2 group by 9 kcal/mol; with *p*-formylaniline it is favored by 11 kcal/mol, and with *p*-cyanoaniline it is favored by 3 kcal/mol.

However, the results are disappointing in that they do not give correct results for aniline itself. B3LYP predicts C-protonation whereas MP2 predicts N-protonation, whereas both experiments and CCSD(T) calculations find that the two species have essentially the same energy. The error probably results from the difficulty in correctly accounting for the difference in correlation energy associated with the two sites of protonation. It would be desirable to carry out calculations for all of the compounds at the CCSD(T) level, but this is beyond the capability of our computational resources.

Calculated Energies of the Anilines and the Acidity of the Anilinium Ions

Although there is a problem associated with N- vs C-protonation, the MP2 results previously obtained with benzoic acid and phenols suggest that the relative energies for N-protonation might be reasonably well represented by MP2 calculations, and that proton affinities calculated at this level may agree with the experimental results.

The energies of the anilines were determined at the same theoretical levels as used for the anilinium ions, The results are given in Table III, and the acidities derived from these data are also given in the table. The calculated values may be compared with the observed gas phase proton affinities of the anilines (Table III)[10]. The larger basis set calculations lead to ΔH_{acid} that are uniformly 2 kcal/mol smaller than the observed values.

Analysis of the Substituent Effects

We are interested in separately examining the effects of substituents on the anilinium ions and the anilines[11]. With the ions, there is a positive charge adjacent to the benzene, whereas with the anilines, there is a lone pair that can interact with the aromatic ring. The following isodesmic reactions (Scheme 1) allow the effects to be separated (Table IV).
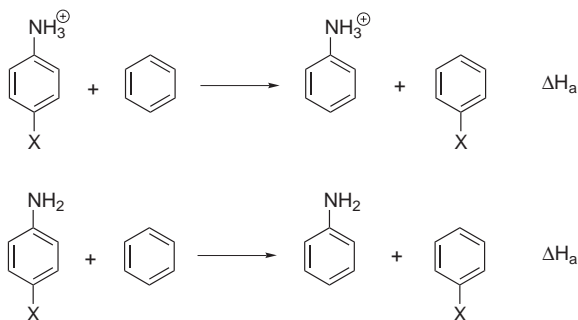
The electron releasing substituents, Me, NH_2 and OH, stabilize the positive charge in the substituted anilinium ions, whereas the other substituents destabilize it. The latter substituents compete with the anilinium center for the charge density in the benzene ring, whereas the former substituents will donate electron density to the ring. With the anilines, the electron-releasing substituents along with SH and Cl destabilize the substituted amines with both groups trying to donate electron density into the

TABLE III
Calculated energies of anilines and proton affinities[a]

p-ArNH$_2$ X	B3LYP 6-311+G*	MP2 6-311+G*	MP2[b] ++G**	MP2[c] (2df,2pd)	H$_{corr}$[d]	ΔH$_{acid}$ B3LYP 6-311+G*	ΔH$_{acid}$ MP2 6-311+G*	++G**	(2df,2pd)	ΔH$_{acid}$ obs
H	−287.62738	−286.76095	−286.81623	−286.98781	0.123531	209.7	209.1	210.2	209.2	210.9
Me	−326.99670	−325.94591	−326.01598	−326.21279	0.152722	213.2	212.0	213.1	212.3	214.3
NH$_2$	−343.04002	−341.97870	−342.04543	−342.24966	0.141676	218.4	215.3	216.2	215.9	
OH	−362.91124	−361.83334	−361.89550	−362.10781	0.128668	212.8	211.1	212.2	211.6	
F	−386.94106	−385.84485	−385.89244	−386.11026	0.116119	206.5	205.3	207.1	206.5	208.3
SiH$_3$	−578.38967	−576.94354	−577.02284	−577.21902	0.140974	208.3	208.0	209.3	207.8	
SH	−685.88378	−684.42269	−684.48543	−684.69735	0.124189	209.4	207.9	209.2	208.8	
Cl	−787.29661	−745.82808	−745.87589	−746.09431	0.115210	205.8	205.4	206.8	205.8	
CN	−379.94445	−378.80958	−378.85662	−379.07213	0.124053	197.2	198.1	199.6	198.1	
CF$_3$	−624.82626	−623.22972	−623.27708	−623.61181	0.131598	200.2	200.2	201.7	201.1	
CHO	−401.03529	−399.84597	−399.90065	−400.12994	0.134828	200.3	201.6	203.1	201.8	217.6[e]
NO$_2$	−492.22961	−490.87763	−490.92464	−491.19254	0.128558	195.1	199.7	199.0	198.0	214.3[e]

[a] The total energies are given in Hartrees, the ΔH$_{acid}$ are given in kcal/mol. [b] MP2/6-311++G**//MP2/6-31+G*. [c] MP2/6-311++G(2df,2pd)//MP2/6-31+G*. [d] Zero-point energy and enthalpy correction to 298 K, derived from B3LYP/6-311+G* vibrational frequencies. [e] The calculated value is for N-protonation; the experimental value is for protonation at the substituent.

ring. The electron-withdrawing substituents stabilize the anilines, but the effect is rather small, and does not suggest much of a conjugative interaction.

SCHEME 1

TABLE IV
Enthalpy changes for isodesmic reactions, MP2/6-311++G(2df,2pd), kcal/mol

X	ΔH_a	ΔH_b	X	ΔH_a	ΔH_b
H	0.0	0.0	SH	–0.6	–0.2
Me	2.6	–0.5	Cl	–3.9	–0.5
NH_2	4.8	–1.9	CN	–9.8	1.3
OH	0.7	–1.8	CF_3	–7.2	0.9
F	–3.9	–1.2	CHO	–4.5	2.8
SiF_3	–0.6	0.7	NO_2	–9.9	1.3

Rotational Barriers

The above results suggest that there is only a small conjugative interaction in the ground state between NO_2 and NH_2 in *p*-nitroaniline, whereas there clearly is a strong interaction in the electronically excited state[12]. In order to try to confirm this result, the rotational barrier for the substituent has been calculated for *p*-nitroaniline and *p*-formylaniline, giving the results summarized in Table V. In the absence of the amine group, these substituents give a significant rotational barrier when attached to a benzene ring, and the quantity of interest is the increase in barrier height when the amino group is present.

TABLE V
MP2/6-311++G(2df,2pd) calculated rotational barriers

X	p-X-aniline	ArX[a]	$\Delta\Delta H$
NO₂	4.7	3.8	0.9
CHO	8.4	7.1	1.3

[a] Lit.[3a]

In both cases, the rotational barrier is increased by only 1 kcal/mol as compared to the substituted benzenes. This small effect should not be surprising since the two groups are relatively far from each other, and charge transfer over this distance represents a significant increase in electrostatic energy.

Conclusions

The accurate calculation of the relative energies for N- and ring-protonation for aniline requires the CCSD level of theory. Neither B3LYP nor MP2 were satisfactory. The MP2-calculated substituents effects for anilines that undergo N-protonation are in reasonable agreement with the experimental values.

Calculations

The calculations were carried out using Gaussian 99 [13].

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