INVESTIGATION OF ORTHO EFFECT, RELAXATION AND SELECTIVE EXCITATION TECHNIQUES IN NMR

by

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Certificate

This is to certify that the thesis titled **"Investigation of Ortho Effect, Relaxation and Selective Excitation Techniques in NMR"** is being submitted by **Ms. Arunima** to the Department of Chemistry, Indian Institute of Technology, Delhi, for the award of the degree of **Doctor of Philosophy**. This thesis is a record of bona-fide research work carried out by her under my guidance and supervision. In my opinion, the thesis has reached the standards fulfilling the requirements of the regulations relating to the degree.

The results contained in this thesis have not been submitted to any other university or institute for the award of any degree or diploma.

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Thank you God, for helping me
through times of joys and sorrows

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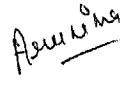

Arunima

Abstract

NUCLEAR spin relaxation is central to the nuclear magnetic resonance phenomenon, providing a wealth of information on global and local motions. There are several mechanisms by which nuclear spins relax. Although known for quite some time, rapid development of NMR methodology and its use for structure determination of biomolecules has in recent years rejuvenated interest in the cross terms between various relaxation mechanisms. This motivated us to exploit such experiments for the determination of physicochemical properties of complex organic systems. In this thesis we exploit cross correlation for the study of the C-H---N hydrogen bonding and the *ortho* effect in fluorobenzenes. We also examine some novel sequences for cross relaxation spectroscopy and selective excitation.

An application of the cross-correlation measurements for providing an evidence for the existence of weak hydrogen bond is described here. The ability of carbon atoms to act as proton donors in a hydrogen bond has been the subject of debate for many years. An increasing number of spectroscopic studies indicate that C-H---X (especially C-H---O) hydrogen bonds occur in many systems. Although intermolecular C-H---X hydrogen bonds are well authenticated and have been the subject of several systematic studies, intramolecular interactions of this type have received scant attention. We report here a cross-correlated relaxation study aimed at probing the existence of such interaction in liquids, specifically in 4,4-Bisphenylsulphonyl-N,N-dimethylbutylamine in which an intramolecular hydrogen

bond has already been reported. These experiments provide a means of measuring a parameter related to the orientation of the chemical shift anisotropy (CSA). This single parameter provides an overall idea about the magnitude and orientation of the CSA tensor. These CSA orientation parameters are measured via determination of the cross correlation rate and the correlation time. We show that the strength of the hydrogen bond reduces in the presence of trifluoroacetic acid, which is reflected in a significant decrease in the CSA orientation parameter of the methine proton, as compared to a minor change in the isotropic chemical shift value. An increased CSA orientation parameter is observed in pyridine due to a competition between the basic solvent and the N atom of the dialkyl-amino group for the methine proton. To our knowledge, this is the first kind of investigation where the variation in the CSA tensor is observed due to the presence of weak hydrogen bond.

We have also performed a systematic study for the assessment of *ortho*-substitution effect on CSA tensors in fluorobenzenes. The variation in the magnitude and orientation of the CSA tensors, on chemical substitution was at first recognized in solid state NMR. Recently it has also been perceived in liquid state through the cross correlation between the tensor (CSA) and dipolar coupling. No systematic study of the *ortho* effect on CSA tensors has been carried out in liquid state NMR before. Experiments we report here for the determination of the cross correlation between the CSA of ^{19}F and its dipolar interaction with the nearby protons are based on the longitudinal relaxation of ^{19}F. The correlation time is measured independently from the ^{13}C relaxation studies. A detailed computational study indicating the variations in the value of CSA orientation parameters, as a function of different *o*-substitution, is also presented in this thesis.

Ab-initio electronic structure calculations are a powerful tool for exploring areas of chemical interest like substituent effects, reaction mechanisms, potential energy surfaces, and excitation energies. In an attempt to extend the scope of our experimental study on the ortho effect we have resorted to *ab initio* calculations of the shielding tensors. From a multi parameter regression analysis of the most shielded tensor element for different fluorobenzenes we find poor correlation with linear free energy parameters. Electrical effects of the substituents are defined in terms of a polar and resonance parameter whereas the *ortho* effect is expressed as the molar refractivity parameter and the steric parameter. The correlation is improved in the absence of groups that have conformational flexibility. The regression analysis shows that the molar refractivity parameter that accounts for both electrical and steric nature of the substituents better represents the variation in the shielding tensor. A similar investigation is shown for the case of the CSA orientation parameter, which is obtained from the anisotropic chemical shielding and the angle subtended by the internuclear vector (FH) and the CSA symmetry axes of the fluorine. This study also illustrates the presence of both electrical and steric nature of the *ortho* effect on ^{19}F anisotropy and provides a physicochemical background for the *ortho* effect.

Nuclear Overhauser effect is one of the cornerstones for relaxation studies of large molecular and supramolecular structures. Transverse cross relaxation spectroscopy (ROESY) is a technique that overcomes the limitations of the nuclear overhauser effect and is used for determining Overhauser enhancements of medium sized molecules. In the present work, we investigated a sequence that suppresses the coherent transfer of magnetization and offset effects during the transverse cross relaxation. Such discrimination is not easily achievable using the usual methods of

phase cycling or randomization of the mixing time. Techniques have been proposed to overcome these drawbacks. Even with these sequences there are still certain regions in the spectrum where cross peaks might arise due to coherent transfer of magnetization. Hwang and Shaka suggested an especially appealing method for ROESY called T-ROESY. It employs a sequence made up of (-180_x -180_{-x} -) pulses on magnetization prepared in the Y-direction. We investigate here the use of amplitude and frequency modulated adiabatic pulses, in the T-ROESY experiment. This is motivated by the fact that adiabatic pulses uniformly invert magnetization over a large bandwidth at modest RF strength. Coherent transfer processes are minimized when amplitude is modulated, and offset effects are minimized by the frequency modulation. Here we explore if a BIR-4 adiabatic pulses could replace the π pulses. Our results indicate that adiabatic pulses perform poorly for this application. The reason for their failure are due to the initial magnetic field being aligned with the RF and the spins being inverted at different times..

Over the past few years, the development of NMR spectroscopy has allowed selective extraction of information from complicated spectra, like those of proteins. The need to tailor radio frequency pulses to create a desired excitation profile has motivated much research into designing various pulse sequences for selective excitation. Here, we examine a simple technique for selectively exciting nuclear magnetic resonance spectra on spectrometers that are not capable of generating an extended series of amplitude, and phase modulated RF pulses. These pulses are similar to DANTE where delays alternate with nutation. However, unlike in DANTE here the pulse width and pulse positions are incremented. This approach can be used to produce single or multiple frequency selective pulses. The main drawback, common to all selective excitations based on DANTE trains, comes from

the presence of sidebands aroused by resonances precessing at frequency multiples of the inverse of the precession delay. We believe that one possible solution for achieving selective excitation with minimized sidebands is to use width or position modulated pulses. The reason they are expected to reduce sideband intensity is that the inter pulse delays are irregular. Experimental confirmation from both one and multidimensional NMR are reported in the present work.

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