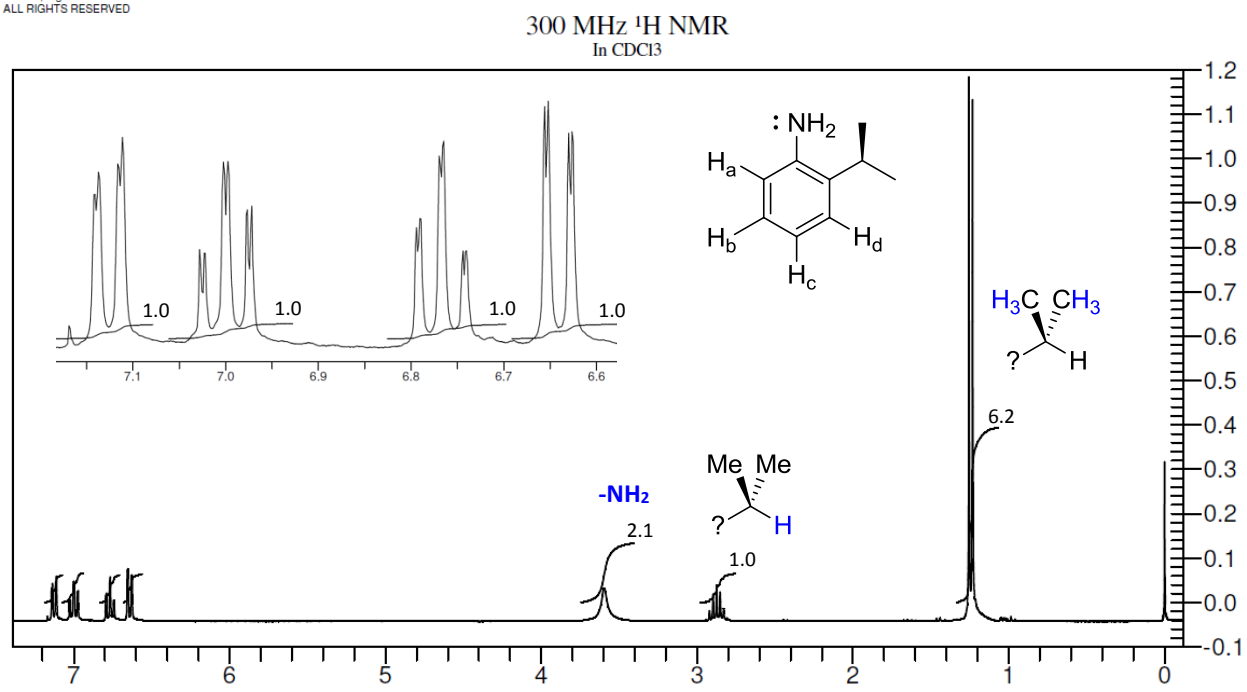
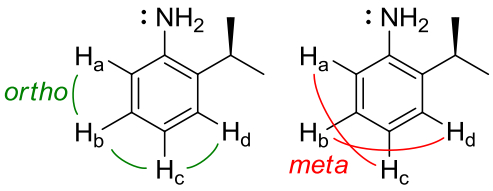
Assigning the ^{1}H-NMR Signals of Aromatic Ring ^{1}H-atoms

Assigning ^{1}H-NMR signals of ^{1}H-atoms on an aromatic ring based upon their chemical shift and coupling can be accomplished in a number of different ways which will be detailed below. These methods which range from very simple to somewhat sophisticated are complimentary to one another. For an example, the aromatic region of the ^{1}H-NMR of *o*-isopropylaniline will be analyzed.



1) Coupling Patterns

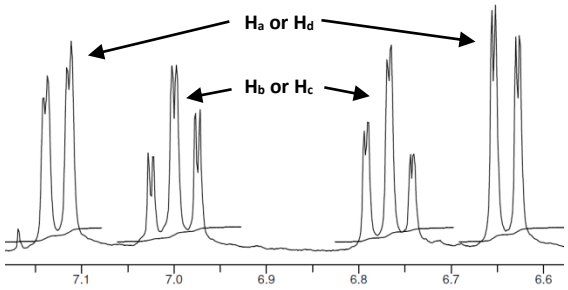
The first analysis should always involve the observable coupling in each of the signals in the aromatic region. In a 300 MHz spectrum, the ***ortho*** and ***meta*** couplings may all be resolved and provide information about the assignments. Remember that J_{ortho} typically is 7 – 10 Hz while J_{meta} is a smaller 2 – 3 Hz for these.



To a simple first order approximation, the appearance of the signals for all 4 ^{1}H-atoms are readily predictable. Depending on the exact value of the three *ortho* couplings and the two *meta* couplings the signals could have slightly different appearances. For instance, if J_{ab} is roughly the same as J_{bc}, then H_b may appear as an *ortho*-coupling triplet in the spectrum. Should J_{ab} be significantly different than J_{bc}, H_b will appear as an *ortho*-coupling doublet of doublets in the spectrum.

	Possible Signal Appearance		
H_a	dd, J_{ortho}, J_{meta}		
H_b	td, J_{ortho}, J_{meta}	or	ddd, J_{ortho}, J_{ortho}, J_{meta}
H_c	td, J_{ortho}, J_{meta}	or	ddd, J_{ortho}, J_{ortho}, J_{meta}
H_d	dd, J_{ortho}, J_{meta}		

The appearance in the spectrum of two triplets of doublets indicates that J_{ab} is almost equal to J_{bc} and J_{cd}. From this information alone, the signals can be identified as H_a or H_d and H_b or H_c as shown below.

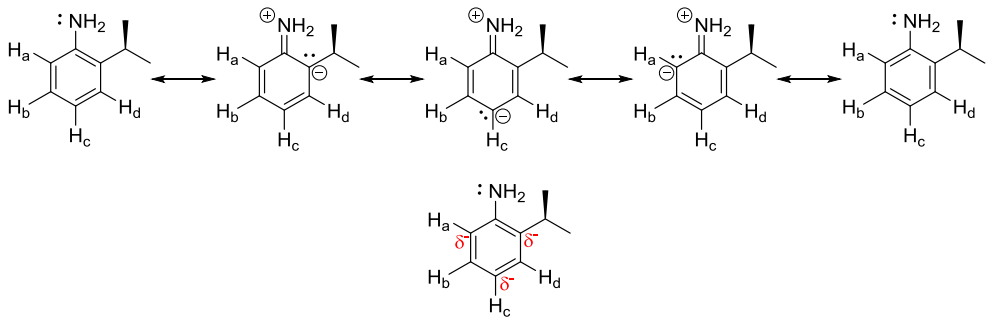


2) Changes in Shielding by Carbon Atom Charge

The magnetic field experienced by each ^{1}H-atom is influenced by the electron density at the carbon atom to which it is attached. The charge can be estimated in several ways, two of which are provided below.

a) Conjugation Depicted by Resonance Structures

Since benzene has an ^{1}H-NMR chemical shift of about 7.3 ppm for its H-atoms, substituted benzenes will have chemical shifts slightly upfield or downfield of 7.3 ppm. For substituents that are conjugated to the aromatic π system, resonance structures are a convenient way to estimate whether a particular position will be relatively shielded or deshielded by the substituent. The amino group (-NH_2) in *o*-isopropylaniline is an electron donating group through conjugation of its p-rich lone pair to the aromatic π system.

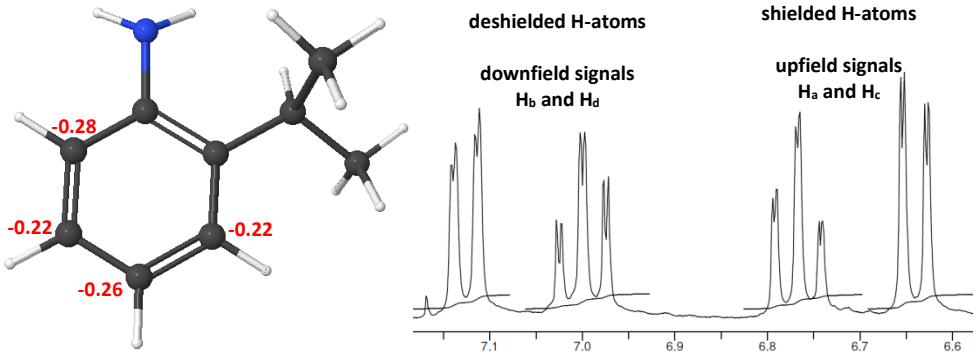


The prediction of extra electron density (negative charge) at the carbon atoms *ortho* and *para* to the amino substituent indicate that the chemical shift of H_a and H_c will be more upfield as the H-atoms

are more shielded. The limitations of this method are significant. The resonance structures indicate that the *ortho* and *para* positions will be more shielded, but does not indicate which one will be most shielded. This method only works for substituents that are conjugated by resonance and offers no way to predict the charge distribution caused by non-conjugated substituents like the isopropyl group. Even for the amino group which is π-donating, there is no straightforward way to think about the electron withdrawing nature of the nitrogen via its σ bond to the ring carbon atom.

b) Natural Bond Orbital (NBO) calculations to estimate the Natural Population Analysis (NPA)

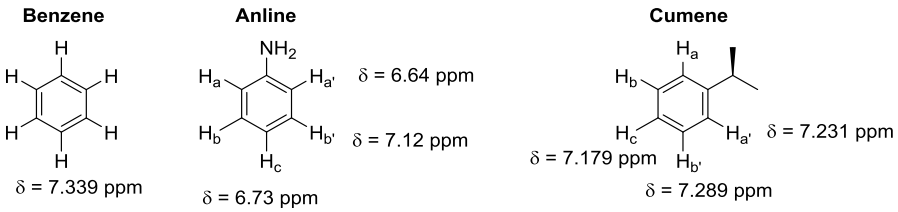
All of the σ and π donating and withdrawing effects of benzene substituents can be estimated via an NBO calculation in WebMO/Gaussian 09. As with all computational approaches, this requires an optimized molecule at a reasonable level of theory and basis set. The calculation presented below was completed at the B3LYP/6-31G(d) level.



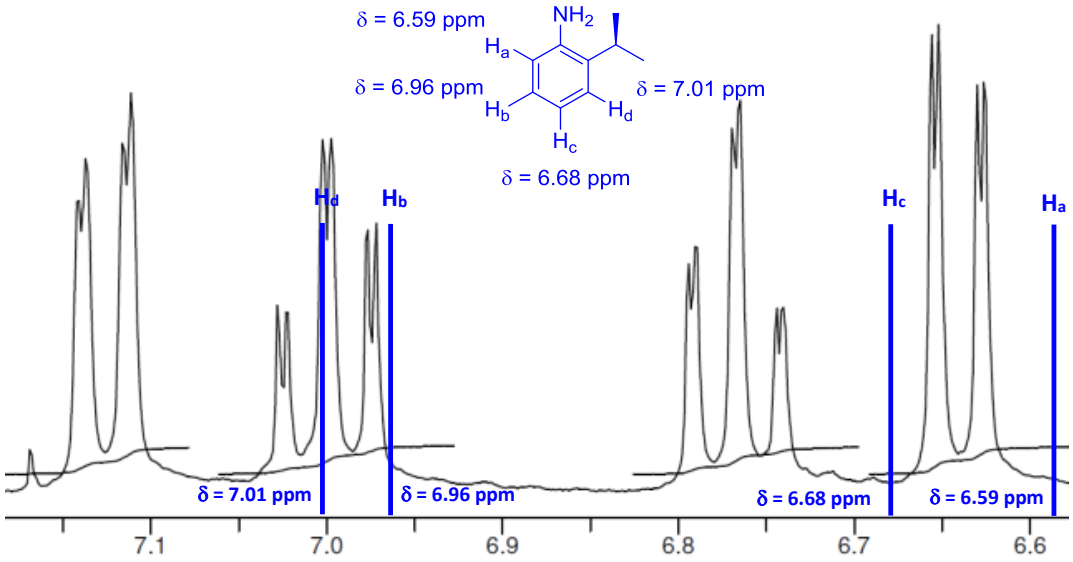
While neither the coupling pattern nor carbon-atom charge estimation are sufficient to assign all of the signals, the combination of the first two methods is sufficient to unambiguously assign all four of the signals in the aromatic region.

3) Model compound

An often over-looked and under-utilized method of assigning the signals in the ^{1}H-NMR region is by comparison to known molecules. Let us assume that the ^{1}H-NMR spectrum of *o*-isopropylaniline is not available in any database. It is very similar to at least three common compounds (benzene, aniline, and cumene) that might provide estimates of the chemical shift of its H-atoms. The Spectral Database for Organic Compounds or SDBS (http://sdbs.riodb.aist.go.jp/sdbs/cgi-bin/cre_index.cgi) provides the ^{1}H-NMR spectra for each of these molecules.



With these known experimental chemical shifts, the impact of each substituent (-NH_2 and -*i*Pr) can be quantified by a comparison of the model compound to benzene and provide a closer approximation of the chemical shifts in *o*-isopropylaniline. The hydrogen atom labeled H_a below in *o*-isopropylaniline should be shifted in a manner similar to the *ortho* H-atoms in aniline (-0.675 ppm) and the *meta* H-atoms in cumene (-0.109 ppm) relative to benzene. Combining these shift effects predicts a chemical shift for the atom labeled H_a in *o*-isopropylaniline shown below.



As can be seen in the comparison between the model compound predictions in blue and the actual spectrum, there is an error of about ± 0.12 ppm in the worst predicted signal location. The relative ordering of the signals from high to low chemical shift is correct and in a simple system such as this, the assignment can be made in an unambiguous manner. The limitations of this method include the availability of spectral data for model compounds in the same solvent as the investigated molecule. While the model compound limitation may be overcome by increasing the amount of data available in the database, this method will always be limited in its ability to account for subtle structural differences in the ring upon substitution of the studied compound caused by multiple substitutions.

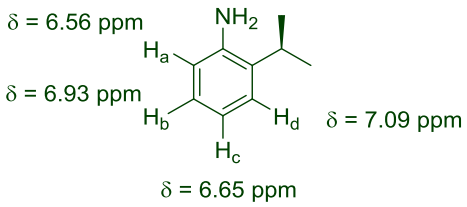
4) Curphy-Morrison Additivity Constants

This method is a more sophisticated extension of the model compound approach detailed above where many molecules with a particular functional group have been studied and parameters for the effect of that substituent on each H-atom on the aromatic ring have been determined. The constants will more accurately predict chemical shifts when fewer of them are required and when the studied compound is similar to those that were used to develop the parameters. A very nice list of the constants is available from Professor Hans Reich via the following links.

Curphy-Morrison Additivity Constants for Proton NMR :
http://www.chem.wisc.edu/areas/reich/nmr/notes-9-hmr-5-curphy-morrison.pdf
Curphy-Morrison Additivity Constants for Proton NMR (vinyl and aryl):
http://www.chem.wisc.edu/areas/reich/nmr/notes-9-hmr-6-vinyl-aryl-shifts.pdf

Each benzene ring H-atom is given a standard shift value of 7.36 ppm and adjusted by up to 5 terms for all of the non-H-atom substituents on the benzene ring. Unfortunately, for estimating the shifts for *o*-isopropylaniline, there is no isopropyl substituent listed. Since many alkyl groups have similar, small shift effects, this will not likely have a large impact on the shift calculation with methyl and *t*butyl groups available. Since the chemical shift effect of an -*i*Pr group is likely somewhere between a -Me and a -*t*Bu group a rough average can be applied with a weight of 1/3 -Me and 2/3 -*t*Bu. An example calculation for H_a is provided below along with the estimates for H_a – H_d.

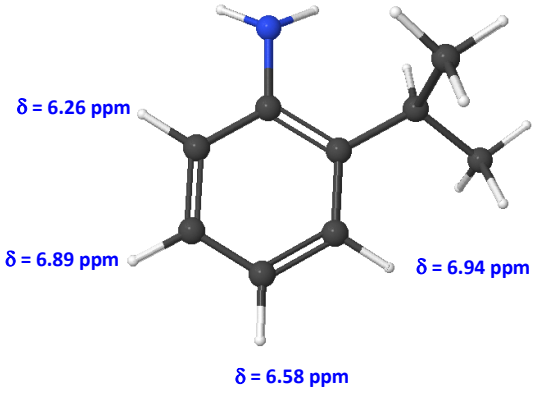
δH_a =	7.36	standard shift
	- 0.71	*ortho* to -NH_2
	-0.09	*meta* to -*i*Pr
	6.56	**Estimated shift**

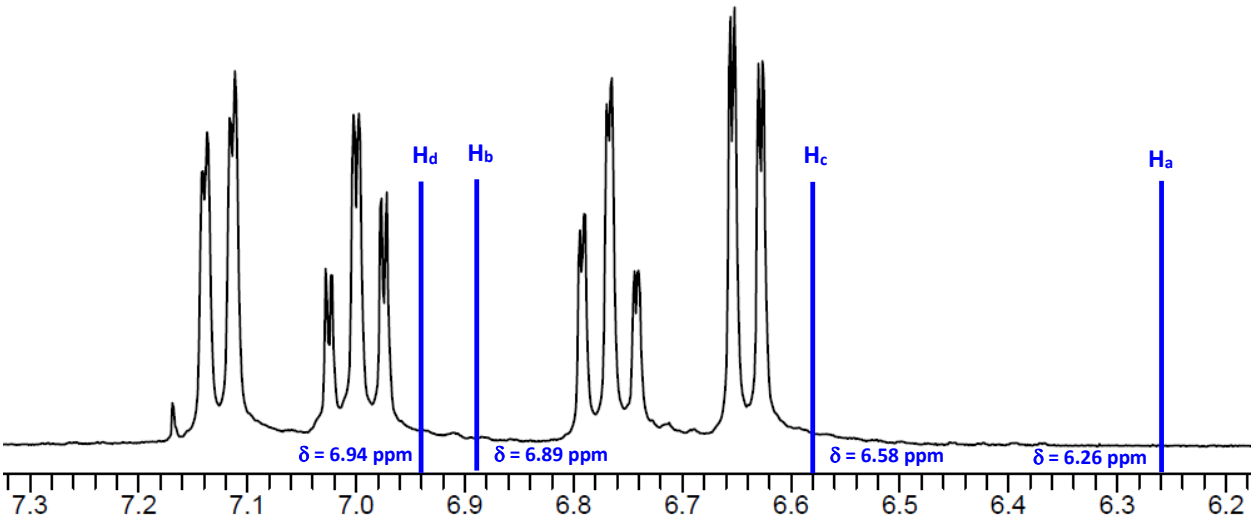


Not surprisingly, the estimate from the Curphy-Morrison Constants is nearly equal to that of the estimation from model compounds. Both of these methods can produce reliable results.

5) NMR calculation using Gaussian 09/WebMO

A computational approach can provide reasonable ^{1}H-NMR shift predictions provided that the level of theory and basis set provide a high-quality estimate of the molecular geometry and the magnetic field of the molecule. A simple approach will be employed below where the lowest energy conformation is optimized and an NMR calculation is performed on that species. As always the nature of the structure as a minimum energy on the potential energy surface should be confirmed by a vibrational frequency calculation. The B3LYP/6-31G(d) ^{1}H-NMR chemical shifts listed below are the unscaled *Isotropic Absolute NMR Shifts* referenced to TMS.





It is highly unlikely that this simple one-conformer approach with a relatively unsophisticated B3LYP calculation will yield quantitatively accurate predictions. This method, however, is likely to be sufficient to produce the correct ordering of the signals from high to low chemical shift as shown above. A more well-conceived computational approach might determine the chemical shift for each H-atom in the molecule in each conformation and weight the shifts according to the relative energies of each species.

With all of this information available, the assignment of the ^{1}H-signals has become trivial.