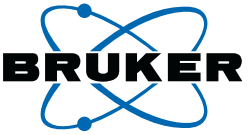

topspin

DAISY

Version 2.0.0

revision state: 03/07/2007 (Version 2.0.0)

Bruker software support is available via phone, fax, e-mail or Internet. Please contact your local office, or directly:

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Contents

Chapter 1

Introduction

1.1 About this manual

This manual is a reference to TOPSPIN structure analysis with 1D spectrum simulation (DAISY). DAISY is a program system designed for simulation and iteration of high resolution NMR spectra. The complete DAISY interface and functionality is described and some examples of simulation will illustrate the power of DAISY.

1.2 Conventions

Fond conventions

daisy - commands to be entered on the command line are in Courier bold italic

Apply - commands to be clicked are in Times New Roman bold italic

`fid` - file names are in Courier

contents - any contents of a text file is in Courier small

name - any name which is not a filename is in Times New Roman italic

1.3 Getting started

1.3.1 Basic program features

The **Spectrum Simulation** is based on the solution of the time - independend Schroedinger equation to calculate the energy levels. To built up the necessary Hamilton matrix the factorisation by total spin values, **chemical equivalence** as well as **magnetic equivalence** and **fragment factorizing** are taken into account to reduce calculation time and memory requirements. Using the selection rules for single quantum transition, frequencies and intensities are determined. Up to 10 nuclei or groups with spin quantum value $I \geq 1/2$ can be treated with one fragment. The **Lorentzian lineshape** is calculated by application of global or individual linewidths to the transitions of as many fragments as you have defined. The calculated spectrum will be stored in the pdata directory under procno 999 by default.

The **Spectrum Iteration** uses the method of **total-lineshape fitting**. Adjustable parameters are **resonance frequencies, scalar coupling constants** and **linewidths**. The program uses the digital experimental spectrum as experimental data.

1.3.2 How to start DAISY

As DAISY is now part of **TopSpin**, it will be started as a special analysis option out of the **TopSpin** main window.

When experimental data (processed 1D NMR data) are loaded to the 1D data window, there are two possibilities to start DAISY:

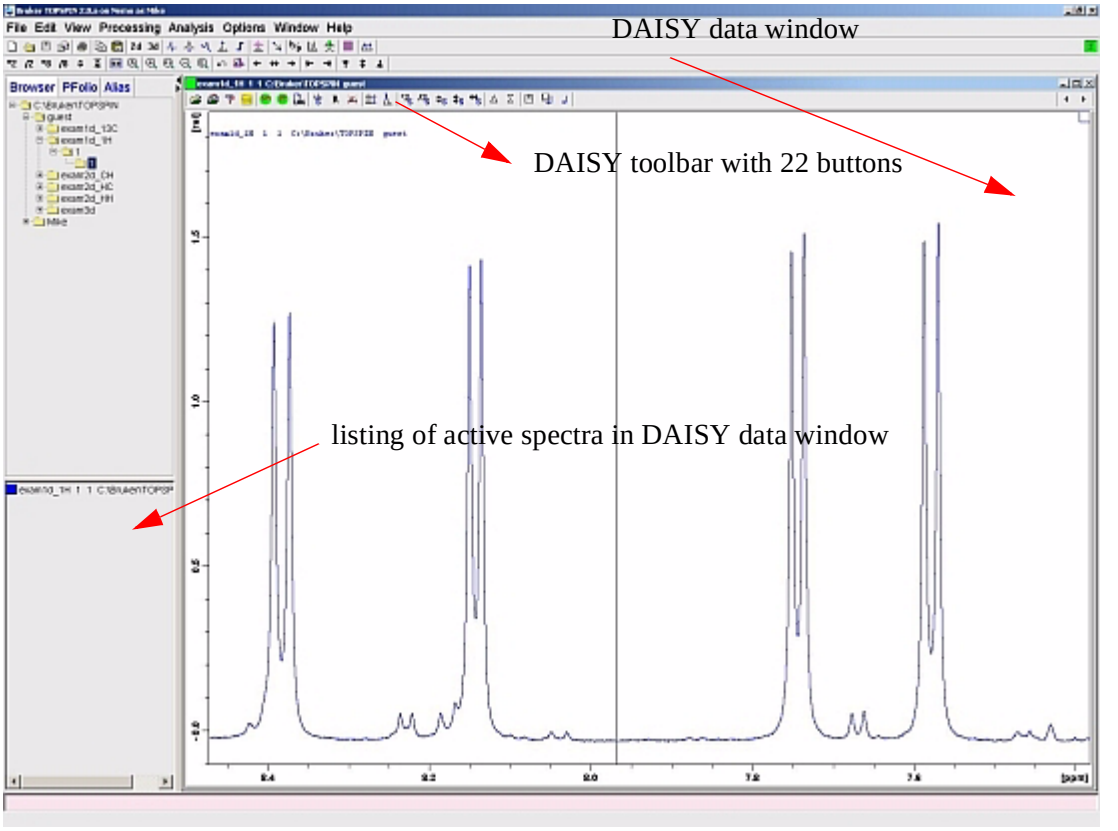
- enter ***daisy*** into the command line

- click Analysis -> Structure Analysis -> 1D Spectrum Simulation [daisy] from the menu

bar

The 1D data window now switches to the DAISY data window.

Figure 1.1: The DAISY data window



1.3.3 How to use the DAISY toolbar

The DAISY toolbar contains 22 buttons for input, data preparation, simulation/iteration, display options, scaling, mathematic operation and data handling.

open Spin-System

This button opens a window for selecting files containing spin system information. The default directory is the TopSpin home directory with the default file type setting MGS file (.mgs). (Chapter 2.1.1)

import multiplets from a dataset

With this button the user opens a window where NMR data sets with multiplet can be chosen and imported to DAISY. (Chapter 2.1.2)

edit Spin-System

This button opens a window consisting of three tables: Parameters like shifts/frequencies, couplings, linewidth etc. will be entered here. (Chapter 2.1.3)

advanced options

Pressing this button opens a window again consisting of three tables. Here simulation sequence options, spectrum options, iteration options and output options can be selected. All possible calculations (simulation, iteration, lineshape or subspectra generation) can be started from this window. (Chapter 2.1.4 , 2.2 and 3)

run simulation

Pressing this button will execute a spectrum simulation resulting in a 1D NMR spectrum with the displayed simulated name. (Chapter 2.2.)

run iteration

This command will execute a spectrum iteration. The iteration statistics are available from the protocol list and the resulting 1D NMR spectrum is written. (Chapter 2.2 and 3)

show DAISY logfile

Pressing this button wil display the Simulation/Iteration Protocol List

(extension 'lst'/'rst') with the defined windows editor. (Chapter 4.1.1 and 4.2.1., 4.2.2., 4.2.3)

deselect all datasets

This command will deselect all datasets displayed in the DAISY window.

reset individual scaling and shifts

This command resets individual scalings and shifts for the selected dataset.

remove all selected datasets from display

Pressing this button wil remove all selected datasets from display.

toggle the display layout

This button switches the display layout from seperated spectra to overlayed spectra and vice versa.

switch on/off the display of dataset name and scalings

Pressing this button the dataset name and scaling will be switched on/off.

increase intensity

Pressing this button the intensity of the selected spectra will be doubled.

decrease intensity

Pressing this button the intensity of the selected spectra will be halved.

expand intensity axis

Decreases or increases intensity of selected spectrum while pressing this button and moving the mouse.

shift up/down

Shifts up and down the selected spectrum while moving the mouse and pressing this button.

shift left/right

Shifts left and right the selected spectrum while moving the mouse and pressing this button.

show a difference between the 1st and the sum of other spectra

Pressing this button calculates the difference between the first and the sum of other spectra and shows the result as a new spectrum.

show a sum of all spectra

Pressing this button calculates the sum of all spectra and shows the result as a new spectrum.

export Spin-System

The spin system of the actually loaded DAISY calculation will be stored in the directory <home>NMRSIM/ham (default path) or another directory of your choise. Two files are created (*.msg, *.itr)

terminate DAISY mode, save changes

terminate DAISY mode, do not save changes

Chapter 2

DAISY Simulations

DAISY calculations can be either simulations or iterations. A simulation means quantum mechanical synthesis of a high resolution NMR spectrum based on given NMR parameters, as there are Resonance frequencies, Scalar Coupling Constants, and linewidths. A spectrum iteration needs all these NMR parameters as well as a starting guess for the iterative refinement of these NMR parameters. In addition experimental data is required for adjustment of the calculated spectrum. As a consequence, both calculation types need the same basic data input, while for iterative calculations simulation data can be extended.

2.1 Parameters for a DAISY Simulations

This chapter will teach the user to prepare a new DAISY simulation input document by explaining all available features and options, to execute the calculation and display the result.

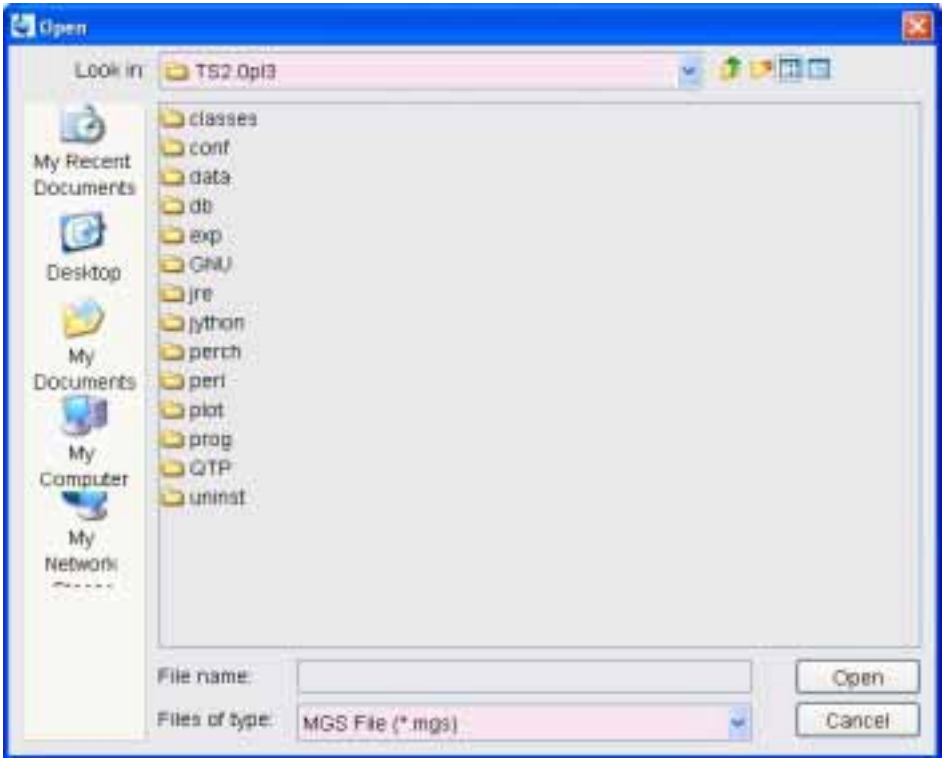
First of all you have to load the spectrum you want to simulate. It is recommended to choose a special region of your spectrum to simulate. This can be done by using the ***int*** command. Otherwise the whole spectrum will be used as basic data for a following iteration. This can cause bad results. You should also do peak picking and multiplet definitions using the commands ***pp*** and ***mana.*** Then switch to the DAISY window by typing ***daisy.***

Now the TopSpin data window looks like it is shown in Figure 1.1. The chosen region of the spectrum is shown on the screen and the toolbar of the data window indicates the DAISY mode.

2.1.1 Open Spin System

If simulation data already exists or has been stored with the  button, it can be loaded by clicking the  button on the toolbar. The window shown in figure 2.1 will appear. It shows the TopSpin home directory with the default file type setting MGS File (.mgs).

Figure 2.1: The open-spin-system window



In general DAISY allows to use the following spin system definition formats:

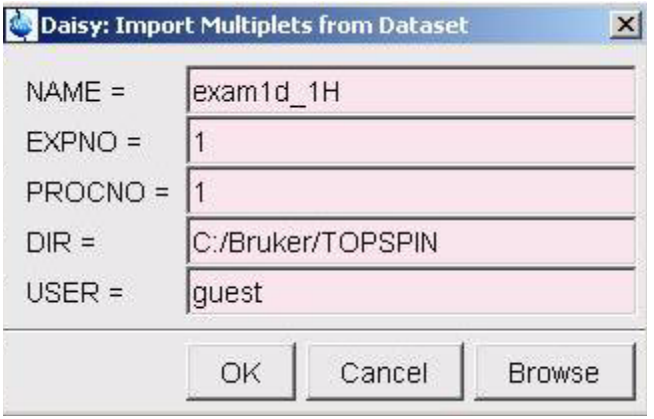
- DAISY file format (*.mgs file)
- NMR-SIM format (*.ham file)
- ACD prediction format (*.acd file)
- Perch prediction format (*.prp files)

2.1.2 Importing data

If you have done a multiplet definition you can import the multiplets from the data set. Multiplet analysis is described inthe manual Structure Analysis Tools . DAISY reads out the information from the file `daisymultiplet.txt` in the **procno** directory. Multiplet definition scans the spectrum for identical line distances. It is possible to do this automatically or manually. The more complex the system is, the more manual analysis has to be done. For really complex second order spin systems a normal spin analysis of the spin system is recommended.

Click on the  button in the toolbar and the window shown in figure 2.2 will appear. Here you can type in the file informations or use the browse button. Click the **OK** button. Now you can decide if you want to subdivide the multiplets and if the found coupling constants shall be used.

Figure 2.2: The DAISY import multiplet window



2.1.3 The 'Edit Spin System' window

In this window all relevant parameters for the simulation of the chosen spectrum have to be set. Click the  button in the toolbar and a new window will appear. This 'Edit Spin System' window is divided into two parts. The left part is a listing of all fragments for your simulation. It depends on the imported multiplet data, how many fragments will appear. Here fragments can be added, copied or deleted.

The right part consists of three tables, described in the paragraph below:

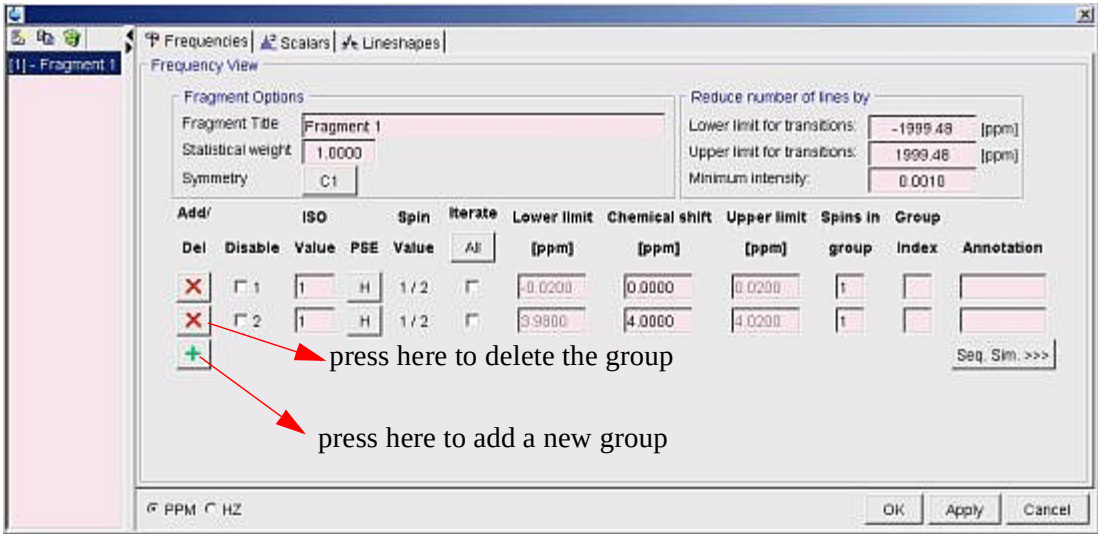
2.1.3.1 The Frequency table (of the 'Edit Spin system' window)

The 1st table (shown in figure 2.3) contains all information about the frequency range of your simulation. It is devided into three blocks.

A) Fragment Options:

In the first line a suitable title can be selected. After pressing the ***Apply*** button this title will be displayed in the listing at the left side of the window.

Figure 2.3: Frequency view of 'Edit Spin System' window



For the creation of the first fragment in a new document you don't need to care about the **Statistical weight** (second line) yet. This value will start to affect the data when more than one fragment is defined. For more information see chapter 2.3.

In the third line a symmetry group can be selected. The default setting for the Symmetry is the point group C1, actually meaning no symmetry at all. As opposed to magnetic equivalence, molecular symmetry leads to chemical equivalence. It is not always necessary to use the maximum symmetry defined by the molecular structure. In general the lower symmetries are much easier to describe and even a simple twofold symmetry greatly improves calculation speed.

Symmetry is useful and saves computer time and memory. Inform yourself about symmetry and gain experimental experience by doing (more in chapter 5.1).

If the selected point group remains C1, the Symmetry Description (available by clicking the symmetry button) can be omitted, because C1 consists of only one symmetry operator , the identity operation. Consequently, further user definitions are not required. If you change the point group selection, all following parameters for this fragment will be affected.

B) Reduce number of lines by:

The default limits of transitions are in normal cases big enough to cover all important lines. The **Minimum intensity** defines the quantum mechanical intensity limit to include a transition into the transition list or not.

C) ISO Value/PSE/Spin Value/Frequencies/Disable:

Below block A and B a frequency block is displayed. It contains the values of the actual fragment. If you have imported data, it is displayed here. Of course, the above declared symmetry directly influences the input.

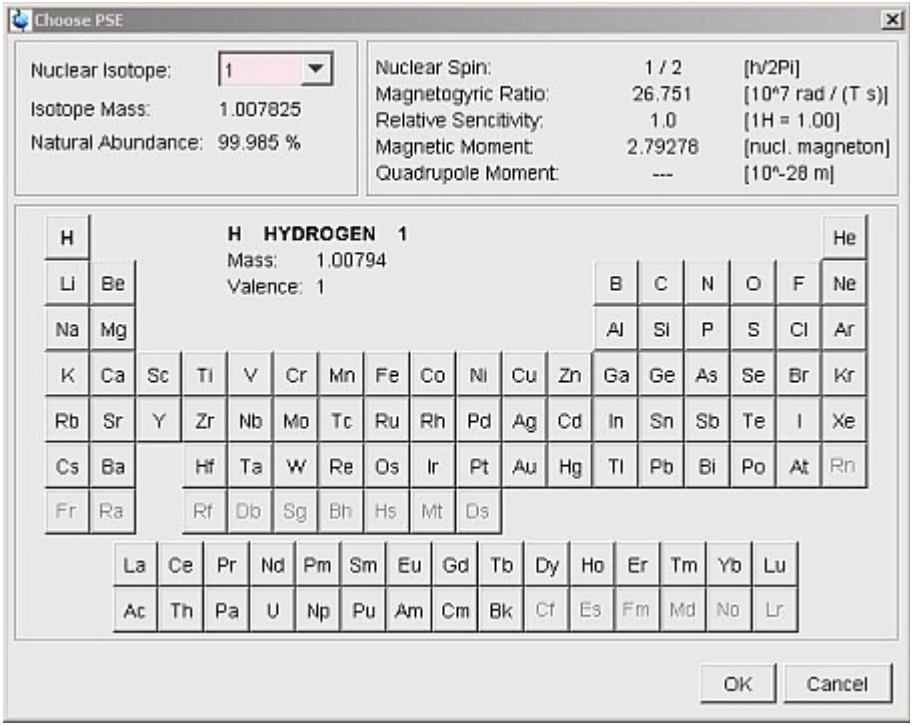
The list also contains ISO Values, Spin Values, Spins in group and Group Indices. In figure 4 the default values are displayed.

In order to define the nucleus type press the ***PSE*** button (see figure 4) for each shift/frequency. The 'Choose PSE' window will appear (figure 2.4).

The values from the frequency block are the initial values. Change the element by

pressing the corresponding button in the Periodic table. In the **Nuclear Isotop** combo box the available spinactive nuclei can be selected. According to this selection the element data in the upper right part of the window are updated. Exiting the window by pressing the ***ok*** button will take the following data to the corresponding nucleus of your spin system: **ISO Value, Element Symbol (on *PSE* button) and Spin Value**

Figure 2.4: 'Choose PSE' window



The parameters for **Element Symbol** and **Spin Value** are only changeable via the ***PSE*** button. The **ISO Value** can be changed by user request to apply X-Approximation for homonuclear spin systems, too. X-Approximation will be executed if the element symbol or the ISO value (or both) are different.

The selection of the Isotope and the number of magnetically equivalent spins in a group defines if a single spin or composite particle simulation shall be executed.

The **Resonance Frequency [Hz]/ Chemical Shift [ppm]** values are imported at the start of DAISY or have to be given by the user manually. This is for example necessary when a manual spin analysis has been done. The sum of the spins in group defines the total size of your spin system in the actual fragment.

If we take, for example, an ethoxy-group A_2B_3, we have two spins in group for A and three spins in group for B.

You can also activate some or all nuclei for iteration (discussed in chapter 4.1.1) and set the upper and lower limits for the frequencies here.

The **Disable** option in the frequency block offers the user to neglect the transitions, which belong to the disabled spin/group. **It does not simulate a decoupling effect!** The coupling information to the disabled nucleus remains in the spin system, only the transitions of the disabled nucleus are suppressed.

This is necessary if you define a fragment in which you have to include one spin/group because of its coupling information towards other spins of this fragment, but for this certain spin/group not all coupling partners are defined. Therefore you want to neglect the transitions of this this special spin/group. This may be possible by restricting the frequency limits. But if the resonance frequency of this special spin/group is located in the same spectral region as the other transitions, it is impossible to supress its transitions by changing the frequency limits. You have to use the disable options for this spin/group.

Another use for this option is to look at a multiplet pattern of a complex spin system if its transitions are overlapped by other signals.

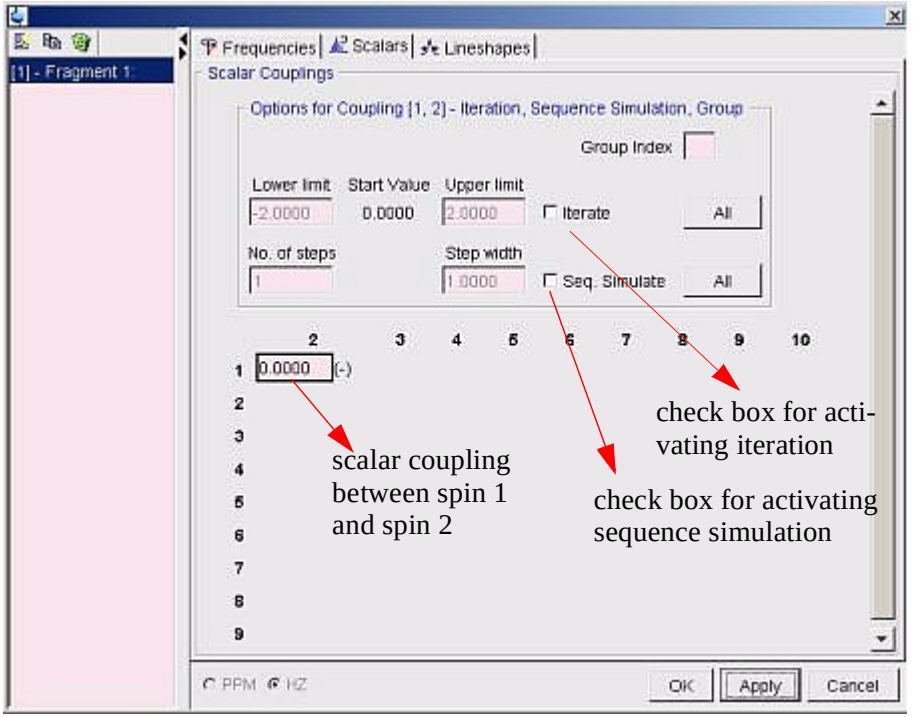
Due to the fact, that this transition suppression is based on the detection of the transition origin nucleus via eigenvectors, this option may not be exact for strongly coupled systems. Combination lines may not be possible to assign.

In this block you can activate the iterate option for resonance frequencies in the chosen fragment by pressing the iterate ***All*** button (iteration of all freqencies) or tagging the frequencies you want to iterate. Now it is necessary to set the lower and upper frequency limits. By pressing the ***Apply*** button all changed values will be stored.

2.1.3.2 The Scalars table (of the 'Edit Spin system' window)

The 2nd table (shown in figure 2.5) contains all information about the scalar couplings.

Figure 2.5: Scalar Couplings table of 'Edit Spin System' window



This table shows the possible indirect (=scalar) coupling constants. If you have imported the couplings by starting **DAISY** they will appear now. Otherwise you have to fill in your desired values. Correspondingly the selected symmetry affects the coupling table. For fragments with symmetry the minimum number of parameters will be presented. In an unsymmetrical case the maximum number of coupling constants is given.

The coupling constant values are always in Hertz. The table is not influenced by the number of magnetically equivalent spins within a group, because the inner-group scalar coupling constant does not affect the spectrum at all if we consider isotropic solutions only. **DAISY** is not able to calculate NEMA spectra at moment and hence does not read in dipolar coupling constants D_{ij}. Therefore the quantum mechanical calculation ignores this value and no input is required.

After setting all values press the ***Apply*** button.

Similar to the frequencies table, you can check iteration of the coupling constants. Again it is necessary then to set lower and upper limits. When choosing a sequence simulation you have to set the number of steps and the step width additionally.

To take over the new values press the ***Apply*** button.

2.1.3.3 The Lineshapes table (of the 'Edit Spin system' window)

The 3rd table (shown in figure 2.6) displays all lineshape parameters. By default a **global linewidth** of 0.3 Hz is set.

The **global linewidth** means that this parameter is applied to every transition of the fragment resulting in the Lorentzian lineshape spectrum. The option to use the **Fast Lorentzian Lineshape** is faster but in case of poor digital resolution the resulting spectrum might be inexact. This way the lineshape determination does not calculate every digital point of the spectrum, but picks up values from a model line with the global linewidth. Therefore the transition frequency is moved to the nearest digital point of the spectrum. For this reason the **Fast Lorentzian Lineshape** calculation is not suitable for spectrum iteration.

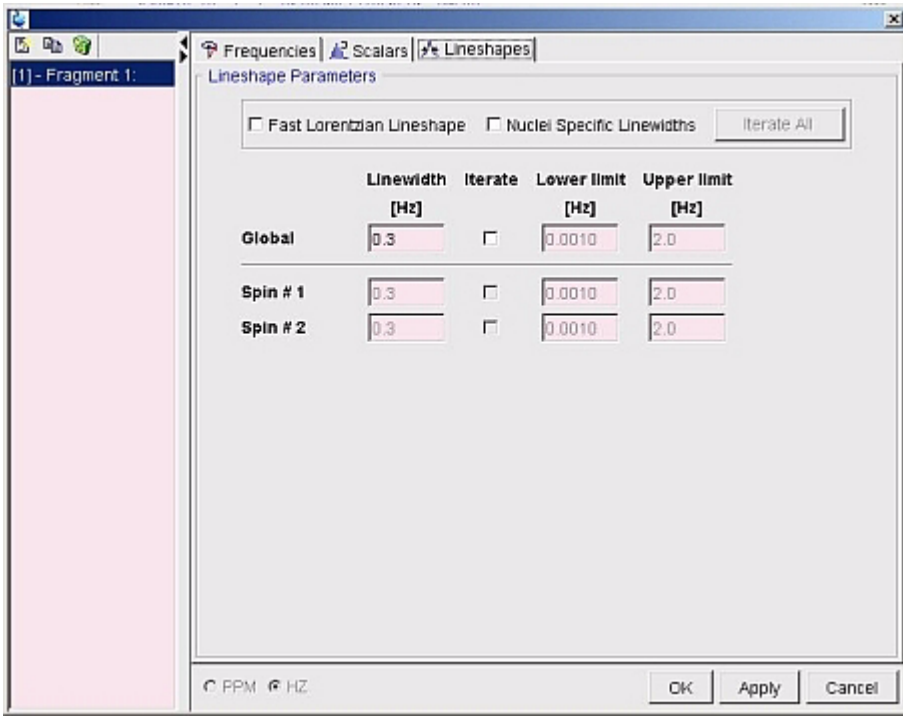
When checking the option **Nuclei specific linewidth**, the **Fast Lorentzien Lineshape** is no longer available. The display than disables the **global linewidth** and offers to set an **individual linewidth** parameter for every spin/group. The algorithm detects the contribution of the nuclei to every transition based on the eigenvectors.

There are many possible cases where nuclei specific linewith parameter are needed:

- an hydroxyproton exchanging with water residue
- neighbor nuclei with quadrupole momentum
- unresolved long range couplings

Pressing the ***Apply*** button will store these parameters.

Figure 2.6: Lineshape Parameters of 'Edit Spin System' window



The input of linewidth has to be given in Hertz. Only independant linewidth parameters are offered for input.

You can check the iteration option like in tables 1 and 2. Now the default iteration limits are available and can be individually modified here.

Press the apply buttons to store the new values.

By pressing the ***OK*** button you leave the 'Edit Spin System' window.

After setting your individal parameters a simulation can be started by pressing the

button in the toolbar.

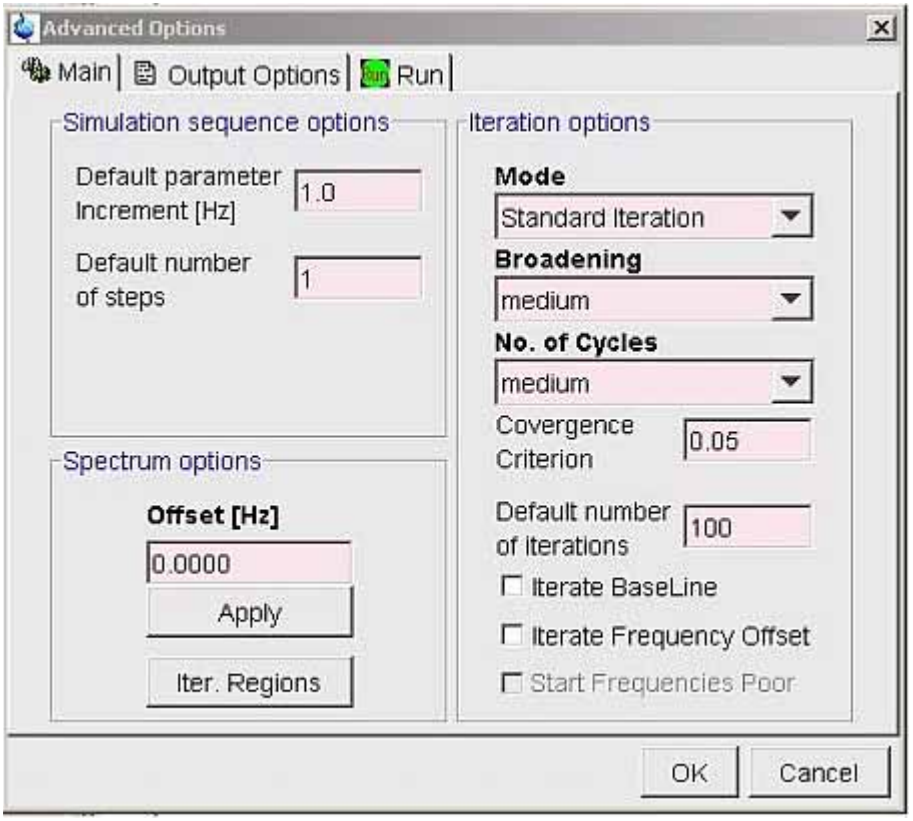
2.1.4 The 'Advanced Options' window

For more detailed simulations (and, especially, better iterations) you should set some parameters in the 'Advanced Options' window. This window also consists of three tables. To open this window press the  button in the toolbar.

2.1.4.1 The Main table of the 'Advanced Options' window

The first table contains the main options for sequence simulation, iteration options and spectrum options. It is shown in figure 2.7.

Figure 2.7: Main table of the 'Advanced Options'window



The values displayed in figure 2.7 show the default parameters. For a normal simulation you can use these values.

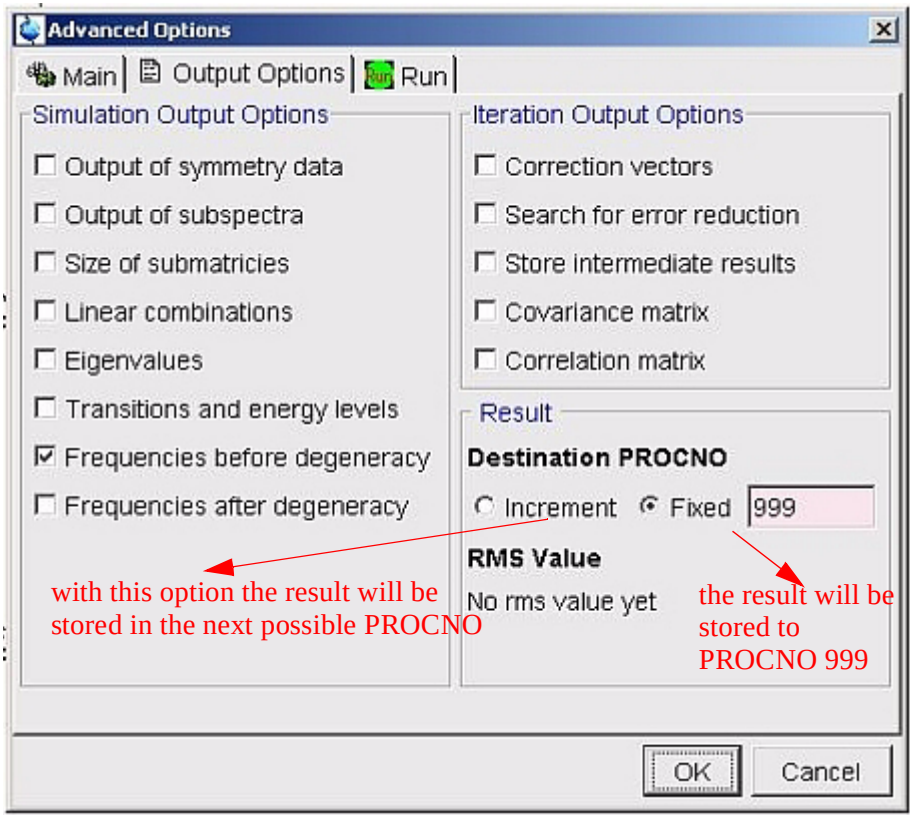
If you enter a frequency offset this value is applied to all resonance frequencies in all fragments when the ***Apply*** button is pressed.

For more information regarding the Iteration Options see chapter 3.1.2.

2.1.4.2 The Output Options table of 'Advanced Options' window

The second table consists of selectable output options. Figure 2.8 shows the table.

Figure 2.8: Output Options of the 'Advanced Options' window



In this table you can activate simulation and iteration output options as well as result options. In this chapter only the simulation output options will be described. More information about the iteration output option can be found in chapter 3.1.2.3.

Output of symmetry data:

DAISY is can use symmetry factorization (chemical equivalence factorizing) to block out the Hamiltonian matrix more efficiently in order to speed up calculation. Select this item to inspect the character table of the point group symmetry. In case of additional magnetic equivalence (e.g. methyl groups) in your spin system the program lists the symmetry (subsymmetry) of the subspectra.

Output of subspectra

This option writes the irreducible representation character of the subspectra into the output protocol in case of symmetry. If Composite Particles are present in the spin system the actual term with weighting of the subspectra is reported.

Size of submatrices

In the absence of magnetic equivalence the program writes a table containing the submatrices for every irreducible representation arranged according to descending total spinvalues. The last column shows the total spin factorization in case of no selected symmetry. If magnetic equivalence is present the program detects the size of submatrices at runtime, so the information is given in the output protocol, when the appropriate matrix is composed (not at the beginning of the calculation).

Linear combinations

This option gives a total representation of the symmetrized basic spin functions used for setup of the Hamiltonian matrix. These linear combinations are NOT the eigen vectors, they are just the symmetrical functional basis.

Eigenvalues

All calculated eigenvalues are saved into the protocol file in the order of their determination.

Transitions and Energy levels

For every submatrix the transition frequency and intensity and the pair of corresponding energy levels are listed.

Frequencies before degeneracy

Towards the end of the calculation all frequencies obeying the quantum mechanical restrictions as defined are listed in decreasing order. In addition a file with the extention 'fre' is created containing the same list. The existence of this file enables the additional **Run** command **Generate Lineshape**. Executing this command will not lead to a quantum mechanical recalculation of the spectrum, but the 'fre'-file containing the determined transition list will be read in. The actual global line width of the corresponding fragment will be used to create the simulated NMR-spectrum. Be careful, only the lines of a fragment for which this option is checked, is listed in the file.

Frequencies after degeneracy

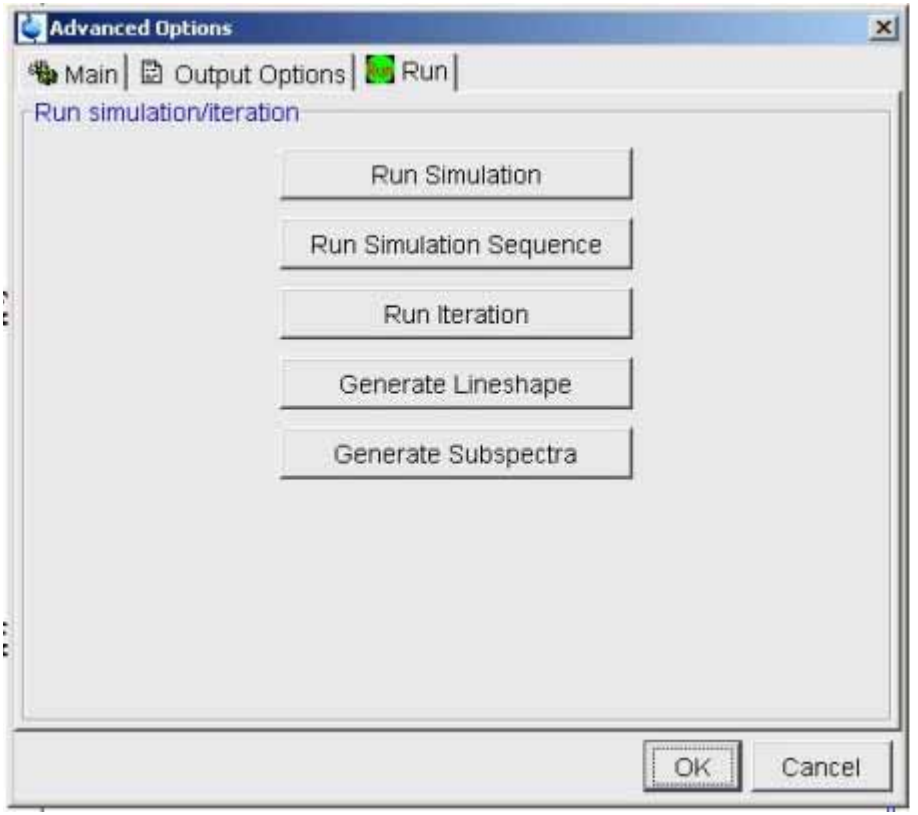
Similar to the latter option, but the transitions belonging to the same frequency are combined and corresponding intensities are summed up. No 'fre' file is written.

In the '**Result block'** of this table you can set the Destination PROCNO. It is recommended to choose 'Increment'. The simulation gets the next possible PROCNO of the experimental spectrum. If you check 'Fixed' you can choose a PROCNO. This will be used for every simulation if you don't change the value.

2.2 Starting a DAISY Simulation

After setting the output options, switch to the 3rd table, the 'Run table' of the 'Advanced Options' window, which is shown in figure 2.9. Press the ***Run Simulation*** button in this table or leave the 'Advanced options' window by using the ***OK*** button and press the  button in the toolbar.

Figure2.9: 'Run table' of the 'Advanced Options' window



The 'Run table' offers five possibilities to calculate spectra with DAISY.

2.2.1 Run Simulation/Run Iteration

The buttons ***Run Simulation*** and ***Run Iteration*** correspond to the - and - buttons in the toolbar of the DAISY window.

2.2.2 Run Simulation Sequence

The ***Run Simulation Sequence*** button allows to calculate spectra with systemati-

cally changed NMR parameters (resonance frequencies and/or coupling constants). The number of steps and the step width for frequencies must have been activated by pressing the ***Seq. Sim.*** button and checking the frequencies in the Frequencies table (see Chapter 2.1.3.1.). This calculation is called Run Simulation, because quantum mechanical calculations will take place for every individual calculation. The first simulation will be the reference calculation - without variation of any parameter.

2.2.3 Generate Lineshape

If you have selected the Output Option **Frequencies before degeneracy** (see Chapter 3.1.4.2.) a list of transitions and intensities of this fragment is written to a 'fre'- file. After a simulation/iteration with this option checked, pressing the **Generate Lineshape** button reads this list and generates a lineshape based on the defined spectrum parameters and the global line-width of the lineshape parameters of this fragment. Even if the option 'nuclei specific linewidth' has been selected, this command cannot deal with specific lineshape parameters, because no eigenvectors (on which the individual linewidths are detected) are available. This command does not take care of if you have selected the output option for all the fragments. It just takes the transitions of these fragments, for which the option has been selected. For small spin systems this calculation is not faster than a quantum mechanical calculation, because the lines have to be read from the harddisk. For large fragments, however, (e.g. 10 spins) this option might be useful.

2.2.4 Generate Subspectra

In case the spin system contains either Composite Particles (groups of magnetically equivalent nuclei and/or Spin Values >1/2) and/or Symmetry (for definition of symmetry refer to section (2.1.3.1).

2.3 Special Simulation Features

There are different situations conceivable where the option ***statistical weight*** is indispensible for spectrum simulation. It is only effective if more than one fragment is defined:

Calculation of an unequal mixture of compounds in the solution, e.g. isomeric mixtures, impurity signals.

When a compound contains not only pure, spin-active elements, the spectrum consists of the main and a satellite spectrum. The latter one includes the not 100%-abundant spin interactions.

If parts of the molecule give equal patterns they may be defined just once and weighted according to their presence.

Chapter 3

Daisy Iterations

DAISY iteration input documents are based on simulation input files with some additional information required. The basic features and definition of indispensable parameters will be described. References to the DAISY simulation will be mentioned if the features are already described there.

3.1 Parameters for a DAISY Iterations

The following chapter will teach you setup and start a DAISY iteration. If you have simulated the spectrum you can use the input parameters of this simulation. Some additional parameters for an iteration have to be added.

If you don’t have simulation parameters, start DAISY and follow the parameter setup as described in chapter 2.

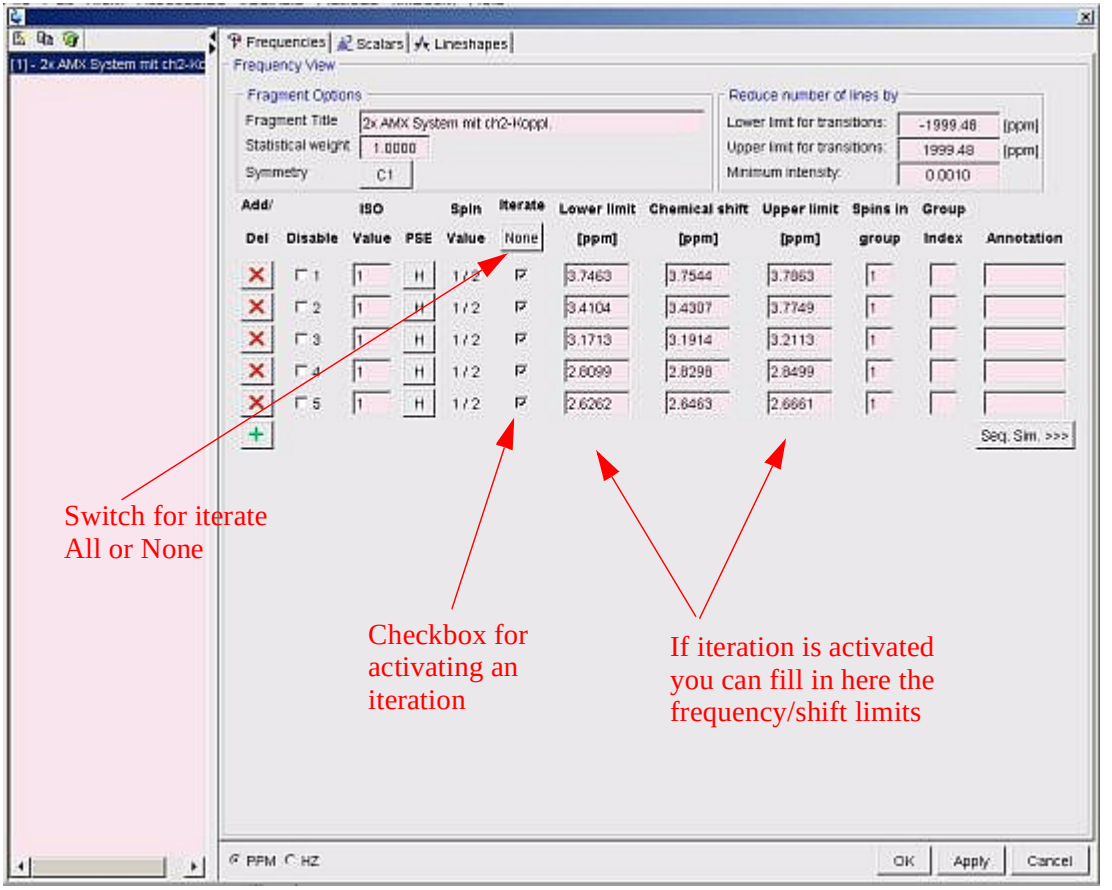
3.1.1 Additional parameters in the ’Edit Spin System’ window

For iteration setup some additional inputs in all the tables of the ’Edit Spin System’ window are required.

In the ’Frequencies’ table, the spin(s) you want to iterate have to be checked. Now

it is possible to fill in the lower and upper limit for the chemical shift or resonance frequency (depending on what is checked ppm or Hz). An example for such a table is shown in figure 3.1.

Figure 3.1: 'Frequencies' Table of 'Edit Spin System' window with iteration parameters



- **Group Index**

  Some NMR spectroscopists may not want to define chemical equivalence via Point Group Symmetrie or due to other reasons parameters shall be kept identical for optimization although they are not tied together by symmetry. Therefore

a feature has been added to DAISY allowing to tie parameters of the same type together, with the purpose to keep them identical. Valid types are Resonance Frequencies and Coupling Constants.

IT IS NOT POSSIBLE TO COMBINE SYMMETRY AND GROUPING!

To visualize the difference, if parameters are dependent either because of chemical equivalence or because of manual grouping, in the latter case the edit fields are shown, but disabled. In case of symmetrical dependent parameters these fields are invisible. For grouped parameters only the first appearing group member is enabled for editing, all others are disabled. Their connection can be seen from the identical number in the Group Index entry. The number zero means no grouping.

The group index is a nonzero integer number and is valid for the actual parameter type over all fragments. This means, parameters can be grouped together over all fragments of a DAISY document. For example all resonance frequencies having the group index ’1’ in the whole DAISY document will get the same properties, except the disable option in the ’Frequencies table’. Properties are:

- parameter values
- iteration options
- iteration limits

and for frequencies the same number of:

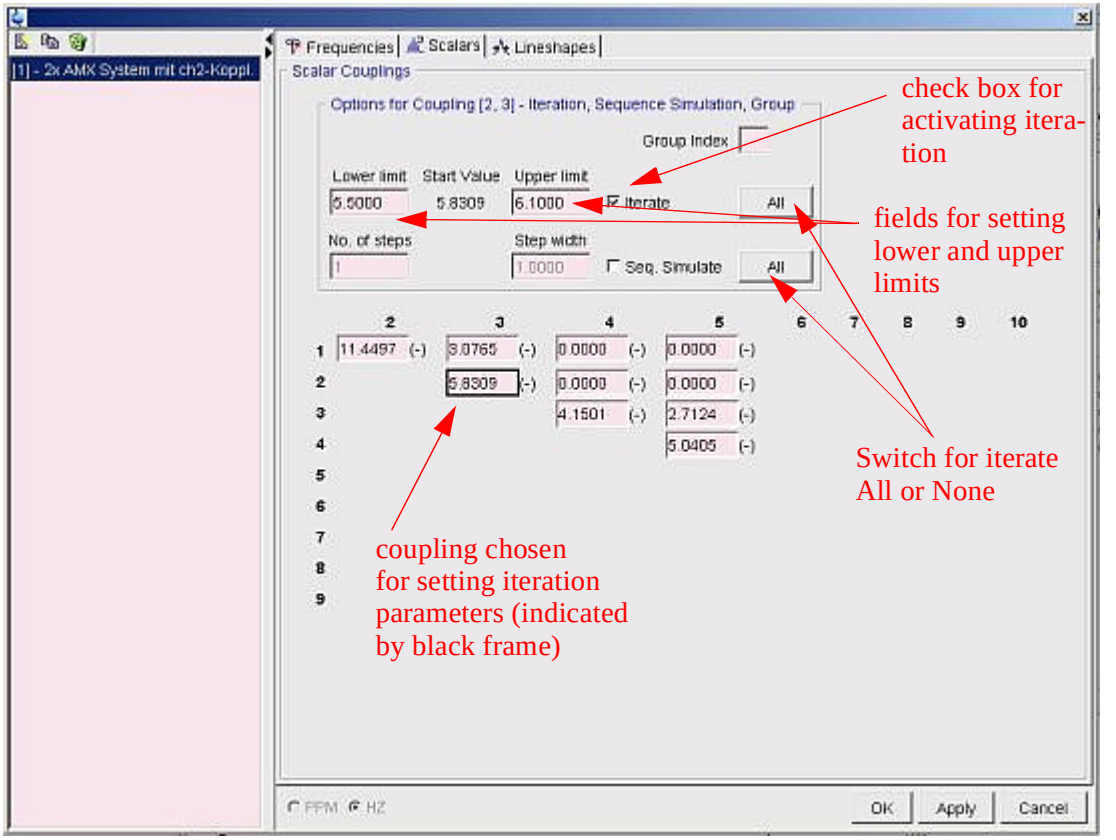
- spins per group
- spin value
- isotope value
- element symbol etc.

Group indices can be set in the ’Frequencies’ table and/or the ’Scalars Couplings’ table.

In the ’Scalar Couplings’ table the iteration of the coupling(s) must be activated, too. This can be done by checking the box beneath ’Iterate’. Now the fields with lower and upper limits are available and the desired values can be filled in. As distinct from the ’frequencies’ table with its check box for each frequency, here you have to choose the coupling first by clicking on it. The value of the chosen coupling is now the ’Start Value’ of the iteration parameters. Checking the iteration

box activates this coupling for iteration. An example is shown in figure 3.2 .

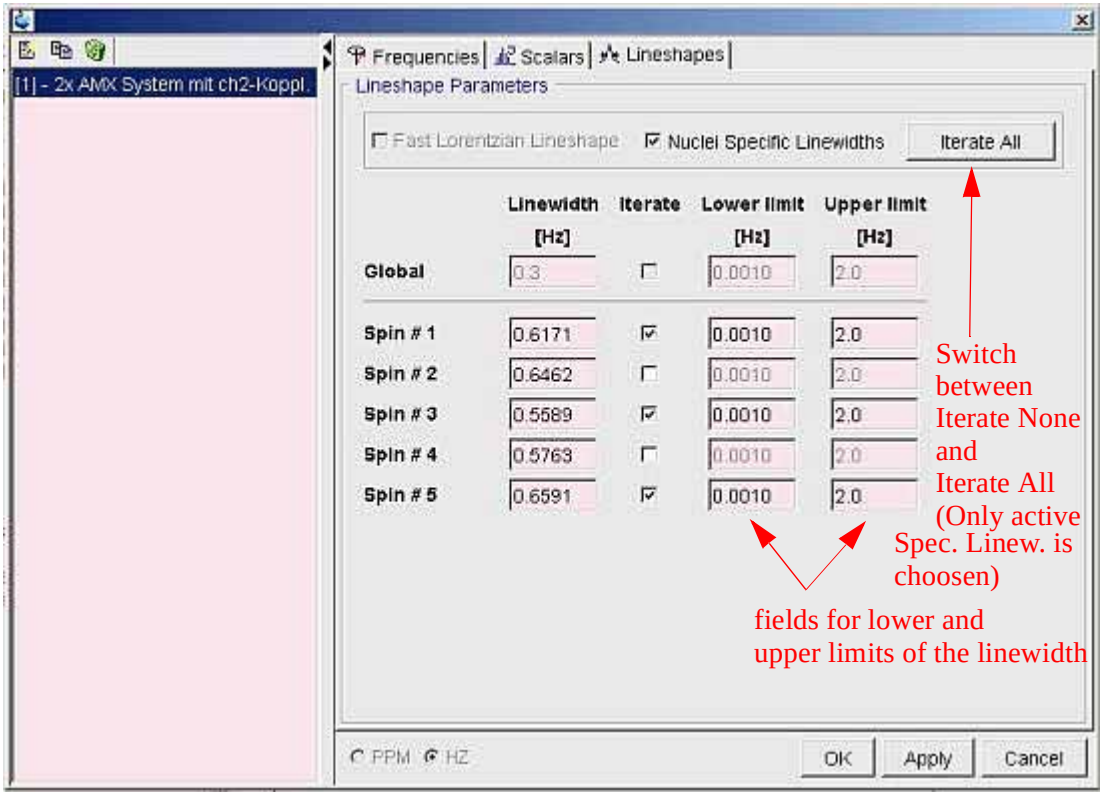
Figure 3.2: ’Scalars Couplings’ Table of ’Edit Spin System’ window with iteration parameter



In the ’Lineshapes’ table you have the possibility to do Lorentzian Lineshape calculation with a global linewidth or a calculation with a Nuclei Specific Linewidth (see Chapter 2.1.3.3). An iteration with Lorentzian Lineshape calculations iterates all lines of the spectrum with the same global linewidth. If you check the **Nuclei Specific Linewidth** box, an iteration for all or only some spins with their specific

linewidth is available. An example is shown in figure 3.3. **Do not use *Fast Lorentzian Lineshape* for spectrum iteration!**

Figure 3.3:'Lineshapes' Table of 'Edit Spin System' window with iteration parameter



For each table the new value will be taken over by pressing the ***Apply*** button. To leave this window press then the ***OK*** button.

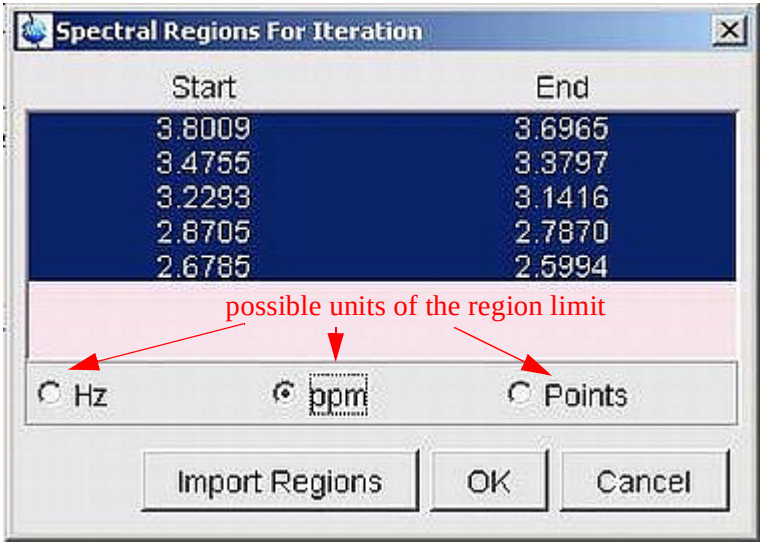
3.1.2 Additional parameters in the 'Advanced Options' window

The three tables of the 'Advanced Options' window contain some iteration specific parameters, too. They are explained in the following section.

A DAISY iteration is more time efficient when iterating only regions containing NMR signals of the spins of interest. To define the regions for the signal groups, each signal group in you experimental spectrum should be integrated and the integration saved.

For a DAISY iteration it is possible to import these integration regions in the ’Main’ table of the ’Advanced Options’ window. Press the ***Iter.Regions*** button (see figure 2.7 in chapter 2.1.4.1). A new popup window will appear as shown in figure 3.4.

Figure 3.4: Window with import data for iteration regions



Select the regions for the iteration and press **Import Regions** button.

In the ’Iteration options’ block of the ’Main’ table you can select your desired iteration mode. Two modes are available, both of them are total-lineshape fitting methods.

- **Standard**
  The Standard iteration mode represents the original spiral algorithm written by Binsch et al, which was optimized by Boenigk [9d]., based on the combination of

steepest descent and Gauss-Newton corrections for the parameters. (Chapter 5.2.2.1)

- **Advanced**
  The Advanced modus uses successive steepest descent and Gauss-Newton correction, optionally with a double-sum-target function, introduced by Höffken[11]. (Chapter 5.2.2.2)

By default the Standard iteration mode is set.

3.1.2.1 Smoothing Parameters

The parameters **Broadening** and **No. of Cycles** in this options block are connected to the Iteration mode. The combination of these parameters define the smoothing of the spectra. A brief explanation of the meaning of these parameters without going deep into theory:

Total-lineshape fitting is designed to avoid letting the iteration fall into local minima and to reach the global minimum. The starting parameters for iteration can be quite poor. The poorer the parameters the stronger the starting smoothing has to be in order to enable the system to find correct solution. E.g. if your simulated spectrum with your initial parameter guess for iteration is already quite good (or even almost correct), use only low smoothing (or even none).

- **Broadening**

  Possible values are **none**, **low**, **medium** and **high**. **None** means, the original experimental data will directly be used for iteration without smoothing.

  Low, **medium** and **high** define the initial strength of spectrum smoothing.

  The stronger the starting smoothing is selected, and the more points the spectral regions contain, the longer the iteration will take in the first iteration cyclus.

- **Number of Cycles**

  You can select **low**, **medium** and **high**.

  This value defines the factor for reducing the smoothing during iterations. Here the same effect is valid: The higher the value is selected, the longer the iteration will take, but the worser the starting NMR parameters can be.

3.1.2.2 Additional Options and other Iteration Parameters

- **Iterate baseline**

  Checking this option will include the correction of the experimental spectrum with a baseline increment and a baseline tilt in the last phase of iteration. But this baseline iteration parameter does not substitute a proper baseline correction with the TopSpin processing command ***bas*** before using **DAISY**.

In case of the Standard Iteration Mode an additional parameter may be selected:

- In case the relative differences of resonance frequencies are well known, it is useless to iterate all resonance frequencies independently. For this purpose the iteration of only one resonance frequency (the first in the first fragment) shall be selected for iteration and the option **Iterate Frequency offset** shall be checked. When this option is used ONLY the very first resonance frequency in the first fragment must be selected for iteration, NO other frequency is allowed to be selected. During optimisation the freqency differences from the very first shift to all other shifts is kept constant! This feature is e.g. very useful to analyse spectra of compounds in anisotropic solutions, when isotropic NMR parameters are well known.

In the case of the **Advanced Iteration Mode** an additional parameter may be selected:

- **Starting Frequencies poor**

  If this option is checked, the Advanced iteration will start with the double-sum target function in the first phase.

There are two other parameters which are important for iteration:

- **Convergence Criterion**

  The convergence criterion (default 0.05, means the difference between consecutive error values) defines the limit, when to change to the next iteration cycle to decide no further improvements can be made with the actual smoothing.

  Normally this value doesn’t need to be changed.

- **Default number of iterations**

  This value can be entered to stop the iteration, when no minimum can be reached. For normal cases this number of iterations won’t be reached.

3.1.2.3 Additional output options in the ’Output Options’ window

In the ’Output Options’ window there are five additional output options besides the simulation output options.

- **Correction vectors**

  For every iteration the parameter vector together with the gradient vector and (Standard)/ or (Advanced) the Gauss-Newton vector is combined and written into the output file.

- **Search for error reduction**

  For Standard iteration three different spirals with four testing points on each spiral are used and for Advanced iteration the distance is halved to achieve error reduction. This option informs about the spiral geometry and the actual error for each test point.

- **Store intermediate results**

  Especially when a time-consuming iteration is started, this option is very useful. When it is activated the resulting parameters of every single iteration are stored in a file with a consecutive number as part of the file extension. So instead of file name <name>.mgs, the first iteration result will be <name>.mgs1, the second <name>.mgs2 etc.. Be careful, because 100 iterations will generate 100 files in the procno directory of the experimental NMR spectrum. If you check this option you have to delete these files manually, if you don’t need them anymore.

- **Covariance matrix**

  The parameter covariance matrix is written in the output file.

- **Correlation matrix**

  The correlation matrix is written in the output file.

Now all parameters are set and you can start an iteration by pressing the  button in the toolbar or out of the ’Run’ table in the ’Advanced Options’ window. In the procno-directory of NMR-spectrum (<TopSpin>\pdata\procno) 4 files will be created by >DAISY:

- daisy.itr
- daisy.log

- daisy.lst
- daisy.mgs

If you want to keep these files, you have to rename them. DAISY will overwrite them when starting a new simulation/iteration of the choosen spectrum.

After you have done your DAISY calculations it is possible to store the calculated spin system by pressing the  button in the toolbar of the DAISY window. By default two files (*.msg, *.itr) will be stored in TopSin home directory. Any other directory can also be chosen , too. These files contain the data of the tables in the 'Edit Spin System' window. The stored data can be loaded by pressing the  button when needed.

To terminate the DAISY session press the  button or the  button. The first one terminates DAISY saving changes, the second one terminates without saving changes.

Chapter 4

Examples

This chapter illustrates the calculation of experimental spectra with DAISY. A suitable setup will be shown for each example.

Section 4.1 will illustrate the DAISY simulation, whereas section 4.2 will explain some features of parameter optimization by DAISY iteration.

4.1 Spectrum Simulation

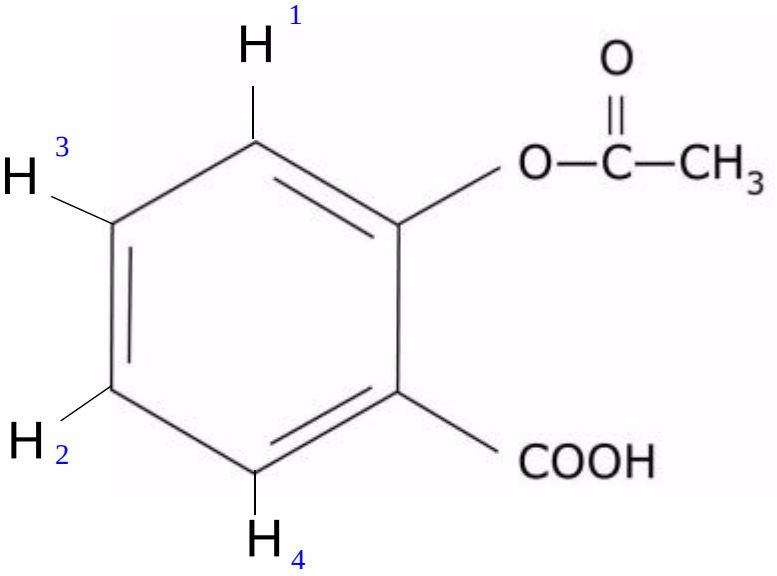
For all simulations and/or iterations you have to treat your experimental spectrum in the same way before entering DAISY.

- After normal processing (ft, pk, cal) you need a peak picking for the whole spectrum or for the signal groups you want to simulate (see TopSpin Users Guide). Without this the multiplet definition will not work.
- It is recommended to integrate the different signal groups of your spectrum. You get information about the number of protons in a signal group. For a possible iteration after your simulation you will need the integration to define your iteration regions (see TopSpin Users Guide).

4.1.1 The ^{1}H-NMR Spectrum of Aspirine (aromatic protones)

The first example of a DAISY simulation is the aromatic proton system of aspirine. The structure is shown in figure 4.1.

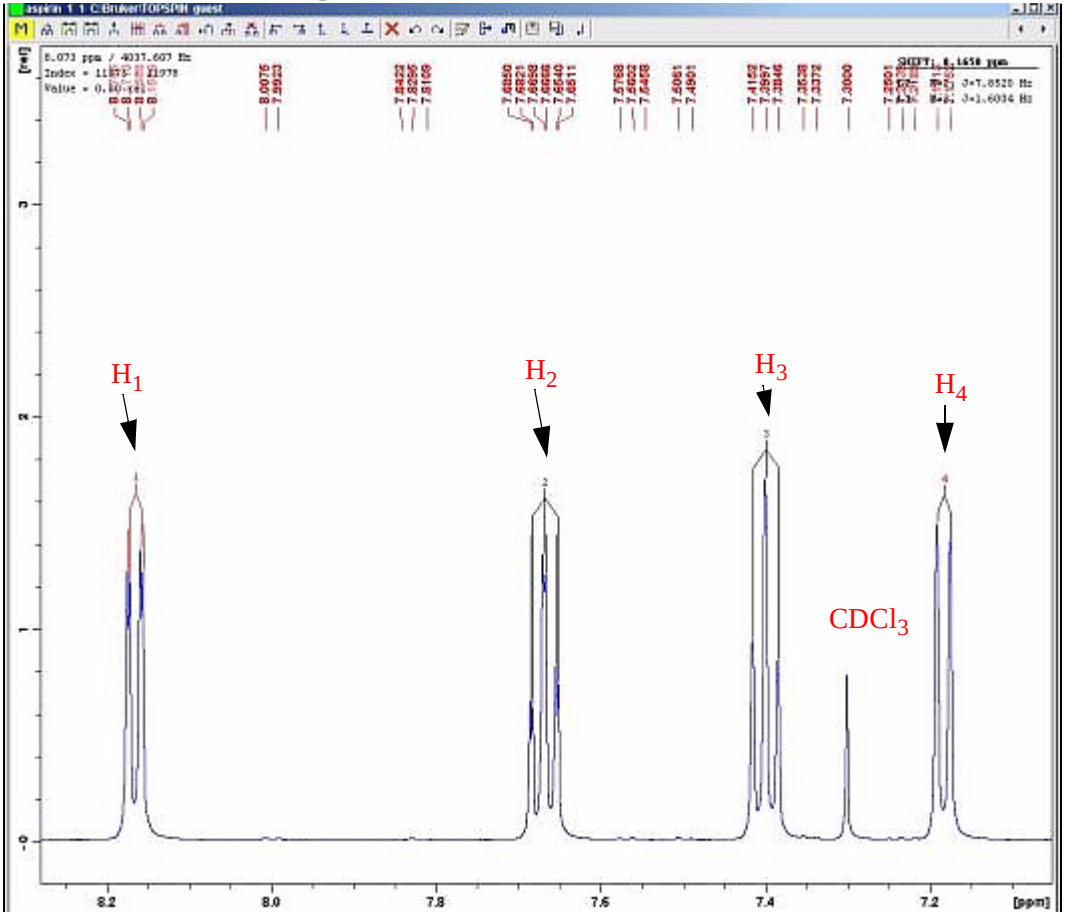
Figure 4.1: Structure of aspirine



The ^{1}H-NMR spectrum shows four seperated signal groups representing the four aromatic protons of the compound. In order to prepare the spectrum for a DAISY simulation a peak picking is requested in the first step. Afterwards it is possible to execute a multiplet analysis with Multiplet Definition (***mana***). As the signal groups are clearly seperated and show good resulution, the automated multiplet analysis is fine. There is no need for manual corrections. The automatic multiplet definition starts at the low-field side of the spectrum. The numbering of the multiplets was adapted to the protons in the structure using the information from other NMR experiments (see figure 4.2.).

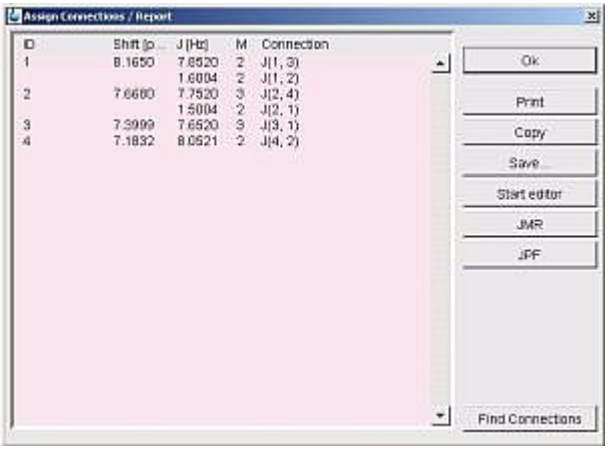
Using the multiplet report available in the Multiplet Definition window you can assign connections between the found shifts and couplings. (see figure 4.3). These determined connections will be transfered to the ’scalars’ table in the ’Edit Spin System’ window when starting DAISY.

Figure 4.2.: ^{1}H-Spectrum of aromatic protons of aspirine with peak picking and multiplet definition



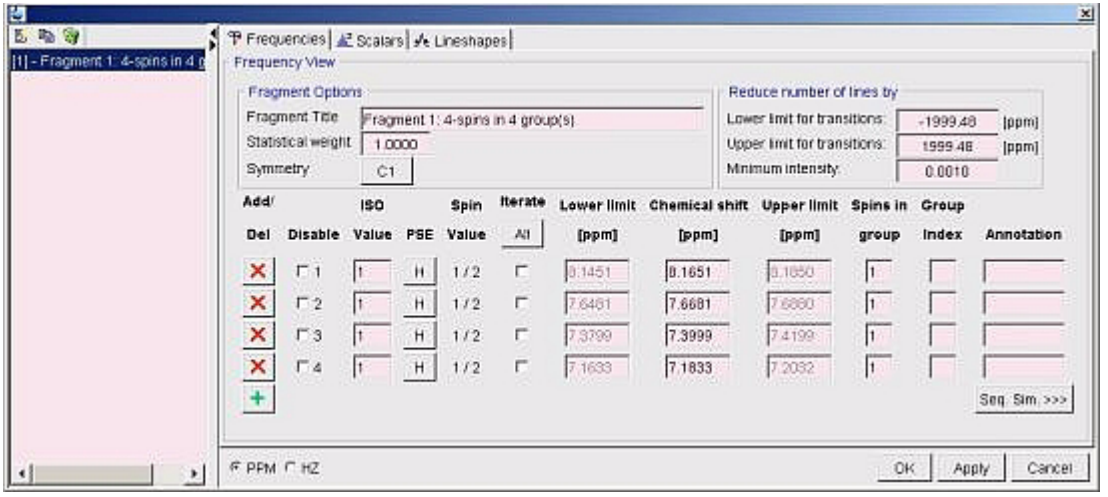
For identical couplings found in several multiplets, the average of these values will be filled in. Looking to the list in figure 4.2, you will realize that there are no couplings J(1,4) and J(2,3) visible. The coupling from H_1 to H_4 is a long range coupling over 5 atoms. It can be set to 0. The coupling J(2,3) is an ortho-coupling like J(2,4) and J(1,3). It must be of the same size like these couplings. This missing value will be set manually in the 'scalars' table of the 'Edit Spin System' window. Before leaving the multiplet definition window save all data by clicking the 'terminate/save changes' button.

Figure 4.3. Assign Connection/Report in from Multiplet Definition window



After starting DAISY you will be asked if you want to import information from the multiplet definition. Click Ok and the following data will appear in the "Edit Spin System window':

Figure 4.4: 'Frequency' table for the aspirine aromatic protons



As multiplet definition had found 4 multiplets, a 4-spin system is built. We clear the iterate check boxes for a first simulation. They are always checked when starting with complete data (frequencies and couplings) from multiplet definition.

Figure 4.5: Scalar Couplings table for aspirine aromatic protones

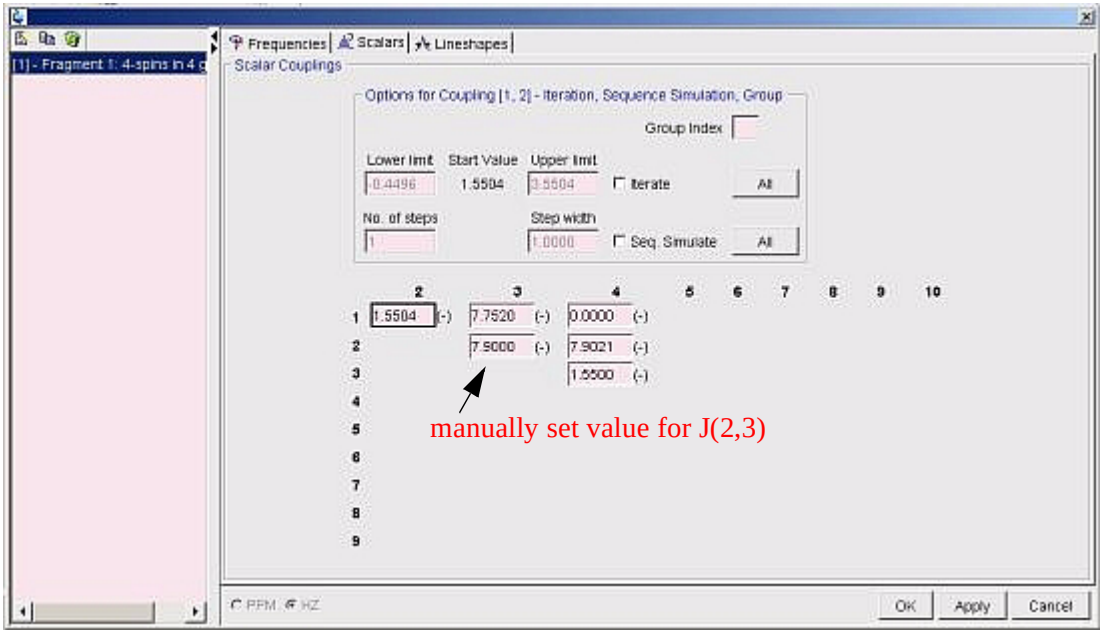
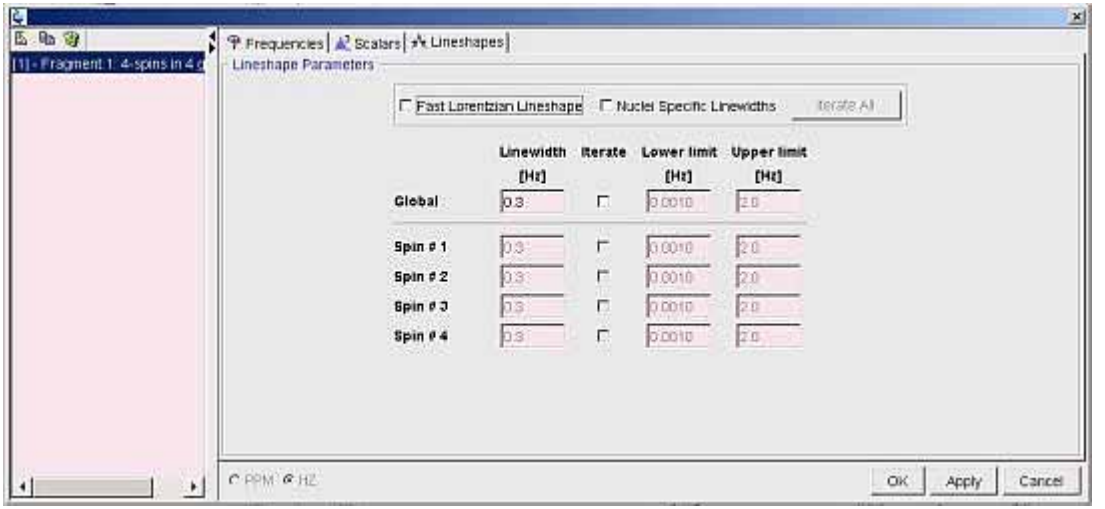
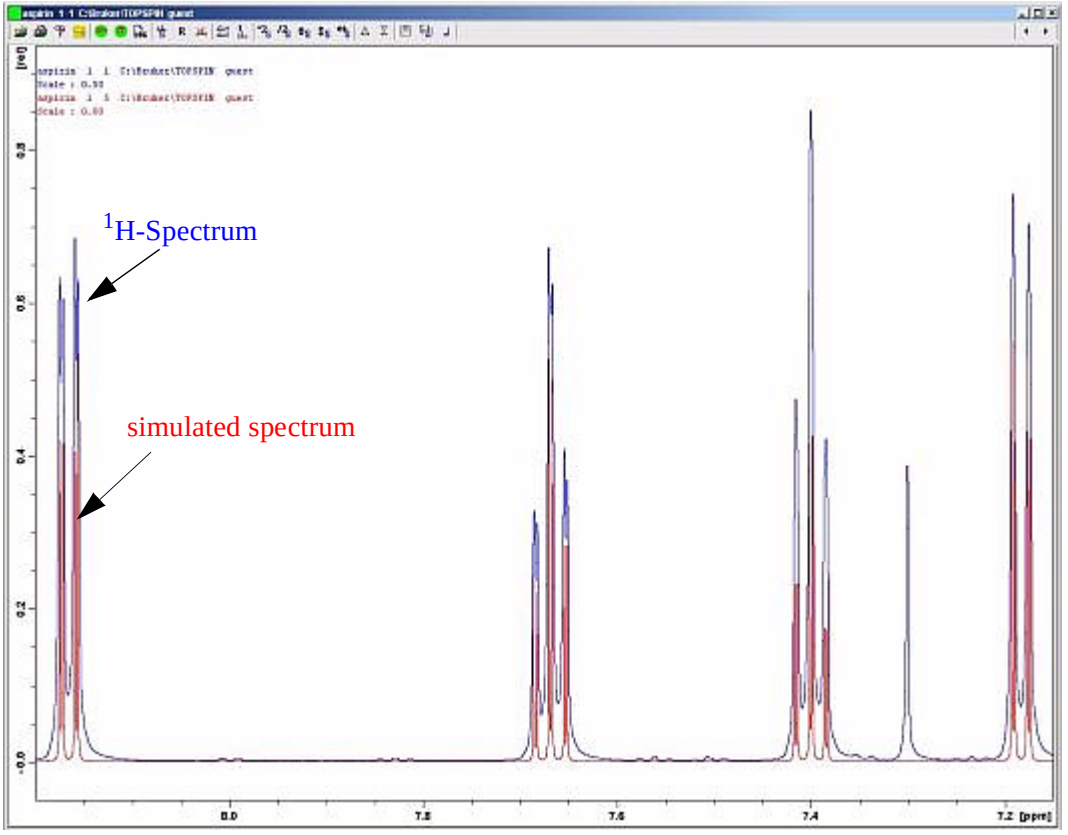


Figure 4.6: Lineshape table fore aspirine aromatic protones



After importing all data, the coupling J(2,3) has to be filled in manually (see above). For a first simulation a global line with of 0.3 Hz is ok. Start the simulation by pressing the  button. Figure 4.7 shows the simulated and measured spectrum.

Figure 4.7: Simulated and measured spectrum of aspirine aromatic protons



Looking at the result we see both resonance frequencies and couplings fit quite well. But the linewidth is not correct. In the simulation the lines of the different multiplets are much better resolved than in the real spectrum. Besides this we need line specific linewidth. The input data of this simulation are quite well for a final iteration of this system (see chapter 4.2.1).

The DAISY report of this simulation contains input data and data chosen in the output options. In this example it was ’Frequencies before and after degeneration’.

The following paragraphs show the DAISY log-file which appears pressing the  button in the DAISY window. You can find this file named `daisy.lst` in the /procno-directory of your spectrum.

```
 SPIN SYSTEM CONSISTS OF 4 NUCLEI
// SINGLE SPIN SIMULATION
========================================
```

Standard Output:
detected by the programm

```
 TITLE: Fragment 1: 4-spins in 4 group(s)
 ------
STARTPARAMETERS DEFINING CALCULATED SPECTRUM
 ============================================
```

Standard output:
the fragment title
Standard Output

```
ISO-VALUE   RESONANCE FREQUENCY
-------------------------------
 1          4083.5864
 1          3835.0218
 1          3700.9119
 1          3592.5588
```

Standard Output:
complete resonance frequencies

```
COUPLINGS    SCALAR      DIPOLAR
-------------------------------------
 1  2       1.5504      0.0000
 1  3       7.7520      0.0000
 1  4       0.0000      0.0000
 2  3       7.9000      0.0000
 2  4       7.9021      0.0000
 3  4       1.5500      0.0000
```

Standard Output:
complete scalar couplings

```
GLOBAL LINEWIDTH :     0.3000
._._._._._.

Expected Number of Calculated Transitions: 56

LINES CALCULATED:              56     32.000
```

Standard output:
the total intensity of all possible
and of all calculated lines is given here

LINES SUPPRESSED BY

- MINIMUM INTENSITY (0.001): 24 0.000
- LOWER FREQ. LIMIT (-1000000.000): 0 0.000
- UPPER FREQ. LIMIT (1000000.000): 0 0.000

LINES BEFORE DEGENERACY: 32 32.000

Frequencies before degeneracy

Transition frequencies and intensities ordered for decreasing frequencies

1 seconds
0.00

FREQUENCY	INTENSITY	LINENUMBER
4088.2795	0.9737	29
4088.2784	0.9738	26
4086.7228	0.9858	20
4086.7213	0.9857	13
4080.5344	1.0136	23
4080.5339	1.0137	15
4078.9777	1.0268	11
4078.9767	1.0267	4
3843.8750	0.9156	30
3842.3183	0.9079	17
3835.9820	0.9739	27
3835.9750	1.0321	24
3834.4249	0.9671	9
3834.4183	1.0143	7
3828.0821	1.1035	16
3826.5248	1.0857	3
3709.3637	1.0631	31
3707.8049	1.0999	28
3701.6187	1.0172	18
3701.4638	0.9495	21
3700.0604	1.0554	10
3699.9050	0.9685	14
3693.7186	0.9128	5
3692.1604	0.9337	2
3597.2153	1.0476	32
3597.2142	1.0486	19
3595.6565	1.0173	25
3595.6559	1.0165	8

```
   3589.3223      0.9803   22
   3589.3207      0.9809    6
   3587.7635      0.9547   12
   3587.7625      0.9539    1
LINES AFTER DEGENERACY:
======================
```

Frequencies after degeneracy

intensities of degenerated lines are added up

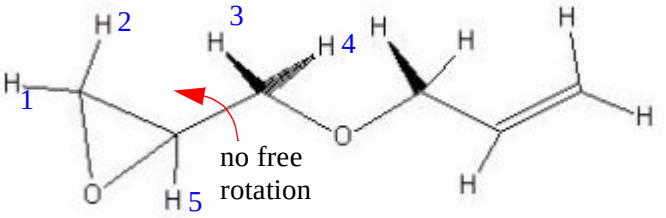
```
   FREQUENCY      INTENSITY   NUMBER
   ----------------------------------

   4088.2795      0.9737     1 +
   4088.2784      0.9738     2 +
   4086.7228      0.9858     3 +
   4086.7213      0.9857     4 +
   4080.5344      2.0274     5 +
   4078.9777      1.0268     6 +
   4078.9767      1.0267     7 +
   3843.8750      0.9156     8 +
   3842.3183      0.9079     9 +
   3835.9820      0.9739    10 +
   3835.9750      1.0321    11 +
   3834.4249      0.9671    12 +
   3834.4183      1.0143    13 +
   3828.0821      1.1035    14 +
   3826.5248      1.0857    15 +
   3709.3637      1.0631    16 +
   3707.8049      1.0999    17 +
   3701.6187      1.0172    18 +
   3701.4638      0.9495    19 +
   3700.0604      1.0554    20 +
   3699.9050      0.9685    21 +
   3693.7186      0.9128    22 +
   3692.1604      0.9337    23 +
   3597.2153      1.0476    24 +
   3597.2142      1.0486    25 +
   3595.6565      2.0339    26 +
   3589.3223      0.9803    27 +
   3589.3207      0.9809    28 +
   3587.7635      0.9547    29 +
   3587.7625      0.9539    30 +

LINES AFTER DEGENERACY:    30
 1 seconds
```

0.01

4.1.2 The ^{1}H-NMR Spectrum of Allyl-glycidyl-ether

The second example for DAISY simulations is one of the two clearly seperated 5-Spin-systems of Allyl-glycidyl-ether. The structure of this compound is shown in figure 4.8.

Figure 4.8: Structure of Allyl-glycidyl-ether



Between 2.5 ppm and 3.8 ppm there are five seperated multiplets which represent the three protons of the epoxy-ring and the CH_2-group.

For a DAISY simulation chemical shift/resonance frequency informations and the coupling constants of the protons are needed. The analysis option **Multiplet Definition** can help to find these parameters. For the protons 1 - 4 (see figure 14) this can be done by automatic multiplet definition. Each of the four protons shows a dublett of dubletts, so there is no problem to find couplings and chemical shifts.

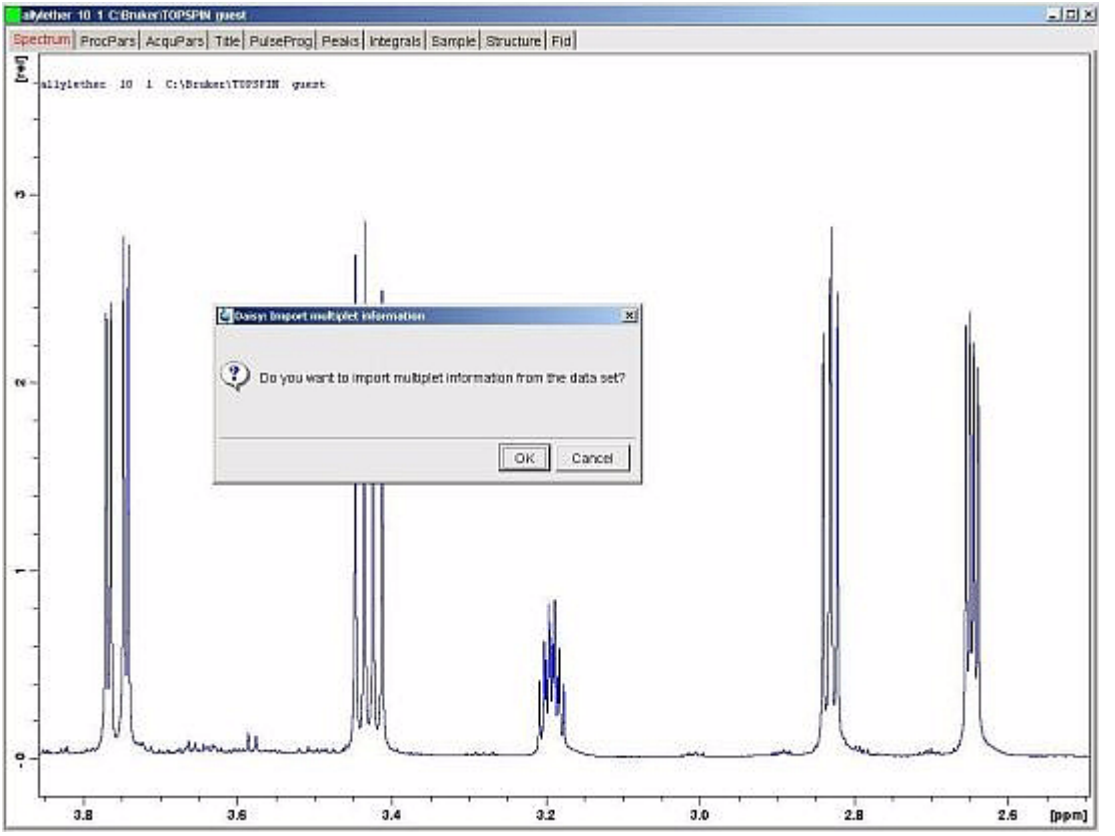
For proton 5 the situation is more difficult. It is in a center position of this group and therefore shows couplings to all four protons. The linewidth of the signal group for proton 5 indicates that some lines are probably not resolved. The multiplet definition is difficult and may lead to wrong couplings and chemical shifts.

The multiplet definition of the other groups contains all required couplings. So we only read out the chemical shift for proton 5 (center of the signal group) and leave the 'Multplet Definition' window while storing the results in the file `multiplet.txt`.

Now we type ***`daisy`*** in the command line or choose Analysis/Structure Analysis/1D Spectrum Simulation from the main menu bar of TopSpin. Figure 4.9 shows

the actual display.

Figure 4.9: Import of data for DAISY calculations (1st step)

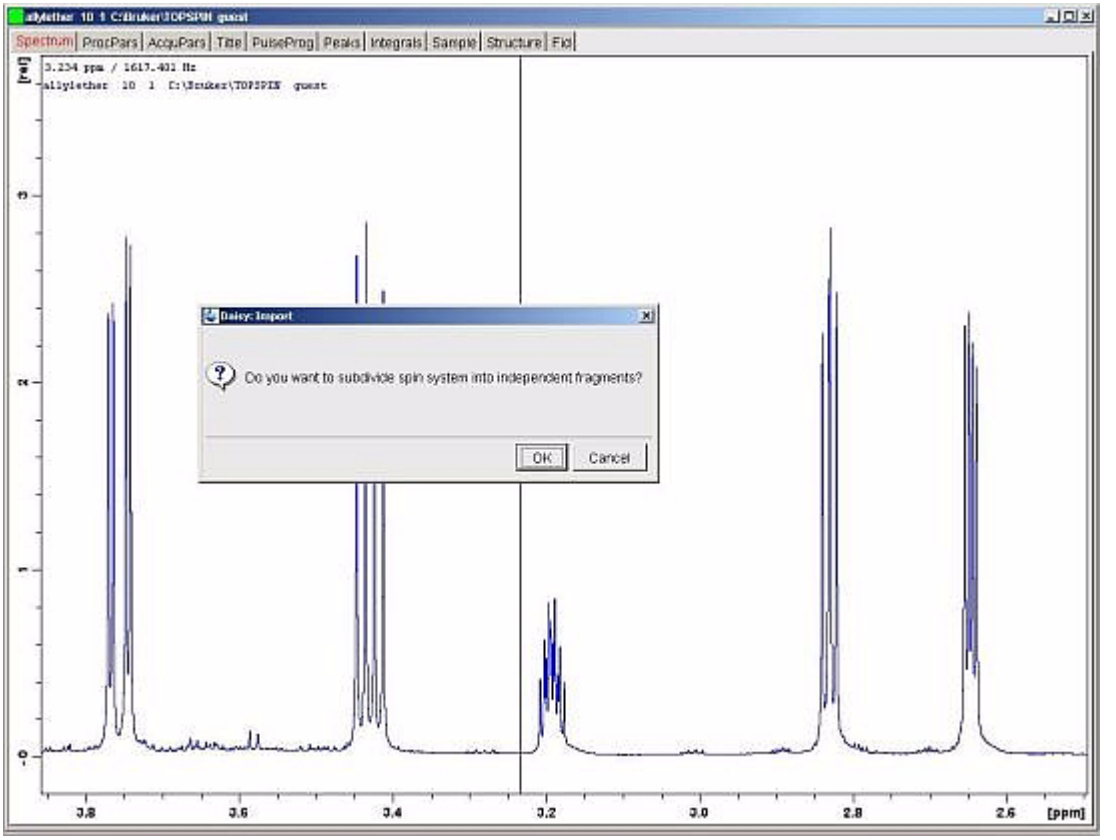


Click **OK** in the popup window and DAISY will import the multiplet information you created with 'Multiplet Definition'.

After clicking **OK** (or **Cancel**) button a new popup window will appear. Now you have to decide where you want to subdivide your system into independent fragents. (see figure 4.10)

In our example we cancel this to calculate our 5-spin-system as one fragment.

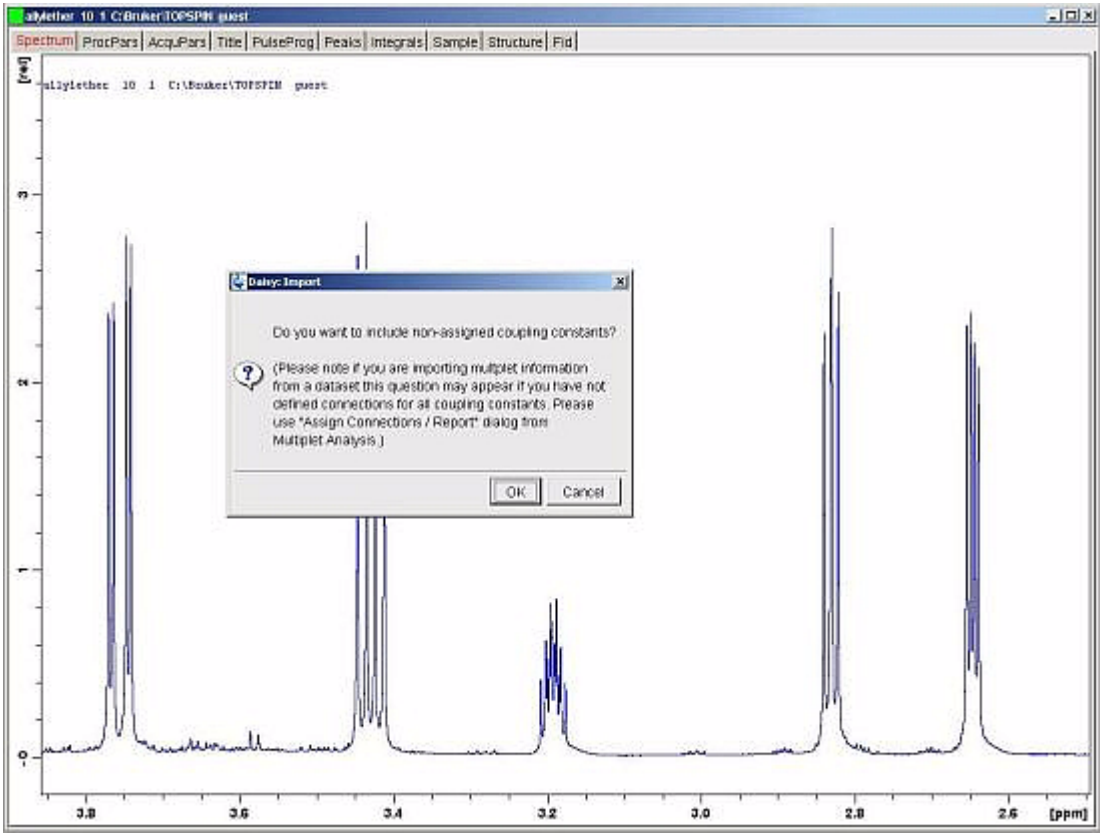
Figure 4.10: 2nd step of data import for DAISY calculation



Finally you can to import unassigned couplings from the `multiplet.txt` file. (see figure 4.11)

We don’t do it for this example because we have to add a frequency and the corresponding couplings manually as explained above.

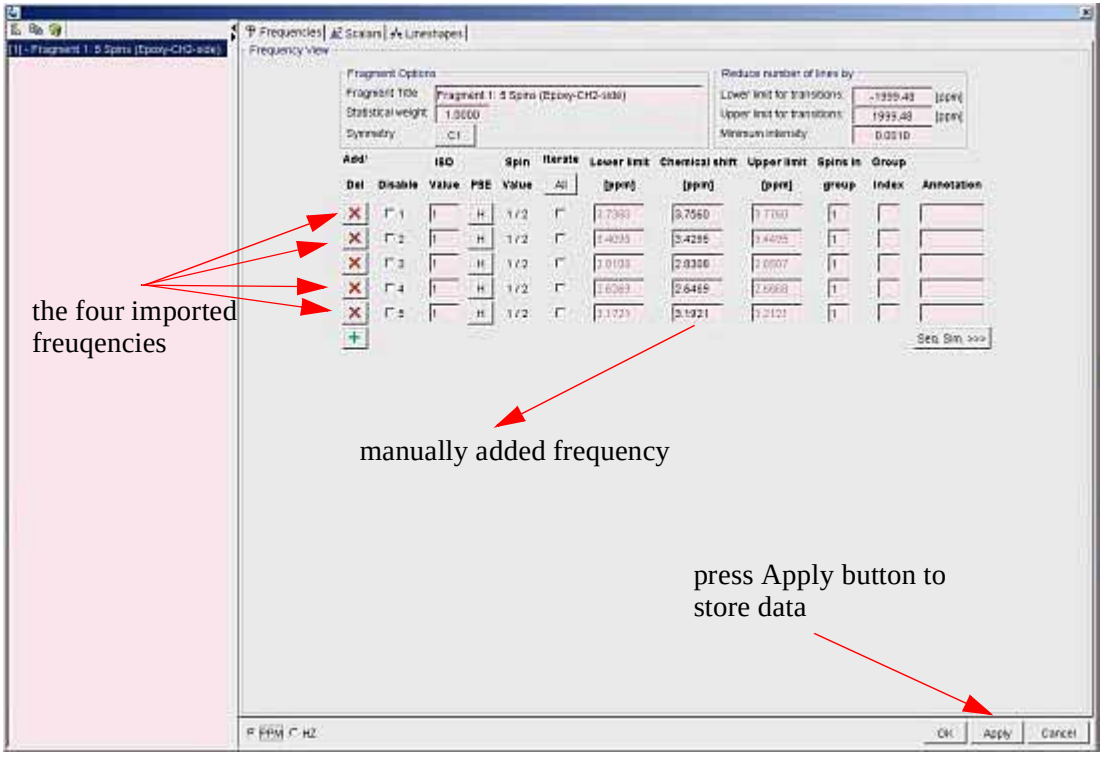
Figure 4.11: 3rd step of data import for DAISY calculation



Now all data gets imported to DAISY. We can check and complete the frequencies and couplings in the different tables of the ’Edit Spin System’ window.

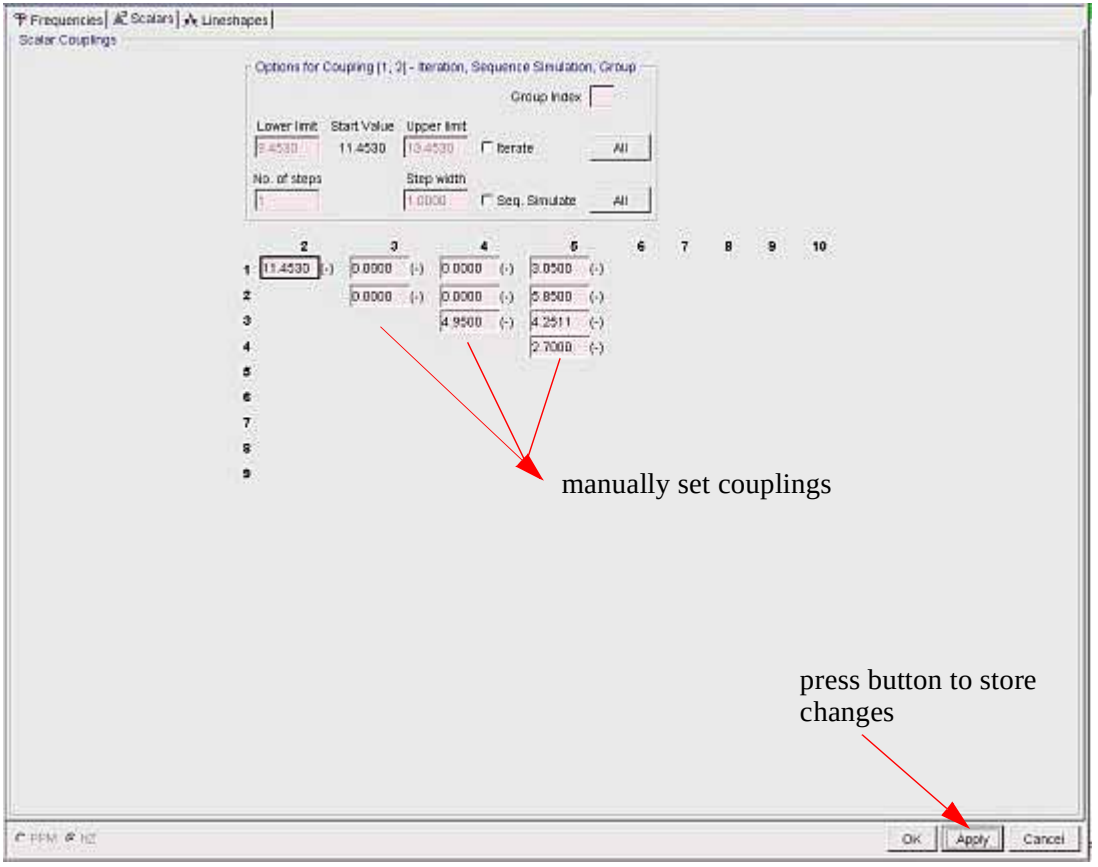
Press the  button in the toolbar of the Data window and the frequencies table will appear (see figure 4.12). The first four frequencies/shifts have been imported from the file `multiplet.txt`, the fifth frequency has been set manually.

Figure 4.12: Frequencies table for the epoxy-CH_2-group of Allyl-glycidyl-ether



Afterwards we have to check and complete the Scalar coupling table (see figure 4.12). As we did not import unassigned couplings, only coupling J_{12} is set in the table. The other couplings are entered in manually.

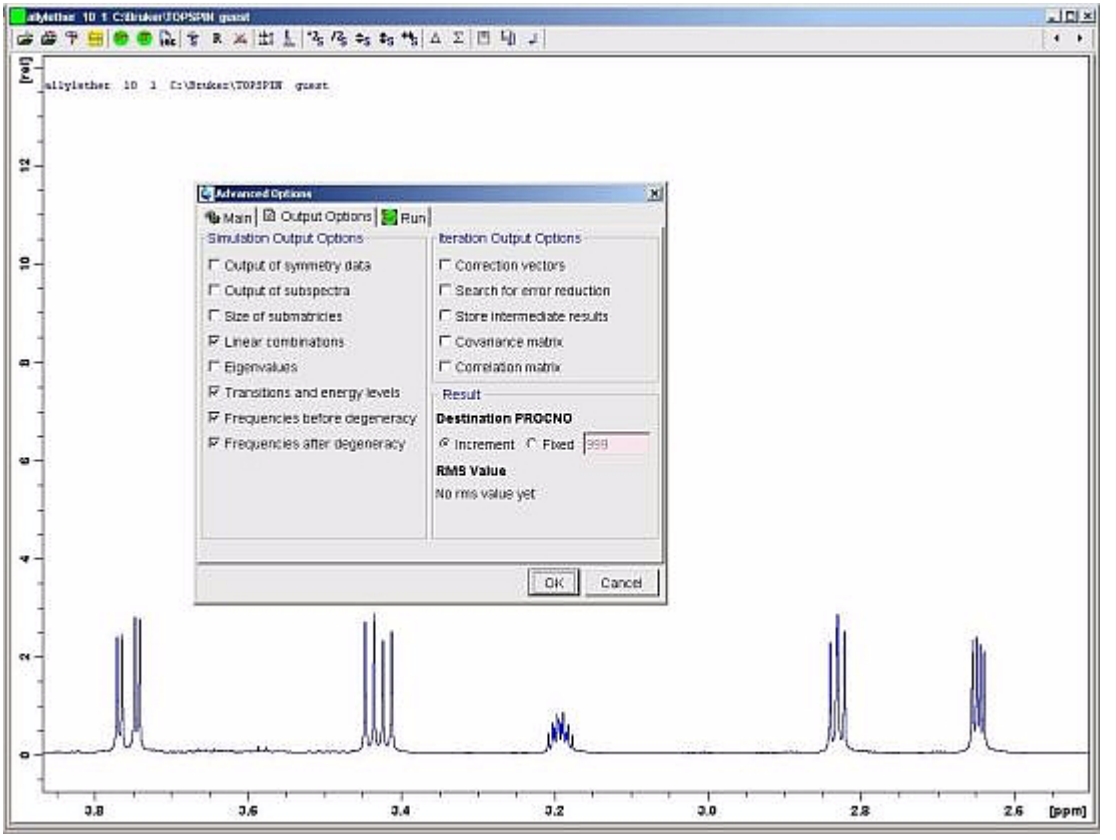
Figure 4.12: Scalar Couplings table for the epoxy-CH_2-group of Ally-glycidyl-ether



The last table, the Lineshape table is important for our example. As explained above, proton 5 (see figure 4.8) shows different couplings to the four other protons of the group. The resulting signals are closely together and don't seem to be resolved. Therefore the signal group representing proton 5 shows linebroadening. For the simulation of the whole spin system we use a global linewidth of 0.5 Hz.

Before starting the simulation some output options and the Destination PROCNO are set. Figure 4.13 shows the chosen values.

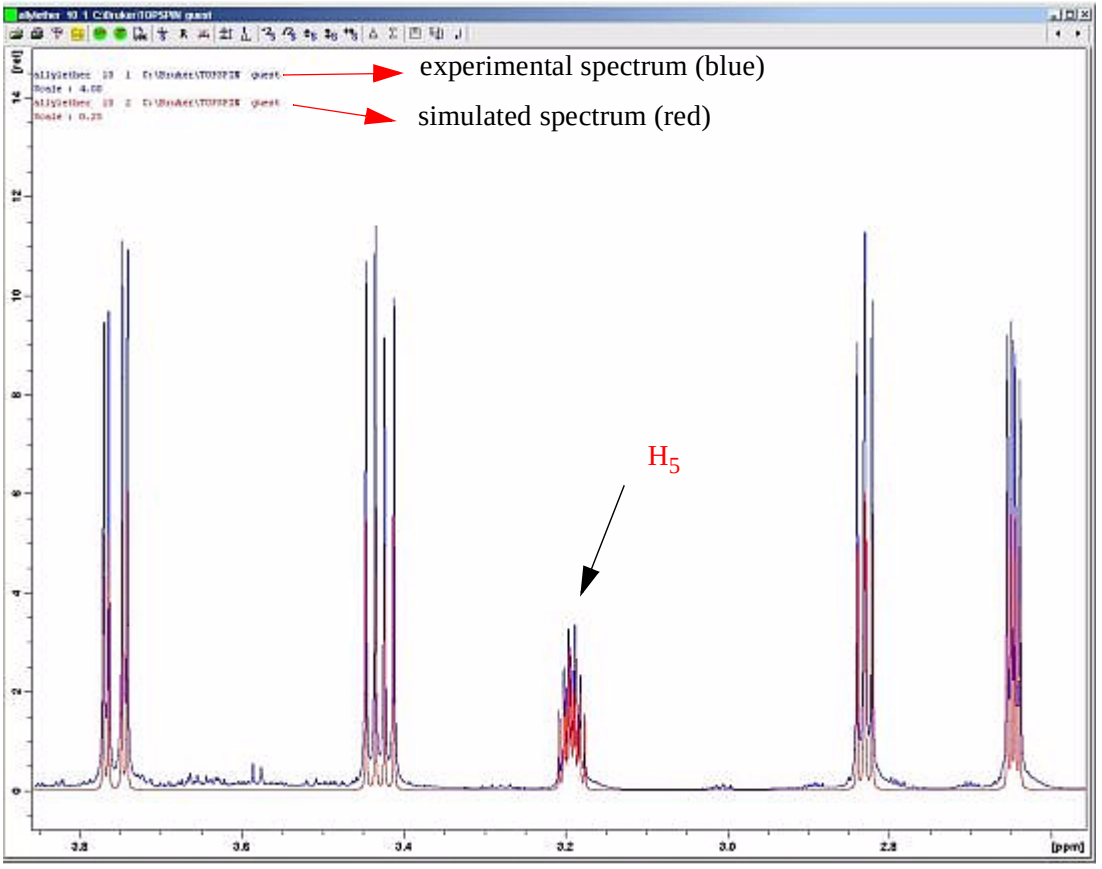
Figure 4.13: Output Options for the epoxy-CH_2-group of Allyl-glycidyl-ether



The simulation of the spectrum using these parameters is shown in figure 4.14. Although it is 'only' a first simulation, experimental and simulated spectrum fit together very well. A closer look at the signal group for proton H_5 (figure 4.15) shows a well chosen linewidth of 0.5 Hz.

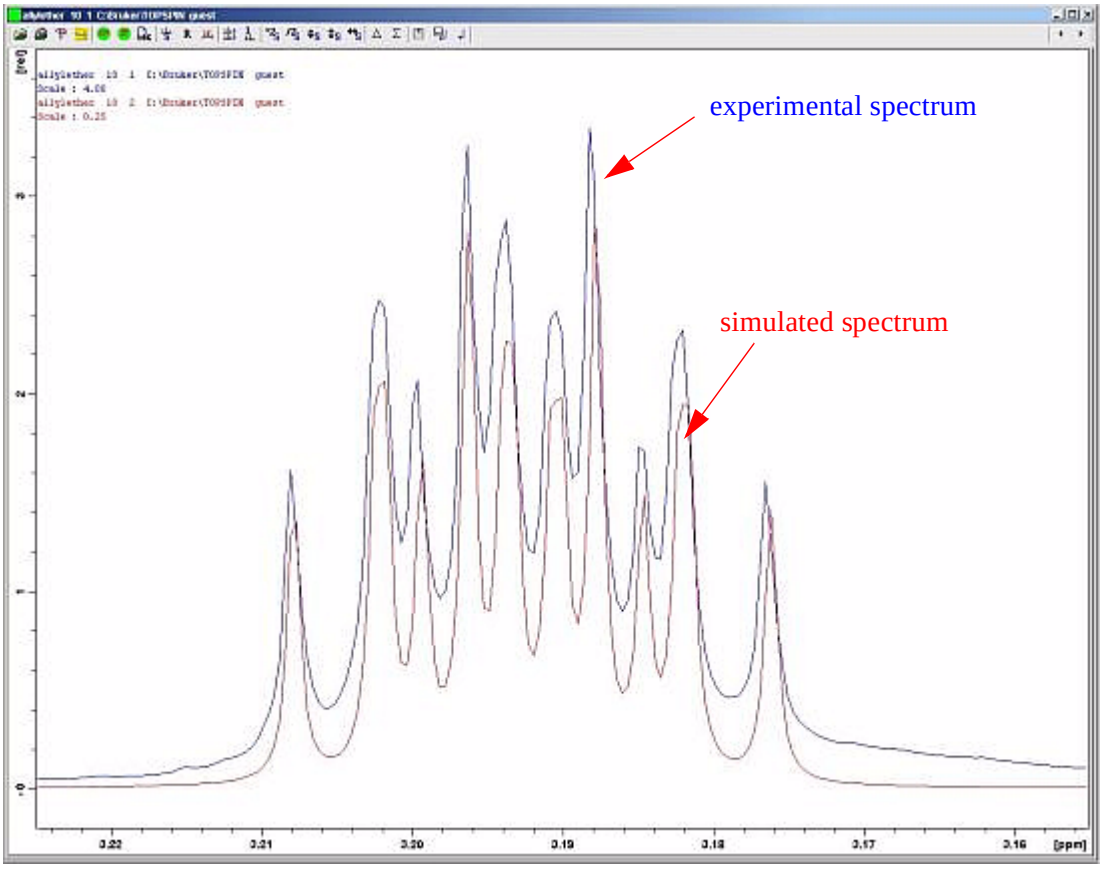
These simulation parameters are good starting values for an iteration of this 5-Spin-System. They are stored together with your chosen output options in the simulation protocol in the file `daisy.lst`.

Figure 4.14: Experimental and simulated spectrum of the epoxy-CH_2-group of Allyl-glycidyl-ether



Resonance frequencies and couplings seem to fit quite well. The global linewidth of 0.5 Hz seems to be better justified for Allyl-glycidyl-ether than for the previous case (aspirine) is better than the one in the first example (aspirine). neverthe less an advanced calculation using spin specific linewidth is requested. (see chapter 4.2.2).

Figure 4.15: Experimental and simulated spectrum of proton H_5



The frequencies, scalar couplings and linewidth used for the simiulation again can be found in the log-file, the `daisy.lst`, respectively in the /procno-directory of you spectrum.

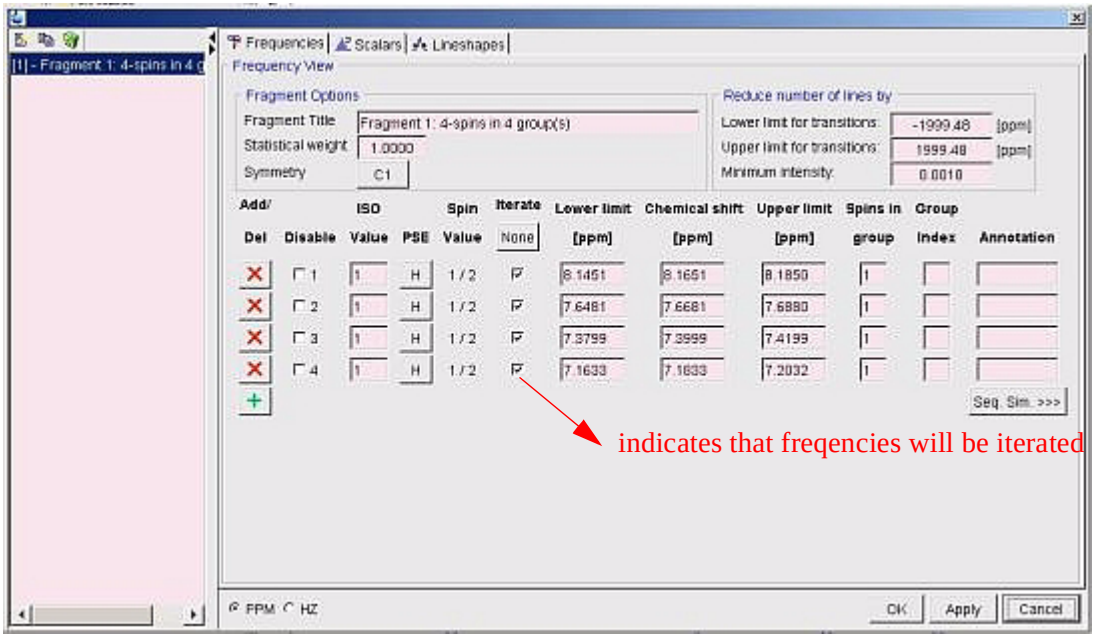
4.2 Spectrum iteration

The DAISY iteration input documents are based on simulation input files with some additional information.

4.2.1 Iteration of the ^{1}H-NMR Spectrum of Aspirine (aromatic protones)

The 4-spin system of the aromatic protons of aspirine shows four clearly seperated multiplets in the ^{1}H-NMR-spectrum. Multiplet analysis and DAISY simulation with determined frequencies and couplings are described in chapter 4.1.1. The simulation results showed that the frequencies and couplings are quite well. So we can use theses values as start input for an iteration. Looking at the simulation we realized the need of a nucleus specific linewidth for an exact calculation of this spectrum.

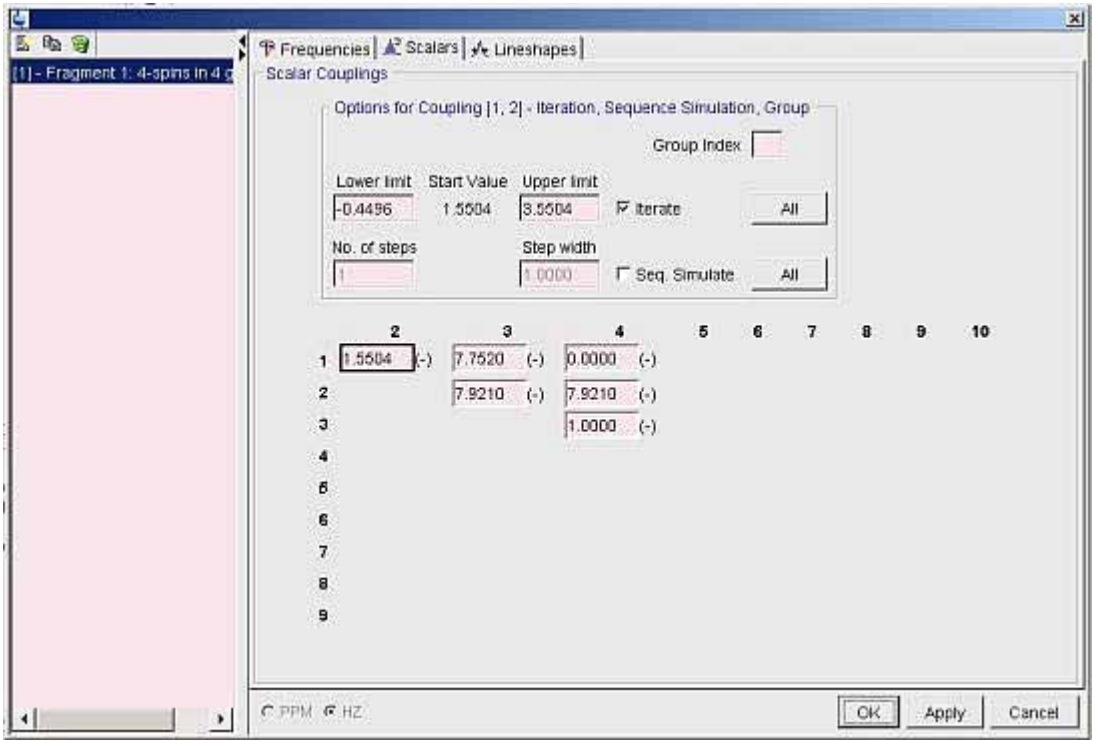
Figure 4.16: Frequency table prepared for iteration



For the following iteration all parameters available in the ’Edit Spin System’ window will be iterated. Therefore click on the iteration check boxes for each frequency, scalar coupling and linewidth. The figures 4.16, 4.17 and 4.18 show the three tables of the ’Edit Spin System’ window.

The upper and lower limits for iteration are automatically set by DAISY to +10 Hz and -10 Hz to the start value (see figure 4.16). These values can be changed manually. Using fine start values, this is not necessary.

Figure 4.17: Scalar coupling table prepared for iteration

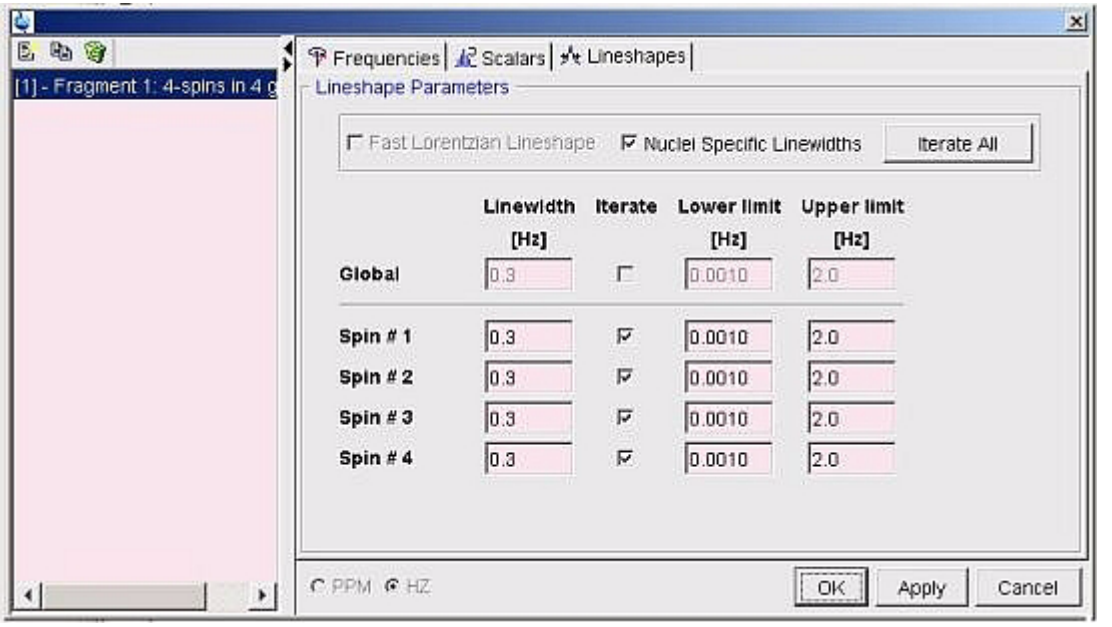


Similar to the frequencies, the upper and lower limits for iteration of the couplings are set automatically by DAISY. For proper chosen start values these limits are fine. In our example the long range coupling 1,4 is not resolved in the experimen-

tal spectrum. So we will leave this value at 0 Hz and do not iterate it.

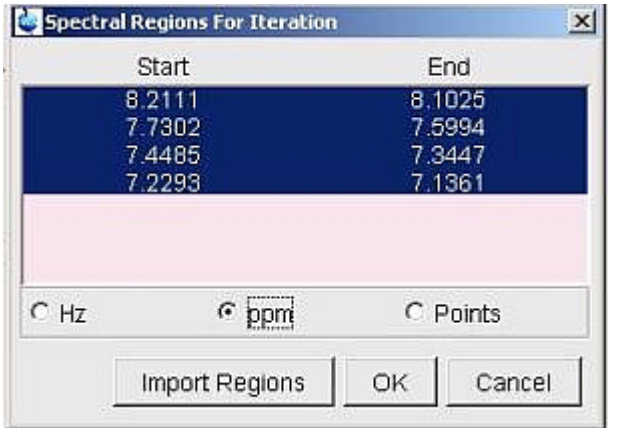
In the lineshape table we choose Nuclei Specific Linewidth and iterate all nuclei. Again DAISY automatically sets the upper and lower iteration limits.

Figure 4.18: Lineshape table prepared for iteration



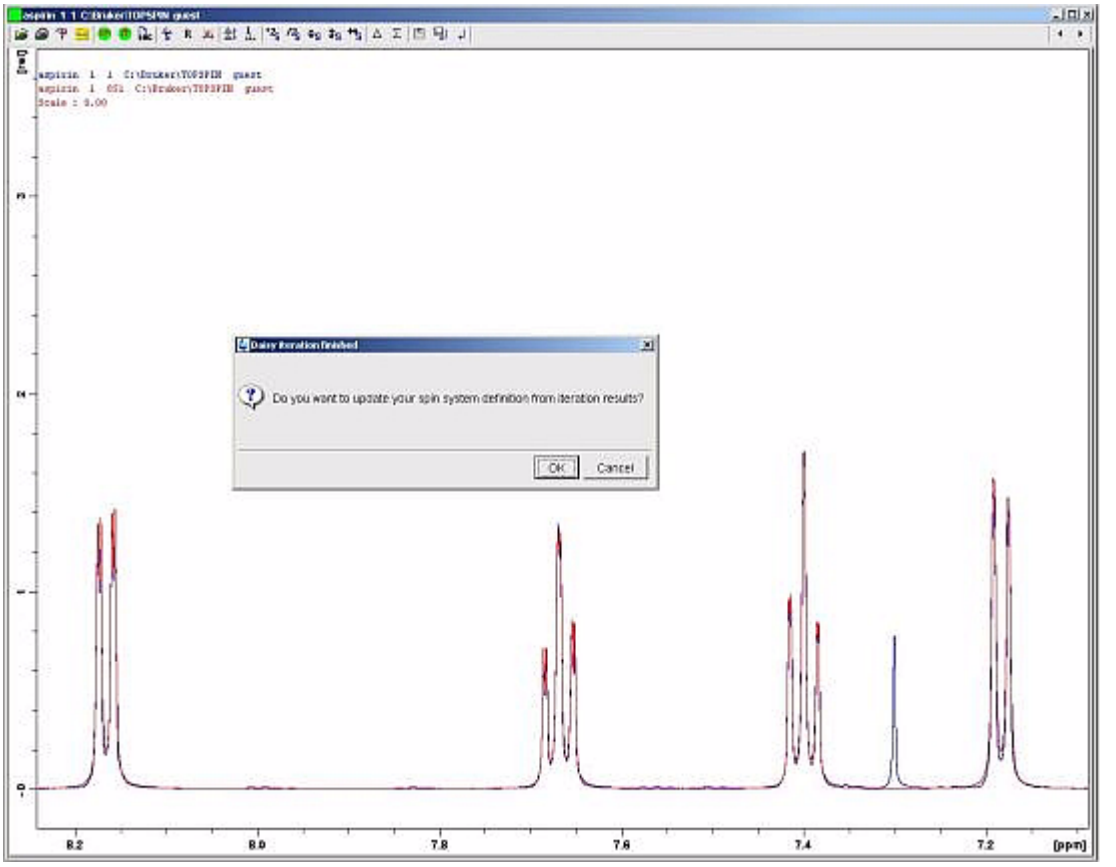
In the ’Advanced Options’ window the additional parameters have to be set as decribed in chapter 3.1.2. To get good results we import the iteration regions of the experimental spectrum and check ’Iterate BaseLine’ (Main table of this window). Figure 4.19 shows the upcoming window for definition of the iteration regions.

Figure 4.19 Importing iteration regions



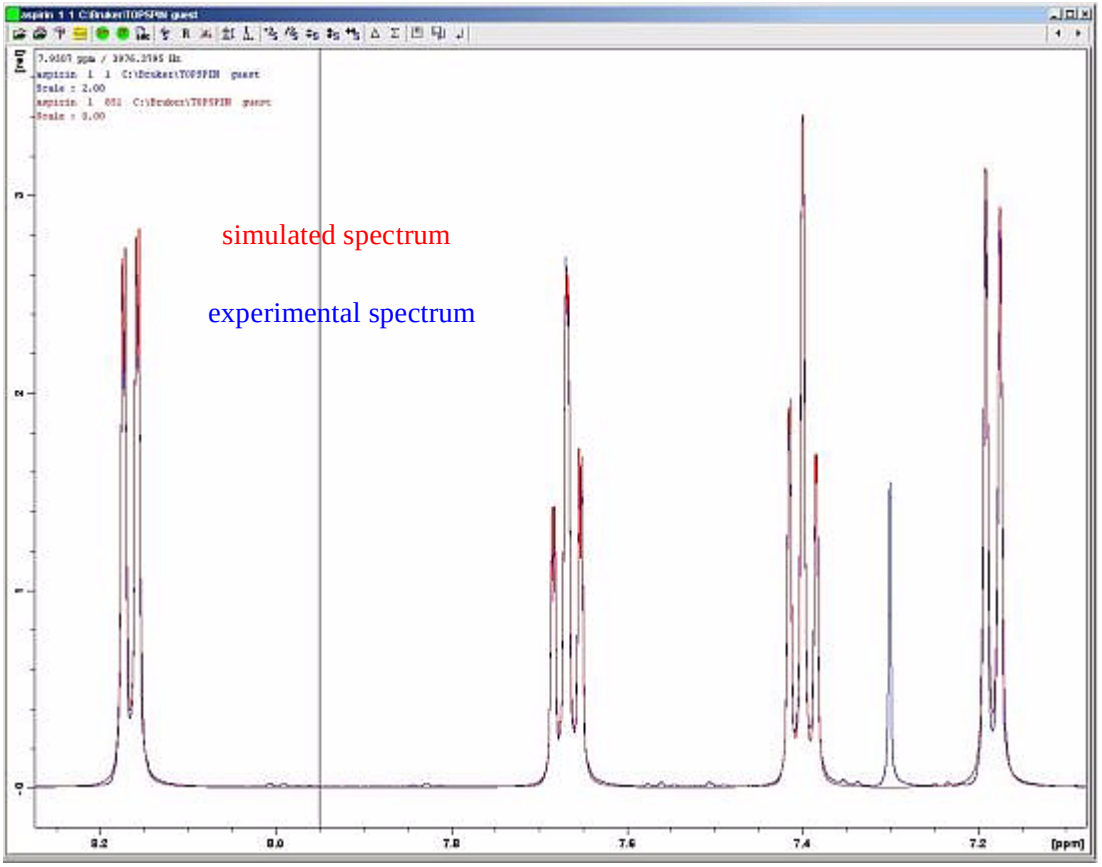
'Start' and 'End' in this table are the start and end points of the integration region of the experimental spectrum. The most relevant information for the spectrum shape is available in the signal regions. So it is only necessary to iterate the spectrum in these regions. The baseline in between will be calculated. Now the iteration can be started. When it is done you will be asked if you want to transfer the calculated values in the input tables (see figure 4.20).

Figure 4.20: DAISY window after end of iteration



Clicking **OK** transfers the calculated values and frequencies etc. to the tables of the ’Edit Spin System’. Now a new iteration could be started with these new start values. Otherwise the input values will be kept. The calculated values can be seen in the log-file.

Figure 4.21: Iterated spectrum overlayed with experimental spectrum



The following paragraph shows the start parameters and the result of the iteration. It was taken from the file `daisy.rst` in the directory <user>/pdata/1. This is also the source for the data available with the  button in the DAISY window.

Parameters to be iterated

==========

Fragment	Type	starting value	lower limit	upper limit
1	F(1)	4083.59000	4073.58640	4093.58640
1	F(2)	3835.02000	3825.02180	3845.02180
1	F(3)	3700.91000	3690.91190	3710.91190
1	F(4)	3592.55000	3582.55880	3602.55880
1	J(1, 2)	1.55040	-0.44960	3.55040
1	J(1, 3)	7.75200	5.75200	9.75200
1	J(2, 3)	7.92100	5.90000	9.90000
1	J(2, 4)	7.92100	5.90000	9.90000
1	J(3, 4)	1.00000	-0.45000	3.55000
1	H(1)	0.30000	0.00100	2.00000
1	H(2)	0.30000	0.00100	2.00000
1	H(3)	0.30000	0.00100	2.00000
1	H(4)	0.30000	0.00100	2.00000
0	Baseline Offset	0.00000	-2.00000	2.00000
0	Baseline Ascent	0.00000	-2.00000	2.00000

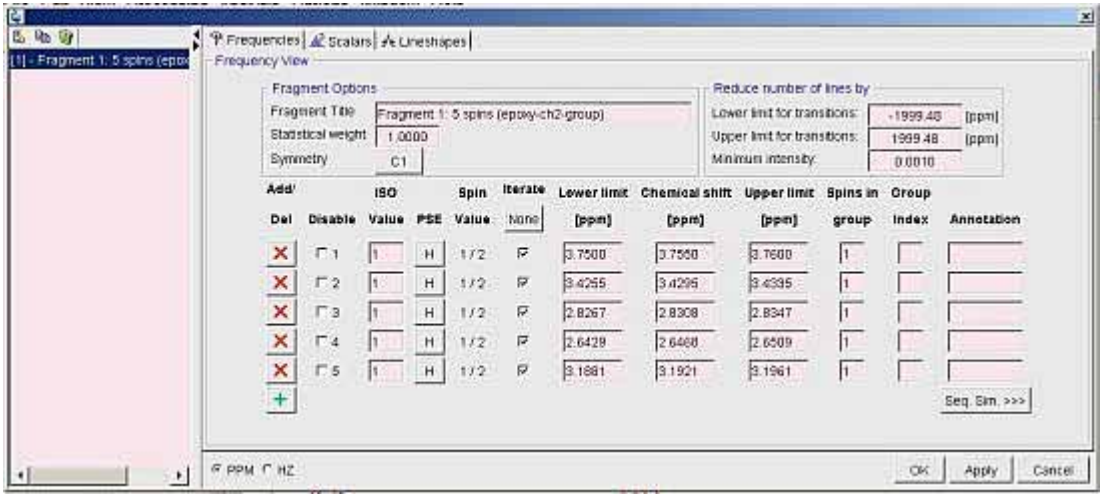
Iteration 21 rms = 1.78270396

Index	Parameter Type	Parameter Value	neg. Grad.	GN-Corr.
0	F(1)	4083.65011	2.891e-004	2.952e-004
1	F(2)	3834.98820	-2.802e-004	-2.614e-004
2	F(3)	3700.91634	3.834e-004	3.713e-004
3	F(4)	3592.53425	3.880e-004	3.802e-004
4	J(1, 2)	1.69580	7.011e-004	1.503e-003
5	J(1, 3)	7.87206	-6.621e-004	-3.382e-004
6	J(2, 3)	7.39957	2.575e-003	1.005e-003
7	J(2, 4)	8.09810	-5.682e-004	1.634e-004
8	J(3, 4)	1.08665	-9.393e-004	2.475e-004
9	H(1)	1.54867	-4.263e-003	-4.733e-003
10	H(2)	1.34961	-5.573e-003	-5.830e-003
11	H(3)	1.29116	-3.844e-003	-3.774e-003
12	H(4)	1.71547	-7.271e-004	-1.068e-003

4.2.2 Iteration of the epoxy group of Allyl-glycidyl-ether

As mentioned in chapter 4.1.2, the simulation input parameters lead to a simulated spectrum which fits well to the experimental one (see figure 4.14 and 4.15). A final iteration of the parameter will lead to a well simulated NMR-spectrum. In this example, the definition of lower and upper limits is of primary importance to obtain a successful results. The values that are automatically by DAISY define a wide range of parameter variation. Is is too big for this example with its 5-spin system and the very different linewidth for each nucleus. But if you confine the range for the parameters, especially for the frequencies and the linewidth, the iteration will be fast and fine. Otherwise the iteration leads to a deterioration of the simulated spectrum. The system probably falls into a local minimum. (see chapter 5.2.2.). The figures 4.22 - 4.24 show the input tables for a sucessful iteration.

Figure 4.22: Frequencies table prepared for iteration of epoxy-CH_2-group of Allyl-glycidyl-ether



The upper and lower limits of the frequencies, scalar couplings and specific linewidth are set manually and preferrably close to the start parameters. This is possible because the simulation shows that the input values are nearly the true values. Otherwise the simulated spectrum would not fit that well to the experimental one.

Figure 4.23: Scalar coupling table prepared for iteration of epoxy-CH_2-group of Allyl-glycidyl-ether

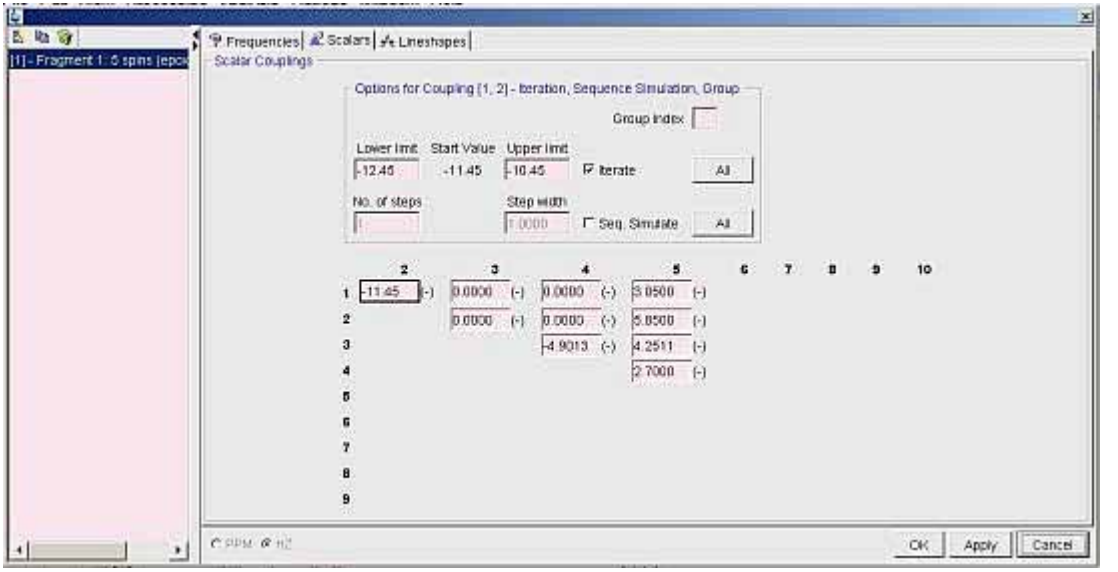
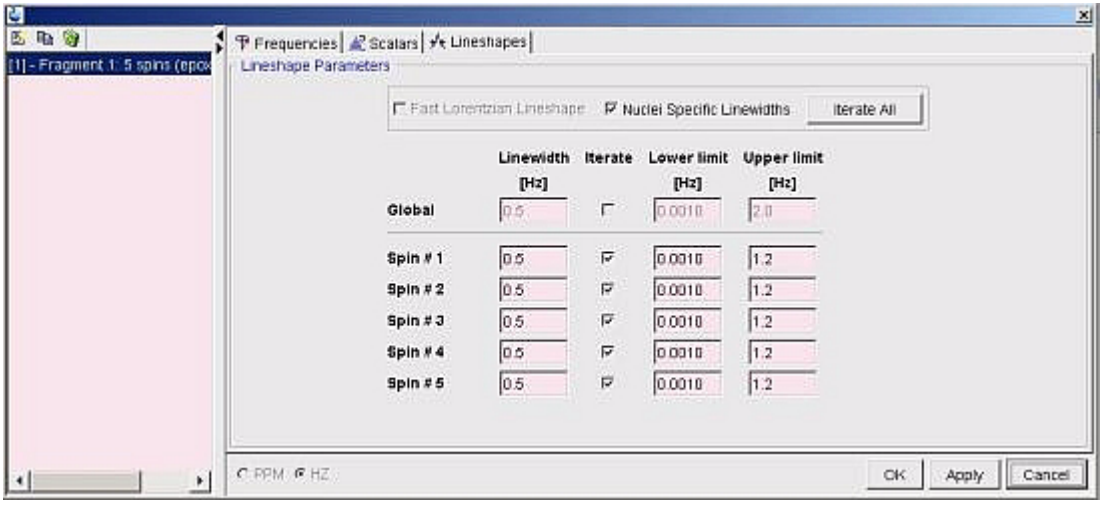
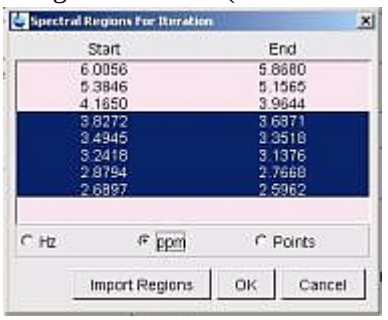


Figure 4.24: Lineshape table prepared for iteration of epoxy-CH_2-group of Allyl-glycidyl-ether



With these parameters and the iteration regions shown in figure 4.25 we start a DAISY iteration.

Figure 4.25: Iteration regions window (available under ’Advanced Options’)



In the iteration regions window the iteration regions of the whole experimental spectrum are available because the whole spectrum was integrated at the beginning of the analysis (see chapter 4.1.2). We choose the five regions between 3.8 and 2.5 ppm and press the button ’Import Regions’. Then the iteration can be started by pressing the  button in the toolbar of the DAISY window or out of the ’Run’ table of the ’Advanced Options’ window. Figure 4.26 shows the result. To illustrate the quality of the iteration the figure also shows the experimental spectrum.

As mentioned above the signal groups in the experimental spectrum have different linewidths. Especially the signal group representing Proton H_5 shows a significant line broadening compared to the other signals. Iterating with specific linewidths for each nuclei leads to a satisfying result which can be seen more detailed in figure 4.27.

Figure 4.26: Experimental and iterated spectrum of epoxy-CH_2-group of Allyl-glycidyl-ether

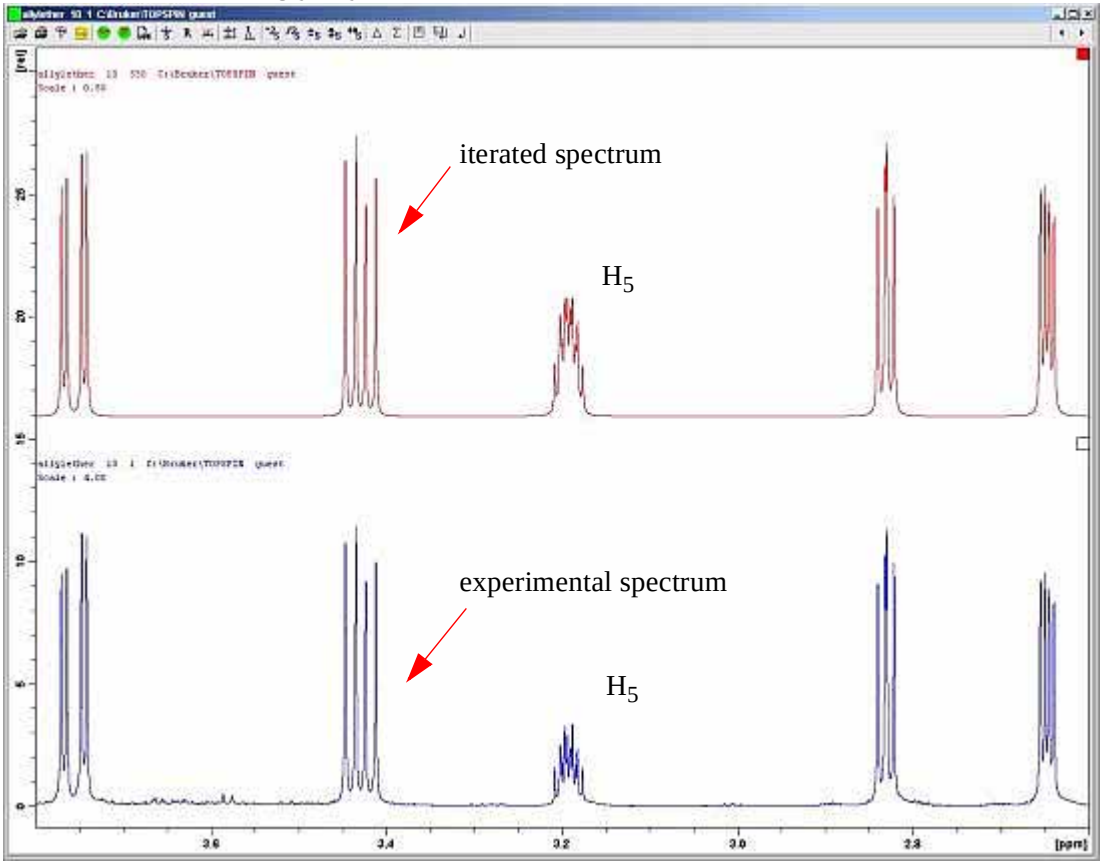
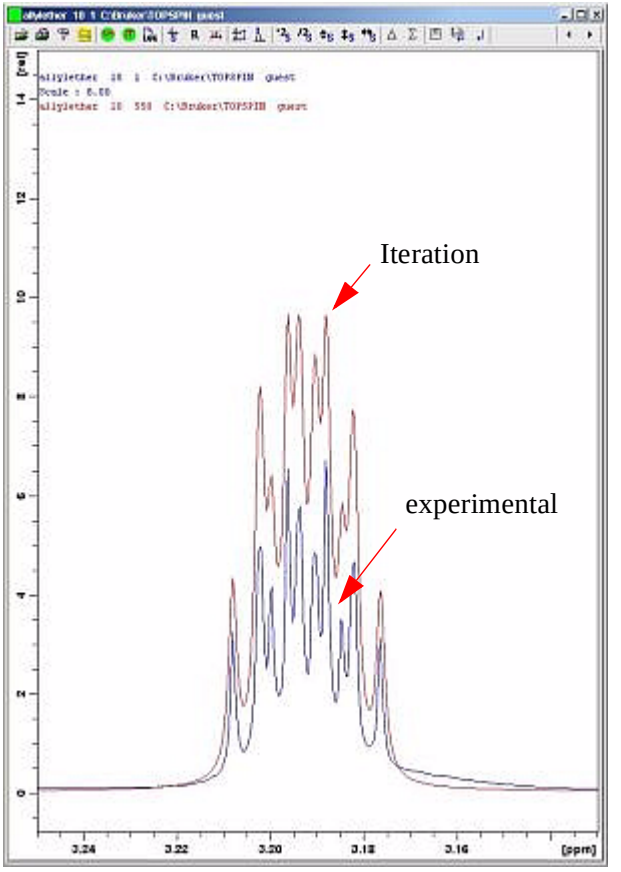


Figure 4.27: Experimental and iterated signals of H_5-protone of epoxy-group of Allyl-glycidyl-ether



The detailed results of iteration can be seen clicking the  button in the menu bar or opening the file `daisy.rst` in <user>/pdata/1. Input values and final iteration value are shown now:

```
Iteration
============================

Maximal number of iterations =          100
Convergence criterion        =      0.05000
Correlation factor           =      0.01000
```

Multiplier = 6.00000
Total number of cycles = 4
Correlation factor lineshape = 0.10000
Iteration of lineshape starting in the 3rd Cycle

Parameters to be iterated
==========

Fragment	Type	starting value	lower limit	upper limit
1	F(1)	1877.98820	1875.49000	1880.49000
1	F(2)	1715.19580	1713.20000	1717.20000
1	F(3)	1415.76800	1413.74000	1417.74000
1	F(4)	1323.74410	1321.77000	1325.77000
1	F(5)	1596.46500	1594.46000	1598.47000
1	J(1, 2)	-11.45000	-12.45000	-10.45000
1	J(1, 5)	3.05000	2.05000	4.05000
1	J(2, 5)	5.85000	4.85000	6.85000
1	J(3, 4)	-4.90130	-5.95000	-3.95000
1	J(3, 5)	4.25110	3.25110	5.25110
1	J(4, 5)	2.70000	1.70000	3.70000
1	H(1)	0.50000	0.00100	1.20000
1	H(2)	0.50000	0.00100	1.20000
1	H(3)	0.50000	0.00100	1.20000
1	H(4)	0.50000	0.00100	1.20000
1	H(5)	0.50000	0.00100	1.20000
0	Baseline Offset	0.00000	-2.00000	2.00000
0	Baseline Ascent	0.00000	-2.00000	2.00000

Statistical Information :
==========

Final sum of squares = 297.999358
Number of spectral points = 1622
Degrees of Freedom = 1606
Standard Deviation of Measurements = 0.430760
R-Factor (%) = 3.918803

Fragm. No.	Parameter type	Initial Parameter Vector	Best Parameter Vector	Standard Deviation
1	F(1)	1877.98820	1878.26984	0.00072

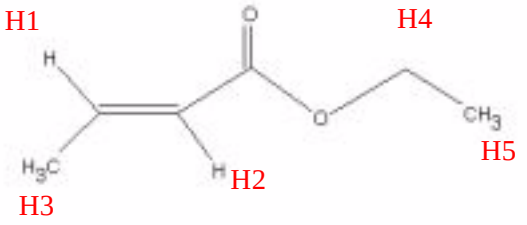
1	F(2)	1715.19580	1715.30507	0.00072
1	F(3)	1415.76800	1415.66754	0.00099
1	F(4)	1323.74410	1323.81176	0.00096
1	F(5)	1596.46500	1596.55872	0.00243
1	J(1, 2)	-11.45000	-11.45124	0.00101
1	J(1, 5)	3.05000	3.07087	0.00137
1	J(2, 5)	5.85000	5.86312	0.00135
1	J(3, 4)	-4.90130	-5.05153	0.00127
1	J(3, 5)	4.25110	4.17002	0.00154
1	J(4, 5)	2.70000	2.73139	0.00176
1	H(1)	0.50000	0.78791	0.00142
1	H(2)	0.50000	0.78866	0.00141
1	H(3)	0.50000	0.93455	0.00198
1	H(4)	0.50000	0.94549	0.00191
1	H(5)	0.50000	1.07432	0.00489

2 seconds
0.83

4.2.3 Iteration of the ^{1}H-spectrum of trans-Crotonic-acid-ethylester

The last example that will be analysed with DAISY is the proton spectrum of the trans-Crotonic-acid-ethylester (s.figure 4.28.).

Figure 4.28.: Structure of Crotonacidethylester



The ^{1}H-spectrum of this substance shows 5 clearly seperated and very well dissolved signal groups (H2 - H6, see annotation in DAISY frequencies table, too). According to the structure of the molecule it is a good example for dividing the spectrum in two independent subspectra. The Ethylester group is totally independent from the system around the double bond. A coupling of the protons via carboxy

group is not possible.

Figure 4.29: Frequencies table for iteration of Fragment 1 (Vinylgroup)

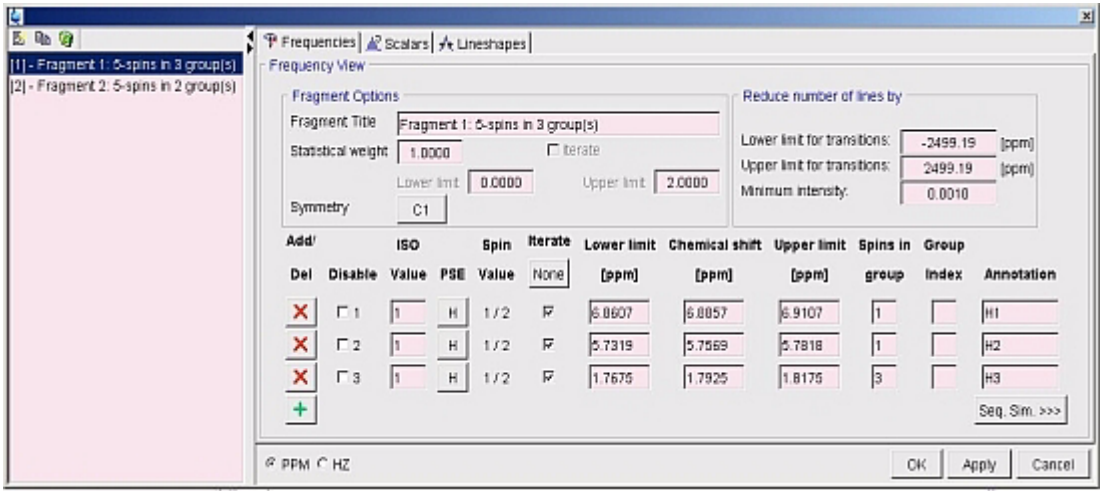
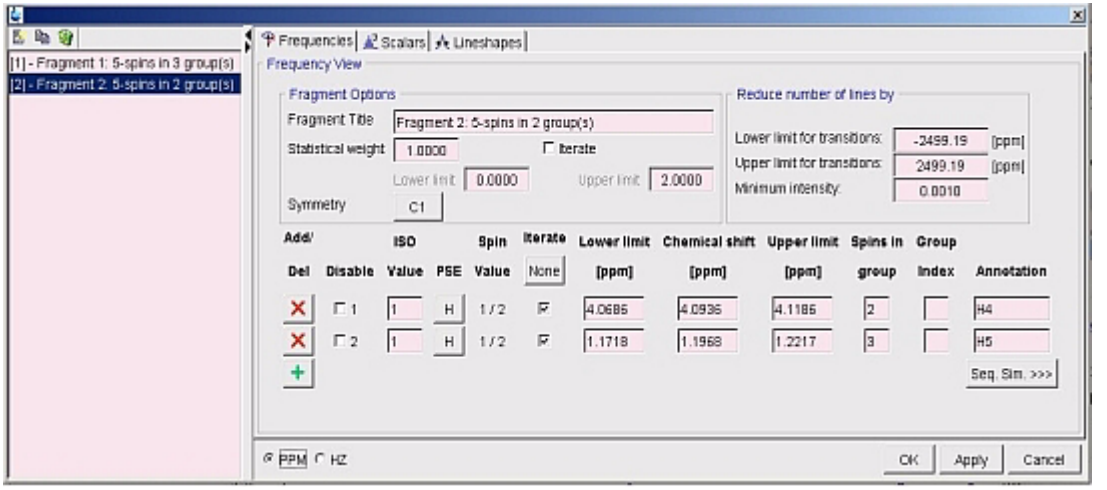


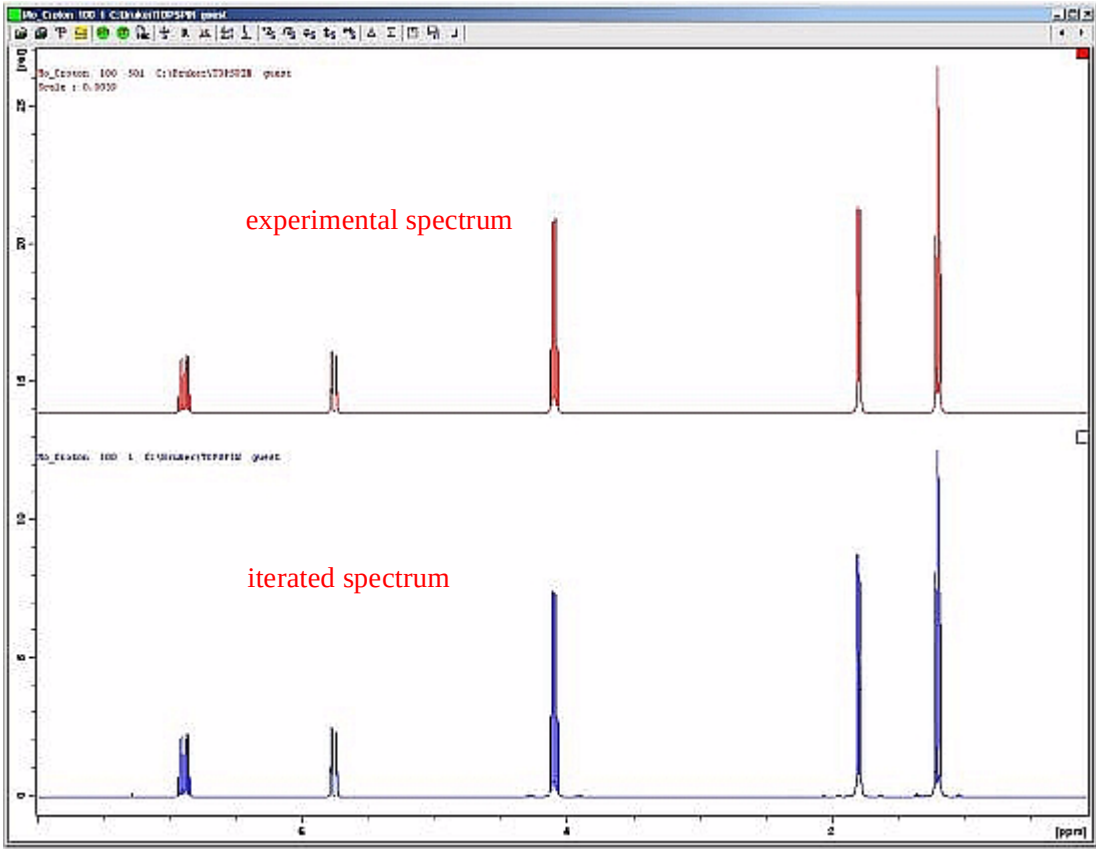
Figure 4.30: Frequencies table for iteration of Fragment 2 (Vinylgroup)



For both fragments a corresponding ’Scalar Couplings’ table and a ’Lineshape’ table is available. The values are filled in directly from the multiplet definition file `daisymultiplet.txt`. For the following DAISY calculation of the spec-

trum all parameters (frequencies, couplings and linewidth) are checked for iteration. In the 'Lineshape' table **Nuclei Specific Linewidth** is chosen and iterated for each spin. The result is shown in figure 4.31.

Figure 4.31 Simulated and original spectrum of trans-Crotonic-acid-ethylester



Again the detailed results of iteration can be seen clicking the  button in the menu bar or opening the file `daisy.rst` in <user>/pdata/1. Input values and final iteration value are shown now:

Iteration
==========

Maximal number of iterations = 100
Convergence criterion = 0.05000
Correlation factor = 0.00010
Multiplier = 6.00000
Total number of cycles = 7
Correlation factor lineshape = 0.02154
Iteration of lineshape starting in the 4th Cycle

Parameters to be iterated
==========

Fragment	Type	starting value	lower limit	upper limit
1	F(1)	2755.16510	2745.16510	2765.16510
1	F(2)	2303.48840	2293.48840	2313.48840
1	F(3)	717.24300	707.24300	727.24300
2	F(1)	1637.97220	1627.97220	1647.97220
2	F(2)	478.85560	468.85560	488.85560
1	J(1, 2)	15.49500	13.49500	17.49500
1	J(1, 3)	6.95560	4.95560	8.95560
1	J(2, 3)	1.72390	-0.27610	3.72390
2	J(1, 2)	7.16570	5.16570	9.16570
1	H(1)	0.30000	0.00100	2.00000
1	H(2)	0.30000	0.00100	2.00000
1	H(3)	0.30000	0.00100	2.00000
2	H(1)	0.30000	0.00100	2.00000
2	H(2)	0.30000	0.00100	2.00000

Statistical Information :
==========

Final sum of squares = 109.752807
Number of spectral points = 1505
Degrees of Freedom = 1491
Standard Deviation of Measurements = 0.271312
R-Factor (%) = 1.062955

Fragm. Parameter type Initial Parameter Best Parameter Standard

No.		Vector	Vector	Deviation
1	F(1)	2755.16510	2755.06463	0.00279
1	F(2)	2303.48840	2303.65185	0.00322
1	F(3)	717.24300	717.15556	0.00104
2	F(1)	1637.97220	1637.93539	0.00115
2	F(2)	478.85560	478.80272	0.00083
1	J(1, 2)	15.49500	15.55628	0.00400
1	J(1, 3)	6.95560	7.01139	0.00181
1	J(2, 3)	1.72390	1.87399	0.00159
2	J(1, 2)	7.16570	7.18705	0.00110
1	H(1)	0.30000	1.10007	0.00547
1	H(2)	0.30000	1.14072	0.00634
1	H(3)	0.30000	1.33525	0.00209
2	H(1)	0.30000	1.25424	0.00230
2	H(2)	0.30000	1.41031	0.00167

2 seconds
1.03

Chapter 5

Appendix

This chapter gives some more information about symmetry groups and symmetry describtion (chapter 5.1) and a short summery about the theoretical background of the DAISY simulator and the DAISY iterator (chapter 5.2)

5.1 Spin Symmetry, Symmetry groups

The spin symmetry in DAISY is described using the Schoenfliess permutation group. The default input is C_1 which means that the molecule does not contain any symmetric element. For the non-symmetry C_1 no input of symmetry description is required. All other symmetries need permutation operators to fix the molecular symmetry. The Schoenfliess symbol have been chosen here, because they are often used in the describtion of molecular symmetry.

To give an overview which symmetry requires how many permutations, the following table is given. The first row gives the total number of permutation operators including the unity operation, so that one permutation less than enumerated has to be defined.

number of permutations	Schoenfliess point group symmetries
1	C_1
2	C_2, C_s, C_i
3	C_3
4	S_4, D_2, C_4, C_{2v}, C_{2h}
5	C_5
6	S_6, D_3, C_6, C_{3v}, C_{3h}
8	D_{2d}, D_{2h}, C_{4h},C_{4v}, D_4
10	C_{5h}, C_{5v}
12	T, D_{3d}, D_{3h}, D_6, C_{6v}, C_{6h}
16	D_{4d}, D_{4h}
20	D_{5d}, D_{5h}
24	O, T_h, T_d, D_{6h}, D_{6d}
48	O_h
60	I

Table 5.1 : Schoenfliess point groups and corresponding permutations

The Symmetry Description dialog box directly depends on the Symmetry Group selection made. For default C1 Symmetry Group no userdefined Symmetry Description is necessary.

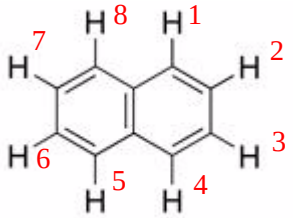
The Symmetry Description dialog box informs about the number of descriptions, which means the number of permutation operators. This value minus 1 represents the number of lines required for permutation input. This defines the layout of the dialog box.

In the headline the point group name and the number of corresponding symmetry description is displayed. The unity-operation is given in the first line and is at the

same time the fixed nucleus numbering. In the first row the name of the symmetry operation is displayed to the user preparing the input properly. It is not allowed to interchange the sequence of symmetry operations. This will lead to errors during calculation and wrong results.

For symmetry higher than C1 all permutations have to be defined before closing the dialog box. This is necessary because the construction of the following input tables (for frequencies/couplings) depends on the symmetry definition.

The creation of permutation operators is described using naphthalene as example:



The spin system of naphthalene can be either described as $[AB]_4$ (C_{2v}) or as $[AB]_4$ (D_{2h}). We will show the creation of the permutation table with the symmetry group C_{2v} and explain that this is the better choice, although D_{2h} strikes the maximum molecular symmetry.

The C_{2v} symmetry consists of 4 symmetry operators: the identity (E), the C_2-axis (C_2) and two vertical symmetry planes (SigV and SigV’)

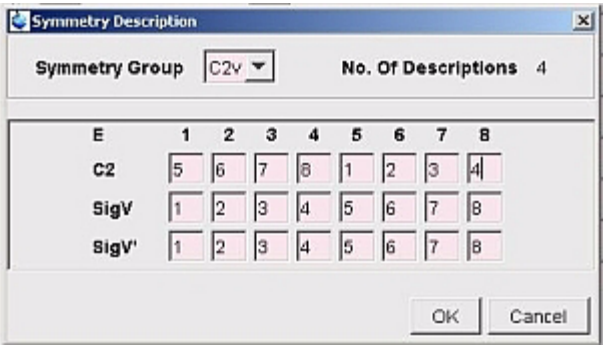
Figure 5.1: Initial Symmetry Description for naphthalene

The identity results in the subsequent spin numbering. The other three symmetry

operators are followed by the initial numbering of the spin system (see figure 5.1).

Now the C_2 operation will be applied to the molecule according to the numbering of the spin system leading to the permutation operators. The C_2 axis is perpendicular to the molecular plane and interchanges spins number 1 into 5, number 2 into 6, number 3 into 7, number 4 into 8 and vice versa (see figure 5.2).

Figure 5.2: Symmetry Description completed with C_2 permutation

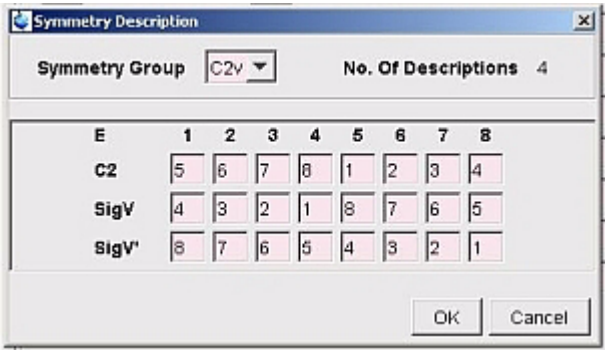


The next operation involves the SigV plane. This (and all subsequent symmetry operations) operate on the spin labelling as defined in the first line (identity operation E). Spins 1 and 4 change places, and so do spins 2 and 3, 5 and 8, and finally 6 and 7 (see figure 5.3).

Figure 5.3: Symmetry Description completed with SigV permutation

The fourth symmetry operation SigV' is now perpendicular to the SigV plane. The effect of this mirrow plane transfers spin 1 to 8, 2 to 7, 3 to 6 and 4 to 5 (see figure 5.4).

Figure 5.4: Symmetry Description completed with SigV' permutation



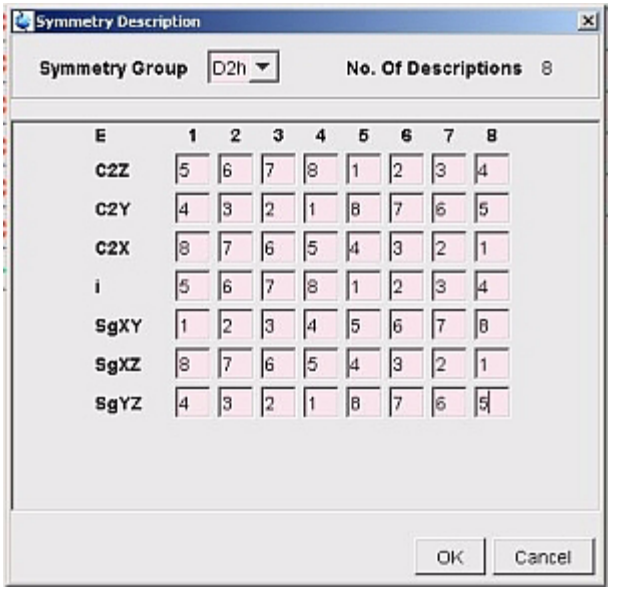
As mentioned before, the spin system of naphthalene satisfies all required symmetry operations of D_{2h} (identity, three perpendicular C_2 axes, one inversion center and three perpendicular mirror planes - every plane is constructed of two C_2 axes). So there are twice as many symmetry operators in D_{2h} than in C_{2v}.

Looking at the additional permutation information about the symmetry of D_{2h} in the naphthalene case (see figure 5.1.5), we will recognize that the permutations are in pairs identical (E = SigXY, C_{2z} = i, C_{2y} = SigYZ, C_{2x} = SigXZ). This does not yield additional information about the molecule.

For DAISY calculation this does not result in a gain of calculation speed. As this is the main reason for symmetry consideration, there is no need to use D_{2h} symmetry group instead of C_{2v} symmetry group in this case.

Conclusion: In many cases it is not necessary to select the highest symmetry that is available in the Symmetry Description window. A partially reduced symmetry will do for fast calculation.

Figure 5.5: D_{2h} Symmetry Description for naphthalene



5.2 Theoretical Background

References: [1-18]

5.2.1 The DAISY Simulator

References: [1-9,12,16-18]

5.2.1.1 The basic Single Spin simulation algorithm

References: [8,9,17]

The simulation of high resulution NMR spectra is based on the time independent Hamilton Operator (here in the first step for Single Spins) to satisfy the Schroedinger equation in the Hilbert space.

$$\hat{H} = -\sum_{i=1}^{N} \frac{1}{2\pi}\gamma_i h B_0 (1-\sigma_i) I_{z,i} + \sum_{i<k}^{N}\sum^{N} h J_{ik} \hat{I}_i \hat{I}_k \qquad \textbf{(1)}$$

H nuclear spin Hamilton operator [Joule]

N number of nuclei in spin system

gamma$_i$ gyromagnetic ratio of the i-th nucleus

h Planck constant

B$_0$ static magnetic field (defines in -z direction)

sigma$_i$ shield constant of the i-th nucleus

I$_{z,i}$ spin operator of the i-th nucleus in z direction

J$_{ik}$ Scalar (indirect Coupling Constant between i-th and k-th nucleus)

I$_i$ spin operator of the i-th nucleus

After dividing the Hamiltonian operator by **h** , using the definition of the resonance frequency

$$\nu_i = \frac{1}{2\pi}\gamma_i B_0 (1-\sigma_i) \qquad \textbf{(2)}$$

$$\hat{H} = -\sum_{i=1}^{N} \nu_i \hat{I}_{z,i} +$$

$$\sum_{i}^{N}\sum_{<k}^{N}(J_{ik})\hat{I}_{z,i}\hat{I}_{(i,z)(z,k)} +$$

$$\frac{1}{2}\sum_{<i}^{N}\sum_{k}^{N}(J_{ik})\hat{I}_{i}\hat{I}_{-k} + \hat{I}_{-i}\hat{I}_{k} \qquad \textbf{(3)}$$

$\boldsymbol{H}$	nuclear spin Hamilton operator [Hz]
$\boldsymbol{I_{+,i}}$	raising operator of spin i
$\boldsymbol{I_{-,i}}$	lowering operator of spin i

called the Zeeman term (field dependent), the coupling term (including the z-spin operator) and the mixing term (including raising and lowering term).

For first order calculation the X-approximation, which neglects the mixing term of the Hamiltonian, is implemented.

The set of basic functions is composed of the product spin function |*Phi*>, defined as the product of the spin functions $|s_k>$:

$$|\phi\rangle = \prod_{k=l}^{N}|s_k\rangle \qquad \textbf{(4)}$$

N = number of nuclei in spin system

For single spin calculations involving spins with I=1/2, the spin functions |sk> are symbolised as |alpha> or |beta>.

The eigenfunctions |Psi> to solve the Schroedinger equation

$$\hat{H}|\Psi_i\rangle = E_i|\Psi_i\rangle \qquad \textbf{(5)}$$

are derived as linear combinations of basic product spin functions.

$$|\Psi_i\rangle = \sum_{j=1}^{2^N} c_{ij}|\Psi_j\rangle \qquad \textbf{(6)}$$

The dimension of the Hamilton matrix is given by the number of different basic function 2^N identical with the number of eigenvalues E.

The eigenvalues E are formed by diagonalisation of the Spin Hamiltonian Matrix. Diagonalisation of matrices is a very time consuming process. Consequently matrices are broken down to submatrices of smaller dimension thus efficiently reducing the time demand. The standard way of factorisation is to use the commutator

$$[\hat{H}, \hat{F}_z] = 0 \qquad \textbf{(7)}$$

with F_z, the total spin operator, defined by

$$\hat{F}_z|\Phi_k\rangle = m_{T,\,k}|\Phi_k\rangle \qquad \textbf{(8)}$$

to obtain the total spin factorization.

5.2.1.2 Using Symmetry

References: [5,8,9,16,17]

Further factorisation is archieved by introducing symmetry considerations. A commutator is used:

$$[\hat{H}, \hat{P}_n] = 0 \qquad \textbf{(9)}$$

where P_n stands for the projection operator resulting from the n-th irreducible representation of the spin symmetry group. The basic functions |Phi> are linear combinations of the product spin functions to create the eigenfunctions:

$$|\tilde{\Phi}_i\rangle = \sum_{j\,=\,1}^{2^N} c_{ij}|\Phi_j\rangle \qquad \textbf{(10)}$$

The coefficients c_{ij} are based on the information of the character table of the point group for spin symmetry.

Using the new basic function |psi>

$$|\Psi_k\rangle = \sum_{j=1}^{2^N} c_{ki}|\tilde{\Phi}_i\rangle \qquad \textbf{(11)}$$

the eigenfuctions are derived as required by the Schroedinger equation.

Each Hamiltonian sub-submatrix is diagonalised individually. Then the allowed transition frequencies and intensities are determined according to known selection rules. The demands for memory and processing time largly depend on the size of these sub-submatrices. So symmetry factorisation is important for saving computer time.

Of course the main factor governing the total computer time will be determined by the number of nuclei involved in the spin system. The advanced DAISY user will quickly learn to select the relevant spin-islands to efficiently calculate certain regions of the total spectrum.

5.2.1.3 The Composite Particle Approach

References: [8,16]

If magnetical equivalence occurs and/or spins with spin values higher than 1/2 are involved, the Composite Particle approach is automatically used for speedy calculations. Here every Composite Particle group is treated like one particle in every term of the system.

The properties of the Composite Particle will be described by the following concept:

The particle is decomposed into a weighted superposition of individual states, which will be dealt with as a Single Spin of I≥ 1/2 and handled as individual quantum mechanical systems. The resulting subspectra are finally combined to give a total spectrum of the spin system. Note that the quantum mechanics to be calculated for composite particles is nearly the same as for single spins. The only difference is, that the basic functions |sk> can be composed of any possible spin value, not just only |alpha> and |beta>.

Symmetry can be applied for the main term - the molecule itself. For all other terms the program detects contained subgroups of symmetry automatically from the implemented subgroup-tree. If symmetry is present some of the terms give identical spectra, so that the spectrum will be calculated once and then summed up including the proper statistical weights as derived from binomial coefficients.

The Hamiltonian for the Composite Particle approach for every subspectrum is of the same type like the Single Spin Hamiltonian of equation **(3)**. The only difference is, that for spin system calculation in anisotropic solution the Hamiltonian can be extended.

5.2.1.4 The nuclei specific linewidth

Reference:[16]

Arising from various effects (neighboring of quadrupolar nuclei, dynamic effects etc.) the presence of different linewidths in one spectrum can often be seen. To solve this problem in the most general way for all possibilities - even for second order systems and overlapping spectral regions - the assignment of specific linewidth to every nucleus is the best theoretical approach.

Based on these specific line width parameter (index i) HWB_i for every resonance (index j) in the spectrum a line specific width hbw_i will be determinedwhich can be traced back to the eigenvector coefficients c_i for the actual transition (j).

$$hwb_j = \sum_{i=1}^{N} c_i HWB_i \qquad \textbf{(12)}$$

For normalization the eigenvectors are re-scaled in the following way:

$$\sum_{i=1}^{N} |c_i|^2 = 1 \qquad \textbf{(13)}$$

5.2.1.5 The X-Approximation: Division into Subsystems

Reference: [18]

For increasing size of spin systems the dimension of the Hamiltonian matrix is growing rapidly . Various methods to break them down into smaller parts have been developed over the years:

- the factorisation by the Total-spin values
- the factorisation by permutational operators
- the factorisation by different molecular terms (Composite Particle approach)

The 'simple' X-Approximation based on different ISO-Values solely makes off-diagonal elements of the Hamiltonian matrix to vanish. The dimension of the matrix itself is not touched at all.

The basic equation for the X-Approximation is the pertubation parameter Lambda$_{ik}$.

$$\lambda_{ik} = \left| \frac{J_{ik}}{\nu_i - \nu_k} \right| \qquad \textbf{(14)}$$

As an approximate value for neglection, the mixing term from the Hamiltonian Lamba$_{ik}$ should be much smaller than 0.01. For different isotopes the numerator (difference between the Resonance Frequencies) is in the order of 10^{-6} Hz (MHz), so that this condition is always fulfilled for different types of nuclei, even if a Coupling Constant of 10^3 Hz is present. For nuclei of the same isotope the limit for X-

Approximation is more difficult to fix.

However a very simple case occurs when the Coupling Constant is zero. Then independent from the denominator the numerator is zero. The absolute value of a spectral parameter is zero by definition and that's the smallest value obtainable:

$$\lim \lambda_{ik} = \lim \left| \frac{0}{\nu_i - \nu_k} \right| = 0 \qquad \textbf{(15)}$$

But the neglection of the off-diagonal elements is not the only consequence, also the diagonal elements are not affected by any Coupling Constant contribution. The sole influence of the other nucleus is an additive contribution to all energy levels, so that the transition frequencies are not affected.

An extreme situation occurs when a whole cluster of nuclei present the property against another cluster of nuclei. Here the 'intelligent' X-Approximation starts:

Real factorization according to the membership of a cluster (subsystem, fragment) leads to independent quantum mechanical systems - with much smaller matrix-dimension - in which the former described factorization takes place. To deal with these systems different input cases can be combined to a complete input document. The calculation will be executed in a sequence of simulation runs for all the fragments.

5.2.2 The DAISY Iterator

References: [8-18]

DAISY includes a powerful simulation and iteration algorithm. The iteration may be classified as a total line shape fitting or - more generally - as an intensity iteration. This approach is different from traditional frequency iterations based on LAOCOON type programs.

No trial-simulation and no line assignments are required for iterations with DAISY. The iteration environment uses effient simulators for Single Spins and Composite Particles described in the preceding chapter.

The iteration algorithm is a modification of previous results obtained or used by

Binsch et al.[15] in DAVINS, e.g. the iteration routine is based on the spiral algorithm published by Jones[14]. Previous DAISY versions[8,9] were designed in FORTRAN IV and FORTRAN77 to run on mainframe computers and work stations. The FORTRAN versions were able to handle up to 8 spins. Considerable progress was made with WIN-DAISY, the new modified C-version using totally dynamic memory allocation. The 1994 version coveres up to 10 spins/groups (Composite Particles) per fragment. The current DAISY version, now implemented in TopSpin, is based on this 1994 version of WIN-DAISY, which was developed as a cooperative project between the research team of G. Hägele in Düsseldorf and Bruker Spectrospin, Karlsruhe[8-12,16-18].

As mentioned above the iteration routine uses the spiral algorithm, which is based on previous studies from D.W. Marquardt[13] and K. Levenberg[13]. The error of the initial parameter guess (which has to be minimized) is calculated using a Gaussian least square treatment for all spectra data points.

$$\sum_{i=1}^{n} (res_i)^2 \qquad \textbf{(16)}$$

n number of data points

res_i residual in the i-th data point

The residual is defined as:

$$res_i = f_i(p) - exp_i \qquad \textbf{(17)}$$

$f_i(p)$ = calculated intensity in the i-th data point

exp_i = experimental intensity in th i-th data point

p = NMR parameter

The Jacobian matrix J, consisting of first differentials of the Lorenzian line shape and the NMR parameters, are determined.

$$J = \begin{bmatrix} \frac{\partial}{\partial p_1} f_1(p) & \frac{\partial}{\partial p_n} f_1(p) \\ \frac{\partial}{\partial p_1} f_k(p) & \frac{\partial}{\partial p_n} f_k(p) \end{bmatrix} \qquad \textbf{(18)}$$

n = number of data points

k = number of parameters to be iterated

p = NMR parameter

The Hessian matrix, the second derivative matrix , is built by multiplying an exponential weighting vector to the approximate Hessian, briefly defined by the expression Jacobian (transposed) * Jacobian.

$$Hess_{appr} = J^T J \qquad \textbf{(19)}$$

The Gauss-Newton correction is defined as

$$c_{Gauss-Newton} = -Hess_{appr} J^T res \qquad \textbf{(20)}$$

$c_{Gauss\text{-}Newton}$ = Gauss-newton correction

$Hess_{appr}$ = approximated Hessian matrix

J^T = transposed Jacobian matrix

res = residual

The negative gradient can be defined as:

$$c_{neg,\,grad} = -J^T res \qquad \textbf{(21)}$$

The corrections applied to the NMR parameter are composed of negative gradients and Gauss-Newton correction, which can be done in different ways.

In many cases, sharp local minima occur in the total line shape fitting, consequently an efficient smoothing adopted to the iteration algorithm is required which can be done again in different ways.

5.2.2.1 The Standard Algorithm

References: [8,9,12,15,16]

Iteration theory derives, that one of the best error reductions in these complicated cases is situated in the plane between the Gauss-Newton correction and the negative gradient.

Corrections applied to parameters are thus not simple Gauss-Newton corrections used in traditional frequency iterations, but composed of the Gauss-Newton vector and the negatively scaled gradient.

The error reduction starts with applying the total length of the Gauss-Newton correction to the parameters under iteration. If no reduction of the error is archieved, a spiral is constructed and three more testing points in the plane are inspected to reduce the error value. If this is not successful, the same procedure will be retried with other test spirals starting from a lower Gauss-Newton correction (reductions: division by a factor of three).

Altogether twelve error reduction tests are made, if necessary, for every iteration.

The effective correction can be defined as:

$$c_{eff} = \lambda c_{negGrad} + (1 - \lambda) c_{Gauss-Newton} \qquad \textbf{(22)}$$

with 0 ≤ lambda ≤ 1

The differentials forming the Jacobian matrix are calculated numerically. For each parameter two spectral simulations with small changes in the actual parameter values in positive and negative direction are performed. This iteration procedure is valid for the linewidth as well. Base line increment and base line tilt are determined directly.

5.2.2.2 The Advanced Algorithm

References: [10,11,17]

As it is essential to have properly adjusted main spectral parameters for the use of the Standard Algorithm, a novel double sum target function (17) was developed. This function was created to be used with conjugated gradients ("starting frequencies poor").

$$\sum_{i=1}^{n} \sum_{j=1}^{i} (res_j)^2 = min$$

The result of this iteration is not exact, so the standard target function with quasi-Newton minimization is applied afterwards. The difference to the former described Gauss-Newton method is the substitution of the Hessian matrix by proper matrices to avoid the inversion procedure.

This calculation is faster than the standard method but there is no general rule, which approach (Standard or Advanced) would be the optimum to reach the cor-

rect result. Even more, there is no exact solution to predict the iterability of a given spectrum.

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