

Using Jaguar to predict NMR shifts

To calculate NMR shift using QM methods, a standard must first be determined. The experimental NMR shifts are relative shifts, while the calculated shielding values are absolute, although dependant on method and basis set. In general, the highest level method and basis set should be used.

Ideally, the shift (δ) should be equal to $\sigma_{\text{standard}} - \sigma_{\text{calc}}$. The normal standard is TMS, and thus if the hydrogens on TMS has a calculated $\sigma=30$, and the studied hydrogen has a calculated $\sigma=24$, the predicted ^1H NMR shift $\delta=6$ ppm.

However, in reality the shielding appears to vary somewhat with magnitude, leading to a relationship $\delta = k \cdot \sigma_{\text{calc}} + m$, where k and m are determined by fitting the calculated shielding values for several known standards to their experimental shifts. For example, TMS has a $\delta=0$ ppm and benzene has a $\delta=7.27$ ppm. Using B3LYP/LACV3P**, the calculated averaged shielding for the TMS hydrogens is 31.929633, and for benzene 24.350454. A linear fit between these two points show that $\delta = -0.957887412 \cdot \sigma_{\text{calc}} + 30.58499337$.

Including more than two data points is suggested. Remember, all shielding values must be calculated using the same method, or the k and m parameters will be off. Also, the same experimental conditions (particularly solvent) should preferentially be used for all experimental data.

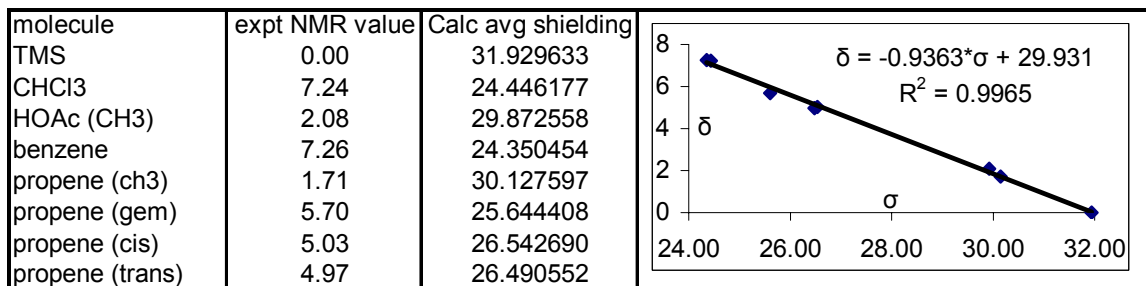


Table 1: standard shifts used to determine $\delta = k \cdot \sigma_{\text{calc}} + m$

Evaluation:

Prediction of ^1H shifts for organic compounds. (No evaluation of other nuclei is included here, mainly because ^1H shifts are expected to be less accurate than any other commonly used shifts)

Jaguars shielding values are expected to be accurate within +/- 0.4 ppm for organic compounds. Indeed, most calculated shifts have been found to be within +/- 0.2 ppm. For example, as this calculation of but-3-enyl isobutyrate shows, the calculated averaged shifts of the olefinic hydrogens (H3, H5 and H6) and methyl hydrogens (H19 – H24) are within 0.1 ppm of experimental values. The allyl hydrogens (H8, H9) are also within 0.1 ppm accurate, while the hydrogen alpha to the carbonyl (H16) is off by 0.16 ppm. The largest error is found in the hydrogens next to the ether (H10, H11), which are off by 0.25 ppm, all in all quite acceptable.

but-3-enyl isobutyrate				
	Expt NMR	Calc. shield	Calc. NMR	Averaged NMR
H3	5.1	26.505496	5.11	5.11
H5	5.8	25.806066	5.77	5.77
H6	5.1	26.611561	5.01	5.01
H8	2.38	29.803628	2.03	2.28
H9		29.261551	2.53	
H10	4.13	27.125786	4.53	3.88
H11		28.523534	3.22	
H16	2.54	29.425770	2.38	2.38
H19	1.17	31.001361	0.90	1.12
H20		30.794784	1.10	
H21		30.369621	1.50	
H22		30.598517	1.28	
H23		30.694535	1.19	
H24		31.173504	0.74	

Table 2: lowest energy conformer of but-3-enyl isobutyrate

This example also highlights the importance of averaging the calculated shielding of equivalent hydrogens. For the methyl hydrogens (H19 – H24) the calculated shift is spread between 0.74 and 1.50 ppm, which most likely reflects the reality of this particular configuration. Since the experimentally measured shielding is a partition function of all possible configurations, a reasonable estimate of this is the average of the calculated shielding numbers.

For methyl hydrogens this approach is normally very accurate, as the three most important conformers are just rotations around the methyl carbon bond. For other hydrogens, such as H10 and H11, it is somewhat more problematic. In the C_{2v} symmetric conformer these hydrogens are of course identical, but in reality the C_{2v} conformer is a transition state for rotation around a C-C axis. The lowest energy conformer is staggered, which renders H10 and H11 non-identical. The result of this can be seen in table 2, where the calculated shift for H10 = 4.53 ppm, and H11 = 3.22 ppm. By averaging the shift of the two hydrogens a reasonable estimate of the experimental shift is obtained.

A more rigorous approach would involve the minimization of several of the lower energy conformers, and then weigh the calculated shifts for each hydrogen by the partition function. For example, a 60° rotation around the C-O axis leads to a stable local minima, 0.2 kcal/mol higher in energy than the global. By using the relationship $\Delta G = -RT \ln K$, we can establish that the two conformers should exist in an equilibrium with $K=0.71$, and the partition quotients $Q_{\text{global}} = 0.58$, $Q_{\text{local1}} = 0.42$. By multiplying the calculated shifts of each conformer by the partition quotient and summing the two calculated shielding values, we obtain a more accurate shielding constant for each hydrogen, as seen in Table 3. The calculated shifts for H10 and H11 are now 4.06 and 3.64 ppm, i.e. significantly closer to the experimental value. It's expected that this molecule will have a significant number of low-level rotamers, and weighing in the shielding for the other rotamers should improve the calculated shift even more.

but-3-enyl isobutyrate				
	Expt NMR	Calc. shield	Calc. NMR	Averaged NMR
H3	5.1	26.459490	5.16	5.16
H5	5.8	25.846015	5.73	5.73
H6	5.1	26.600420	5.03	5.03
H8	2.38	29.529698	2.28	2.32
H9		29.454294	2.35	
H10	4.13	27.636399	4.06	3.85
H11		28.080552	3.64	
H16	2.54	29.435849	2.37	2.37
H19	1.17	30.939799	0.96	1.12
H20		30.817968	1.08	
H21		30.467308	1.40	
H22		30.508131	1.37	
H23		30.748345	1.14	
H24		31.164694	0.75	

Table 3: Weighted averages of two lowest configurations of but-3-enyl isobutyrate

CAVEAT

The only persistently problematic case found thus far is aromatic systems, such as pyridine. As seen in table 4, the calculated shifts are off by a quite substantial margin, -1.44 ppm, -0.68 ppm and +1.20 ppm. A spread of 2.64 ppm effectively prohibits the use of calculated shifts for even qualitative determinations. This problem is present even for all-carbon aromatics, although less pronounced. It is thus suggested that for complexes containing aromatic moieties the prediction of shifts should be contained to the non-aromatic parts.

It should be noted that this does not seem to be a Jaguar-specific problem. Control calculations using Turbomole and DeMon-NMR exhibits similar errors.

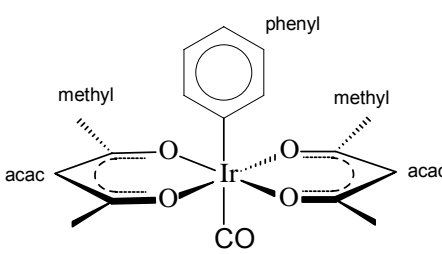
Pyridine				
	Expt NMR	Calc. shield	Calc. NMR	
pyridine (para)	8.74	24.173263	7.30	
pyridine (meta)	7.58	24.601512	6.90	
pyridine (ortho)	7.22	22.974458	8.42	

Table 4: Pyridine

Organometallics

The predictions of shifts for organometallic complexes is somewhat less accurate than pure organics, mainly due to relativistic effects of the metal. Thus, for a fairly uncomplicated Ir complex ($\text{Ir}(\text{acac})_2(\text{Ph})(\text{CO})$), we get relative errors on the order of 0.3 ppm. Considering the more individual shifts in organometallic complexes, this should be accurate enough for comparison to experimental numbers.

$\text{Ir}(\text{acac})_2(\text{Ph})(\text{CO})$	Expt NMR	Calc. shield	Calc. NMR	Averaged Calc. NMR
acac	5.24	26.704906 26.703403	4.93 4.93	4.93
phenyl	7.0 - 7.2	24.256103	7.22	ortho: 7.22
		24.256165	7.22	meta: 6.87
		24.627411	6.87	
		24.627251	6.87	para: 6.78
methyl	1.95	24.722299	6.78	
		29.746940	2.08	
		30.226140	1.63	
		30.237646	1.62	
		29.757997	2.07	
		29.716300	2.11	
		29.722283	2.10	
		29.755045	2.07	
		30.235764	1.62	
		30.235941	1.62	
		29.758233	2.07	
29.721561	2.10			
29.727157	2.10			



The results are expected to be improved by comparison to other Iridium complexes.

As with the organic case above, though, we get very large errors for organometallic complexes featuring aromatics. For example, the predicted shifts of the Periana $\text{Pt}(\text{bpim})\text{Cl}_2$ complex yields errors of -0.75, -0.90 and +0.25 ppm, and can thus not be used for experimental comparisons. As above, however, this does not seem to be a Jaguar specific problem.

$\text{Pt}(\text{bpim})\text{Cl}_2$			
	Expt NMR	Calc. shield	Calc. NMR
para	9.35	22.785610	8.60
meta	8.00	24.386099	7.10
ortho	9.68	21.357137	9.93

