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The Site of Protonation in Aniline

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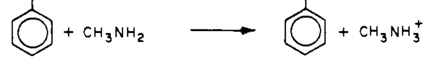
Abstract: We have applied experimental pulsed ion cyclotron resonance spectroscopy and ab initio molecular orbital theory to the problem of the identification of the preferred site of protonation in aniline. Our analysis concludes that, in the gas phase, (1) aniline is a nitrogen base and (2) that protonation on the aromatic ring is some 1–3 kcal/mol less favorable than protonation at nitrogen. The small magnitude of this difference indicates that both substituent and solvent effects should be capable of bringing about observable shifts in the order of nitrogen and carbon basicities of anilines.

The question of the preferred site of protonation of substituted aromatics in the gas phase has been the subject of numerous recent publications.[2] The techniques of high pressure mass spectrometry[3] and ion cyclotron resonance (ICR) spectroscopy[4] make possible the accurate determination of the relative stabilities of ions in the gas phase. However, such methods provide no direct information as to the geometrical structures of the species under scrutiny since the concentrations of ions present are too small to permit their absorption spectra to be obtained.[5,6] It has been necessary, therefore, to turn to a variety of indirect approaches in order to extract structural information from the gas-phase experiments. These have included the detailed comparison of experimental and theoretical relative ion stability data[2c,d] and the employment of isotopic labels as tracers to the course of reaction.[2a,b,d] Another approach, in which substituent effects are used to distinguish between ring and substituted protonation, is illustrated by the study presented herein.

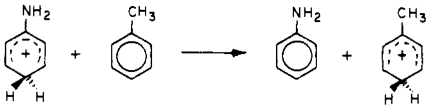
Theoretical and Experimental Methods, Results and Discussion

The enthalpy of nitrogen protonation in aniline may be estimated theoretically[7] by combining the calculated energy for the *isodesmic*[11] processes (eq 1) with the experimental proton affinity of methylamine (211.2 kcal/mol[12]). The value which results, 208.7 kcal/mol, is in good agreement with the experimental proton affinity of aniline, 208.8 kcal/mol.[12,13] Consider, however, the possibility for aniline to protonate at a site other than on the nitrogen, in particular, on the aromatic ring para to the NH_2 substituent. An estimate for this quantity may be obtained by biasing ΔE for the *isodesmic* reaction 2 by the experimental proton affinity of toluene (188.7 kcal/mol),[12] The resultant affinity is 208.5 kcal/mol, which, well within the limits of confidence of the theory, is identical to both the calculated nitrogen affinity and to the experimentally determined quantity.[14] It is apparent, therefore, that the calculated ring and nitrogen proton affinities of aniline are too close to enable the theory to cleanly assign which, in fact, is the higher.



(1)

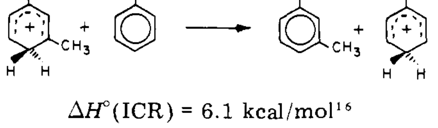
$\Delta E = -2.5$ kcal/mol



(2)

$\Delta E = 19.9$ kcal/mol

If the theoretical prediction regarding the closeness in stabilities of ring and substituent protonated aniline is correct, then it should be possible to shift the energetic balance to either side by the use of substituents. For example, we might expect that the ring methyl substituent present in *m*-toluidine would lead to only a very small increase in the affinity of aniline to protonate at nitrogen. Thus, the difference in the observed proton affinities of *N,N*-dimethyl, *m*-toluidine, and *N,N*-dimethylaniline[15] (both of which are, of course, nitrogen bases) is only 1 kcal/mol. On the other hand it is likely that the effect of the methyl group on the energy of protonation on the aromatic ring would be much more substantial. For example, we have found that the proton affinity of *m*-xylene is 6.1 kcal/mol greater than that for toluene, indicating a significant level of stabilization to the ion because of the second "ortho" Methyl group.[16] The observed difference in the proton affinities of *m*-toluidine (211.6 kcal/mol) and aniline is, however, only 2.8 kcal/mol, far smaller than that expected on the basis of comparison of the relative proton affinities of *m*-xylene and toluene,



(3)

$\Delta H^\circ(\text{ICR}) = 6.1$ kcal/mol[16]

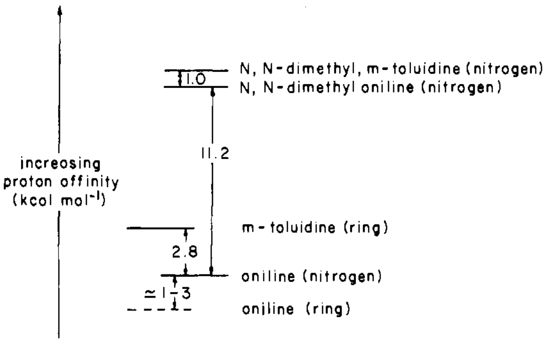


Figure 1. Relative proton affinities of aniline, *m*-toluidine, and the *N*,*N*-dimethyl derivatives of each. The assigned site of protonation is given in parentheses. Except for the ring proton affinity of aniline, the values have been obtained by pulsed ion cyclotron resonance spectroscopy and are relative to a proton affinity of 208.8 kcal/mol for aniline (at nitrogen). See text for discussion of the value for the ring proton affinity of aniline.

yet noticeably larger than is appropriate for a ring *m*-methyl substituent on the nitrogen proton affinity. The observed proton affinity differences may be rationalized by concluding that parent aniline is, in fact, a nitrogen base and that protonation on the aromatic ring is some 1-3 kcal/mol less favorable than on the N substituent. On the other hand, *m*-toluidine is a carbon base in the gas phase, that is, the site of protonation has switched from that in aniline (Figure 1).

It might further be noted that the experimental proton affinities for aniline and *N*,*N*-dimethylaniline show consistent energetic effects for an *N*-methyl vs. an *N*-phenyl substituent. Methylamine has a proton affinity 2.5 kcal/mol greater than aniline, whereas that for trimethylamine is 2.0 kcal/mol greater than for *N*,*N*-dimethylaniline. That is, these results are consistent with N protonation of both of these bases.

Finally, the conclusion that the 2.8 kcal/mol greater proton affinity of *m*-toluidine than aniline is too large to be consistent with N protonation of the former is strongly supported by our observation that the proton affinities of *m*- and *p*-toluidine are identical within the experimental error of ±0.2 kcal/mol. If N protonation occurred for aniline, as well as both *m*- and *p*-toluidine, the latter would have a proton affinity 1-2 kcal/mol greater than that of its meta isomer (*p*-methyl substituent effects always exceed those of *corresponding m*-methyl substituent effects). On the other hand, the 2.8 kcal/mol difference between the proton affinities of *p*-toluidine and aniline is indeed the correct *p*-methyl substituent effect expected from theory for nitrogen protonation of these two bases.


(4)

$$\Delta E^{\circ}(\text{STO-3G}) = 2.4 \text{ kcal/mol}$$

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(15) The proton affinity of *N*,*N*-dimethylaniline is an unpublished result of Dr. M. Taagepera.

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