

Treatment of hydrogen atoms in XD

Synopsis

This tutorial will show how to make a multipole refinement of a molecular system containing a relatively strong hydrogen bond, in the case where neutron data have been used to find the ADPs and positions for all hydrogen atoms. It has to be noted that a successful modeling of hydrogen bonds relies on the presence of accurate information about the ADP and position of the involved hydrogen atom from some other source.

Introduction

Hydrogen bonds (HBs), and particularly the stronger of these, have been at the center of attention in much scientific research for many years for at least two reasons: *Firstly*, the possible existence of a low-barrier hydrogen bond being a key component in the action of a number of enzymes and *secondly*, to establish in more detail the nature of such interactions.

As mentioned in my lecture, an accurate experimental description of the hydrogen electron density in strong HBs can normally only be achieved when a combination of low-temperature neutron and X-ray single-crystal diffraction data are available. However, the neutron experiment requires crystal sizes of several cubic mm, which in particular severely restricts the number of feasible systems. Thus, studies of this kind has only been successfully completed a few times, and this tutorial deals with one of these,^[1] on the compound shown in Figure 1.

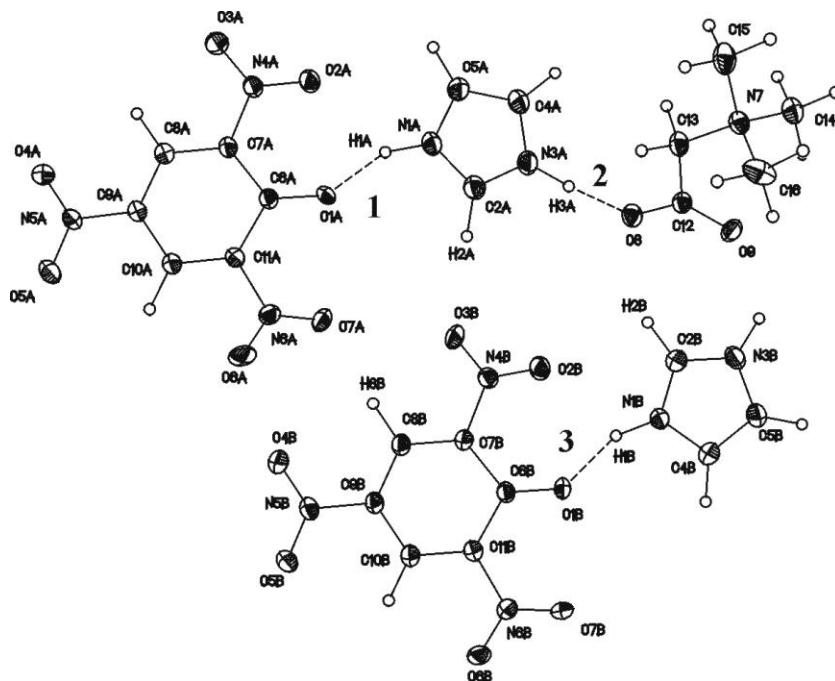


Figure 1. The asymmetric unit of the compound for this tutorial.

For weakly hydrogen bonded systems, or even for hydrogen atoms lacking any nearby acceptor atom, the lack of core electrons on the hydrogen atom still makes it difficult to establish the position and the anisotropic displacement parameters (ADPs) for it with sufficient accuracy. The position and ADPs are much easier determined using neutron diffraction. However, even in the positive case where neutron crystals are available, the resulting parameters obtained using neutrons have to be verified, and in some cases scaled to fit the X-ray data. This is done by comparing the anisotropic thermal parameters from X-ray and Neutron for the non-hydrogen atoms, for instance using the program UIJXN.^[2] If there is a systematic difference between the two sets of ADPs then a scaling also has to be applied to the ADPs for the H-atoms.

Despite its importance, the use of UIJXN is outside the scope of this tutorial, and you are welcome to contact me if you at some point need help in using this program. Below I show how the information from neutron data and the use of UIJXN was implemented in setting up XD files.

THERMAL PARAMETERS.

In the present compound (Figure 1), the comparison using UIJXN of X-ray and Neutron ADPs for data collected at 10 K gave the following result (output taken directly from UIJXN):

```

OMEAN ABSOLUTE DELTA, <|UII (X-RAY) - UII (NEUTRON)|>      =    0.000910 (799)
OMEAN RATIO OF UII VALUES, <UII (X-RAY) / UII (NEUTRON)> =      1.011 (160)
FACTOR(1,1) FACTOR(2,2) FACTOR(3,3) FACTOR(1,2) FACTOR(1,3) FACTOR(2,3)
      1.014      0.999      0.917      0.930      1.108      0.845
    
```

The numbers above shows that for this compound the neutron hydrogen ADPs have to be scaled with the given scale factors before being used for the multipole refinement against the X-ray data. The resulting scaled hydrogen ADPs have already been inserted in the input file for XD that is available for this tutorial.

HYDROGEN POSITIONS.

In addition to the thermal parameters, the H-atomic positions are also obtained from the neutron model. The provided XD.INP file has hydrogen atoms placed such that the bond distances correspond to those found from neutron data.

Cookbook for the tutorial

As mentioned in the synopsis, this tutorial will explain and show how to refine a multipole model for a molecular system containing a hydrogen bond. Many of the elements in the setup of the model are identical to those learned in the previous tutorial on non-HB systems. The following will present a step-by-step description of the process, leading to the final model. Initial XD.INP and XD.MAS files are provided to speed up the process.

The files are found in the folder *“start files/bio”*.

Notes about the structure and the files

The current local coordinate system for the atoms is constructed using four dummy atoms which each represent the midpoint of the 4 different aromatic rings. The atoms that constitute the ring systems all have their x-axes pointing towards the midpoints, while the z-axes are perpendicular to the rings.

The data (hkl-file) is a combination of data collected at the synchrotron and at a conventional diffractometer. This means there are two scale factors to be refined, which can be seen in XD.MAS that has two “1” for SCALE 11. The way that the program knows which reflections to use for scale 1 and which for scale 2 is given in the XD.HKL file, where you will see around line 8100 these two lines:

50	8	7	1	232.4805	51.6816	0.0010
-34	0	10	2	119.9900	9.4328	0.0010

The yellow numbers indicate the scale factor number, and thus this data needs to different scale factors, one for each data set.

How to complete the tutorial

Follow the bulleted list to make the final model:

- Assign a separate kappa to N(7) to give a total of 6 kappa sets.
- Choose, by looking at Figure 1 or the Structure in the WinXD interface, which atoms should be refined with non-crystallographic mirror plane. Possibly identify other non-crystallographic symmetry elements. Write this information to the master file.
- It is reasonable to a first approximation to let the methyl hydrogen atoms be identical using CHEMCON in the ATOM table. Do this now.
- Now, keep all positions and thermal parameters fixed. In XD.MAS set all multipoles you want to refine to “1”. This is most easily done using a text editor. For the non-hydrogen atoms, stop at octopoles, while for hydrogen atoms, only monopole and one dipole that points towards the nearest atom. Include one extra level of multipoles in each step, and end up with the following types of entries:

```
10 111 11111 1111111 000000000 (no non-crystallographic symmetry)
10 110 10011 0110011 000000000 (with non-crystallographic symmetry)
10 001 00000 0000000 000000000 (for hydrogen atoms)
```

For each step, check that the max and min residuals decrease using XDFFT.

- Plot the residual density map in the HB regions. That means use XDFOUR with a GRID-Slant plane with the three atoms defining each HB:
`N(3A) H(3A) O(8)`
`N(1A) H(1A) O(1A)`
`N(1B) H(1B) O(1B)`
 Do the same for the Laplacian distribution in the same planes using XDPROP. A reasonable map is 6 by 6 Å and in steps of not more than 0.1 Å, and preferably less.
- Now use the utilities program XD.RES -> XD.INP and refine ALL dipoles and quadropoles for the three hydrogen atoms in the HBs. Redo the residual density and Laplacian plots and point out changes.
- If time allows, you should try to also refine the non-H atom positions and ADPs. However, this may be quite time-consuming depending on your PC. On my laptop, 5 cycles of only multipoles takes 1-2 minutes, so it is possible to do.
- The source function has been shown to be a strong indicator of hydrogen bond strength, and so calculating this for the three bcps associated with the HBs in this compound is of interest. You can do this in the MODULE XDPROP as follows.

First you locate the BCPs by a search for critical points in the total density. To find these you have to use the following commands:

```
CPSEARCH bond O(1B) H(1B)
CPSEARCH bond O(1A) H(1A)
CPSEARCH bond O(8) H(3A)
```

Then you locate the coordinates of the BCPs in the output file from XDPROP: `xd_rho.cps` where it looks like this:

```
1 (3,-1) O(8) -H(3A) Rho 9.913625 0.897332 4.707479 0.359
```

and the global coordinates are placed in bold. These coordinates are then inserted as the reference points at which to calculate the source function in XDPROP using the TOPINT command:

```
! Local Source Function (only for rho and esp functions):
!The source point here is the HB critical points
SOURCE refpoint 5.673506 2.156185 2.299098 ! O(1A)-H(1A)
SOURCE refpoint 9.897701 0.896144 4.688383 ! O(8) -H(3A)
SOURCE refpoint 13.550304 2.847093 0.784550 ! O(1B)-H(1B)
```

The integration over the different atomic basins and their source contributions to the refoints given above is then carried out by the command:

```
TOPINT atoms all *select H(1A) N(1A) O(1A)
```

This may be preceded by the commands telling the approximate size of the basins (given in the input file already). The numbers in the list are the distances from the atoms to the nearest bcp. An example is given here:

TOPINT spheres H(8A) 0.304 H(10A) 0.305 H(1A) 0.189 H(1B) 0.182

Compare these numbers with the source contributions given in reference 1 for this and two other systems with significantly stronger HBs.

This concludes the tutorial.

Extra assignment

If you have time left, you should try to complete a multipole model of the second compound that is distributed in this tutorial, called “**benz**”, short for benzoylacetone and originally published by Madsen *et al.*^[3]

The goals that you should set for yourself with this tutorial is to reach a full multipole model including all dipoles and quadrupoles for the essential hydrogen X1 that is close to midway between the donor and acceptor atoms, while up to octopoles for the non-H atoms. Do not refine position or thermal parameters for hydrogen atoms, these are taken from neutron data.

Consider the following points as you proceed:

- Non-crystallographic symmetry for C and H atoms
- Different kappa parameters for H(X1) versus the other H-atoms

One thing that could be interesting to do when modeling is complete is to see what the residual density, without H(X1) included, looks like. This can be done by omitting this atom by deleting it from XD.MAS and XD.INP and do 0 cycles of refinement to get a new xd.fou that is used with XDFOUR.

Points of interest to analyse in the final model:

- Integrated source contributions in the H...O bcps.
- Laplacian map in the HB area.

References

- [1] J. Overgaard, B. Schiott, F. K. Larsen and B. B. Iversen, *Chem. Eur. J.* **2001**, 7, 3756-3767.
- [2] R. H. Blessing, *Acta Crystallogr. Sect. B* **1995**, 51, 816-823.
- [3] G. K. H. Madsen, B. B. Iversen, F. K. Larsen, M. Kapon, G. M. Reisner and F. H. Herbstein, *J. Am. Chem. Soc.* **1998**, 120, 10040-10045.