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Density Functional Theory Calculations of ^{17}O NMR Chemical Shifts for Substituted Trifluoromethyl Aryl Ketones

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Abstract: *A good correlation is found between density functional theory calculated carbonyl ^{17}O NMR chemical shifts and those observed in CCl_4 solution for 16 titled ketones. The calculated values are in good agreement, 0-5 ppm in most cases, with observed ones and show a linear relationship against σ^+ constants. The implication of these observations is discussed.*

^{17}O NMR spectroscopy is a sensitive tool to assess the electronic and steric effects exerted on a carbonyl functional group by its substituents.[1,2] Among 13 different types of benzoyl compounds (YC_6H_4COX), the carbonyl group in the trifluoroacetyl group is considered among the most sensitive toward the change of electron donating or withdrawing ability of substituent on the benzene ring.[2b,3,4] In our independent study, we have shown that an excellent linear correlation (correlation coefficient R = 0.998) exists between ^{17}O chemical shifts measured in CCl_4 and σ^+ constants for 12 α,α,α-trifluoroacetophenones, while the correlation between $\delta(^{17}O)$ and the dual-substituent parameters is less satisfactory.[5] Our results demonstrate that ^{17}O NMR spectroscopy could be a good alternative for determination of σ^+ constants and we have successfully redetermined the σ^+ constants for several heteroaromatic rings,[6] even though chemical reactivity is not regarded as directly related to NMR chemical shift.[2] On the other hand, *ab initio* calculations of ^{17}O chemical shifts have been carried out for various classes of oxygen containing compounds, and the calculated chemical shifts for different types of oxygen atoms deviate from experimental values to different extents.[2b,7-10] It is likely that for a series of closely related compounds, such as those employed in determining substituent constants, systematic deviations exist and do not interfere much with the substituent effect. To our knowledge, this notion has never been verified for ^{17}O chemical shifts. In this communication, we would like to report the good agreement between the calculated and observed ^{17}O chemical shifts for trifluoromethyl aryl ketones ($ArCOCF_3$) with a large range of σ^+ constants (-1.03 to +0.946) and with a chemical shift difference of 48 ppm.

Density functional theory (DFT) calculations have been successfully applied to the study of molecular properties and chemical effects.[11] Our calculations on carbonyl ^{17}O chemical shifts for 16 trifluoromethyl aryl ketones, including 12 α,α,α–trifluoroacetophenones (**1a-1l**),[5] 2- and 3-trifluoroacetylfuran (**2o** and **3o**) and 2- and 3-trifluoroacetylthiophene (**2s** and **3s**),[6] were carried out as follows. The lowest energy conformers found for these compounds in AM1[12] conformational analyses were taken as starting points for DFT optimizations at

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Table 1. Calculated and observed ^{17}O NMR chemical shifts (ppm) for trifluoromethyl aryl ketones

$ArCOCF_3$	Ar	σ^{+} [a]	δ(obsd)	δ(calcd)	$\Delta\delta$ [d]
1a	5-coumaranyl	-0.984	531.0	532.9	+1.9
1b	4-$CH_3OC_6H_4$	-0.778	537.1	536.5	-0.6
1c	4-$C_6H_5OC_6H_4$	-0.560	543.2	540.6	-2.6
1d	4-$CH_3C_6H_4$	-0.311	549.7	550.3	+0.6
1e	3-$CH_3C_6H_4$	-0.066	554.4	556.0	+1.6
1f	C_6H_5	0.000	557.6	557.8	+0.2
1g	3-FC_6H_4	0.352	563.8	564.6	+0.8
1h	3-ClC_6H_5	0.399	564.7	563.8	-0.9
1i	3-$CF_3C_6H_4$	0.520	568.5	567.2	-1.3
1j	4-$CF_3C_6H_4$	0.612	572.6	571.2	-1.4
1k	3,5-$Cl_2C_6H_3$	0.701	574.4	569.3	-5.1
1l	3,5-$(CF_3)_2C_6H_3$	0.946	579.2	574.0	-5.2
2o	2-furyl	-1.03	529.6	528.7	-0.9
3o	3-furyl	-0.615[b] (-0.29)[c].	549.2	541.8	-7.4
2s	2-thienyl	-0.928	531.2	534.2	+3.0
3s	3-thienyl	-0.559	543.6	542.1	-1.5

[a] For sources of σ+ of **1a-1l**, see references in ref. 5. For σ+ of **2o, 3o, 2s**, and **3s**, see ref. 6. [b]Based on solvolysis rate constants. [c] Based on ^{17}O chemical shifts. [d]δ(calcd) - δ(obsd).

the level of B3LYP/6-31G(d). The gauge-including atomic orbital (GIAO) method[10,13] implemented in Gaussian 94[14] were then used for NMR chemical shift calculations at the theory level of B3LYP/6-31+G(d,p). The results are listed in Table 1. The calculated gas phase ^{17}O chemical shifts differ from the solution data in general by about 0-5 ppm, with the exception of 7 ppm for **3o**. For **1a-1l**, good linear correlation (R = 0.991) between calculated and measured chemical shifts was observed. (R = 0.991). Large deviations, 3-15 ppm, and poor correlation (R = 0.975) were found if the calculations were carried out at the HF/6-31+G(d) level.

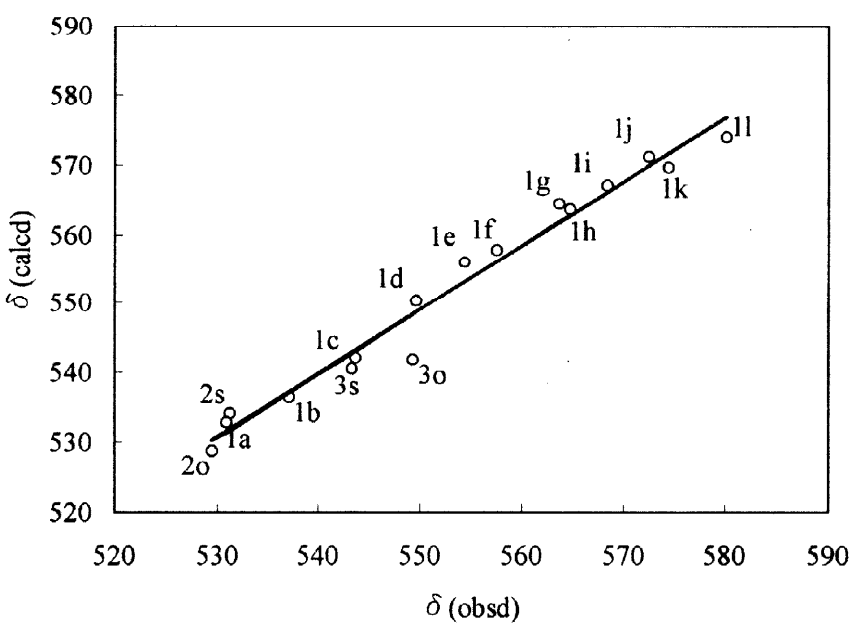

Figure 1. Plot of calculated chemical shifts against observed chemical shifts.

Considering the fact that in the gas phase calculation only a single conformer of each compound, rather than a group of interconverting conformers as in solution, is involved, the good agreement between calculated and experimental results is respectable. Moreover, satisfactory correlation (R = 0.987) was again realized if furan and thiophene derivatives **2o**, **3o**, **2s** and **3s** were included. A plot of the calculated and experimental chemical shifts of all 16 trifluoromethyl aryl ketones (Figure 1) indicated the significant deviation for the point corresponding to 3-trifluoroacetylfuran **3o**. Excellent linear correlations (R = 0.993) can be found as the data for **3o** is not considered. Therefore, ^{17}O NMR chemical shifts calculated with the GIAO method at the B3LYP/6-31+G(d,p)//B3LYP/6-31G(d) level are rather reliable for aromatic and heteroaromatic trifluoromethyl ketones in general.

In the previous study, the σ^+ constants of 2- and 3- furyl and 2- and 3-thienyl groups were redetermined based on the solvolytic reactivities of heteroaromatic analogs of 1-*tert*-butylbenzyl bromides and chlorides, and on the ^{17}O NMR chemical shifts of the trifluoromethyl ketones as well.[6] Inconsistency between the values obtained by those two methods were found only in the case of 3-furyl. It is interesting to note from the plots of calculated and observed ^{17}O chemical shifts against σ^+ constants (Figure 2) that for **3o** δ(obsd) does not correlate well with σ^+ while δ(calcd) does.[15] Linear relationships, R = 0.998 for δ(obsd) without δ(**3o**) and R = 0.993 for all δ(calcd), were found. Moreover, the 3-furyl derivatives, 1-(3-furyl)-2,2-dimethylpropyl bromide and chloride (**4b** and **4c**), were also found to exhibit comparatively poor linear relationships in the Grunwald-Winstein type correlation analysis[16] of solvolytic reactivities in a variety of solvents.[6] Further investigation on such abnormal behaviors exhibited by the 3-furyl compounds, **3o**, **4b** and **4c**, seems to be worthwhile.

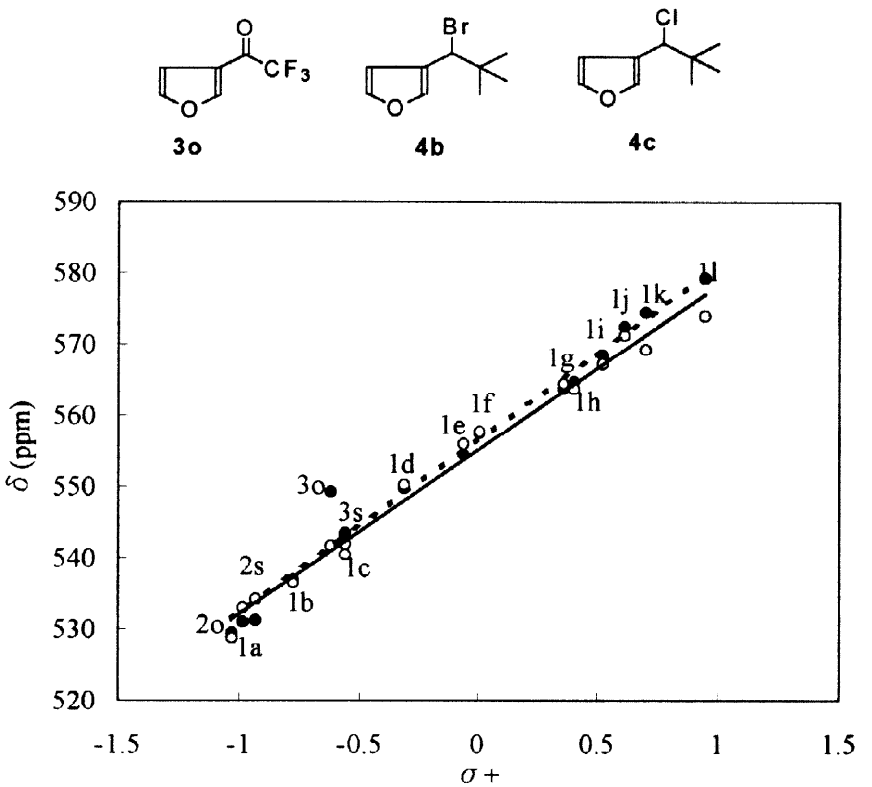

Figure 2. Plot of calculated (open circle, R = 0.993) and observed (close circle, R = 0.998) chemical shifts against σ^+. The observed δ (**3o**) is not taken into account in the fitting.

In short, the measured carbonyl ^{17}O NMR chemical shifts of trifluoromethyl aryl ketones in CCl_4 have been found to show excellent linear correlation with σ^+ constants,[5,6] and in most cases are in good agreement with calculated gas phase values as demonstrated in the present work. Therefore, this powerful and easily available computational technique could be employed to examine the relationship between $\delta(^{17}O)$ and σ^+ constant more extensively, and to probe the anomaly of substituent effect in aromatic and heteroaromatic systems. DFT calculations of ^{17}O NMR chemical shifts for all located conformers and for other carbonyl compounds, such as aromatic acid chlorides, are in progress.

Acknowledgement

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