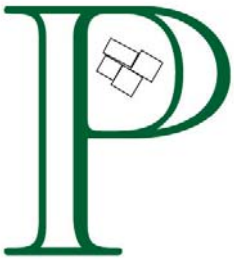
ab initio Structure Determination Using Powder Data

James A. Kaduk
Poly Crystallography Inc.
Naperville IL 60540
kaduk@polycrystallography.com



NORTH CENTRAL COLLEGE 1861

ILLINOIS INSTITUTE OF TECHNOLOGY

ICDD
INTERNATIONAL CENTRE FOR DIFFRACTION DATA

Part 4. Structure Determination

Chapters 4.1-4.10 (137 pages) in *International Tables for Crystallography Volume H: Powder Diffraction* (2019).

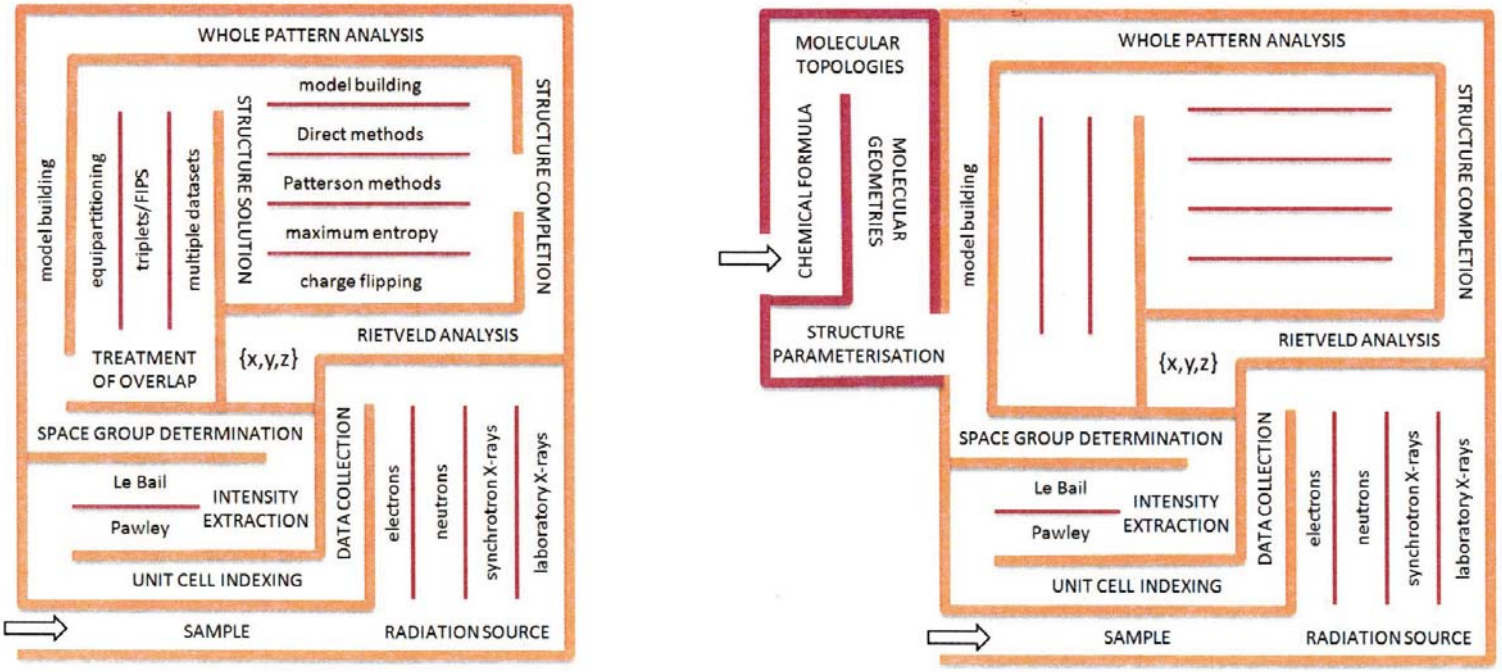


Fig. X.Z.1.1. (*a*) The maze of strategies associated with the determination of crystal structures from powder diffraction data (after Baerlocher & McCusker, 2002) and (*b*) the modified "global optimisation" maze showing the double start point and simplification of the principal maze.

W. I. F. David, Chapter 4.3 (4.3.1), Real space methods for structure solution from powder diffraction data: applications to molecular structures, *Volume H*.

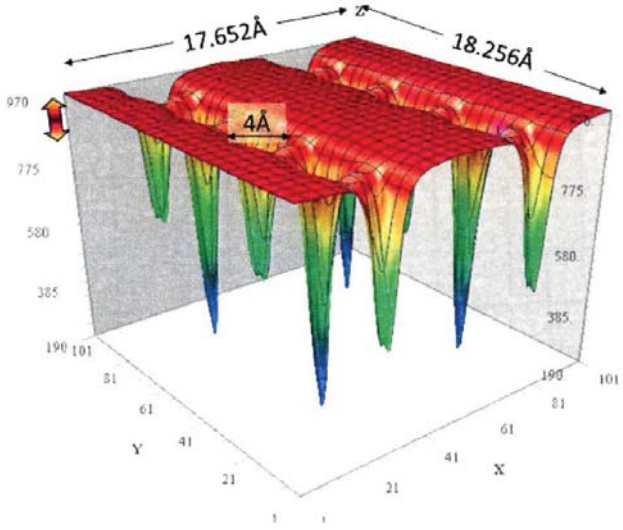


Fig. X.Z.4.4. 2D section of the χ^2_{CI} hypersurface showing the variation in χ^2_{CI} as function of x and z translations.

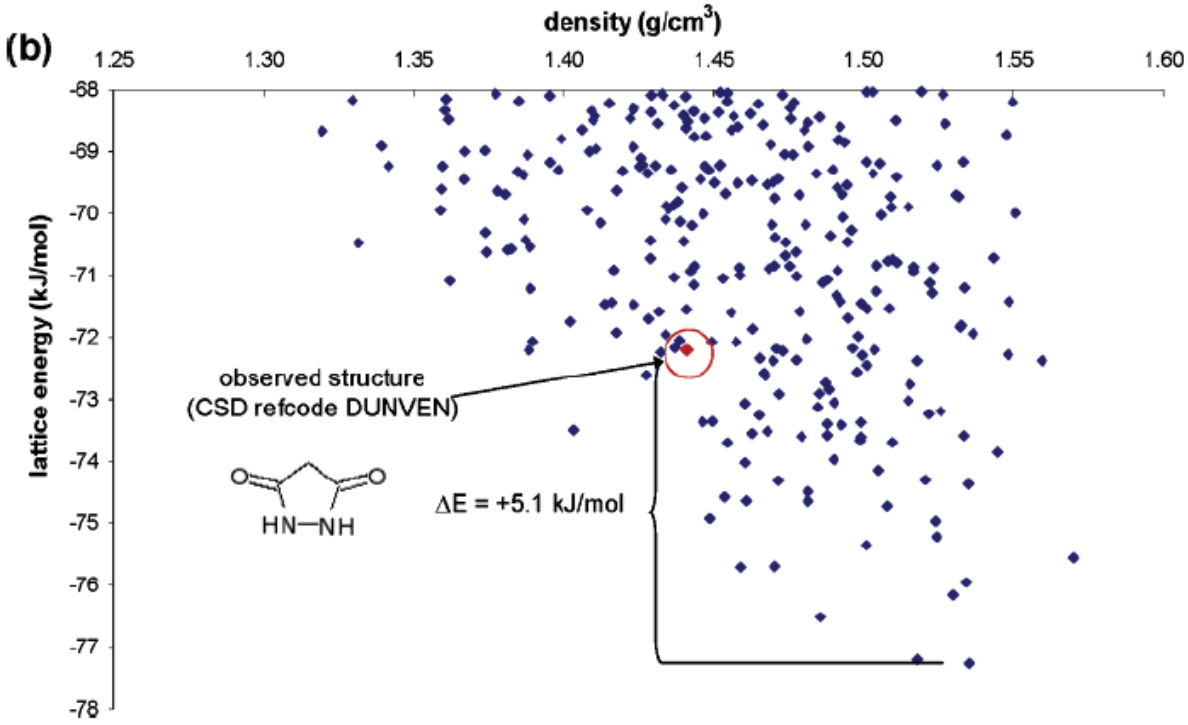


Figure 2. Predicted structures of (a) bicyclo(3.3.1)nonane-2,6-dione and (b) 3,5-pyrazolidinedione.

G. M. Day, J. Chisolm, N. Shan, W. D. S. Motherwell, and W. Jones, *Cryst. Growth Des.*, **4**, 1327-1340 (2004). (Special Issue on crystal structure prediction)

ab initio Structure Determination

- Don't – find an analog
- Reciprocal space methods
- Real space methods

  grid search, Monte Carlo, simulated annealing, genetic algorithms, parallel tempering, particle swarm optimization
- Monte Carlo Simulated Annealing (real and reciprocal space = hybrid)
- Stealth and guile
- Microcrystals (convert powder problem to single crystal) – polycrystals?

Reciprocal Space Methods

Solving Crystal Structures – Reciprocal Space Methods, A. Altomare, C. Cuocci, A. Moliterni, and R. Rizzi, Chapter 4.2 in *International Tables for Crystallography Volume H: Powder Diffraction* (2019).

Reciprocal Space Methods

- Patterson methods

  (really direct methods, but uses some Patterson ideas)

  XLENS; J. Rius, "Patterson-function direct methods for structure determination of organic compounds from powder data. XVI", *Acta Cryst. Sect. A: Found. Crystallog.*, **67**(1), 63-67 (2011)

  EXPO2014 has Patterson functionality
- Maximum entropy methods

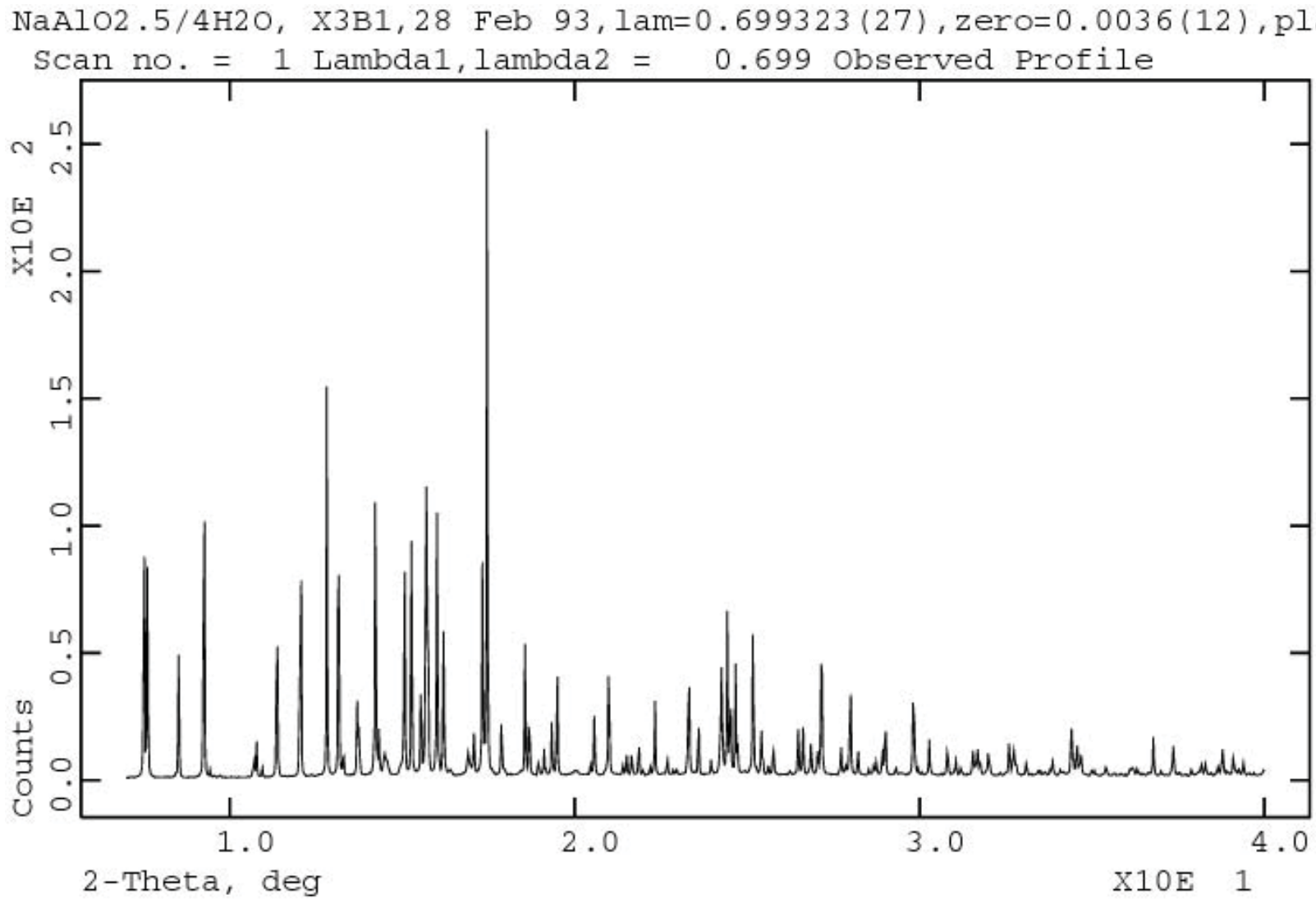
  MICE; C. Gilmore, W. Dong, & G. Bricogne, "A multisolution method of phase determination by combined maximization of entropy and likelihood. VI. The use of error-correcting codes as a source of phase permutation and their application to the phase problem in powder, electron and macromolecular crystallography", *Acta Cryst. Sect. A: Found. Crystallogr.*, **55**, 70-83 (1999)
- **Direct methods**

  Giacovazzo, C. *Phasing in Crystallography*. IUCr/Oxford University Press (2015)
- **Charge flipping**

Direct Methods

$NaAlO_2 \cdot 5/4H_2O$

- commercial "$NaAlO_2 \cdot xH_2O$"
- an important industrial chemical

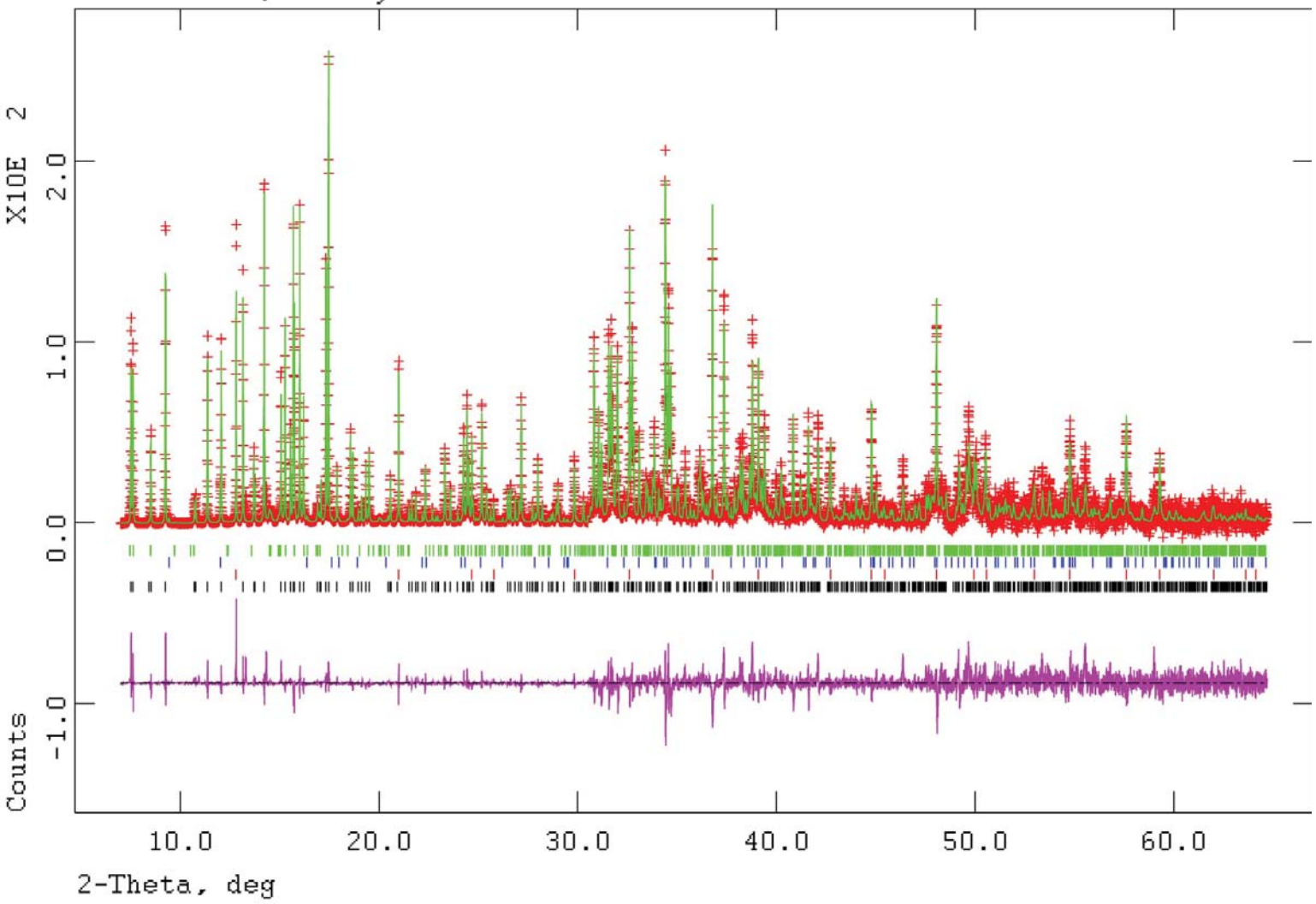

NaAlO2.5/4H2O, X3B1,28 Feb 93,lam=0.699323(27),zero=0.0036(12),pla
Scan no. = 1 Lambda1,lambda2 = 0.699 Observed Profile
X10E 2
Counts
0.0
0.5
1.0
1.5
2.0
2.5
1.0
2.0
3.0
4.0
2-Theta, deg
X10E 1
27-APR-01 14:12:37

Sodium Aluminate

- Commercial $NaAlO_2 \cdot xH_2O$
- TGA: $x = 1.25$
- ^{27}Al MASNMR: 2 T_d Al (1 is impurity)
- *P*-tetragonal, $a = 10.534$, $c = 5.336$ Å
- $P\bar{4}2_1m$ or $P42_12$
- Density: cell contains $Na_8Al_8H_{20}O_{26}$

Sodium Aluminate

- Le Bail extraction, $7 < 2\theta < 50°$
- 357 structure factors ($d > 0.83$ Å)
- Try both $\boldsymbol{P\bar{4}2_1m}$ and $P42_12$
- SHELX direct methods – Al in E-map
- LS/ΔF – 2 O (add others), Na, water O
- Manually place 2 of 3 H



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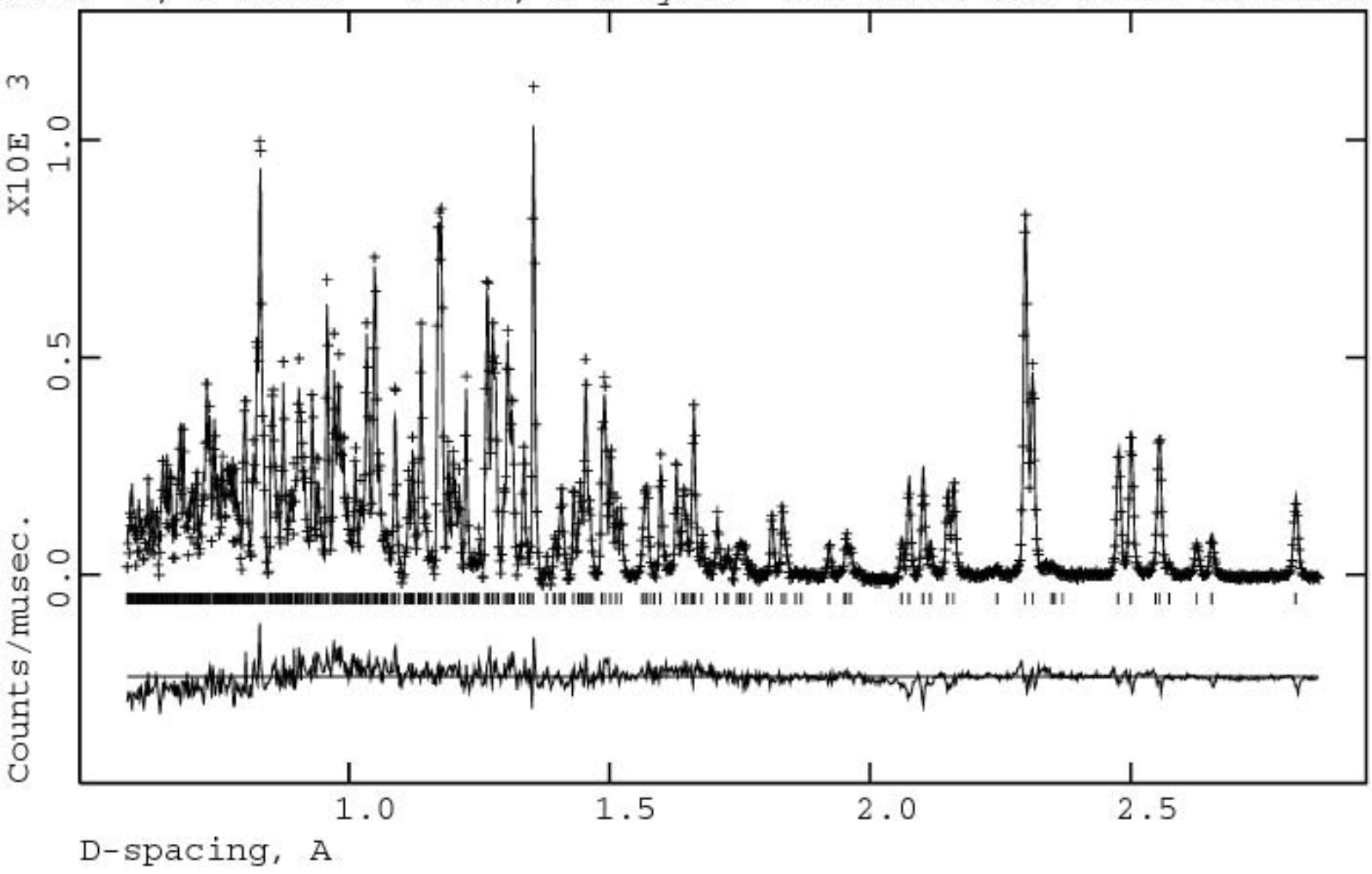
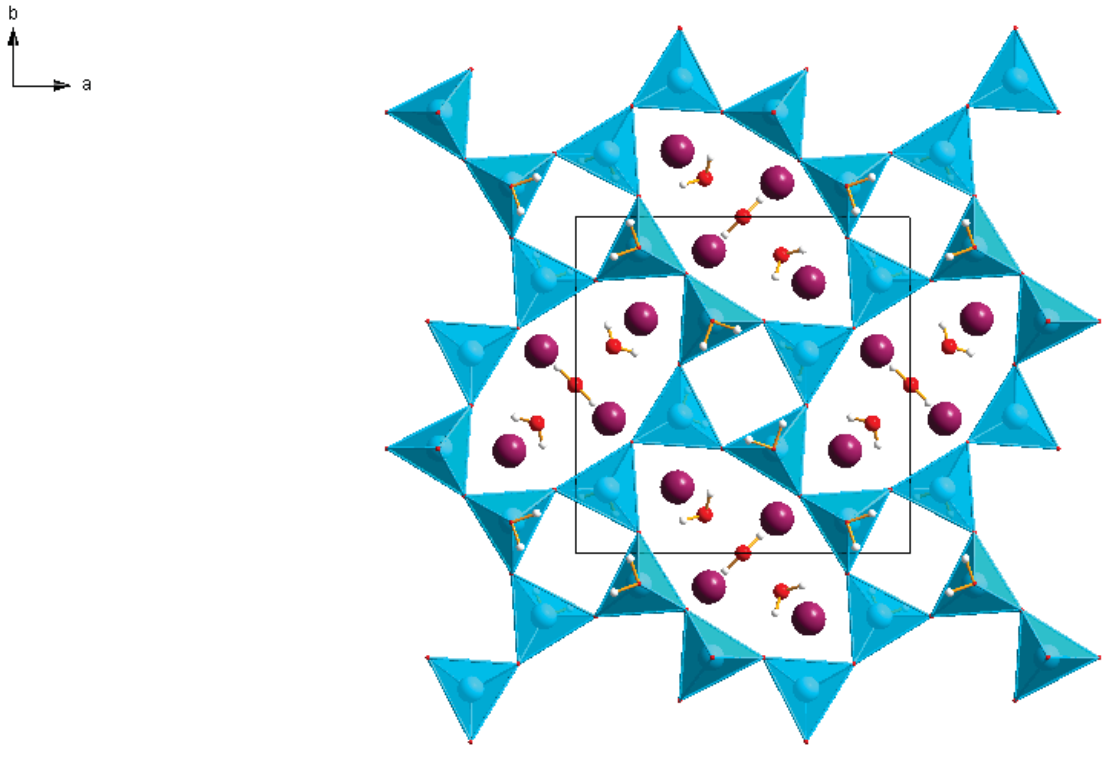
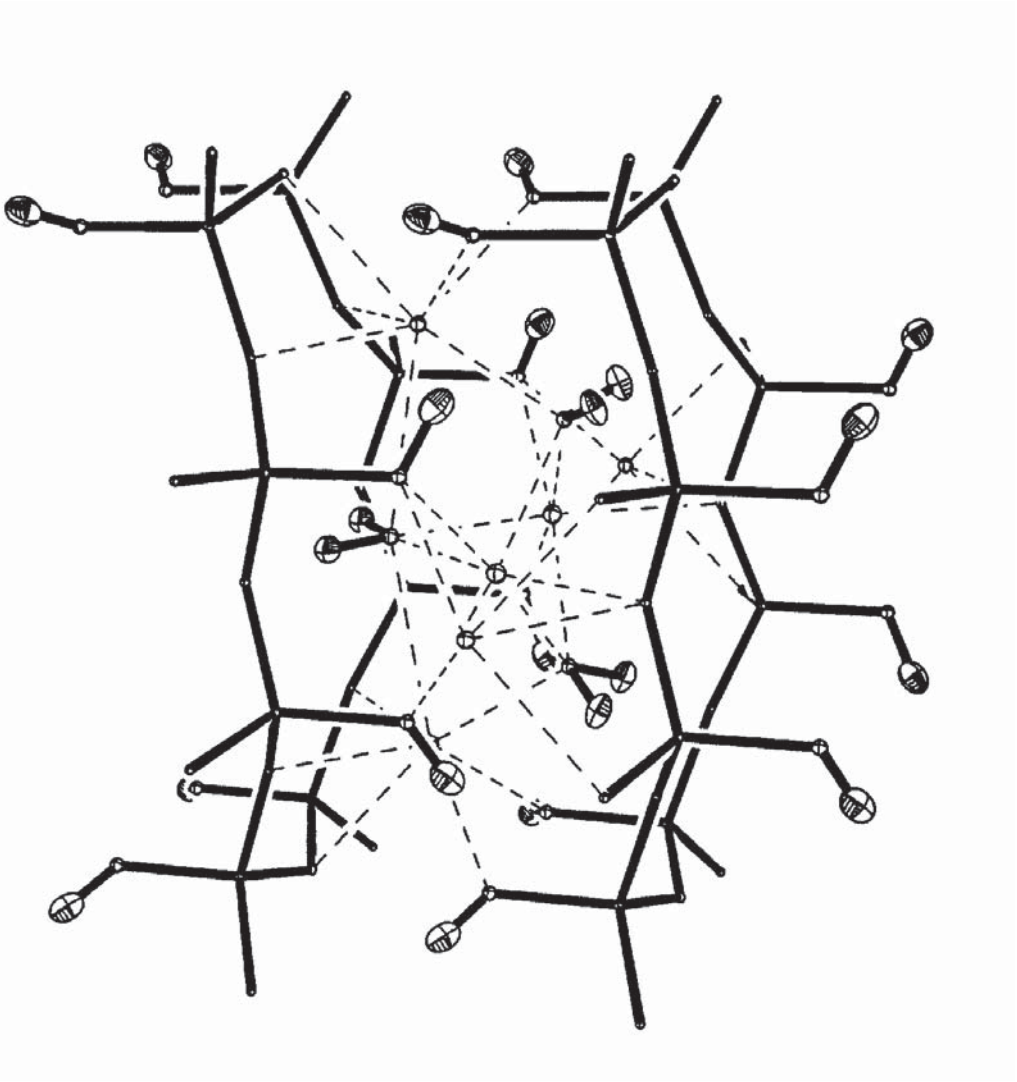

18950-78-1 NaAlO2 . 5/4 D2O, GPPD6981, 20K, 18 May 95
Bank 1, 2-Theta 148.0, L-S cycle 191 Obsd. and Diff. Profiles
X10E 3
1.0
0.5
0.0
Counts/musec.
1.0
1.5
2.0
2.5
D-spacing, A
20-MAY-95 10:49:57



20K



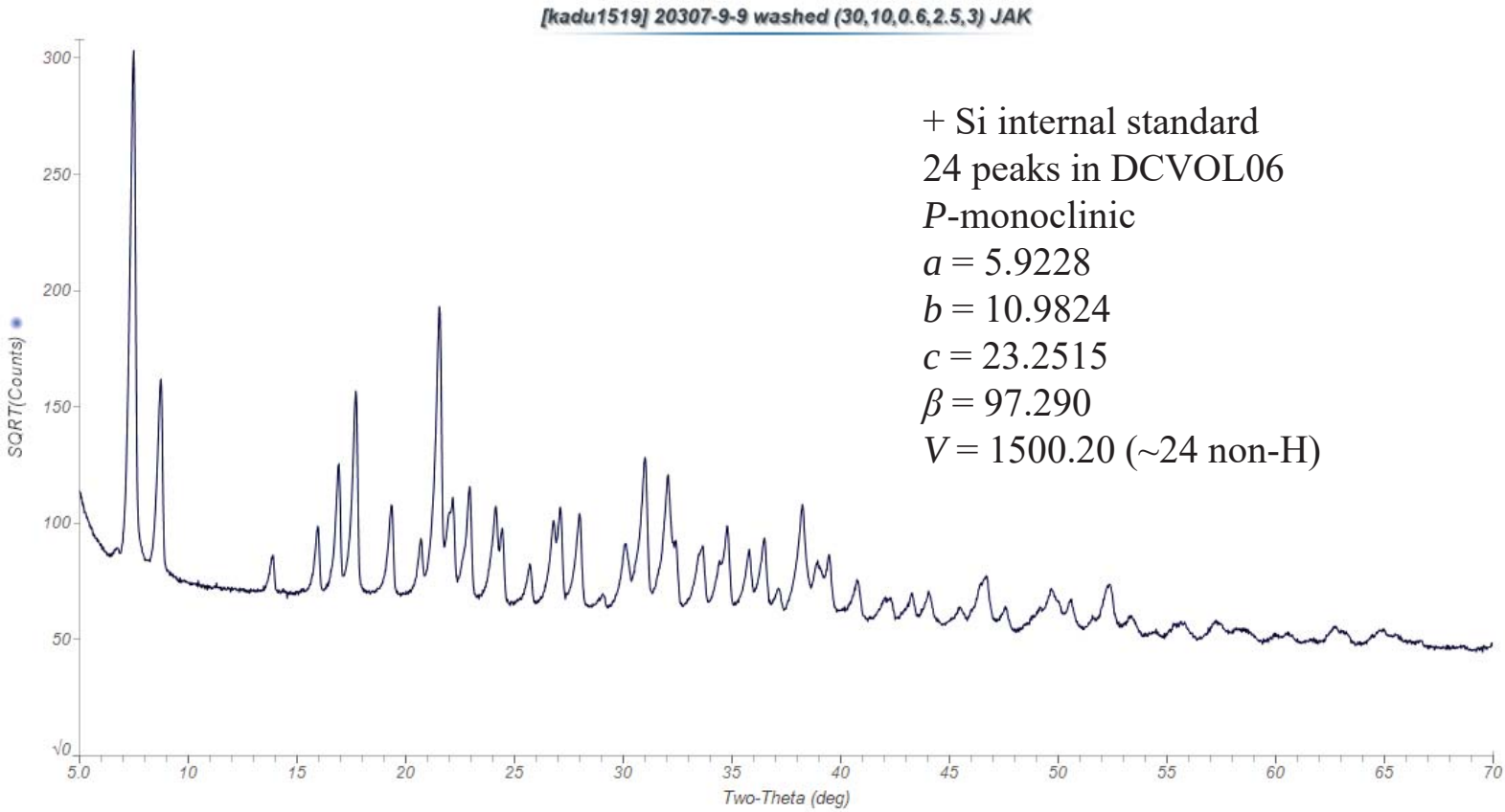
"The Crystal Structure of Hydrated Sodium Aluminate, $NaAlO_2 \cdot 5/4H_2O$, and Its Dehydration Product", J.A. Kaduk and S. Pei, *J. Solid State Chem.*, **115**, 126-139 (1995)

EXPO2014
http://www.ic.cnr.it

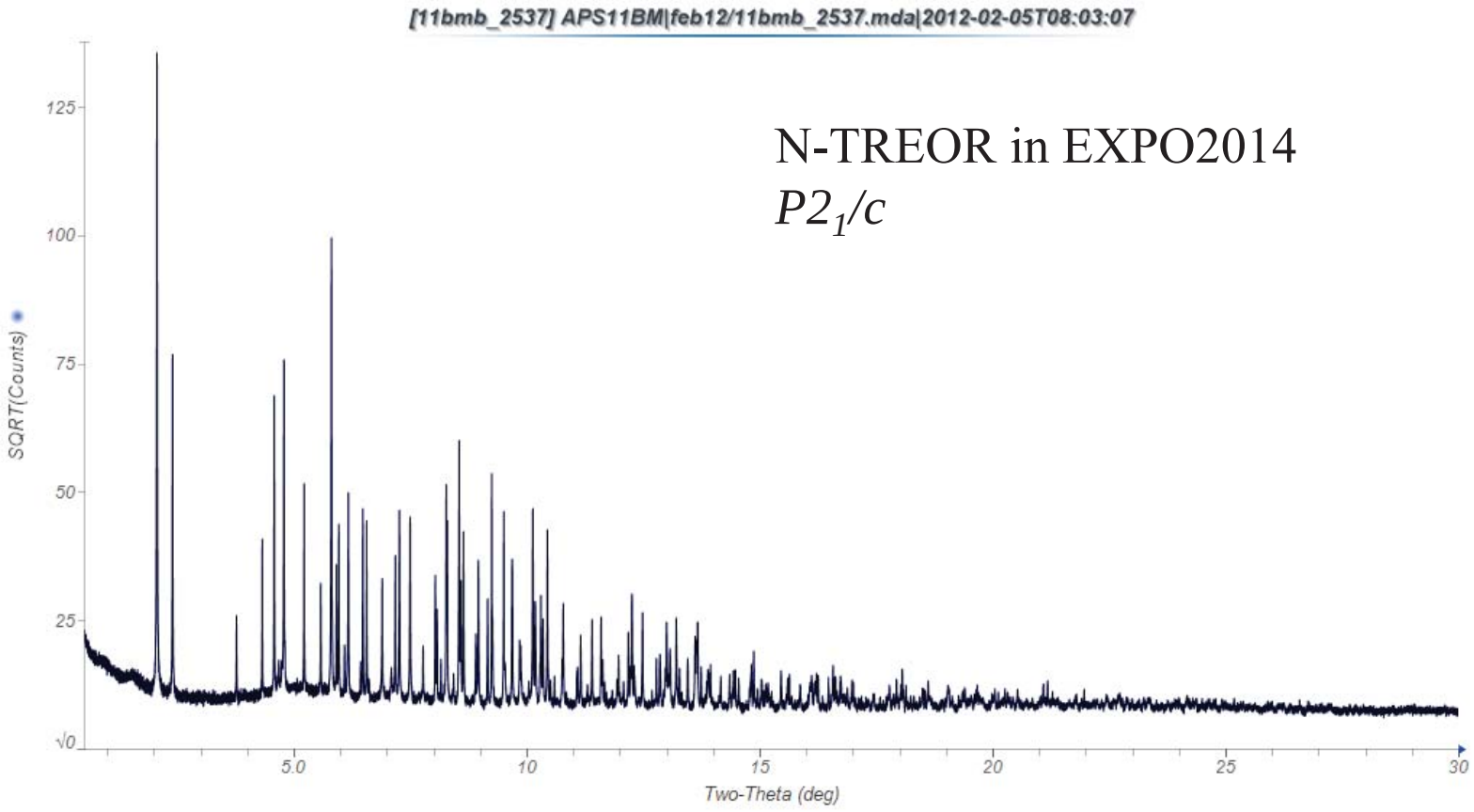
A. Altomare, N. Corriero, C. Cuocci,
A. Falcicchio, A. Moliterni, and R. Rizzi,
"EXPO software for solving crystal structures by powder diffraction data: methods and application", *Cryst. Res. Technol.*, 1-6 (2015)

$Mg(H_2C_6H_5O_7)_2$
bis(dihydrogencitrato)magnesium

The last phase to crystallize when evaporating the Ca/Mg citrate solution left from cleaning a home water still

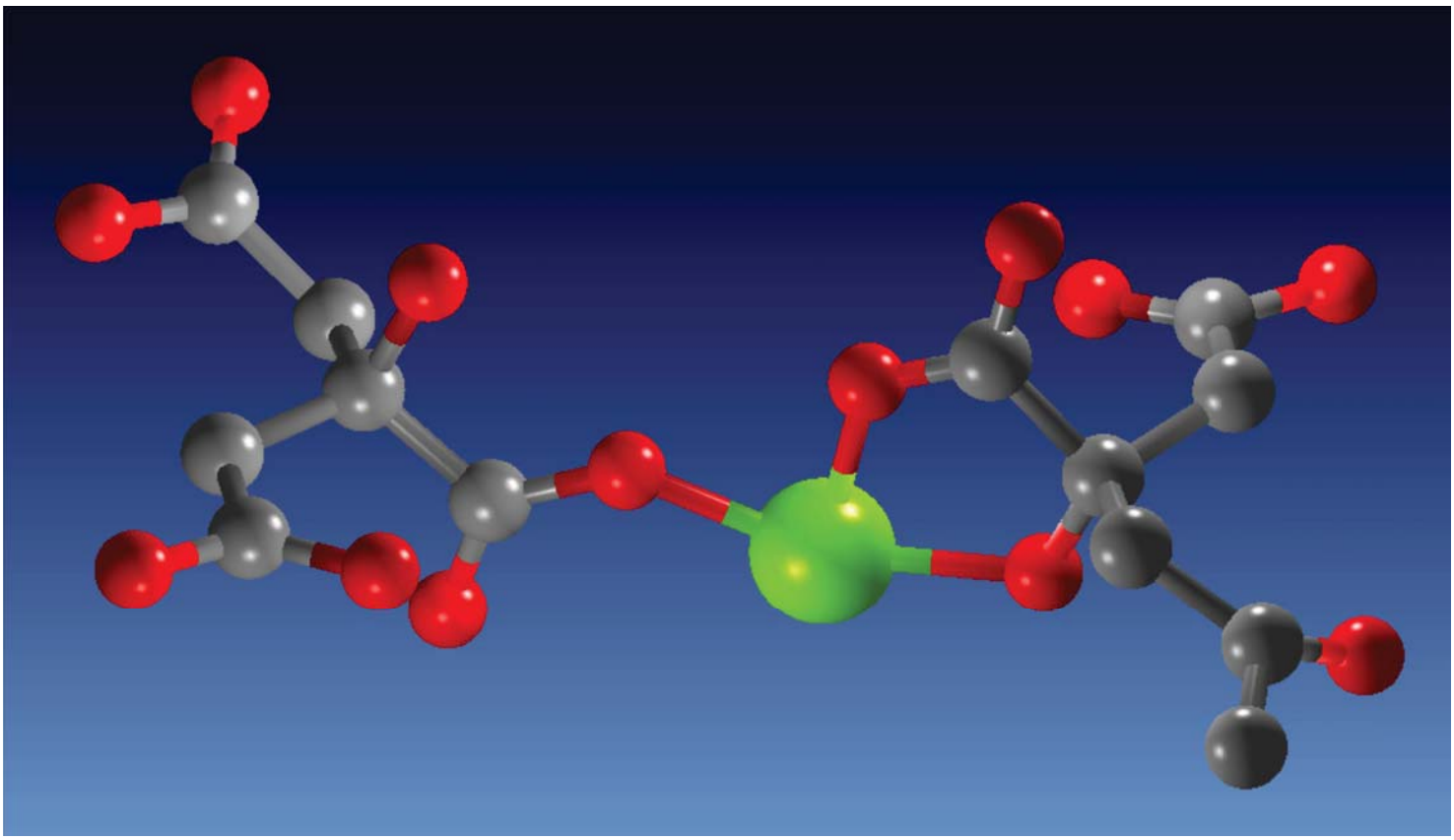


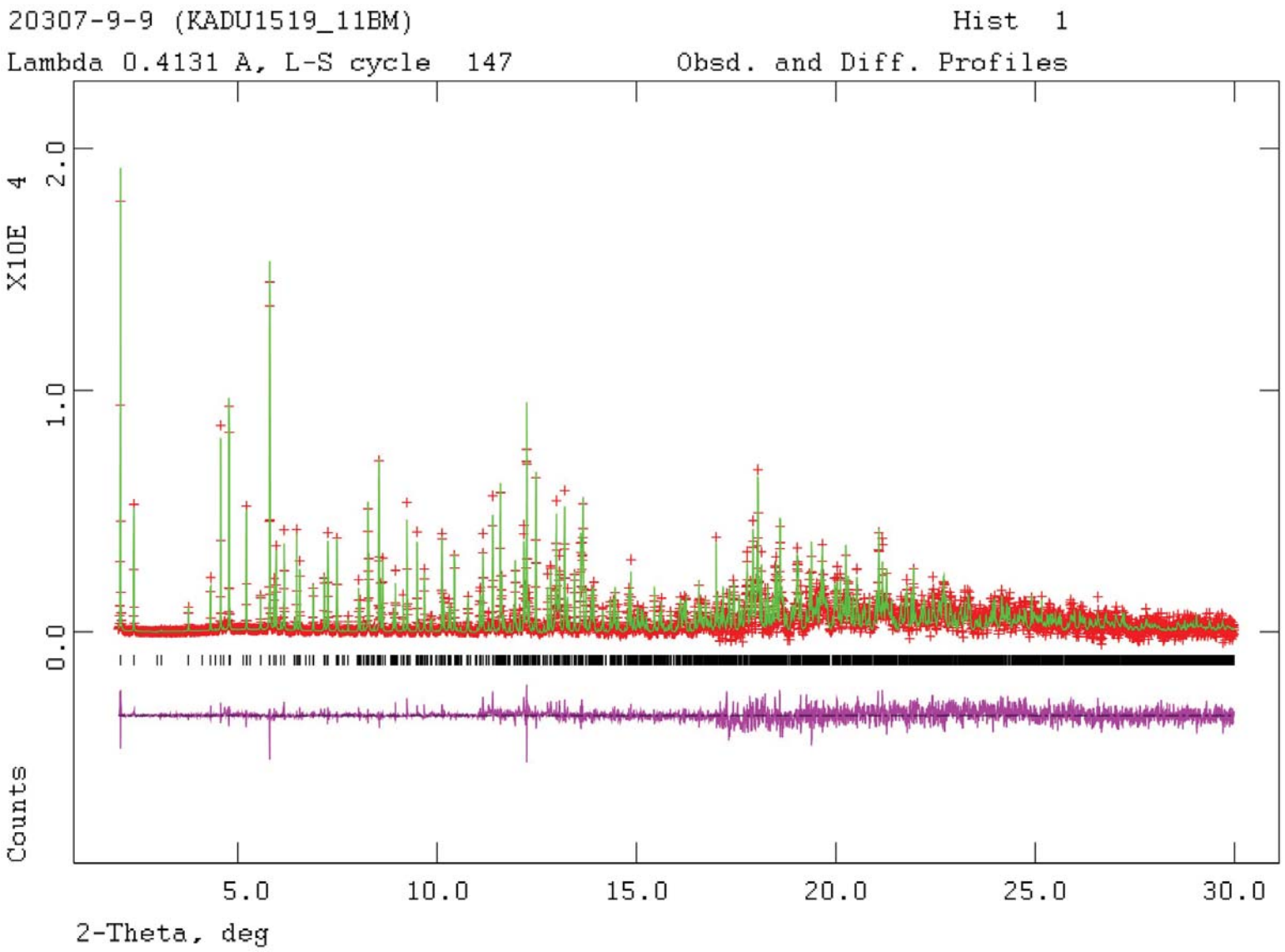
+ Si internal standard
24 peaks in DCVOL06
P-monoclinic
$a = 5.9228$
$b = 10.9824$
$c = 23.2515$
$\beta = 97.290$
$V = 1500.20$ (~24 non-H)



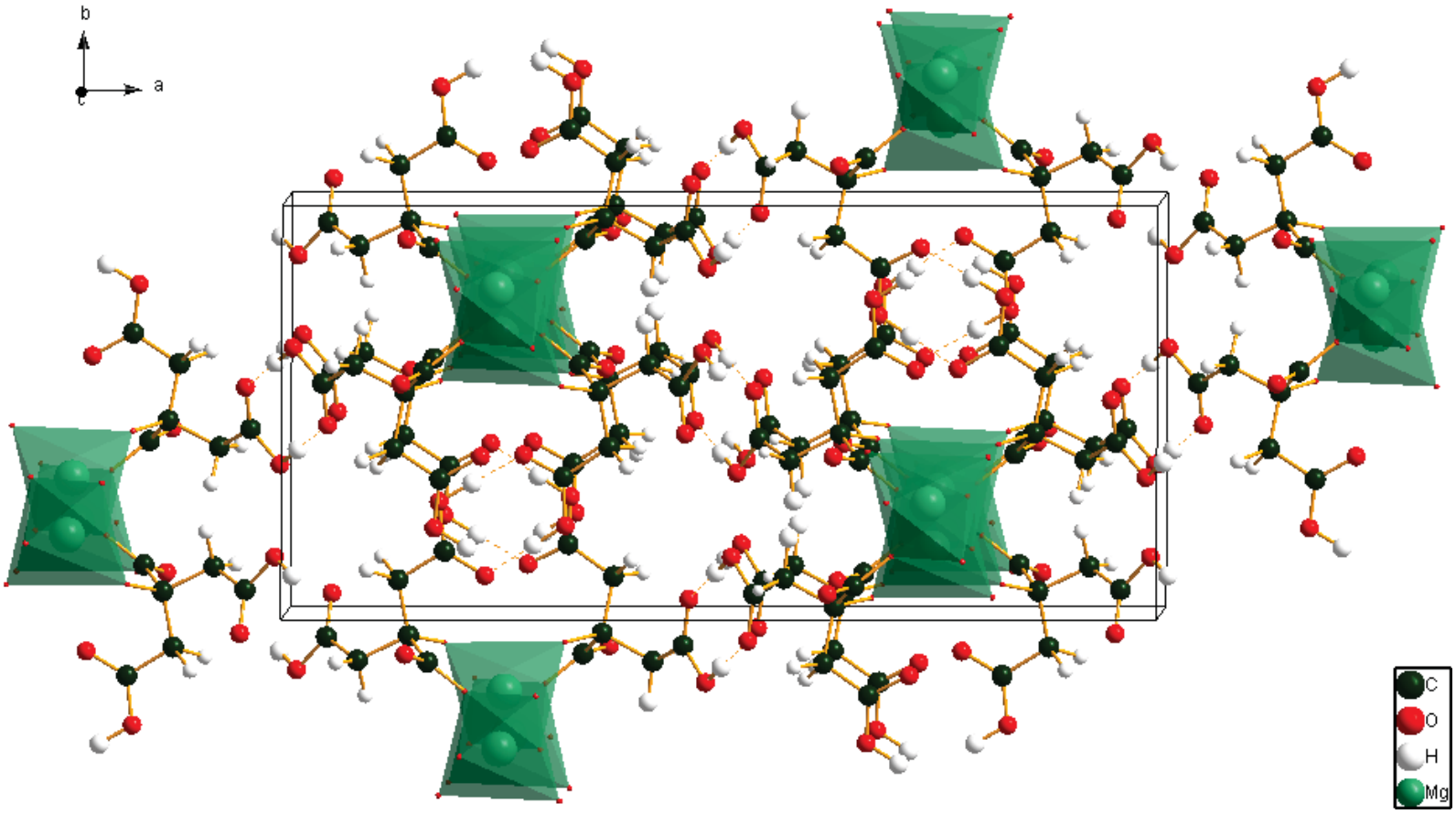
N-TREOR in EXPO2014

$P2_1/c$





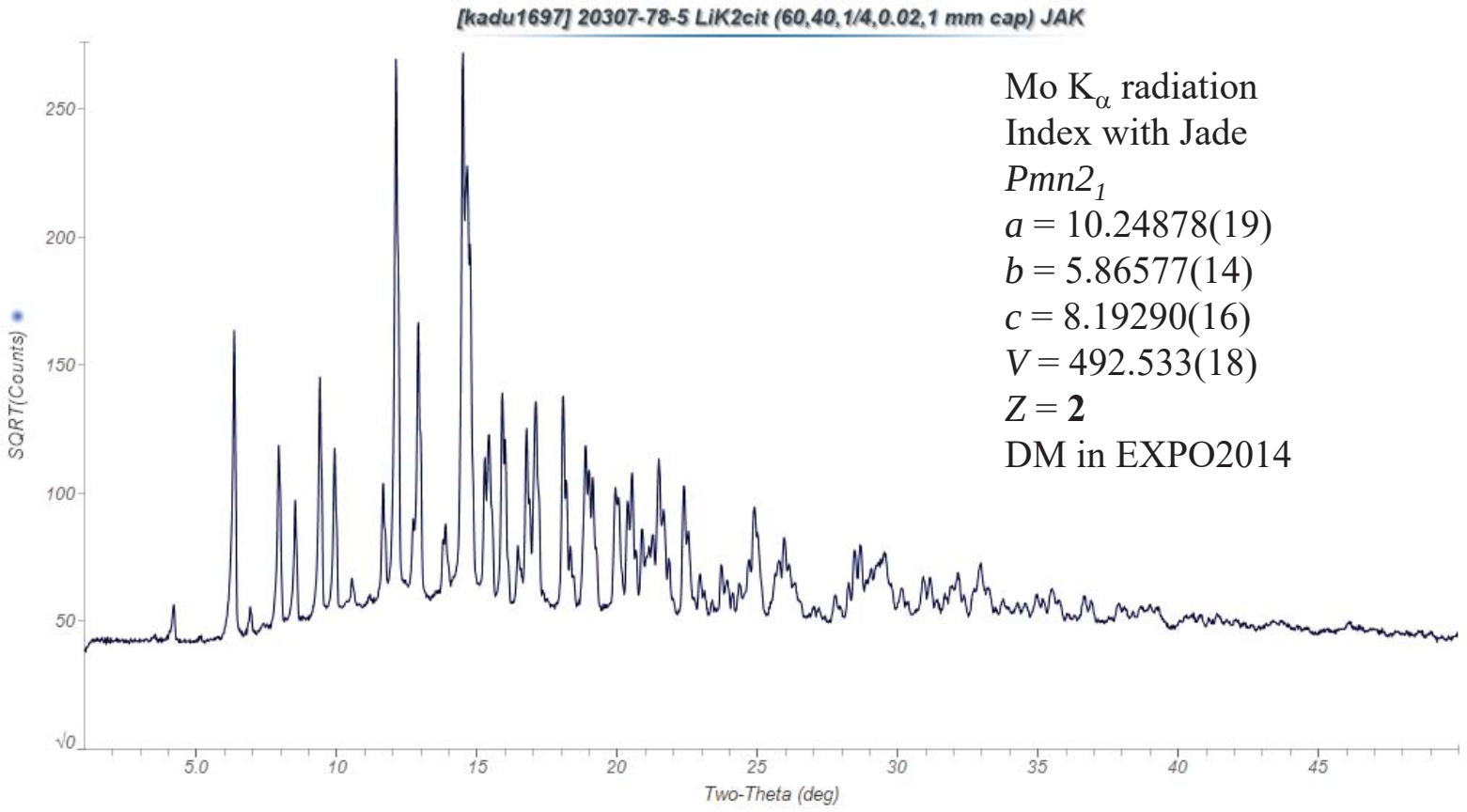
Scaling: 3.0(2.0X) 11.0(10.0X) 17.0(40.0X)


b
a
c
C
O
H
Mg

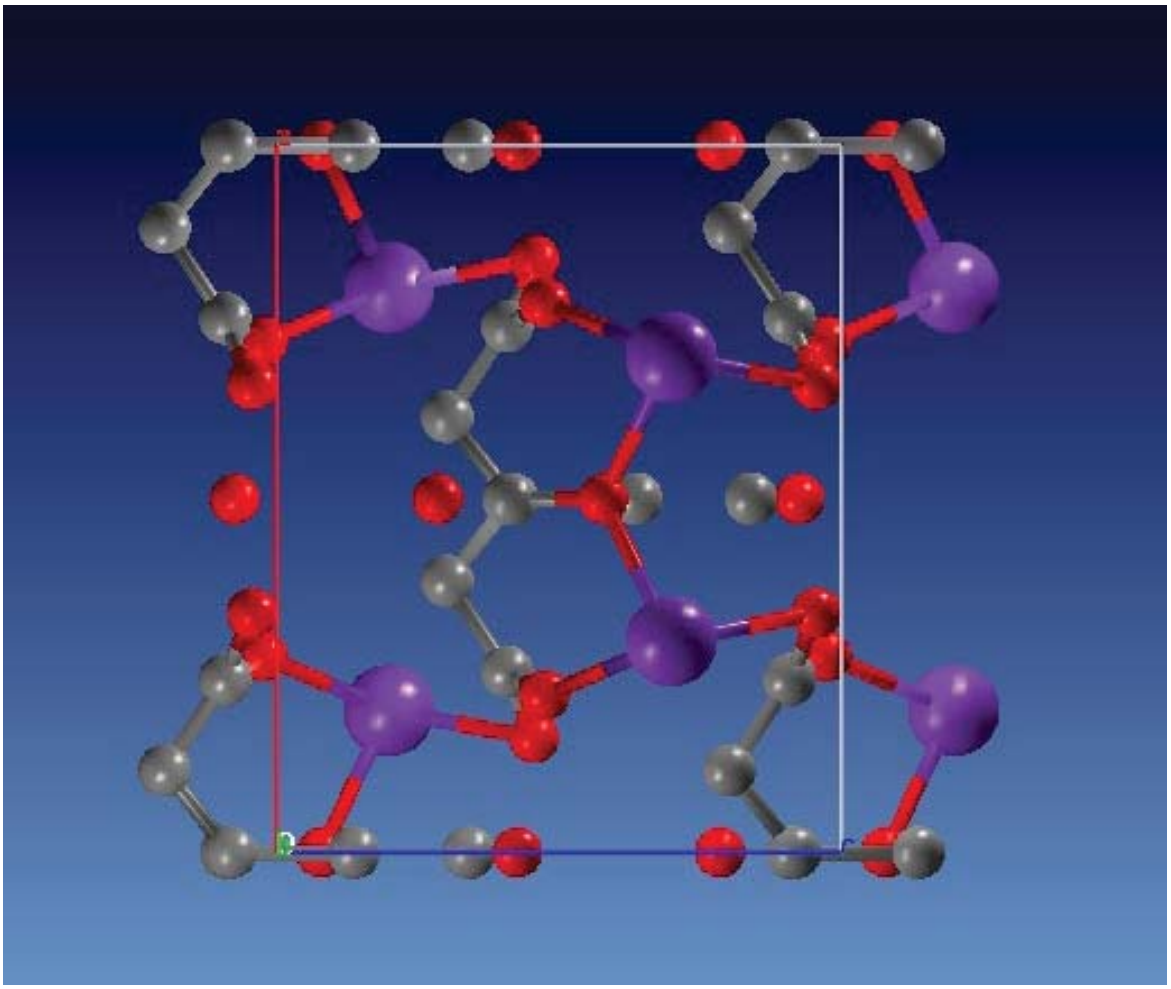
“Crystal structures of two magnesium citrates from powder diffraction data”, J. A. Kaduk, *Acta Cryst. E***76**, 1611-1616 (2020).

$LiK_2C_6H_5O_7(H_2O)$

Andy Cigler
North Central College



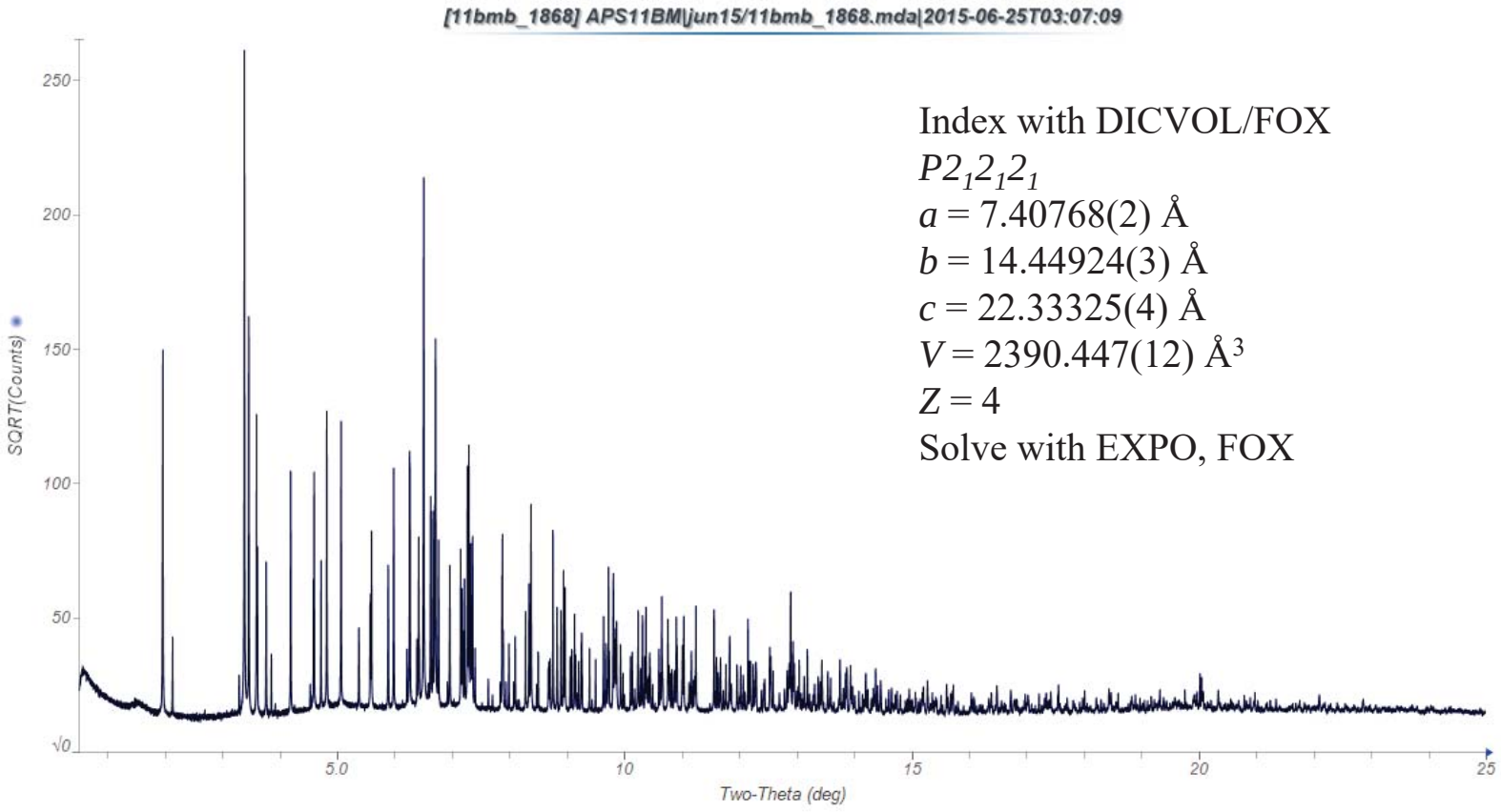
Mo K_α radiation
Index with Jade
Pmn2$_1$
a = 10.24878(19)
b = 5.86577(14)
c = 8.19290(16)
V = 492.533(18)
Z = **2**
DM in EXPO2014



Crystal structure of minocycline hydrochloride dihydrate, $C_{23}H_{28}N_3O_7Cl(H_2O)_2$

Minocin® and Dynacin®

broad-spectrum tetracycline antibiotic



Index with DICVOL/FOX

$P2_12_12_1$

a = 7.40768(2) Å

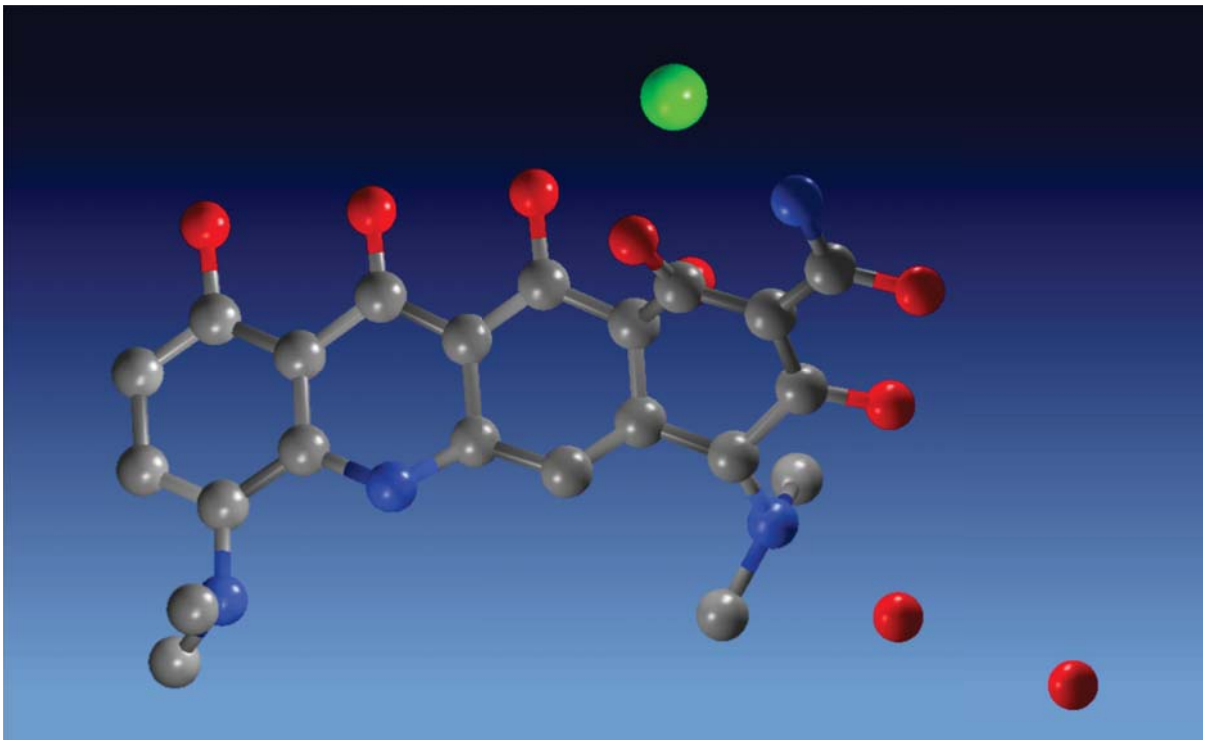
b = 14.44924(3) Å

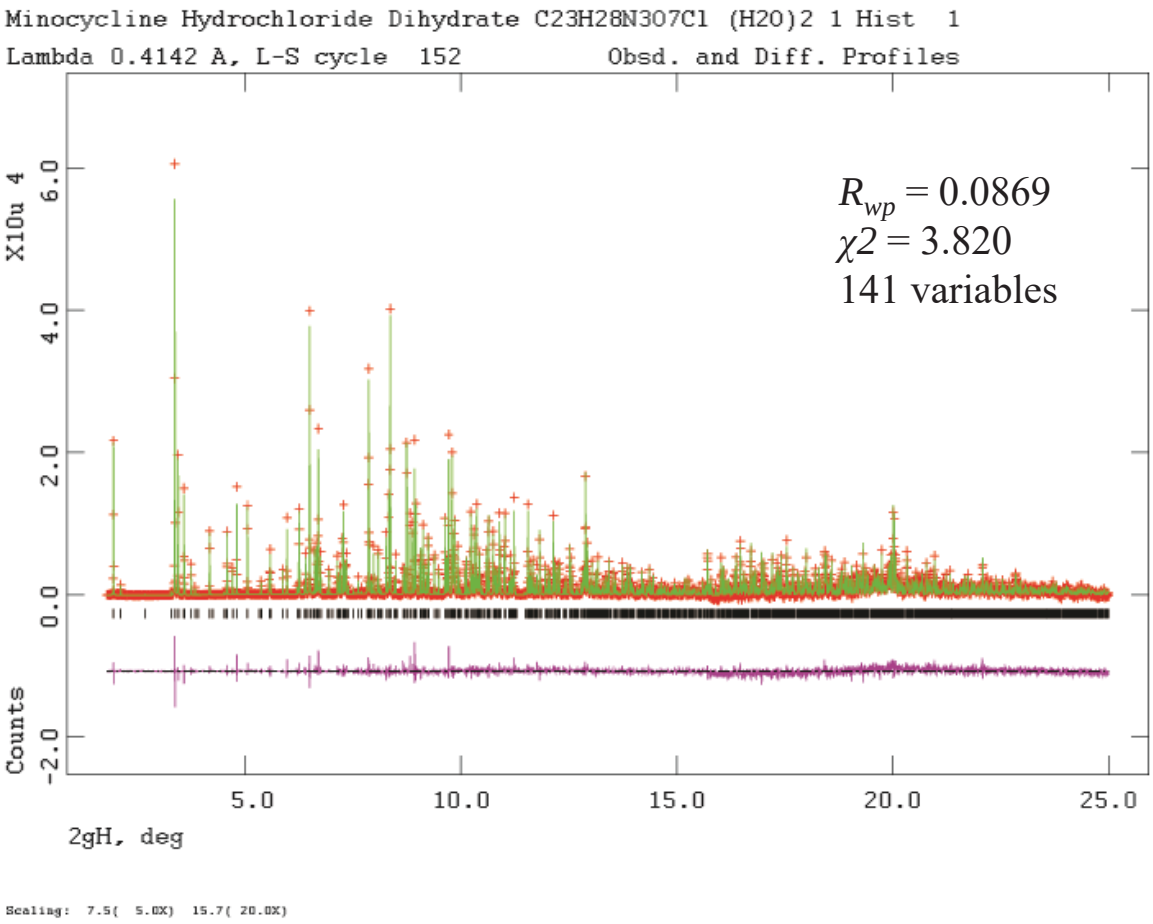
c = 22.33325(4) Å

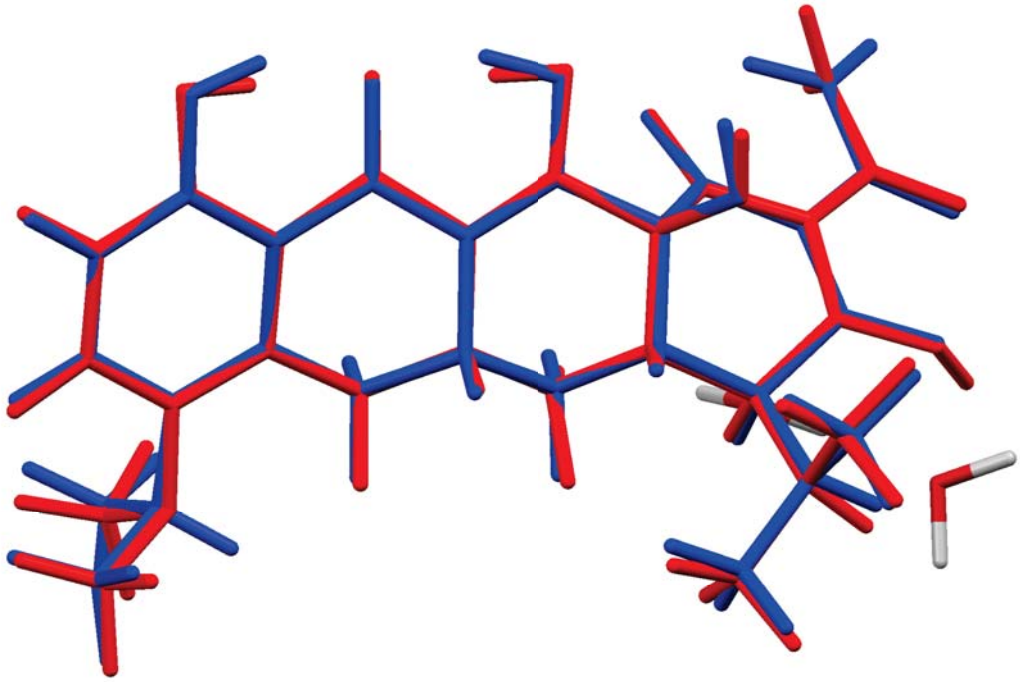
V = 2390.447(12) Å^3

Z = 4

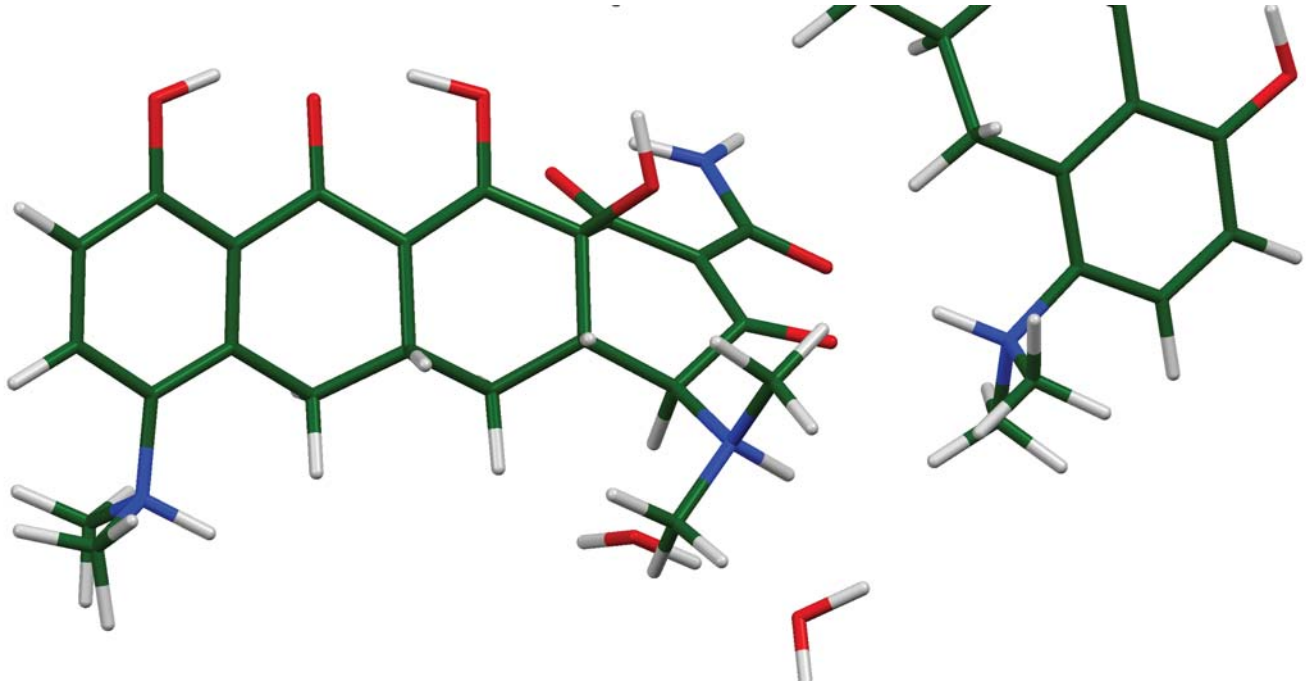
Solve with EXPO, FOX

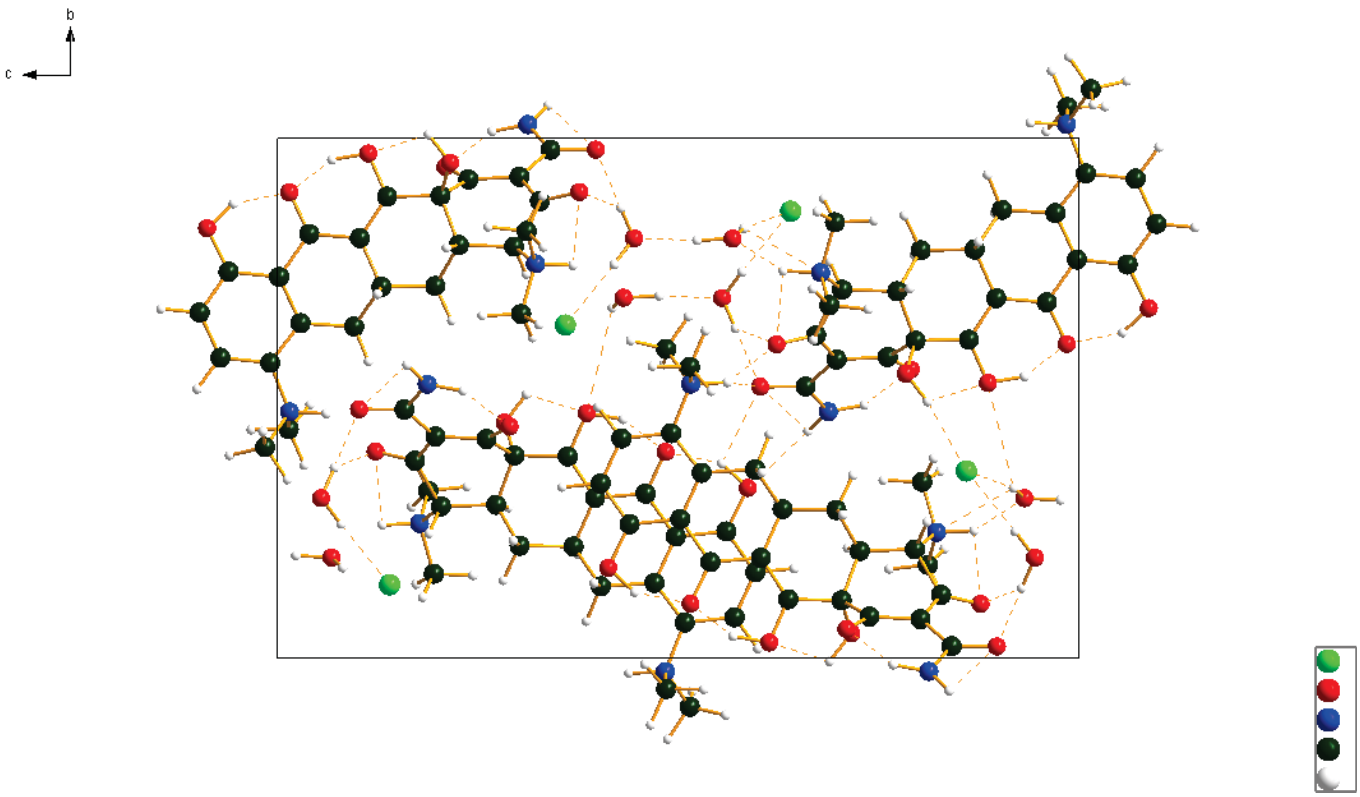



Minocycline Hydrochloride Dihydrate C23H28N3O7Cl (H2O)2 1 Hist 1
Lambda 0.4142 A, L-S cycle 152
Obsd. and Diff. Profiles
R_{wp} = 0.0869
$\chi 2$ = 3.820
141 variables
X10u 4
6.0
4.0
2.0
0.0
-2.0
Counts
5.0
10.0
15.0
20.0
25.0
2gH, deg
Scaling: 7.5(5.0X) 15.7(20.0X)



RMS Cartesian displacement = 0.094 Å




b
c

Charge Flipping

Charge Flipping References

G. Oszlányi and A. Sűtó, "The charge flipping algorithm", *Acta Cryst. A: Found. Crystallogr.*, **64**, 123-134 (2008).

A.A. Coelho, "A charge-flipping algorithm incorporating the tangent formula For solving difficult structures", *Acta Cryst. A: Found. Crystallogr.*, **63**, 400-406 (2007).

L. Palatinus and G. Chapuis, *SUPERFLIP* – a computer program for the solution of crystal structures by charge flipping in arbitrary dimensions", *J. Applied Crystallogr.*, **40**, 786-790 (2007).

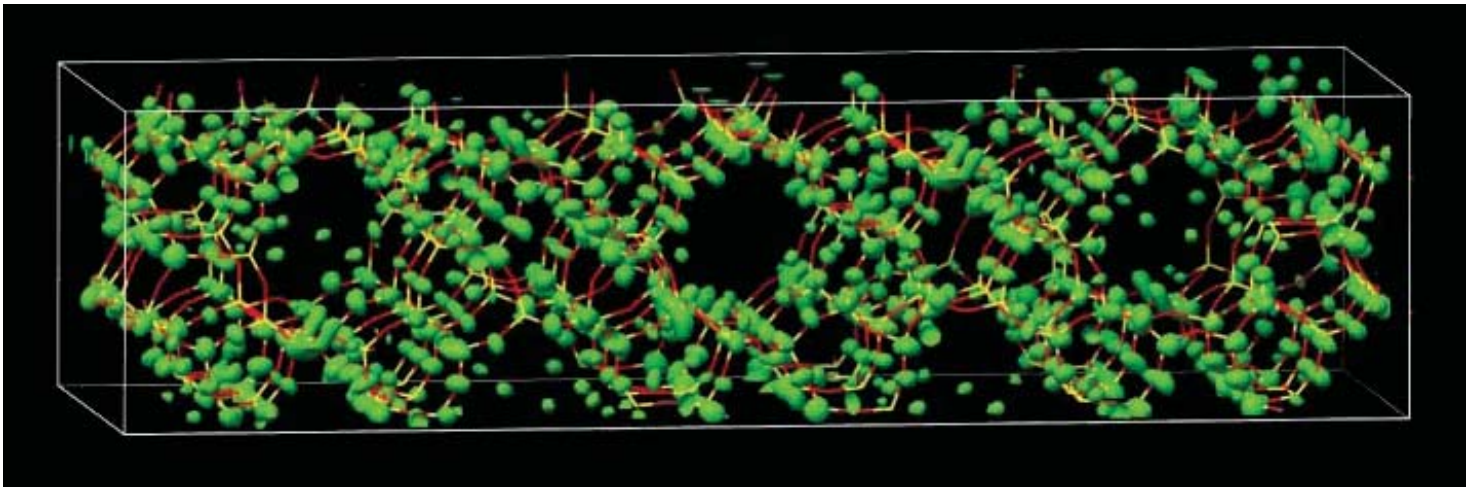
H. Gies, "Charge Flipping and Beyond", *Science*, **315**, 1087-1088 (2007).

C. Baerlocher, F. Gramm, L. Massűger, L. B. McCusker, Z. He, S. Hovmöller, and X. Zou, "Structure of the Polycrystalline Zeolite Catalyst IM-5 Solved by Enhanced Charge Flipping", *Science*, **315**, 1113-1116 (2007).

Jana2006
http://jana.fzu.cz

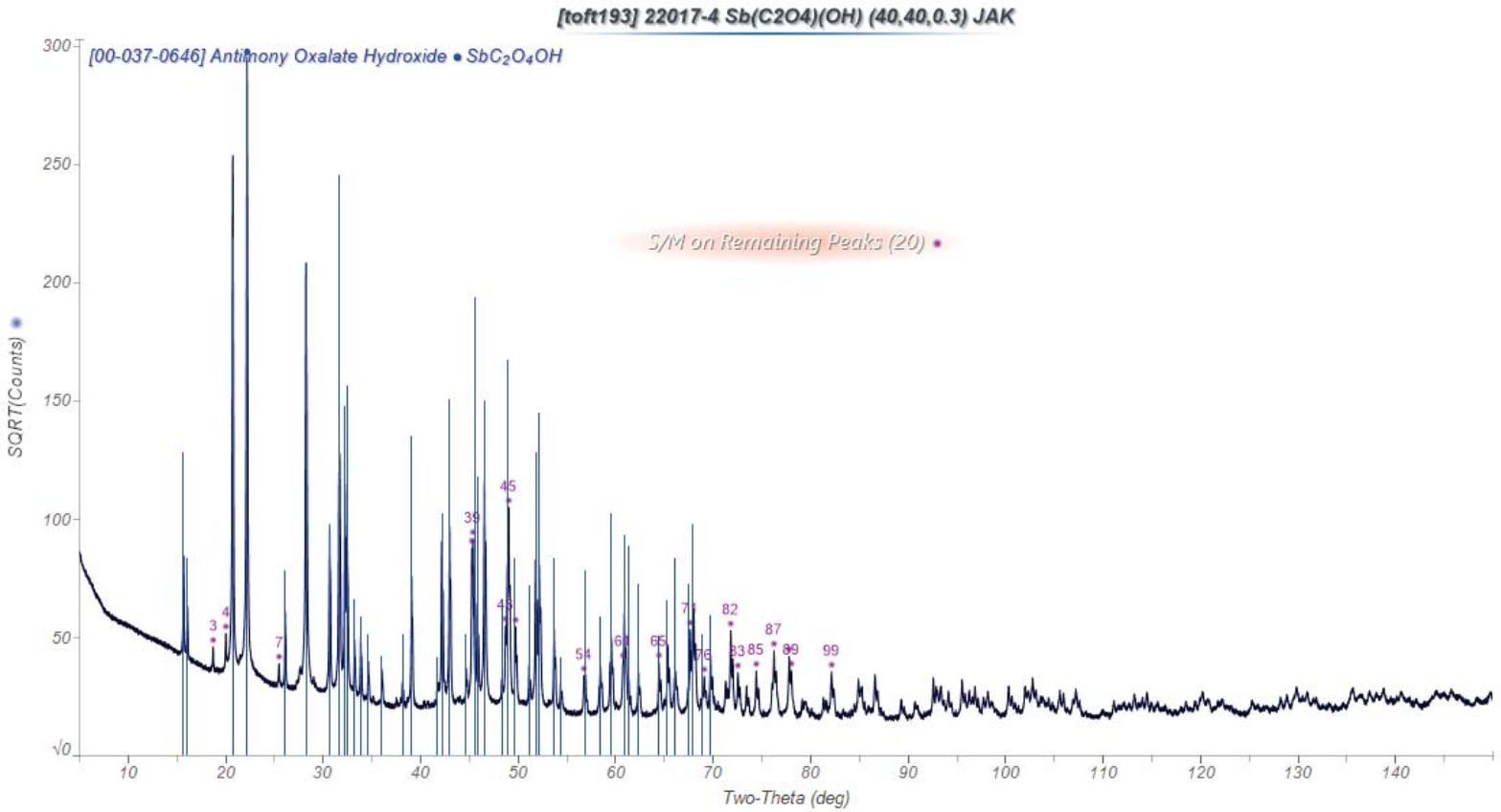
V. Petricek, M. Dusek, and L. Palatinus, L., *Z. Kristallogr.* **229**(5), 345-352 (2014). DOI 10.1515/zkri-2014-173

Electron Density of IM-5



$Sb(C_2O_4)OH$

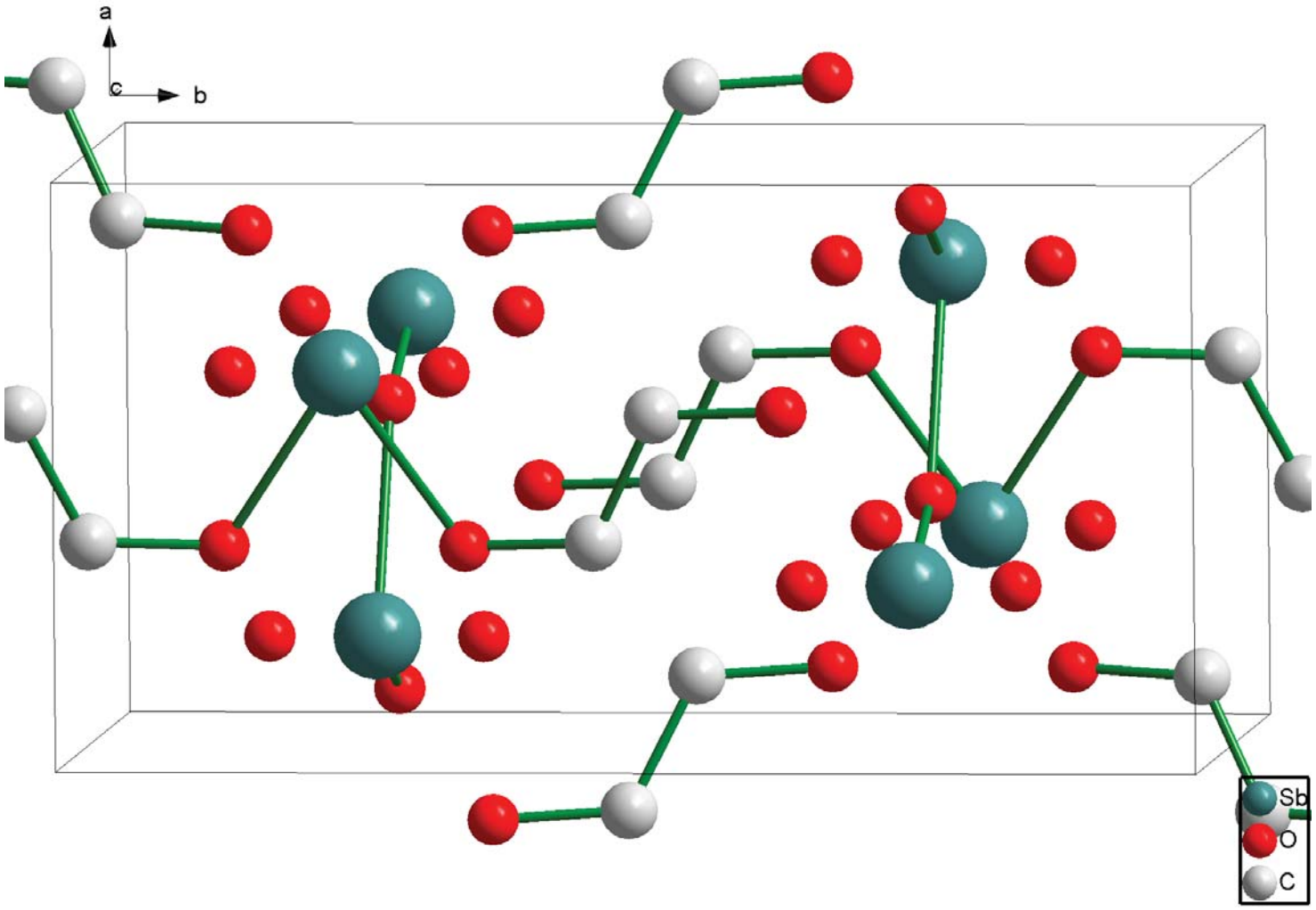
A potential stoichiometric Sb source

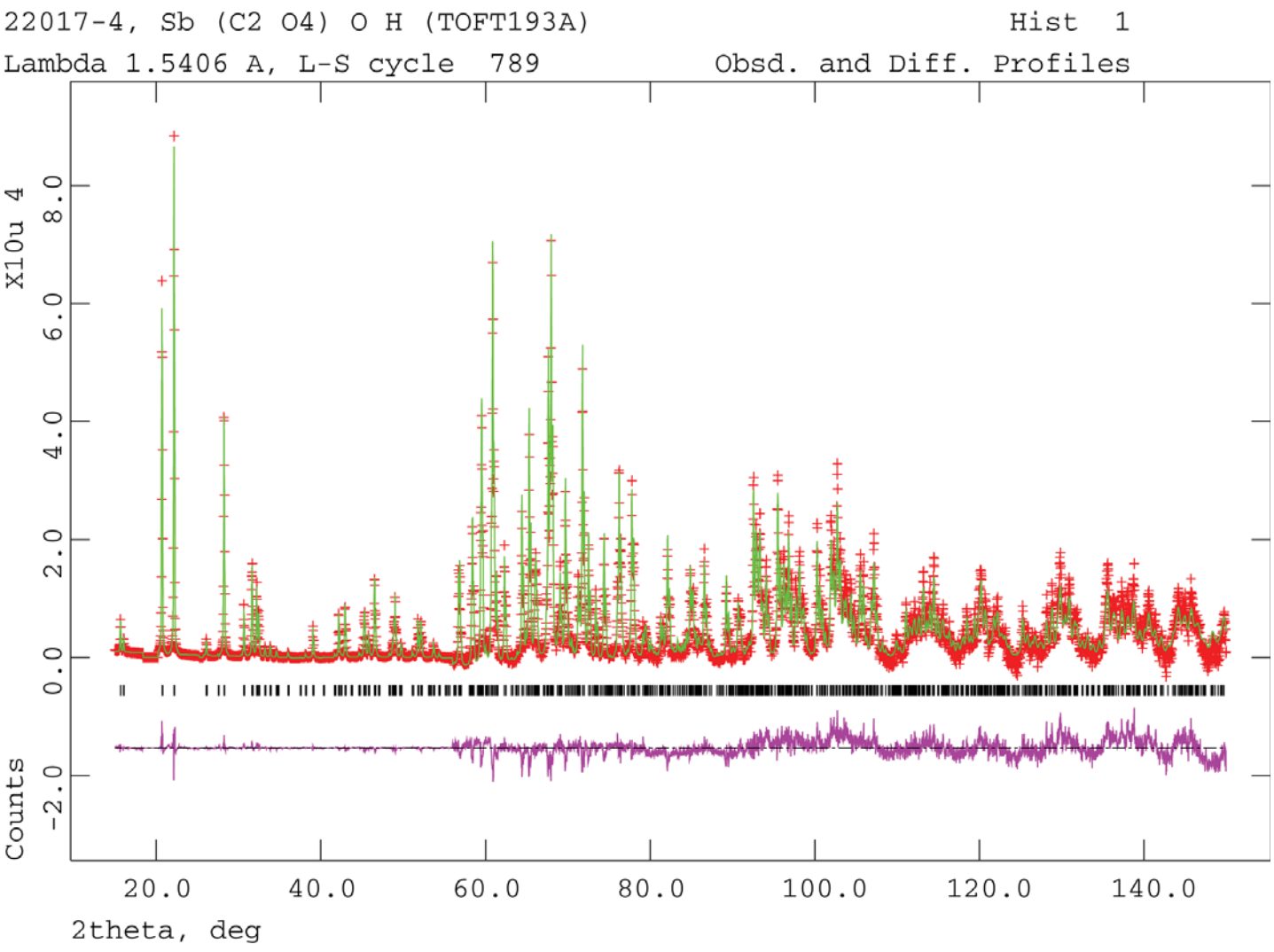

[toft193] 22017-4 Sb(C2O4)(OH) (40,40,0.3) JAK
[00-037-0646] Antimony Oxalate Hydroxide • SbC_2O_4OH
S/M on Remaining Peaks (20)
SQRT(Counts)
Two-Theta (deg)
300
250
200
150
100
50
√0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
3
4
7
39
45
54
65
82
87
99

Structure Solution

- Index (DICVOL06): *M/F*(19) = 123.3/141.1

  5.82713(3), 11.29448(10), 6.31377(3) Å,
  $V = 415.537(5)$ Å^3; *Pnma*, $Z = 4$
- Monte Carlo simulated annealing and direct methods failed (both found Sb on mirror)
- Use charge flipping (Jana2006) – Sb1, O2
- LS/ΔF – O3, C4, O5?


a
c
b
Sb
O
C



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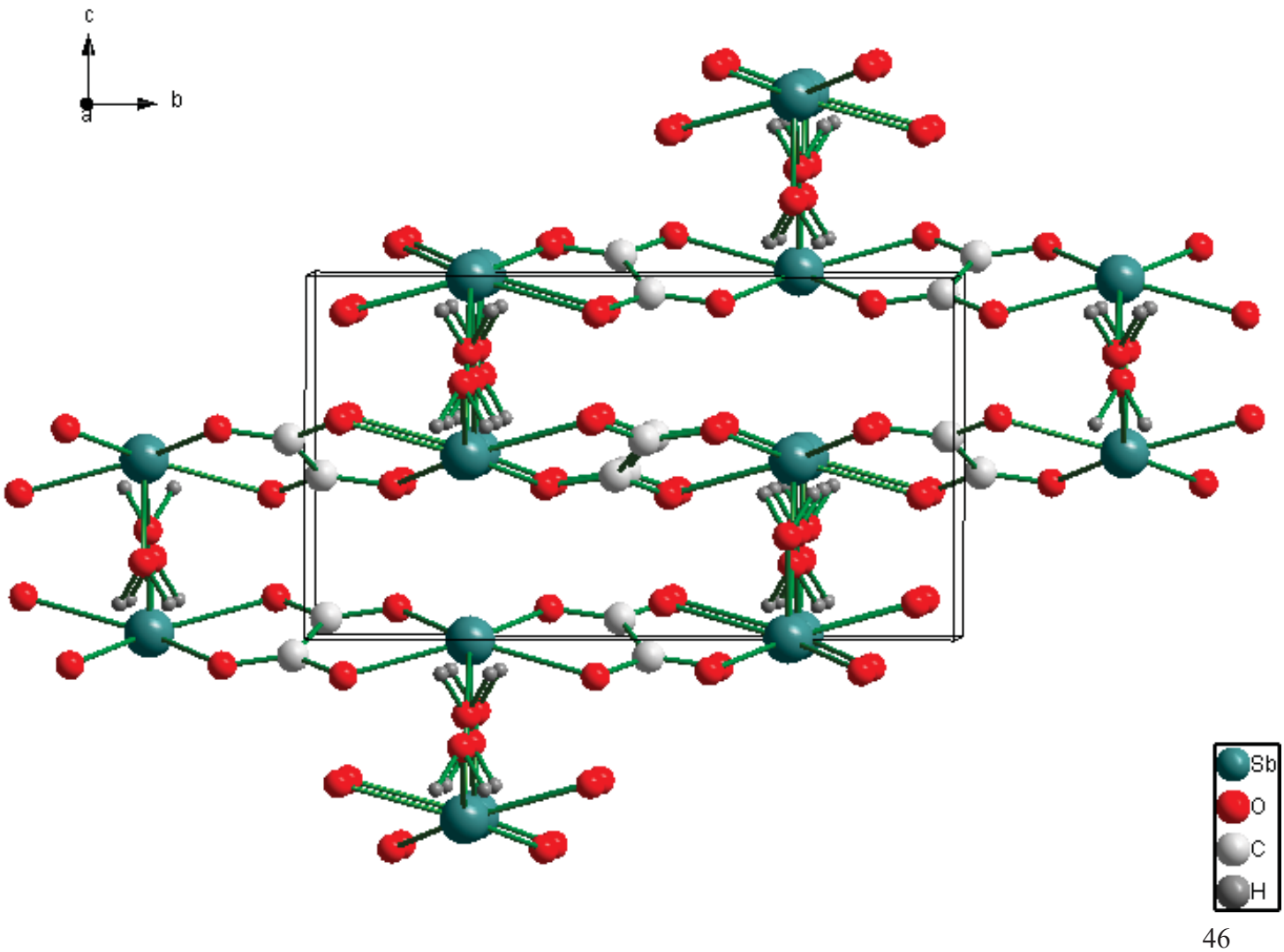
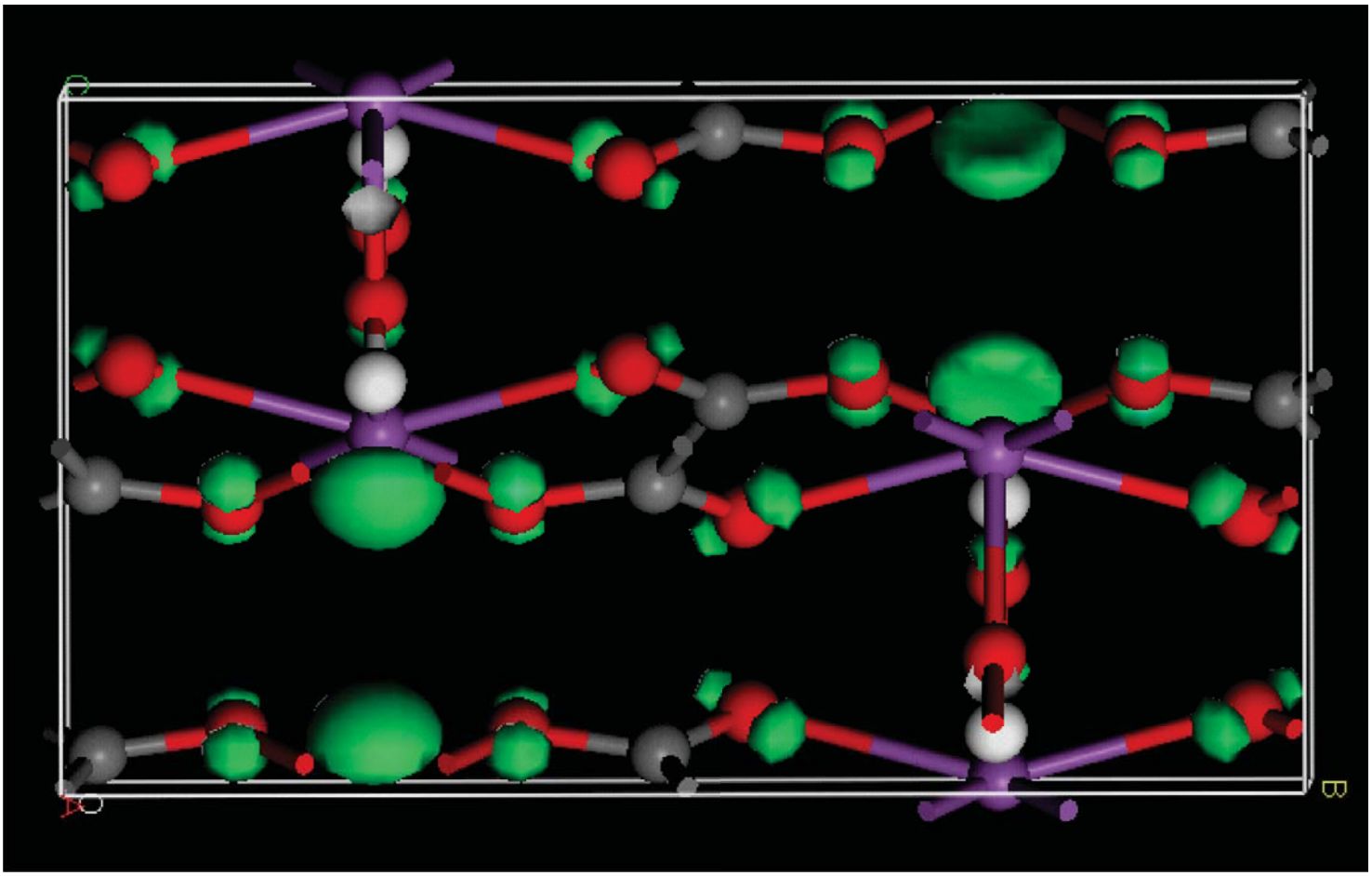
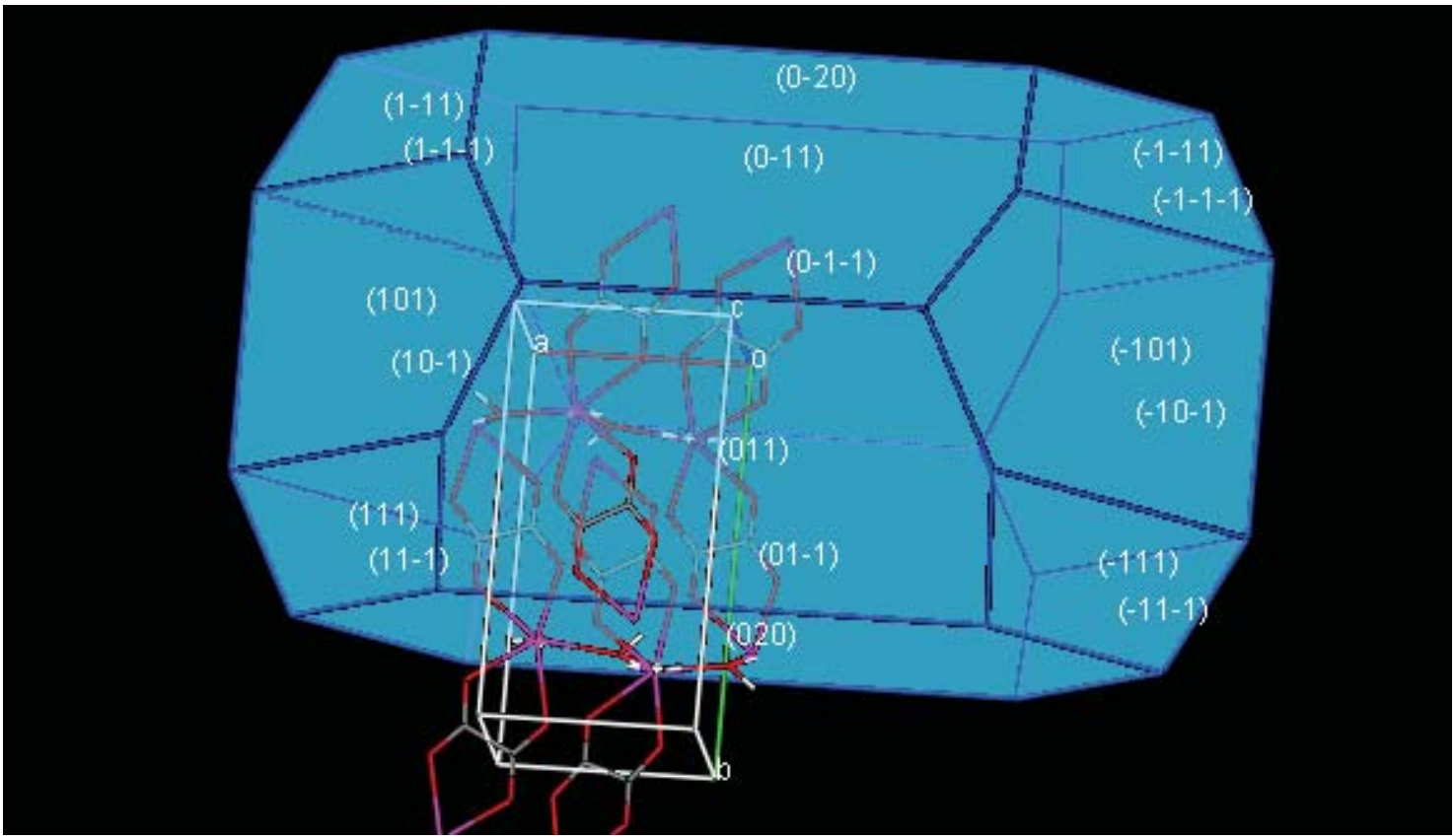

c
b
a
Sb
O
C
H





Texture Index = 1.441

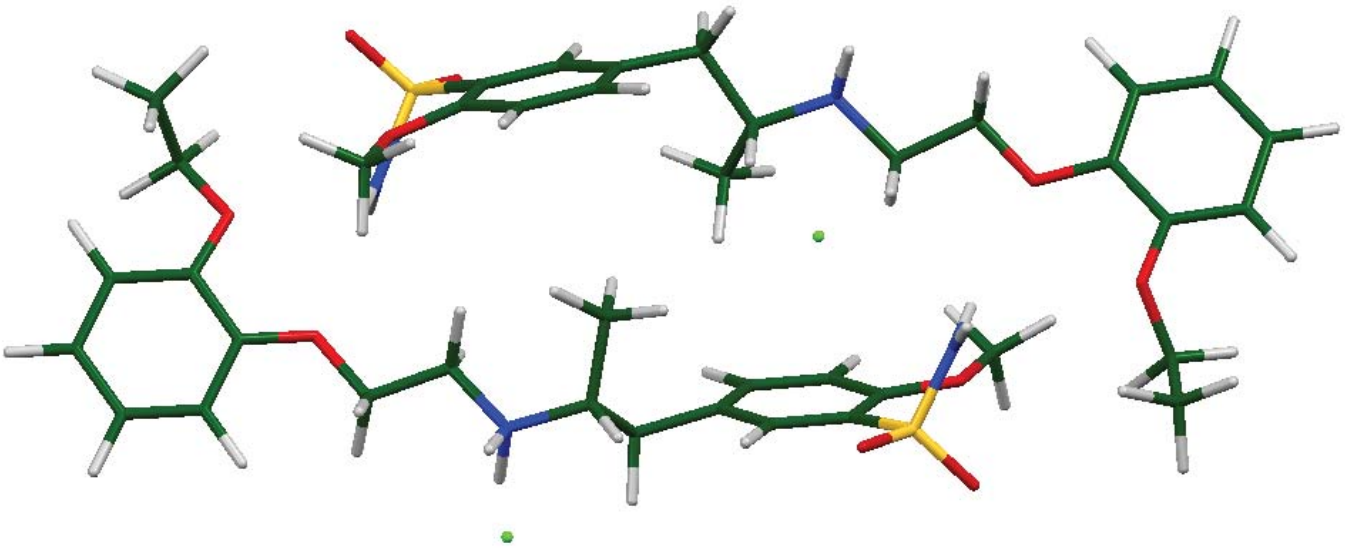
"Crystal structure of antimony oxalate hydroxide, $Sb(C_2O_4)OH$", J. A. Kaduk, M. A. Toft, and J. T. Golab, *Powder Diffraction*, **25**(1), 19-24 (2010).

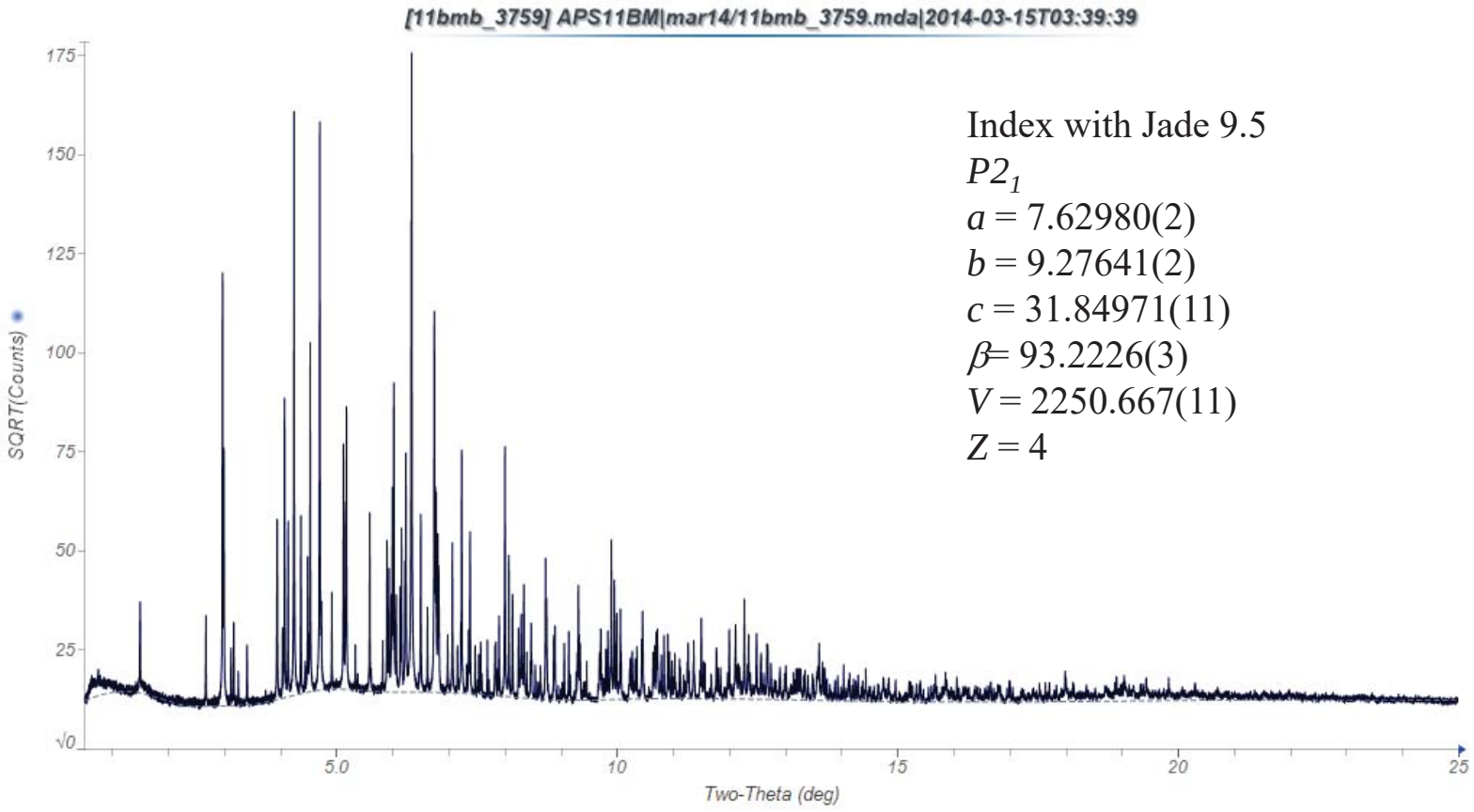
Tamsulosin Hydrochloride
$C_{20}H_{29}N_2O_5SCl$

Flomax (generic in 2010)

benign prostatic hyperplasia (BPH)

Tamsulosin Hydrochloride





Index with Jade 9.5

$P2_1$

a = 7.62980(2)

b = 9.27641(2)

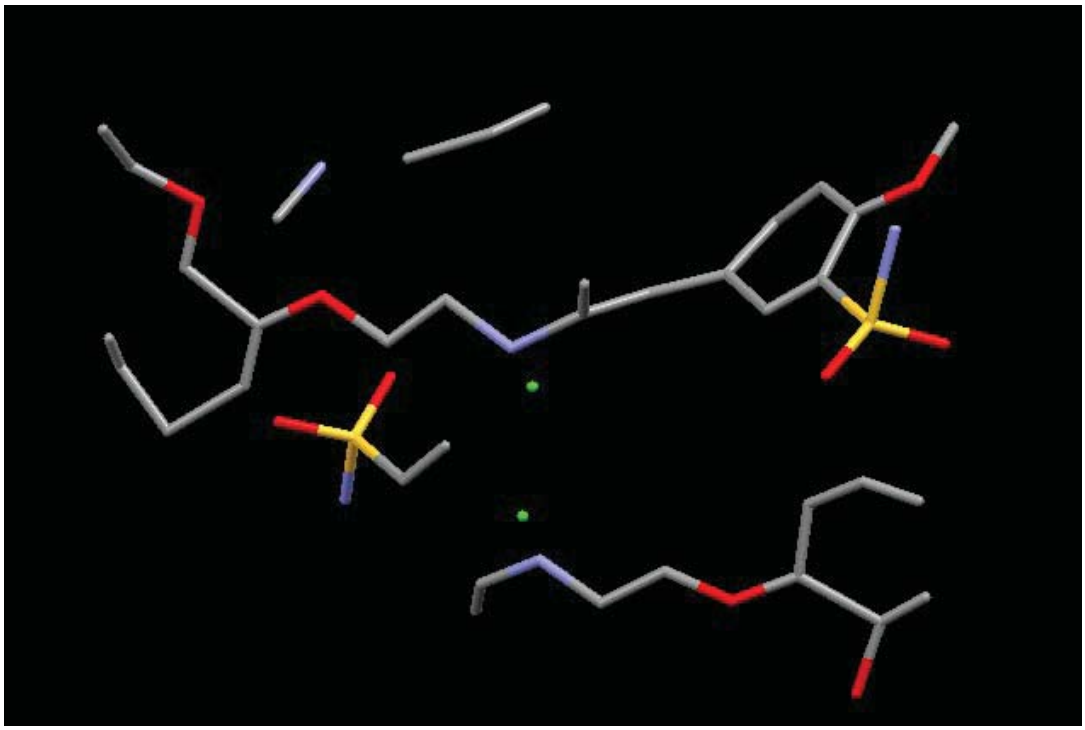
c = 31.84971(11)

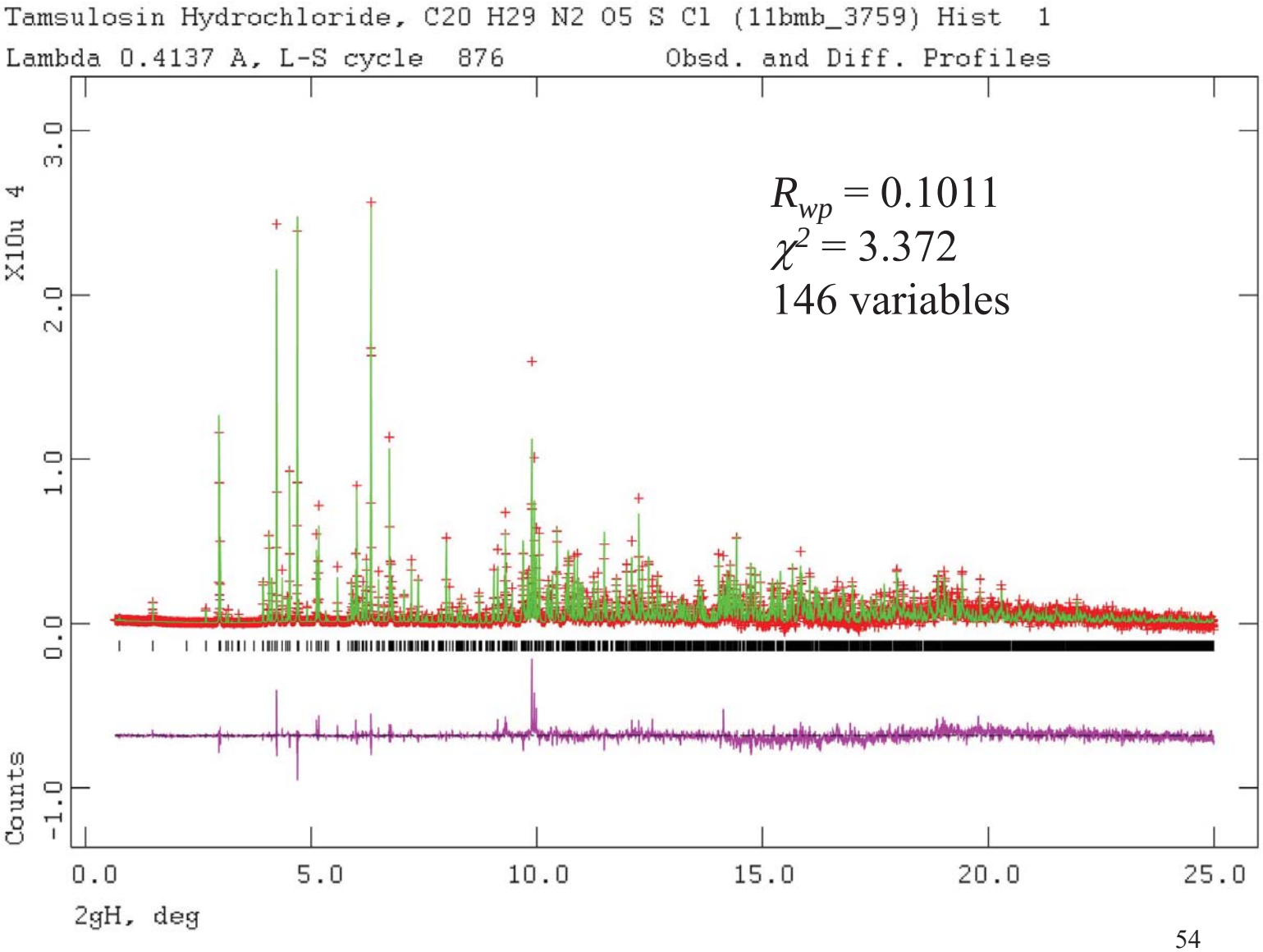
β= 93.2226(3)

V = 2250.667(11)

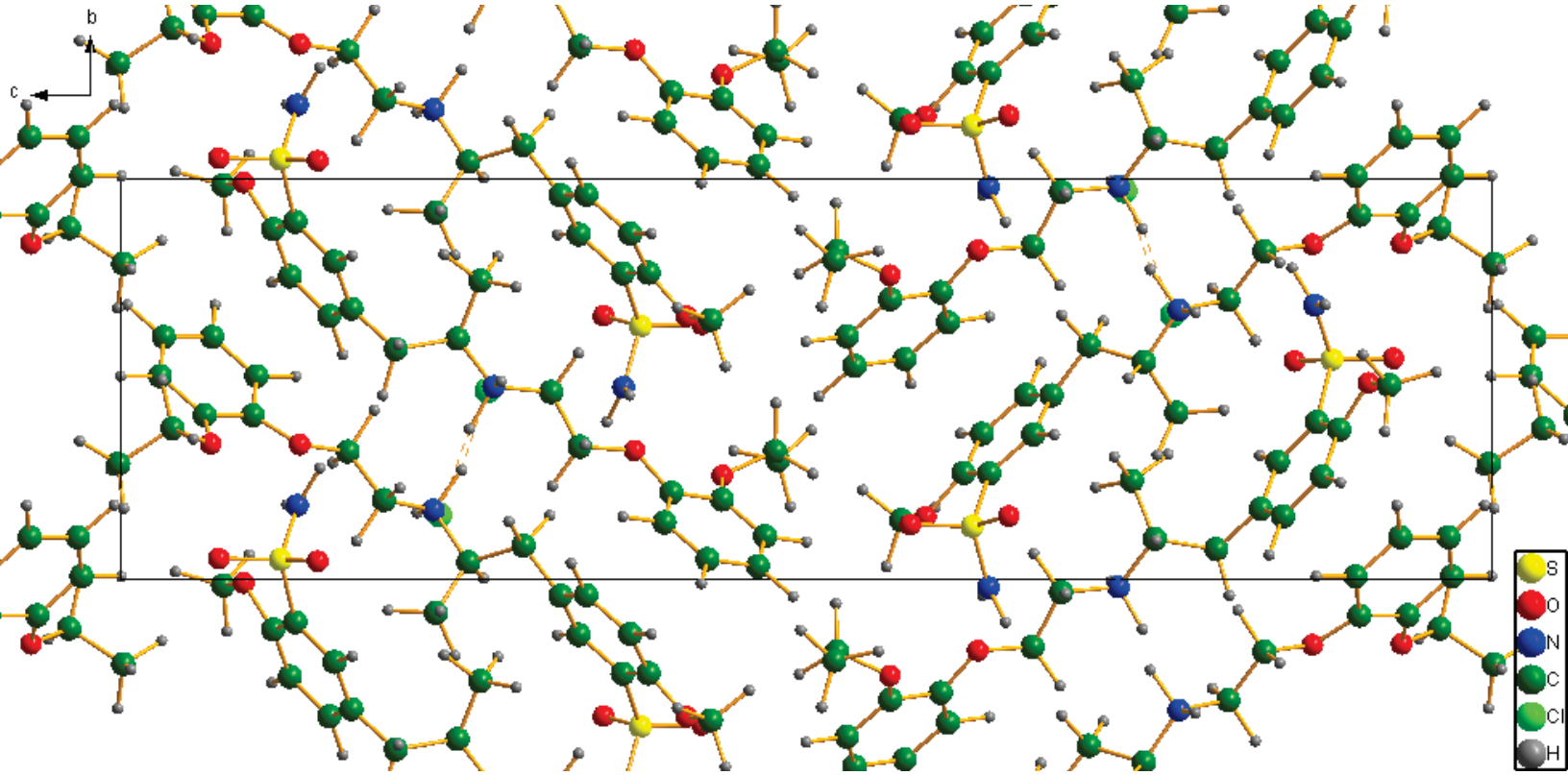
Z = 4

Charge Flipping Result





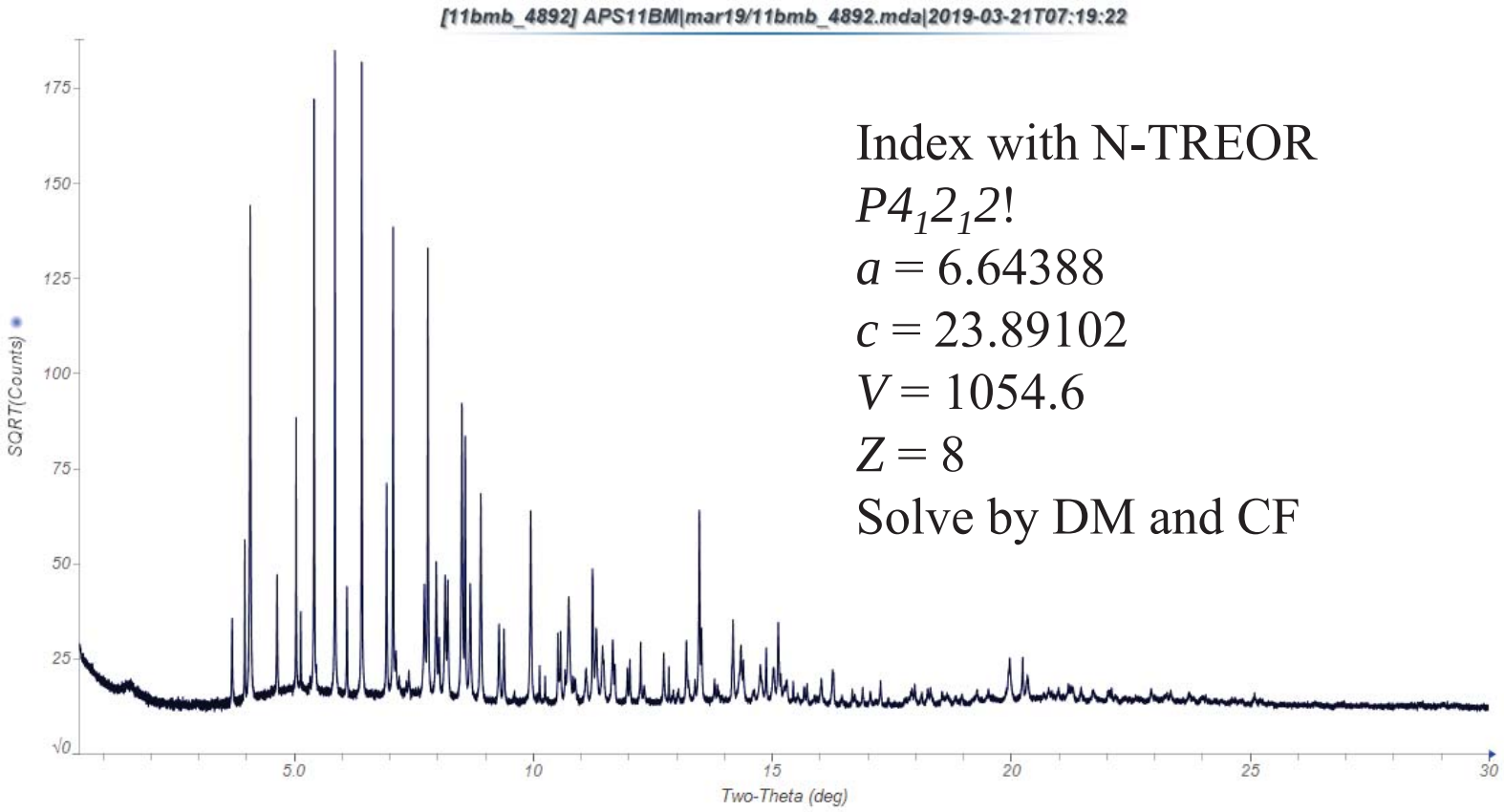
Scaling: 9.0(6.0X) 14.0(20.0X)


b
c
S
O
N
C
Cl
H

Flucytosine, $C_4H_4FN_3O$

Alcobon, Ancobon, Ancotil

antifungal



Index with N-TREOR

$P4_12_12$!

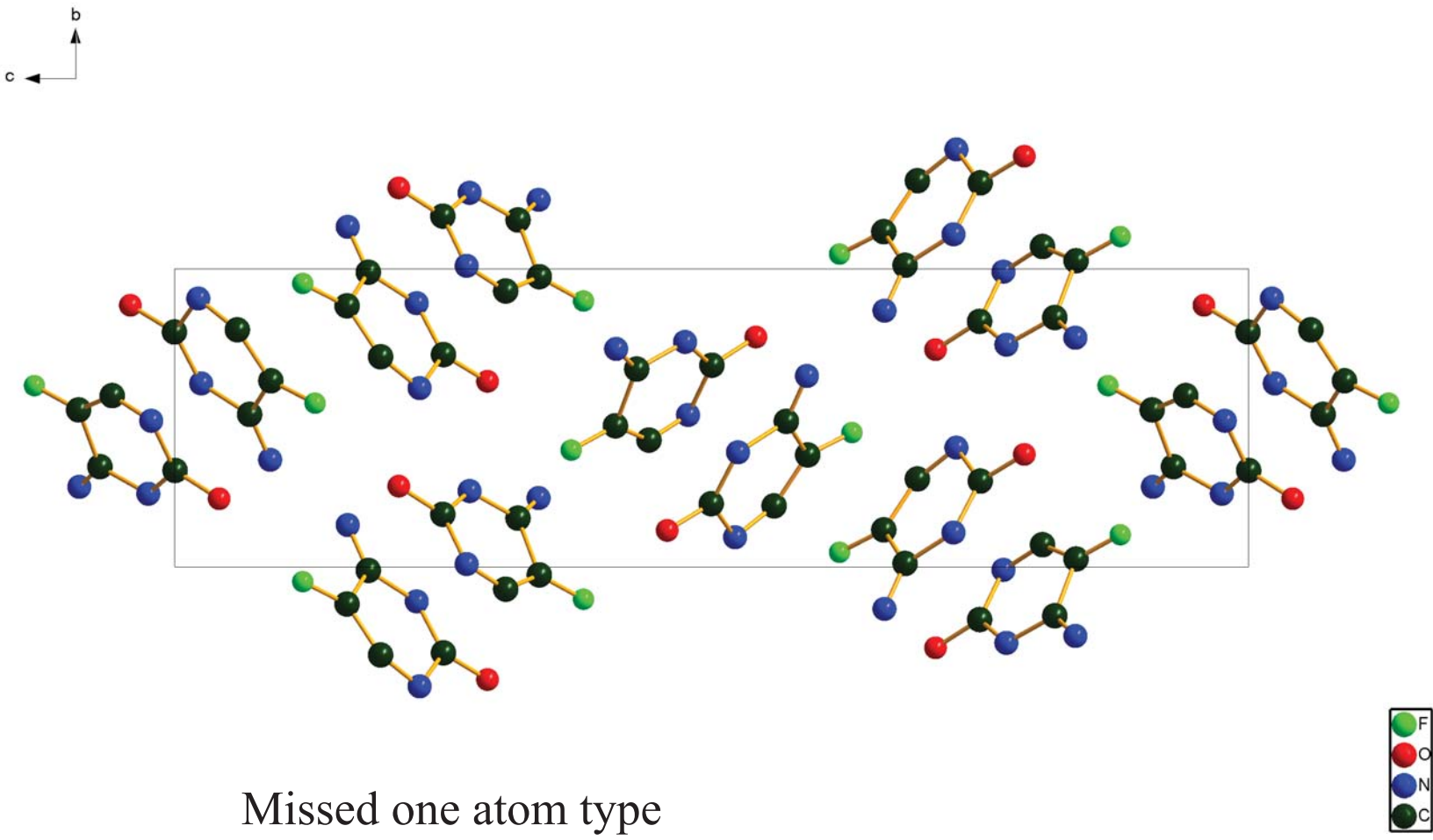
$a = 6.64388$

$c = 23.89102$

$V = 1054.6$

$Z = 8$

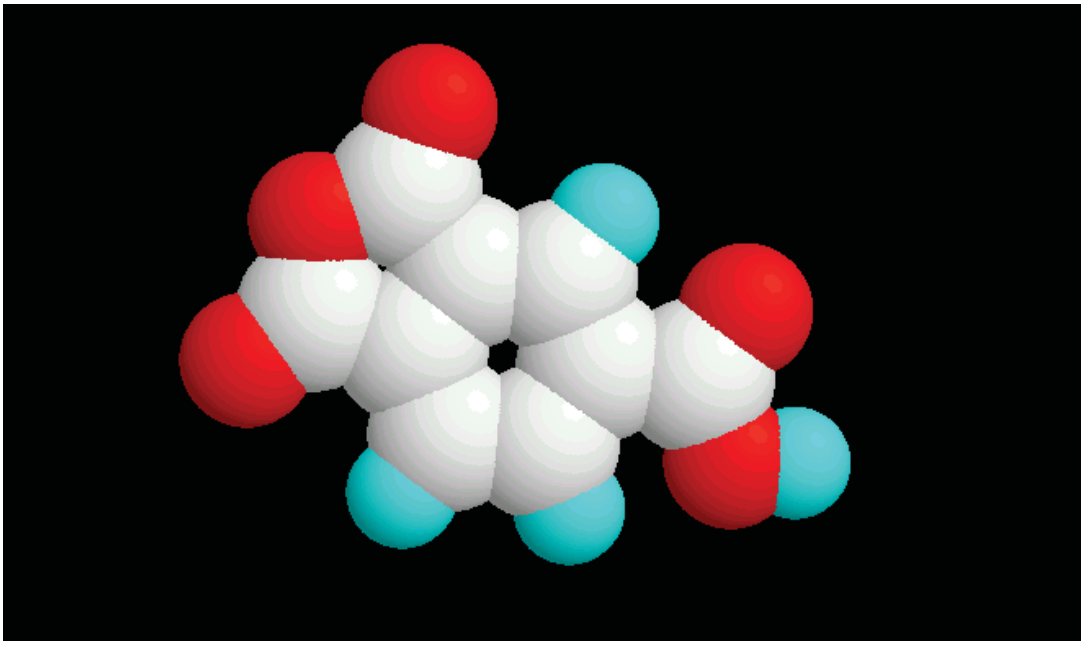
Solve by DM and CF

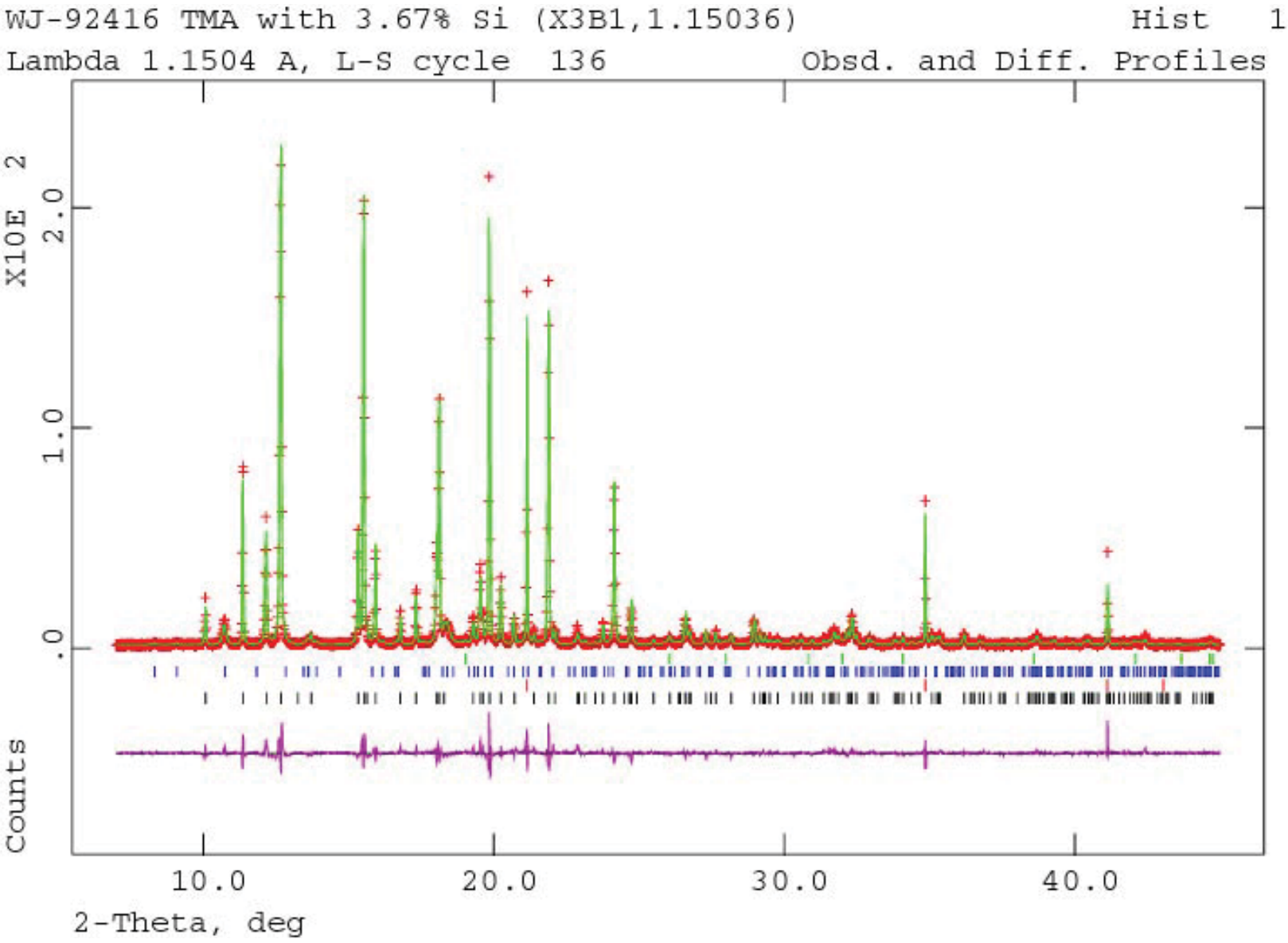


Missed one atom type

Trimellitic Anhydride

a versatile chemical intermediate

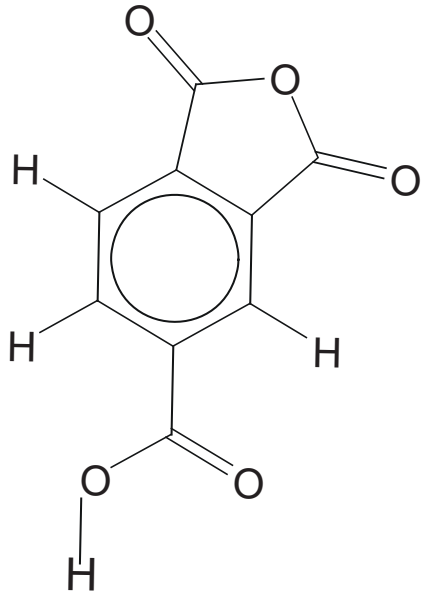



WJ-92416 TMA with 3.67% Si (X3B1,1.15036) Hist 1
Lambda 1.1504 A, L-S cycle 136 Obsd. and Diff. Profiles
X10E 2
2.0
1.0
.0
Counts
10.0
20.0
30.0
40.0
2-Theta, deg

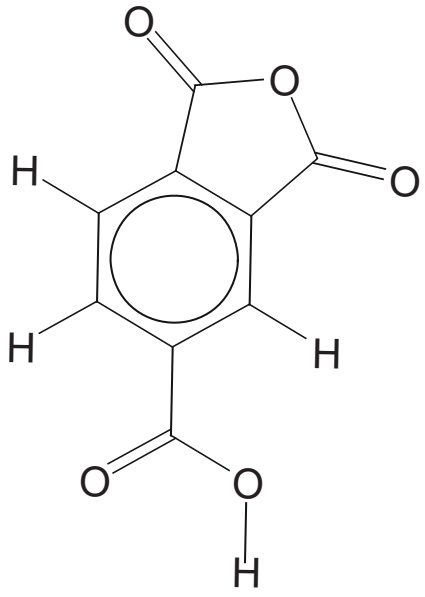
Trimellitic Anhydride

- Try to grow crystals – adducts!
- *P*-orthorhombic
- $a = 5.3684$, $b = 6.8628$, $c = 21.6999$ Å
- $P2_1xx$ – 7 possible space groups
- $P2_12_12_1$, $P2_12_12$, $Pna2_1$, $Pca2_1$ most likely
- $\rho \sim 1.6$ g/mL $\rightarrow Z = 4$!

Two possible conformations:



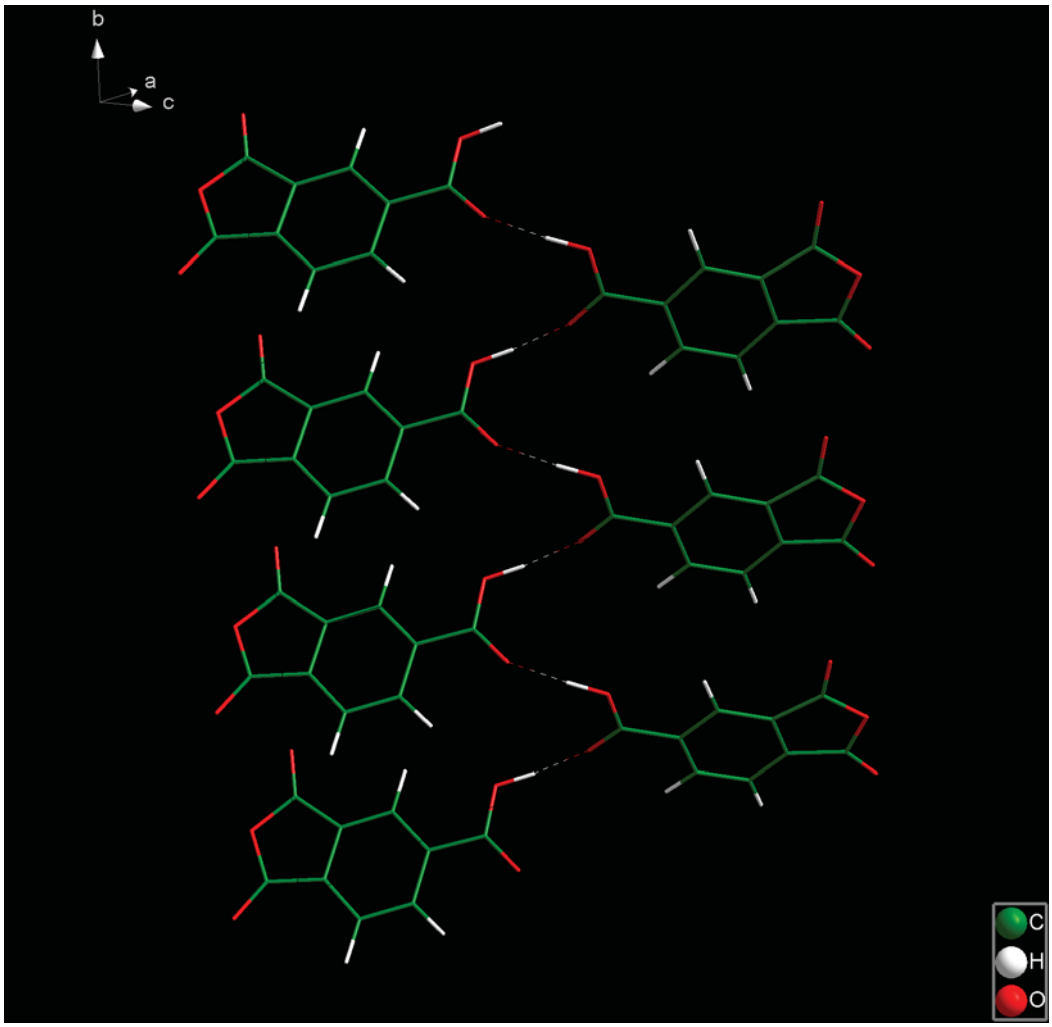
(*E*)-TMA

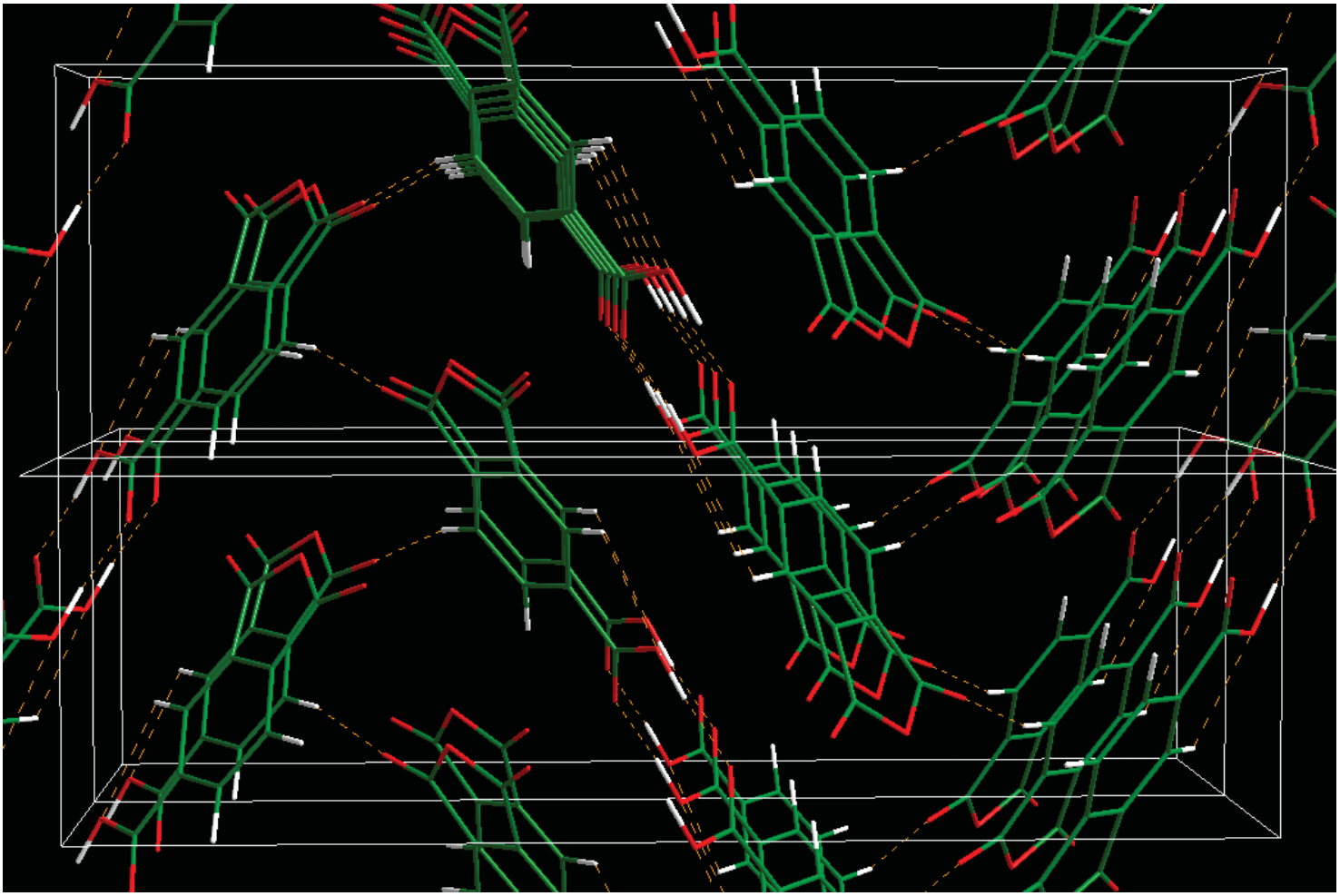


(*Z*)-TMA

Real Space Structure Solution

- Optimize each conformation (Gaussian92)
- 2 conformations × 4 space groups
- Generate “library” of potential low-energy crystal structures
- 2nd-lowest energy in $P2_12_12_1$ had cell similar to observed
- refine


b
a
c
C
H
O



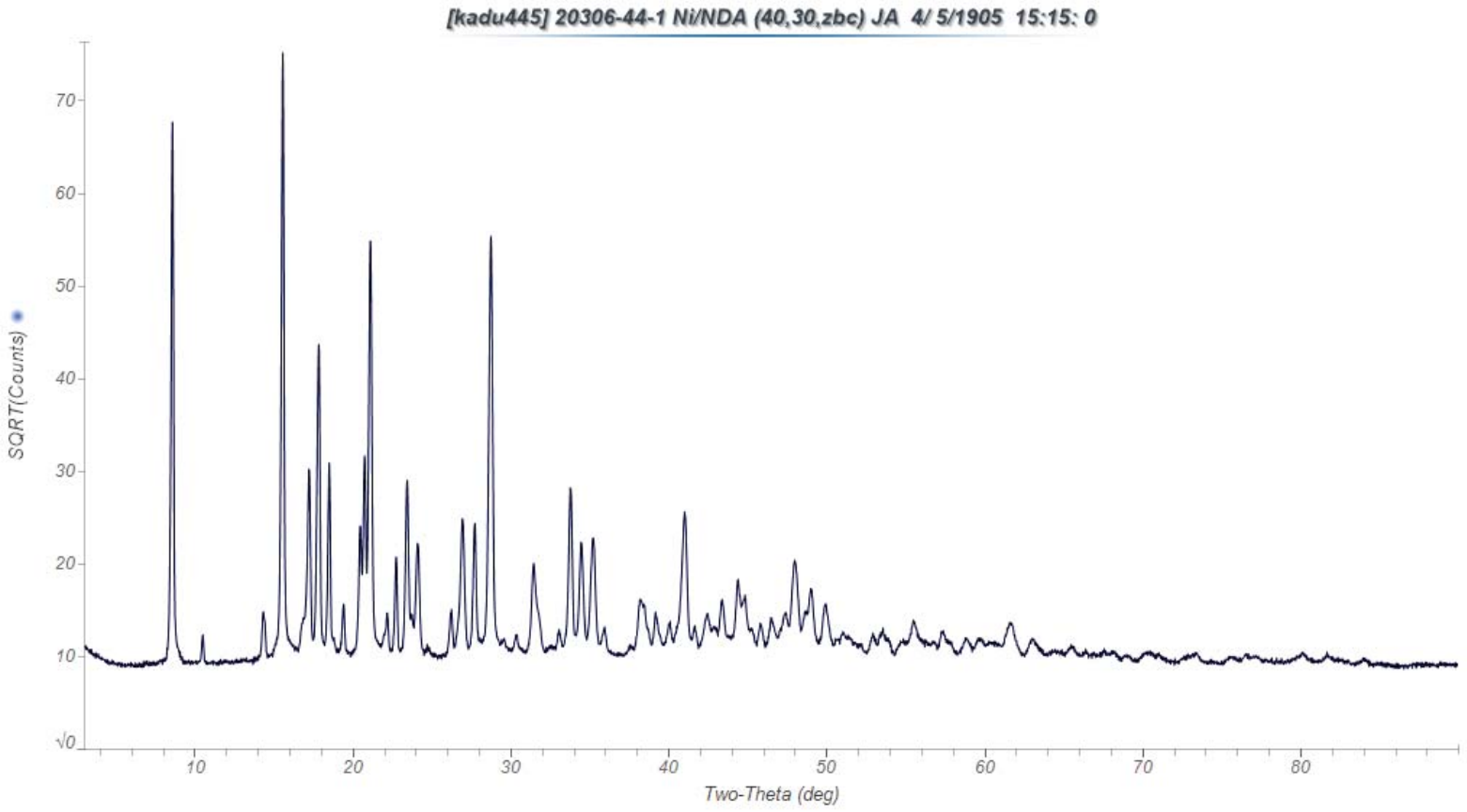
“The Crystal Structures of Trimellitic Anhydride and Two of Its Solvates”, J. A. Kaduk, J. T. Golab, and F. J. J. Leusen, *Crystal Engineering*, **1**(3/4), 277-290 (1998)

Real Space (Hybrid) Methods

Monte Carlo Simulated Annealing
Parallel Tempering

Nickel(II) 2,6-naphthalenedicarboxylate tetrahydrate

- A phase-pure compound synthesized as part of a program to understand commercial plant deposits


[kadu445] 20306-44-1 Ni/NDA (40,30,zbc) JA 4/ 5/1905 15:15: 0
SQRT(Counts)
70
60
50
40
30
20
10
√0
10
20
30
40
50
60
70
80
Two-Theta (deg)

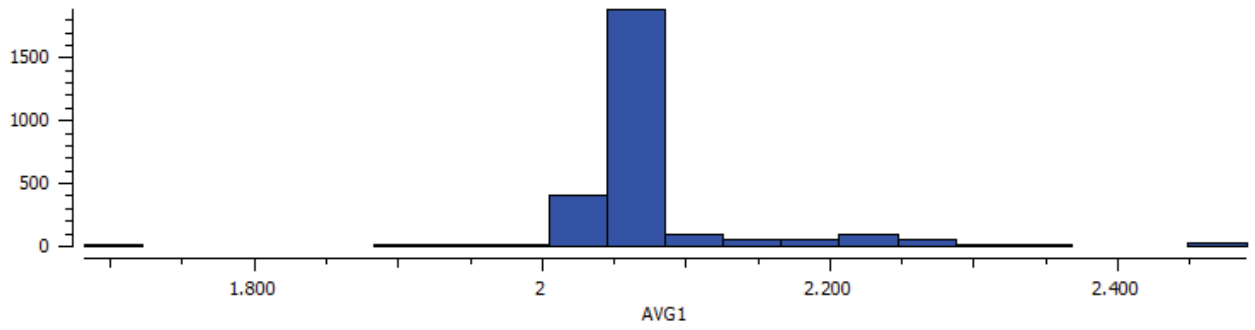
$NiNDA(H_2O)_4$

- Yield $\rightarrow$ Ni:NDA = 1:1
- TGA $\rightarrow$ tetrahydrate
- Index: a = 10.0851(4), b = 10.9429(5), c = 6.2639(3) Å, α = 98.989(2), β = 87.428(3), γ = 108.015(2)°, Z = 2
- *P1* or $\boldsymbol{P\bar{1}}$

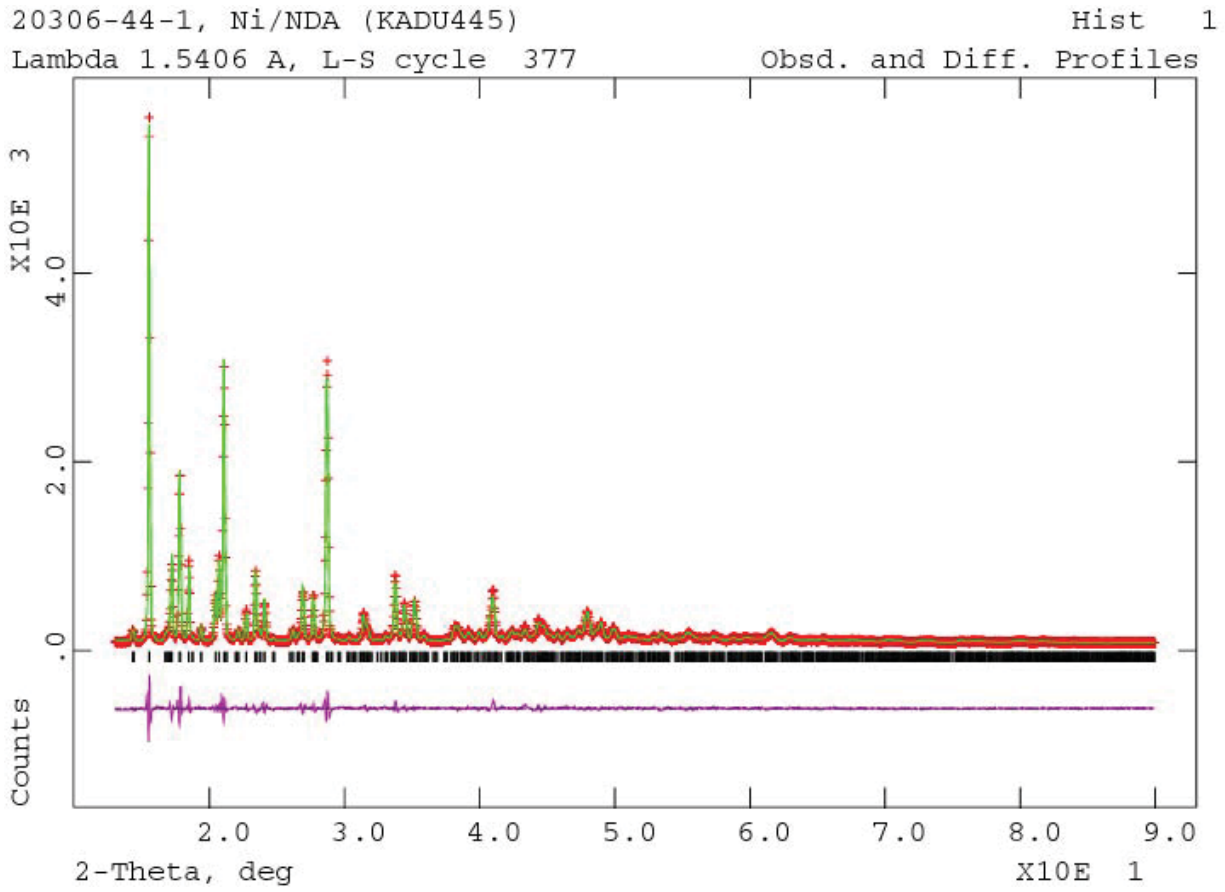
Monte Carlo Simulated Annealing

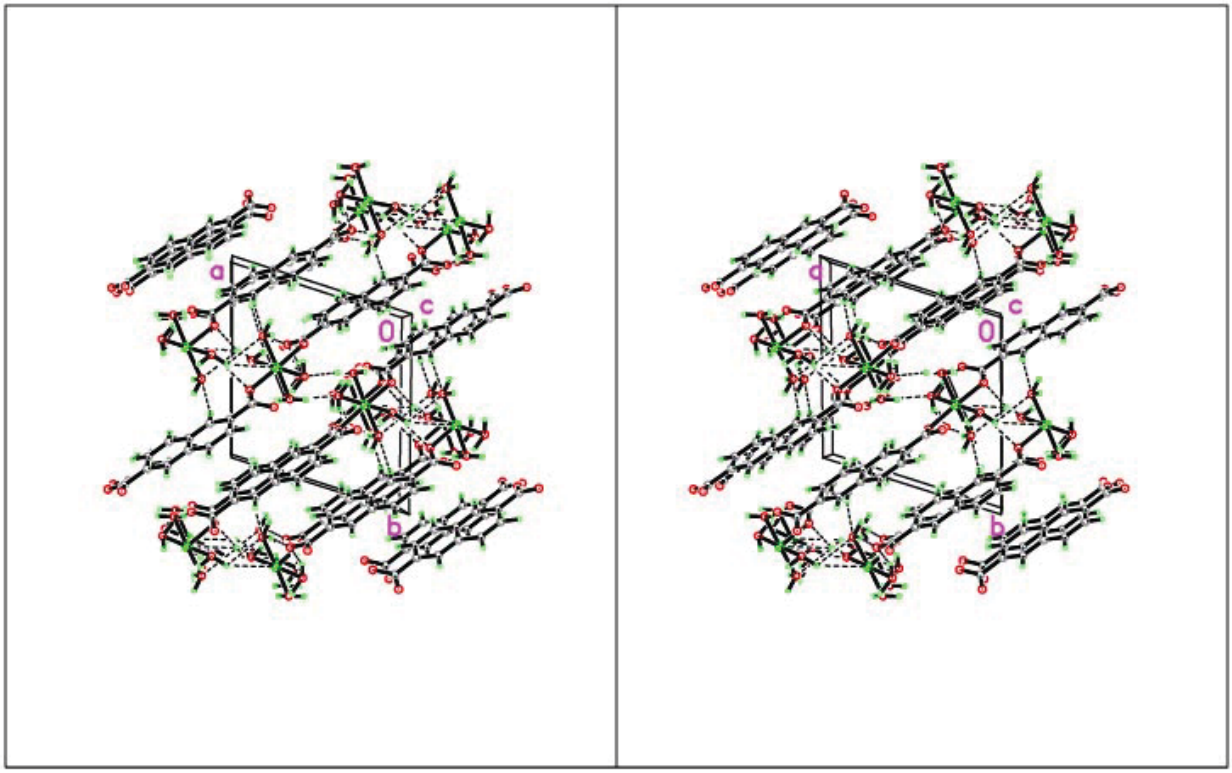
- First try NDA (with 2 torsions) and Ni
- Plausible solutions, but not refinable
- A *trans* octahedral complex?

Ni-O Distances in NiO_6 Coordination Spheres

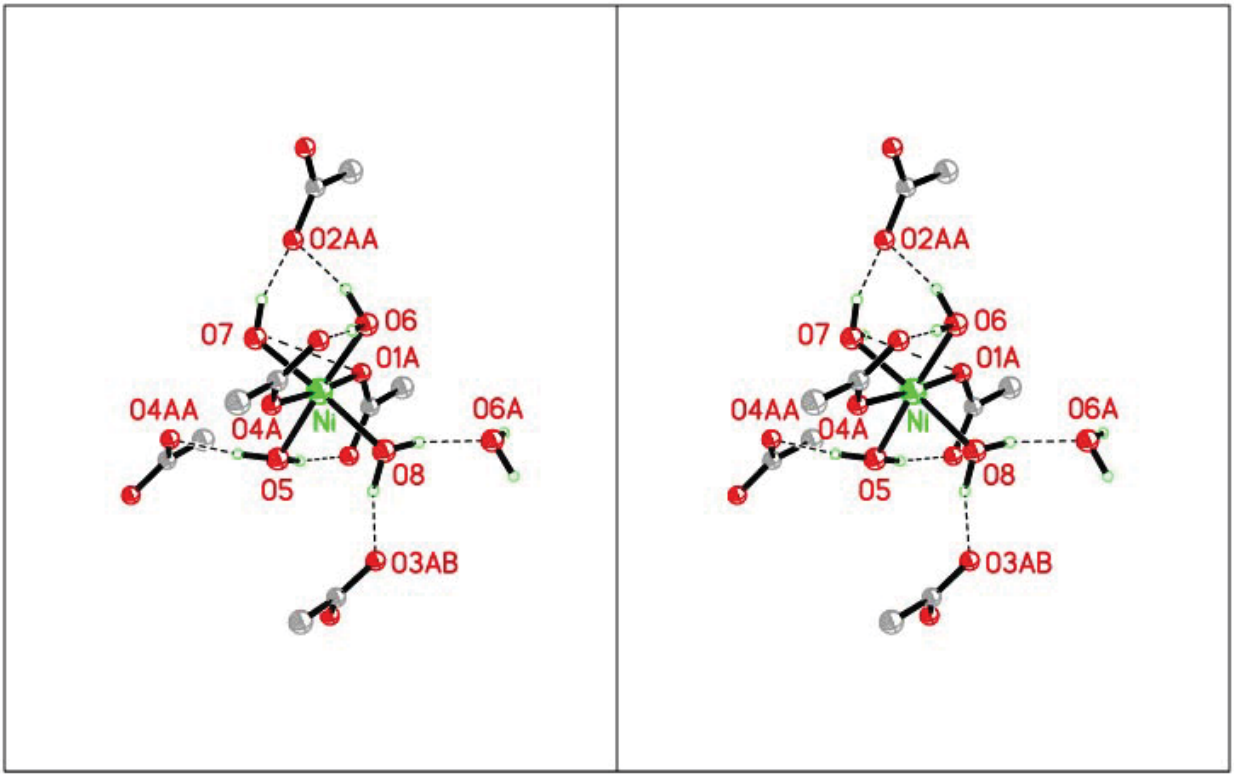


Mean = 2.08(6) Å


20306-44-1, Ni/NDA (KADU445)
Hist 1
Lambda 1.5406 A, L-S cycle 377
Obsd. and Diff. Profiles
X10E 3
4.0
2.0
.0
Counts
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
2-Theta, deg
X10E 1

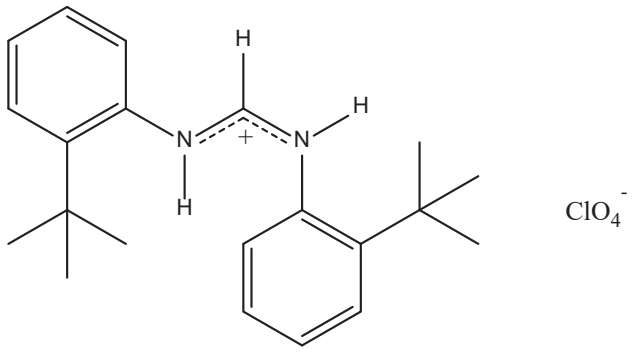


Ni(II) 2,6-naphthalenedicaroxylate tetrahydrate



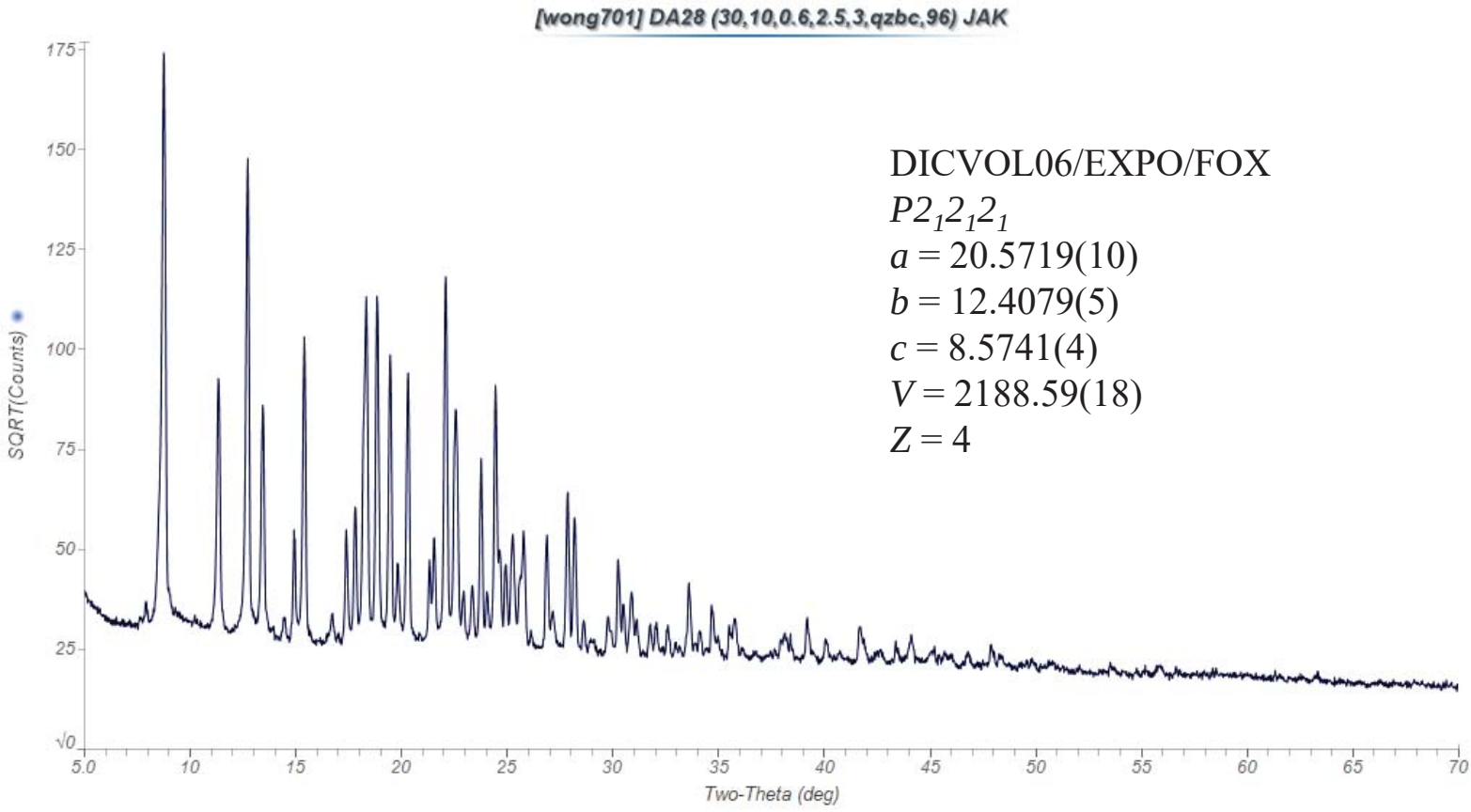
Quantum mechanics to locate hydrogens!

“Salts of aromatic carboxylates. The crystal structures of nickel(II) and cobalt(II) 2,6-naphthalenedicarboxylate tetrahydrate”, J. A. Kaduk and J. A. Hanko, *J. Appl. Cryst.*, **34**, 710-714 (2001).



(*Z*)-*N*,*N*'-*bis*(2-*tert*-butylphenyl)formamidinic perchlorate, $C_{21}H_{29}N_2ClO_4$

Qinliang (Kin) Zhao
University of the Pacific
Stockton CA



DICVOL06/EXPO/FOX

$P2_12_12_1$

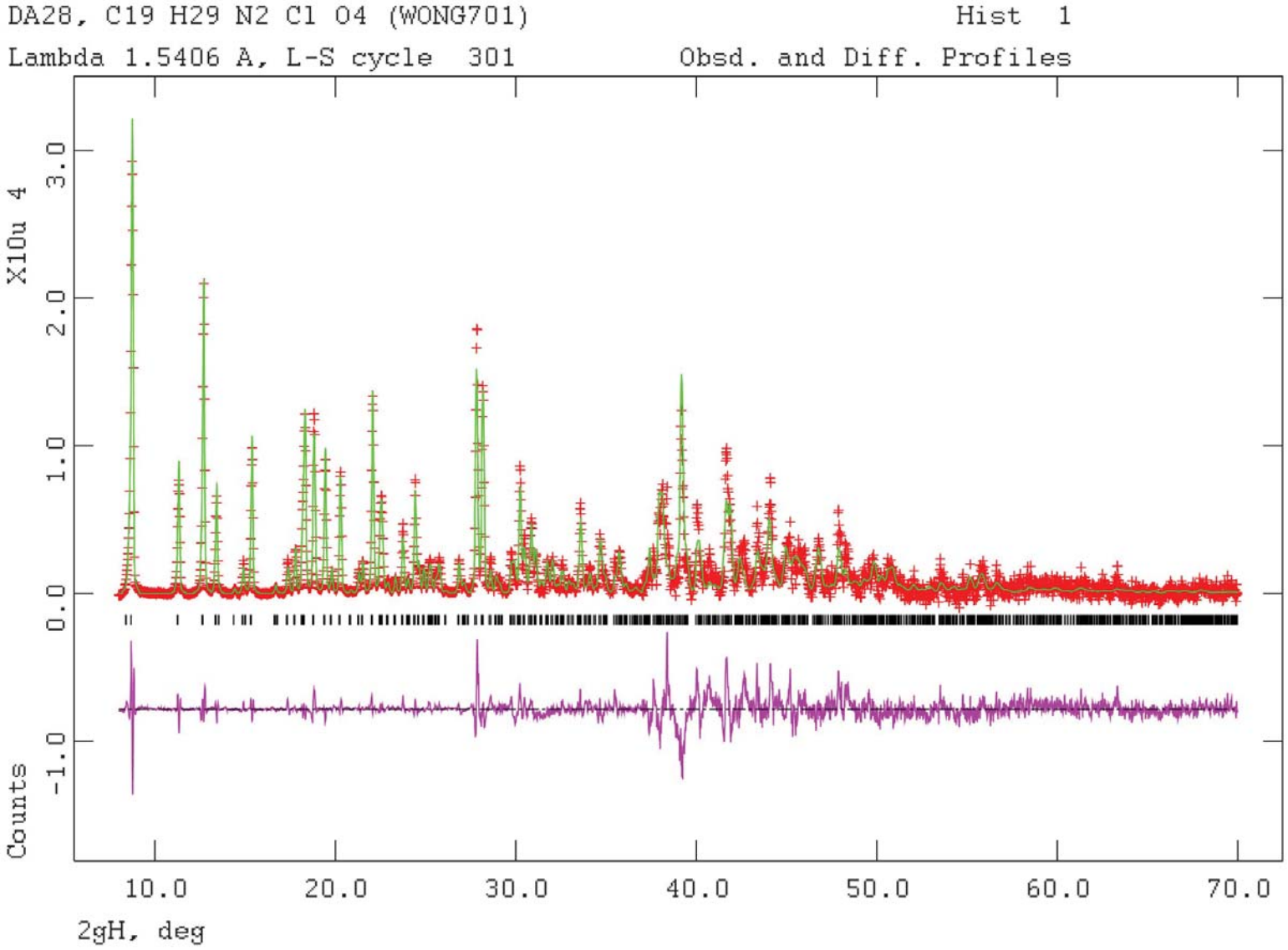
a = 20.5719(10)

b = 12.4079(5)

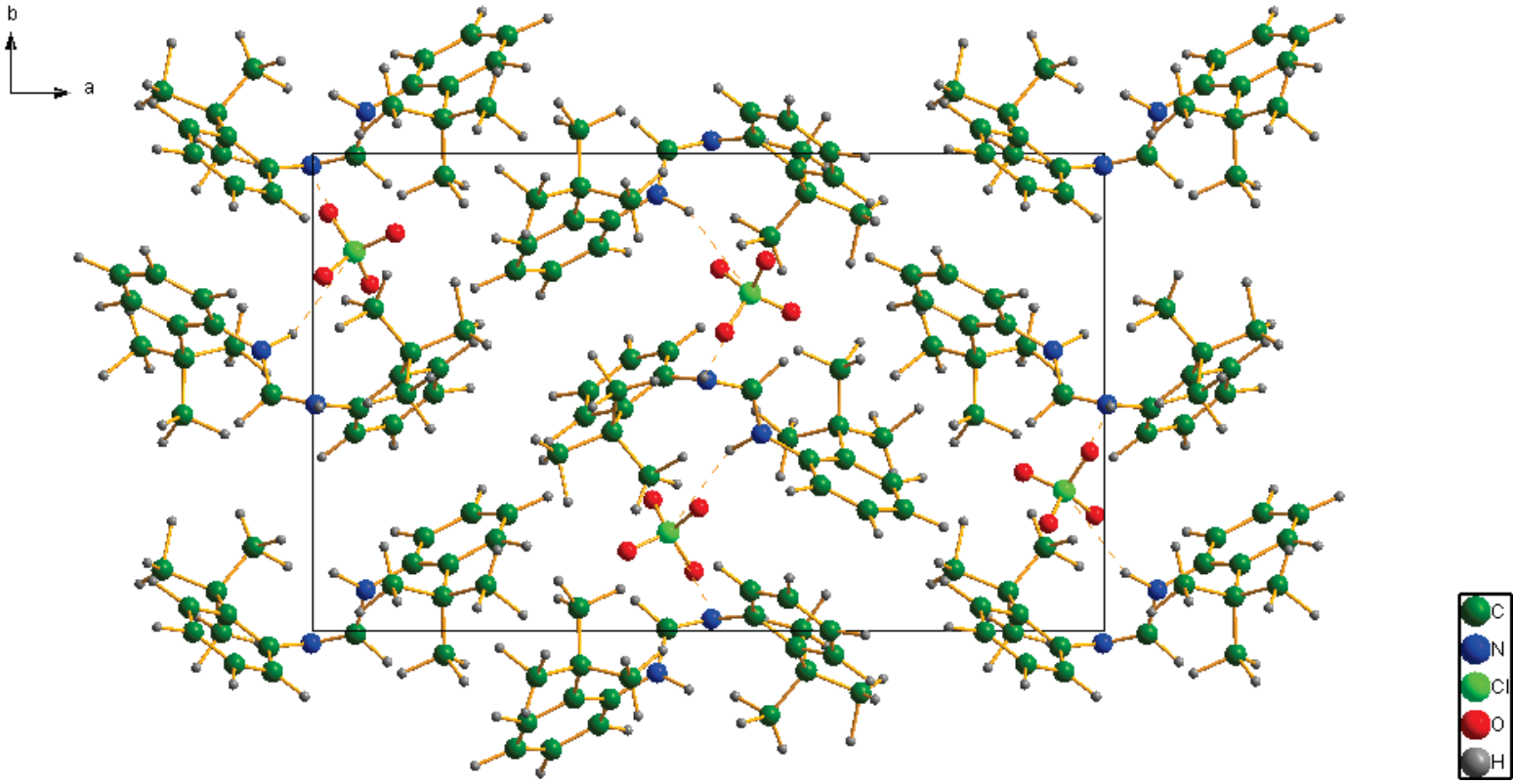
c = 8.5741(4)

V = 2188.59(18)

Z = 4



Scaling: 27.5(5.0X) 37.0(20.0X)


b
a
C
N
Cl
O
H

The Pharmaceutical Project
> 70 structures and counting

"Crystal structure of atorvastatin calcium trihydrate Form I (Lipitor®), $(C_{33}H_{34}FN_2O_5)_2Ca(H_2O)_3$", R. L. Hodge, J. A. Kaduk, A. M. Gindhart, and T. N. Blanton, *Powder Diffraction* **35**(2), 136-143 (2020).

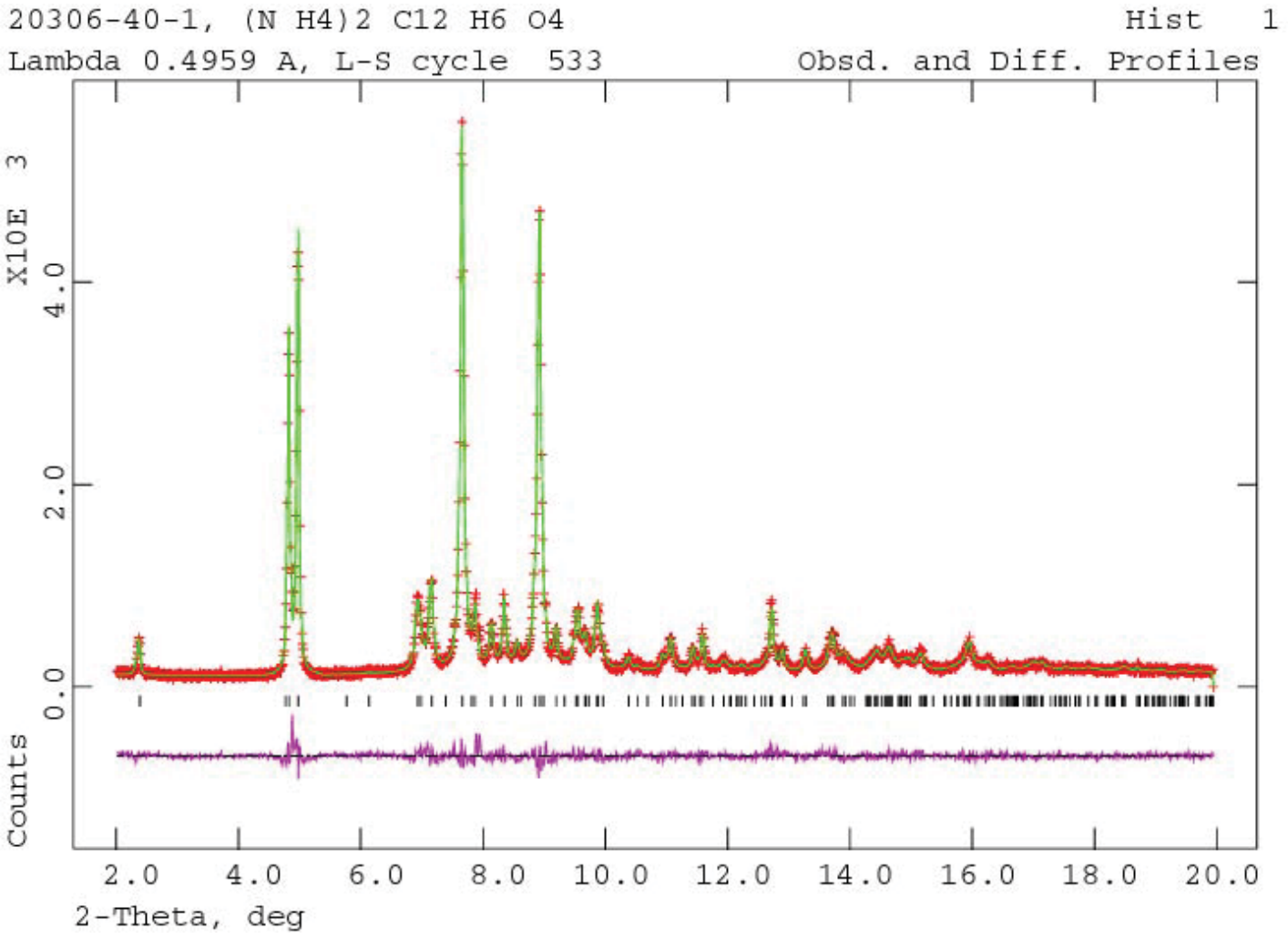
Diammonium 2,6-naphthalenedicarboxylate

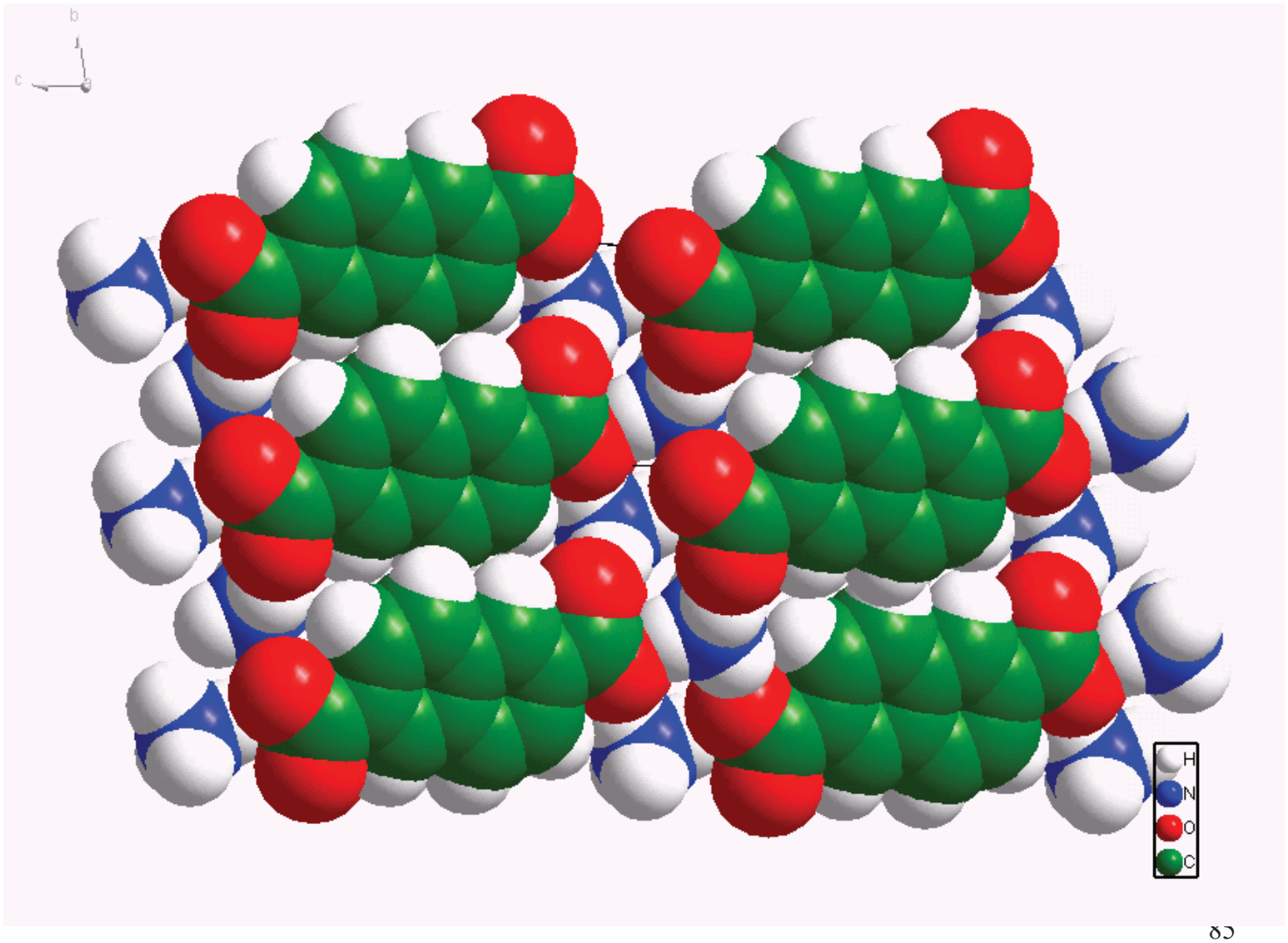
$(NH_4)_2(2,6\text{-}C_{12}H_6O_4)$

$P\bar{1}$, $a = 4.1531(3)$, $b = 5.9937(3)$, $c = 12.2752(10)$ Å, $\alpha = 79.123(7)$, $\beta = 81.040(9)$, $\gamma = 86.781(5)°$, $V = 296.31(4)$ Å^3, $\boldsymbol{\rho = 1.402}$ **g/mL**

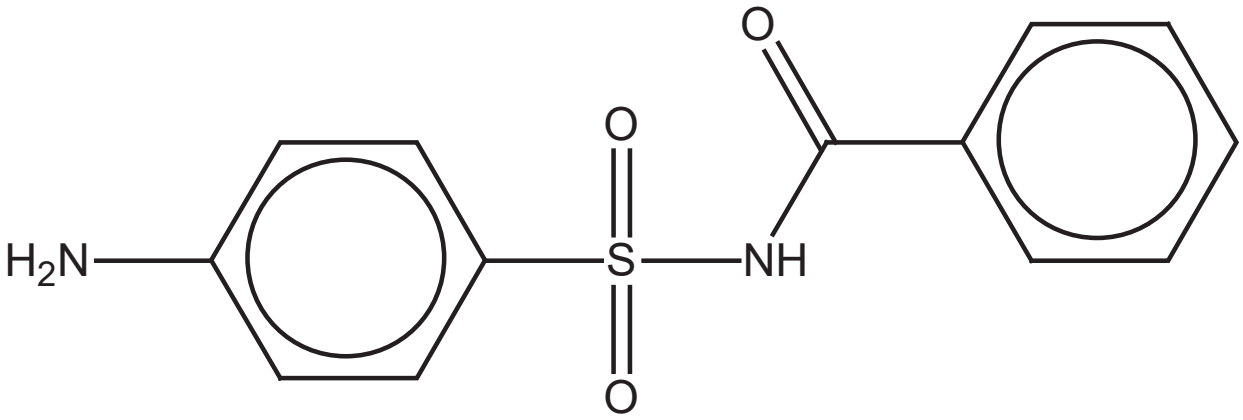
$(NH_4)_2(2,6\text{-}C_{12}H_6O_4)$

- Couldn't index until took to APS (20 min!)
- Cell is 1 wide × 1 long × 1 thick
- Place NDA anion at origin in *P-1*
- Manually adjust so don't overlap
- Place NH_4 in hole, and refine

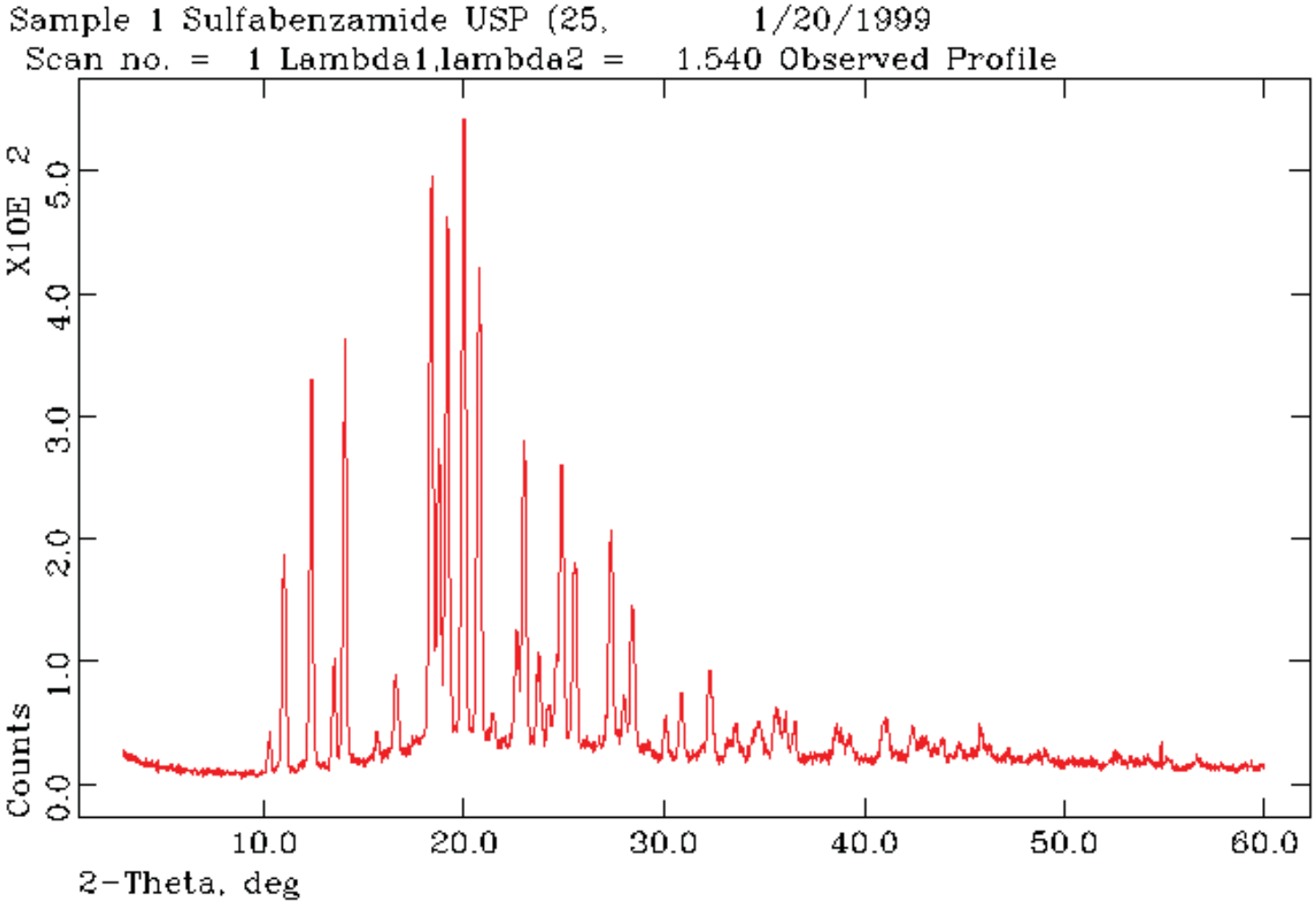

20306-40-1, (N H4)2 C12 H6 O4
Hist 1
Lambda 0.4959 A, L-S cycle 533
Obsd. and Diff. Profiles
X10E 3
4.0
2.0
0.0
Counts
2.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0
20.0
2-Theta, deg


b
c
H
N
O
C

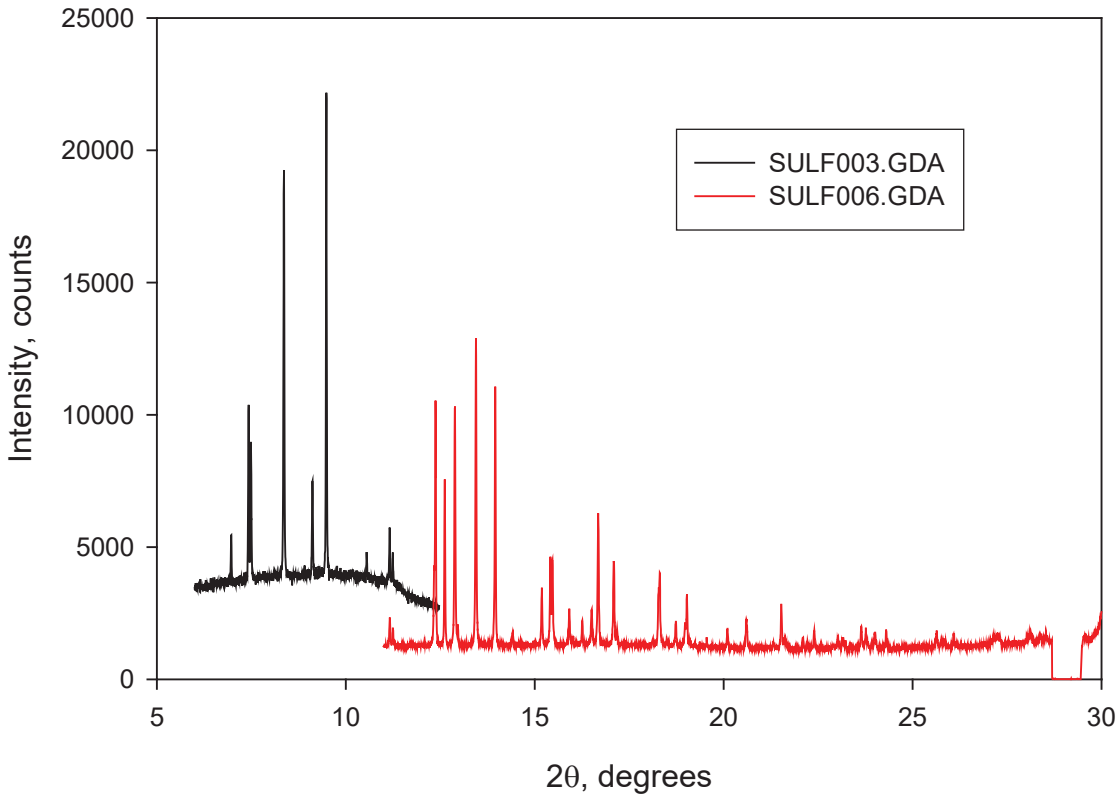
Sulfabenzamide Form I



A polymorph problem?


Sample 1 Sulfabenzamide USP (25, 1/20/1999
Scan no. = 1 Lambda1,lambda2 = 1.540 Observed Profile
X10E 2
Counts
0.0
1.0
2.0
3.0
4.0
5.0
10.0
20.0
30.0
40.0
50.0
60.0
2-Theta, deg

Synchrotron Data for Sulfabenzamide Form I
MR-CAT 10-ID, APS



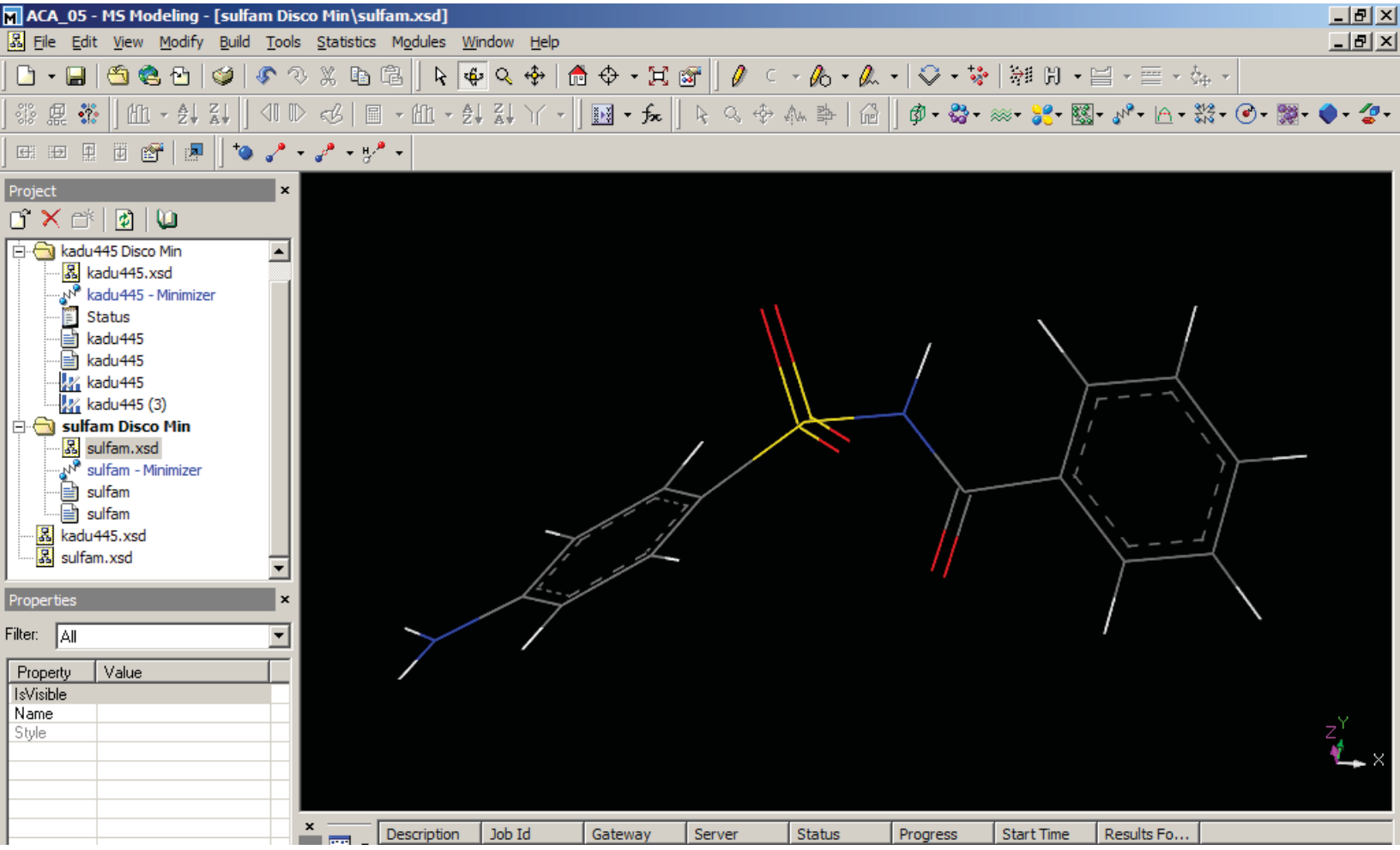
Index the pattern

$a = 8.17063(9)$, $b = 15.98004(18)$,

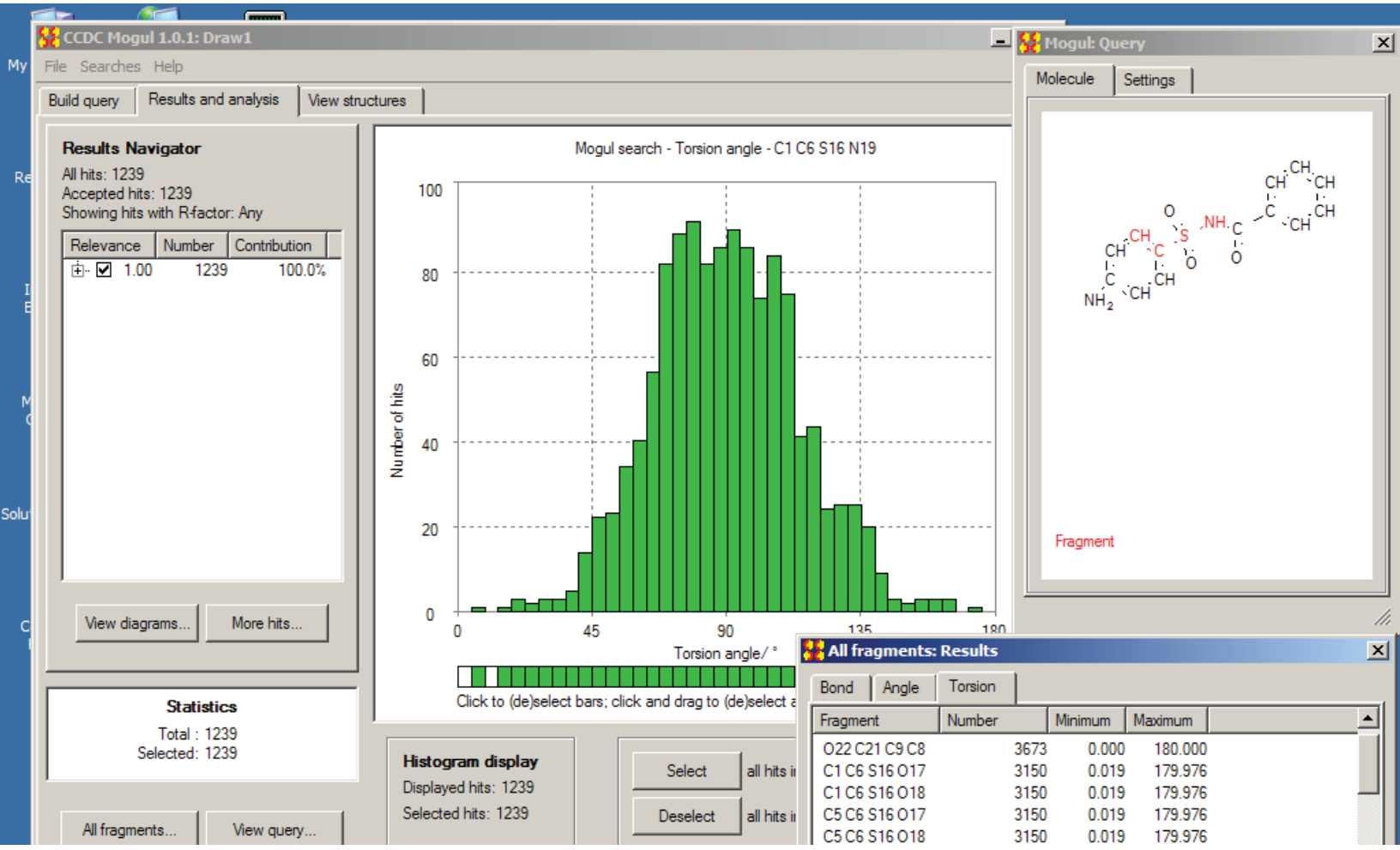
$c = 10.38237(10)$ Å,

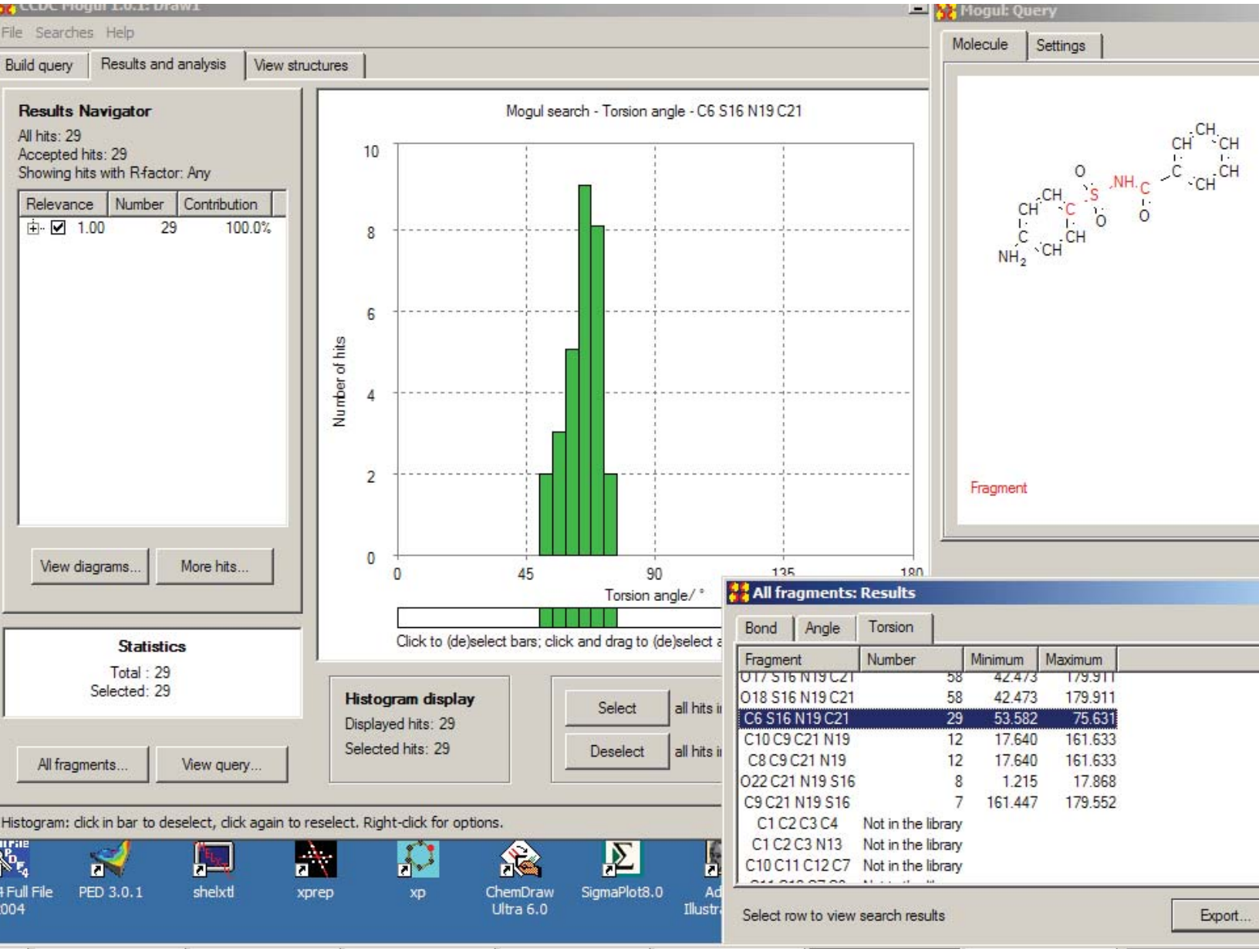
$\beta = 104.1810(9)°$, $P2_1/c$

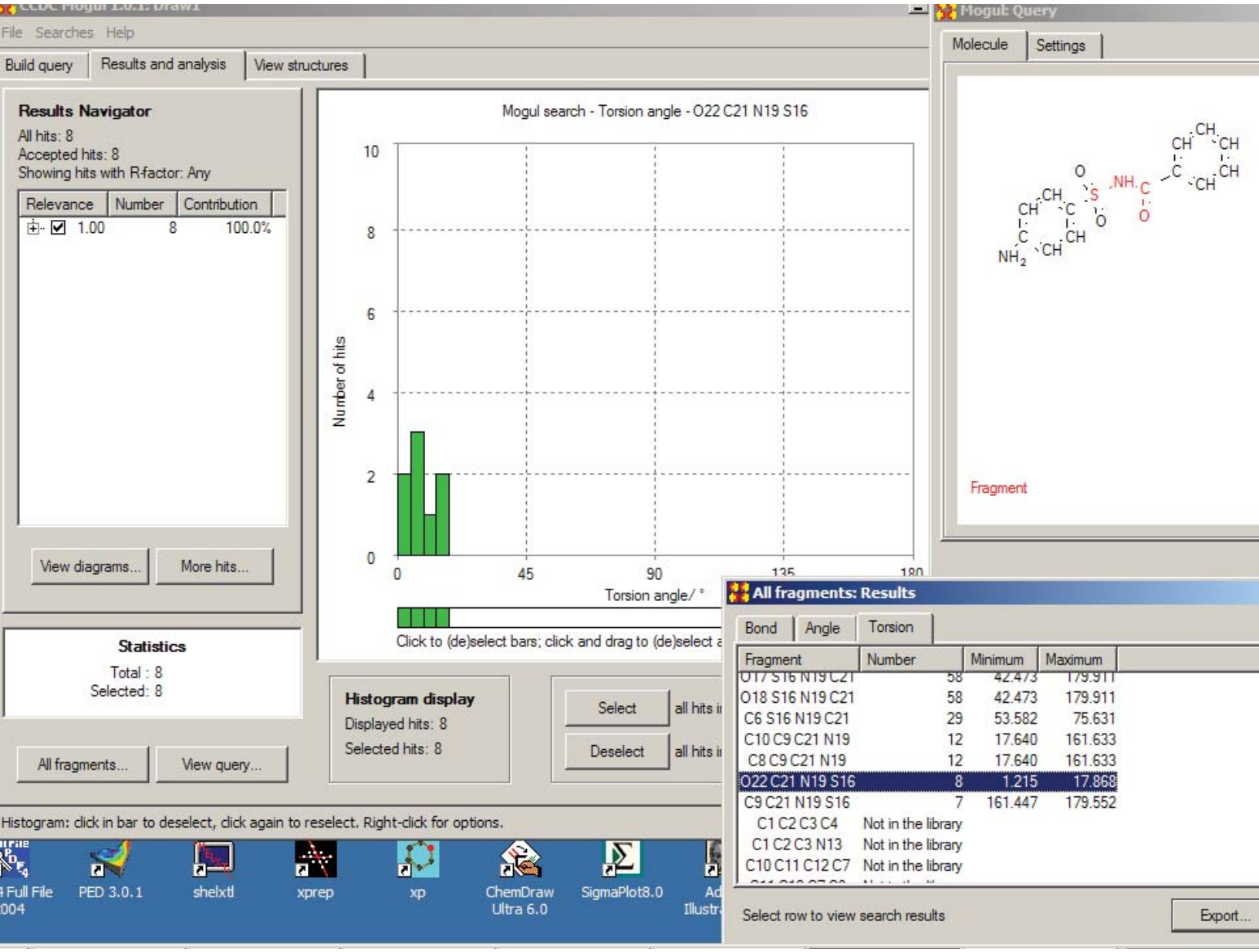
Draw the molecule, and optimize

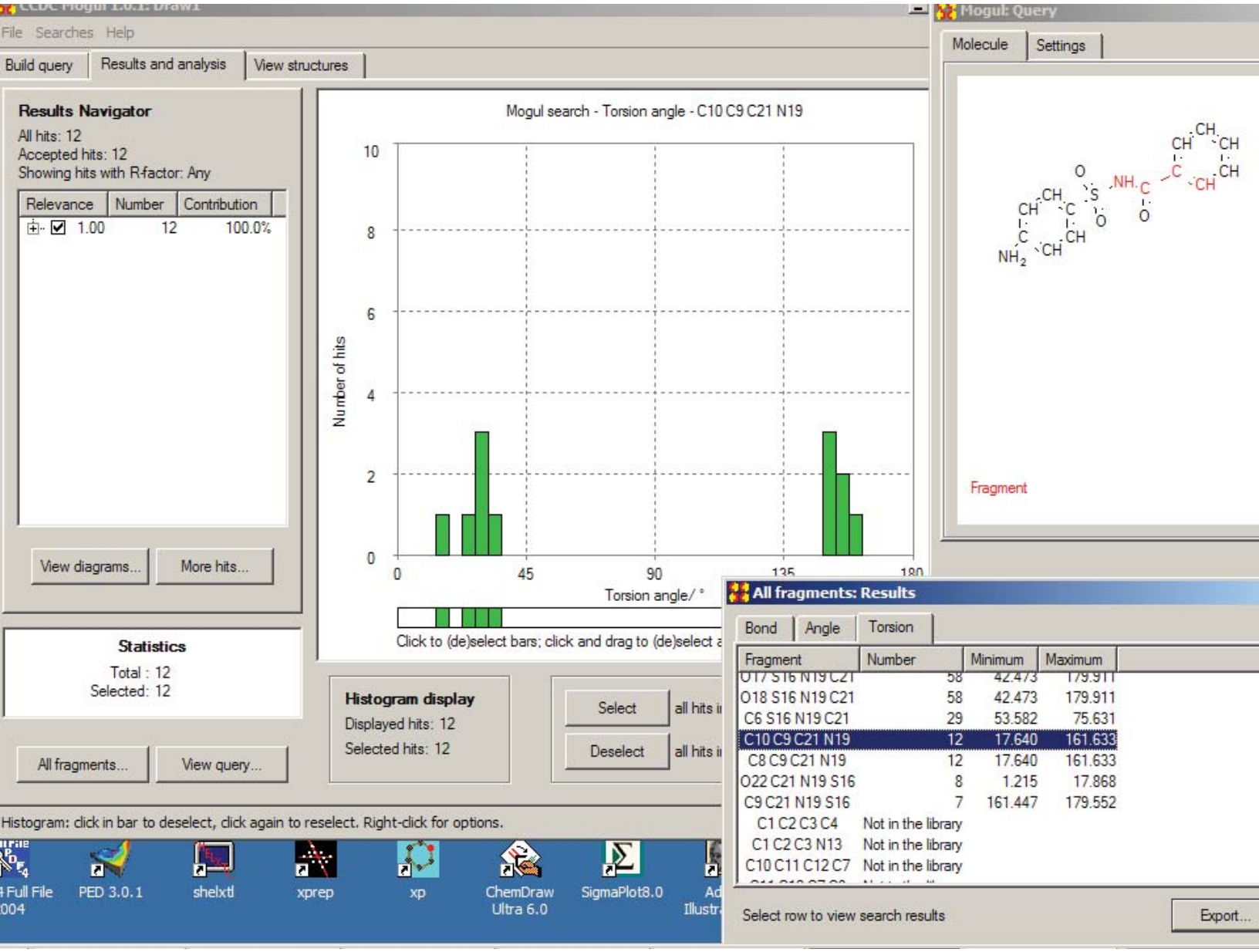


See what torsion angles we can expect

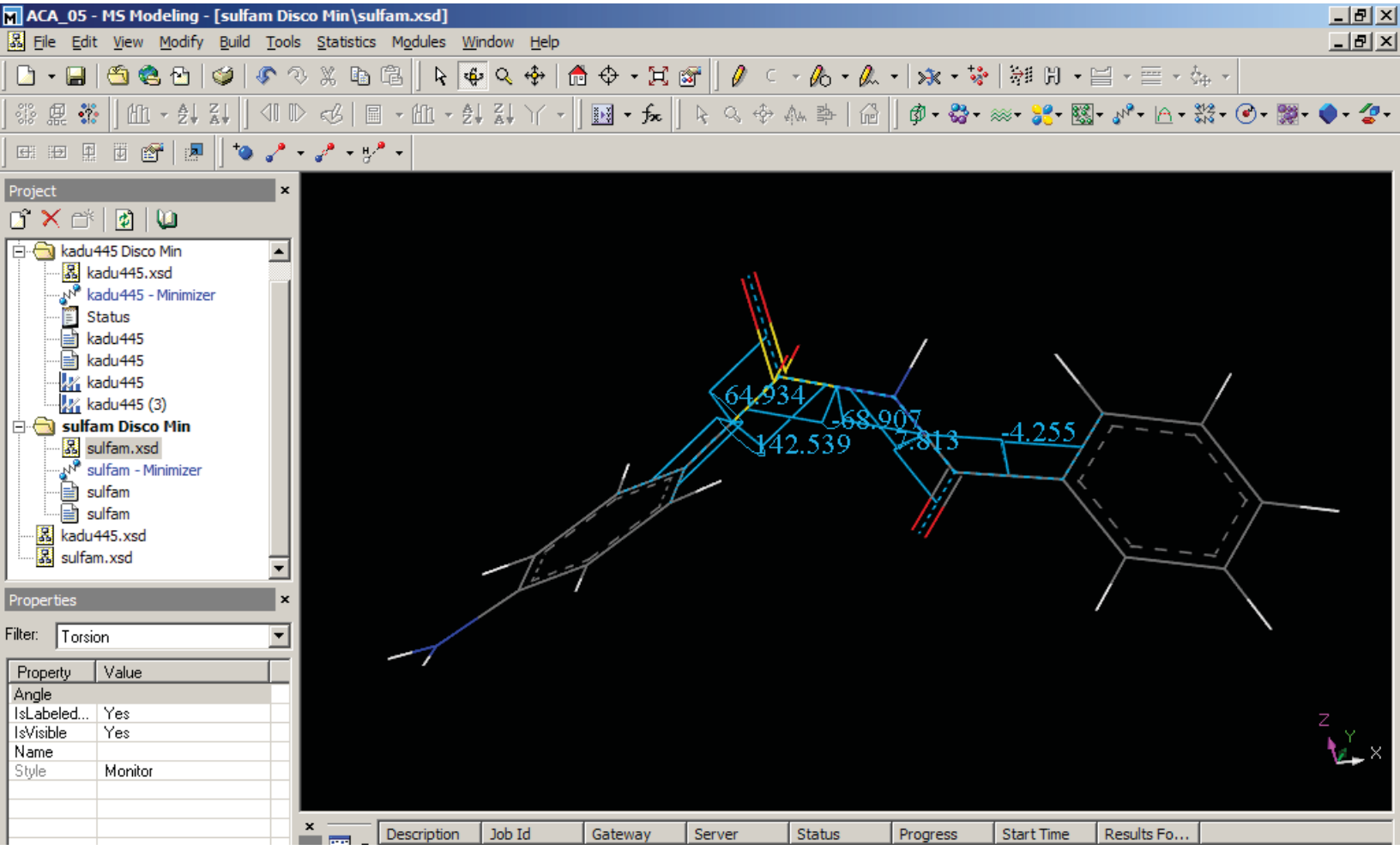



File Searches Help
Build query
Results and analysis
View structures
Results Navigator
All hits: 29
Accepted hits: 29
Showing hits with R-factor: Any
Relevance
Number
Contribution
1.00
29
100.0%
View diagrams...
More hits...
Statistics
Total : 29
Selected: 29
All fragments...
View query...
Mogul search - Torsion angle - C6 S16 N19 C21
Number of hits
Torsion angle/ °
Click to (de)select bars; click and drag to (de)select a
Histogram display
Displayed hits: 29
Selected hits: 29
Select
Deselect
Histogram: click in bar to deselect, click again to reselect. Right-click for options.
Mogul: Query
Molecule
Settings
Fragment
All fragments: Results
Bond
Angle
Torsion
Fragment
Number
Minimum
Maximum
O18 S16 N19 C21 58 42.473 179.911
C6 S16 N19 C21 29 53.582 75.631
C10 C9 C21 N19 12 17.640 161.633
C8 C9 C21 N19 12 17.640 161.633
O22 C21 N19 S16 8 1.215 17.868
C9 C21 N19 S16 7 161.447 179.552
C1 C2 C3 C4 Not in the library
C1 C2 C3 N13 Not in the library
C10 C11 C12 C7 Not in the library
Select row to view search results
Export...
PED 3.0.1
shelxtl
xprep
xp
ChemDraw Ultra 6.0
SigmaPlot8.0

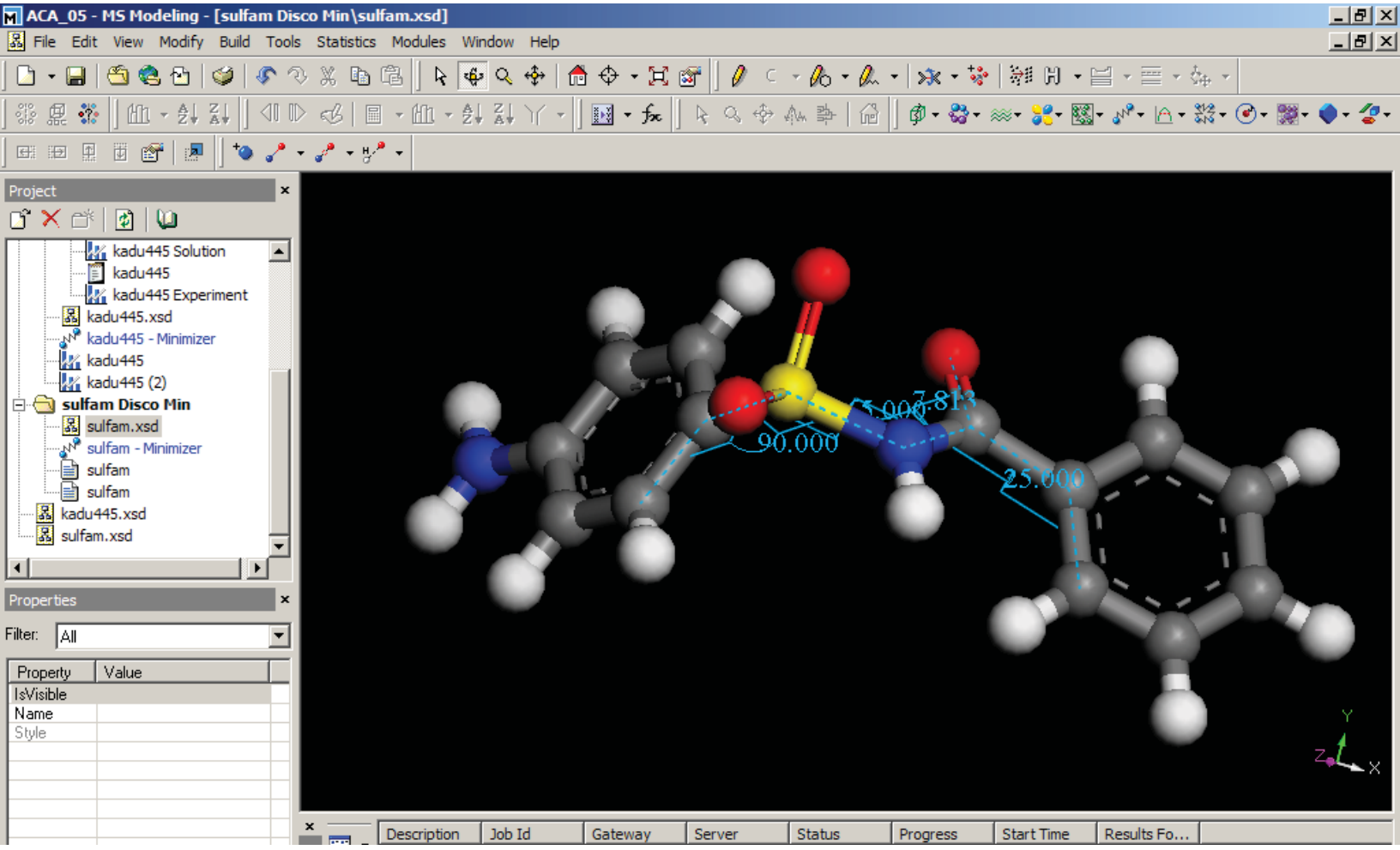

File Searches Help
Build query
Results and analysis
View structures
Results Navigator
All hits: 8
Accepted hits: 8
Showing hits with R-factor: Any
Relevance
Number
Contribution
1.00
8
100.0%
View diagrams...
More hits...
Statistics
Total : 8
Selected: 8
All fragments...
View query...
Mogul search - Torsion angle - O22 C21 N19 S16
Number of hits
Torsion angle/ °
Click to (de)select bars; click and drag to (de)select a
Histogram display
Displayed hits: 8
Selected hits: 8
Select
Deselect
Histogram: click in bar to deselect, click again to reselect. Right-click for options.
Mogul: Query
Molecule
Settings
Fragment
All fragments: Results
Bond
Angle
Torsion
Fragment
Number
Minimum
Maximum
O18 S16 N19 C21 58 42.473 179.911
C6 S16 N19 C21 29 53.582 75.631
C10 C9 C21 N19 12 17.640 161.633
C8 C9 C21 N19 12 17.640 161.633
O22 C21 N19 S16 8 1.215 17.868
C9 C21 N19 S16 7 161.447 179.552
C1 C2 C3 C4 Not in the library
C1 C2 C3 N13 Not in the library
C10 C11 C12 C7 Not in the library
Select row to view search results
Export...
PED 3.0.1
shelxtl
xprep
xp
ChemDraw Ultra 6.0
SigmaPlot8.0


File Searches Help
Build query
Results and analysis
View structures
Results Navigator
All hits: 12
Accepted hits: 12
Showing hits with R-factor: Any
Relevance
Number
Contribution
1.00
12
100.0%
View diagrams...
More hits...
Statistics
Total : 12
Selected: 12
All fragments...
View query...
Mogul search - Torsion angle - C10 C9 C21 N19
Number of hits
Torsion angle/ °
Click to (de)select bars; click and drag to (de)select a
Histogram display
Displayed hits: 12
Selected hits: 12
Select
Deselect
Histogram: click in bar to deselect, click again to reselect. Right-click for options.
Mogul: Query
Molecule
Settings
Fragment
All fragments: Results
Bond
Angle
Torsion
Fragment
Number
Minimum
Maximum
O18 S16 N19 C21 58 42.473 179.911
C6 S16 N19 C21 29 53.582 75.631
C10 C9 C21 N19 12 17.640 161.633
C8 C9 C21 N19 12 17.640 161.633
O22 C21 N19 S16 8 1.215 17.868
C9 C21 N19 S16 7 161.447 179.552
C1 C2 C3 C4 Not in the library
C1 C2 C3 N13 Not in the library
C10 C11 C12 C7 Not in the library
Select row to view search results
Export...
PED 3.0.1
shelxtl
xprep
xp
ChemDraw Ultra 6.0
SigmaPlot8.0

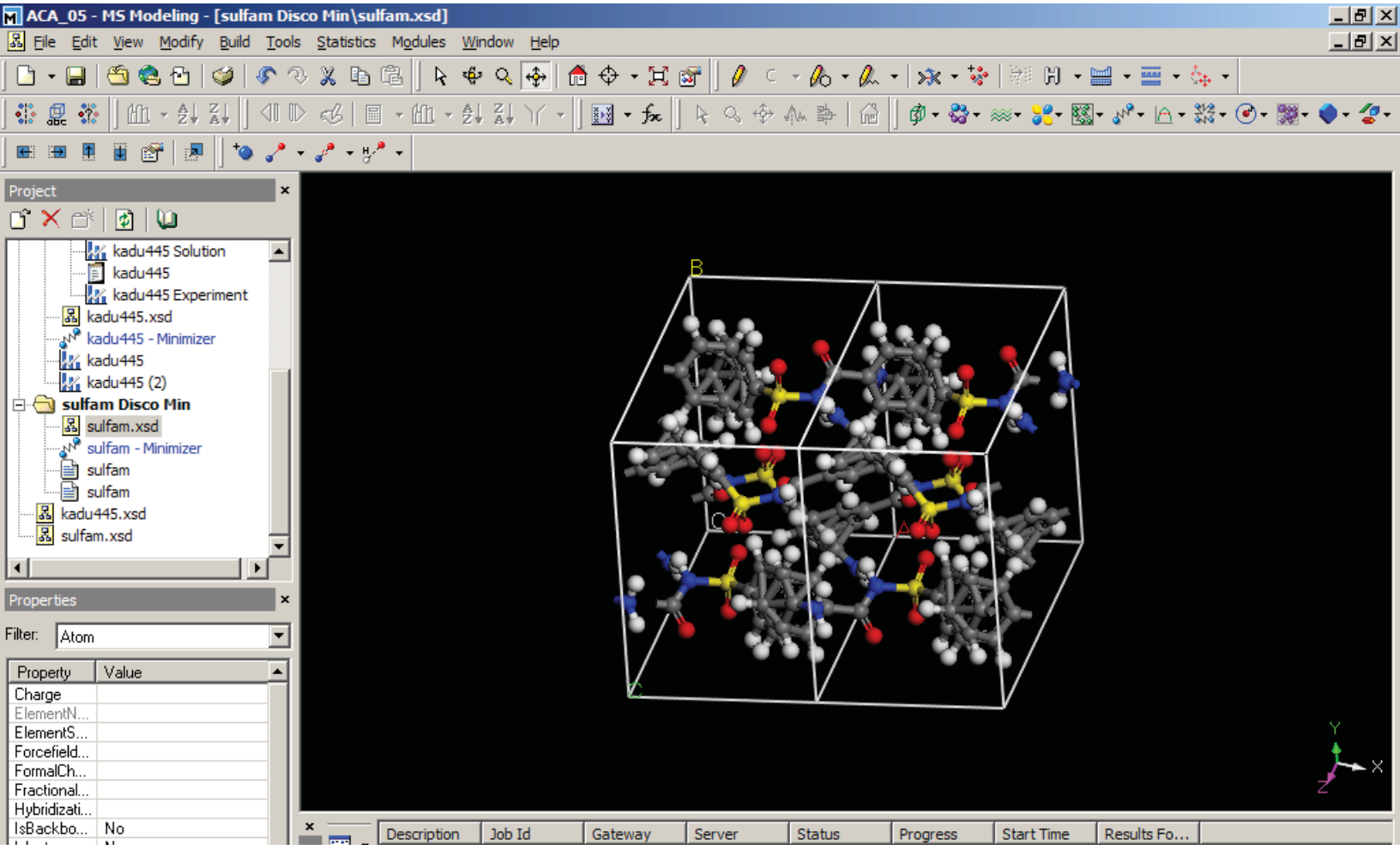
See how reasonable the torsions are



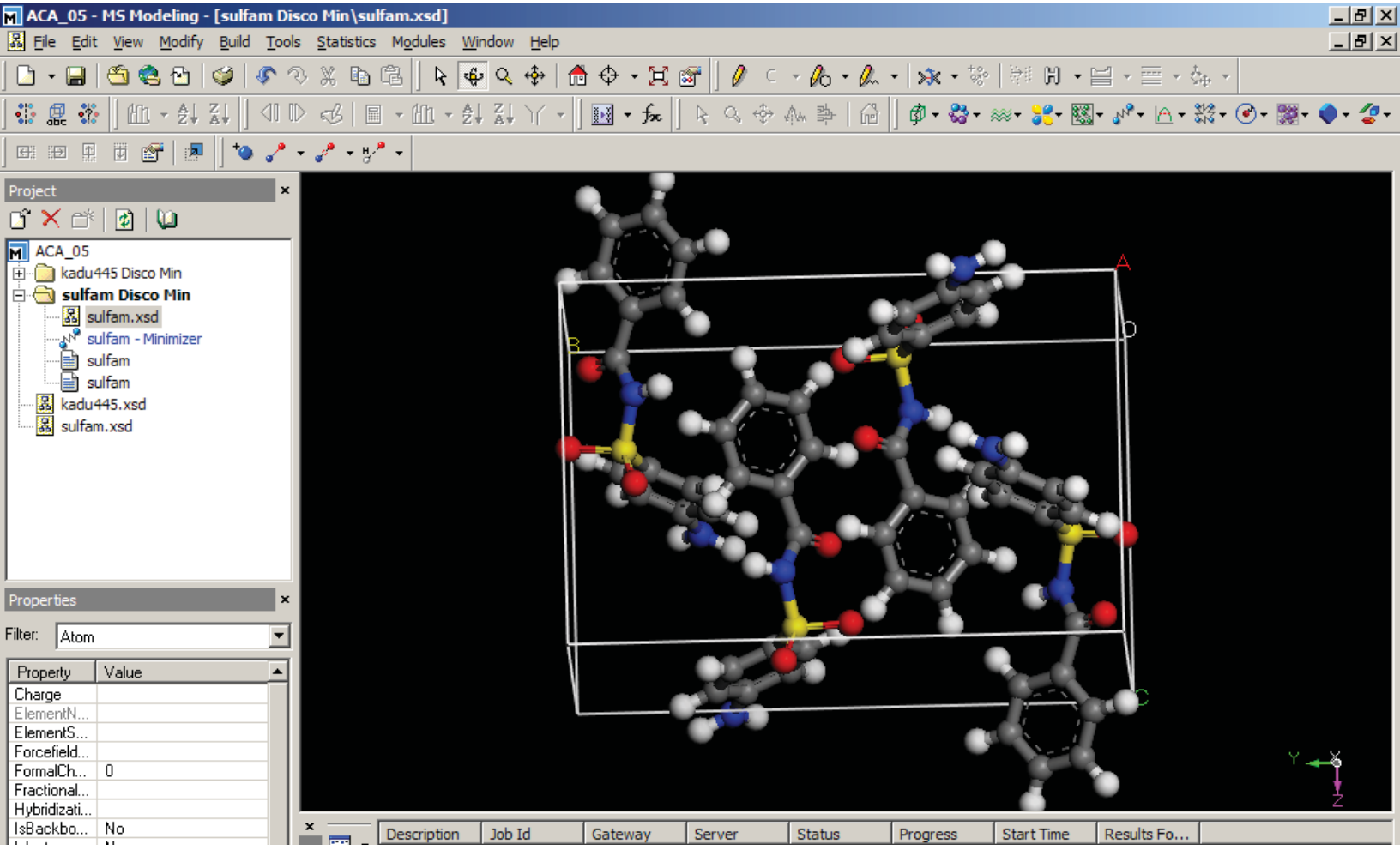
Manually adjust the torsions



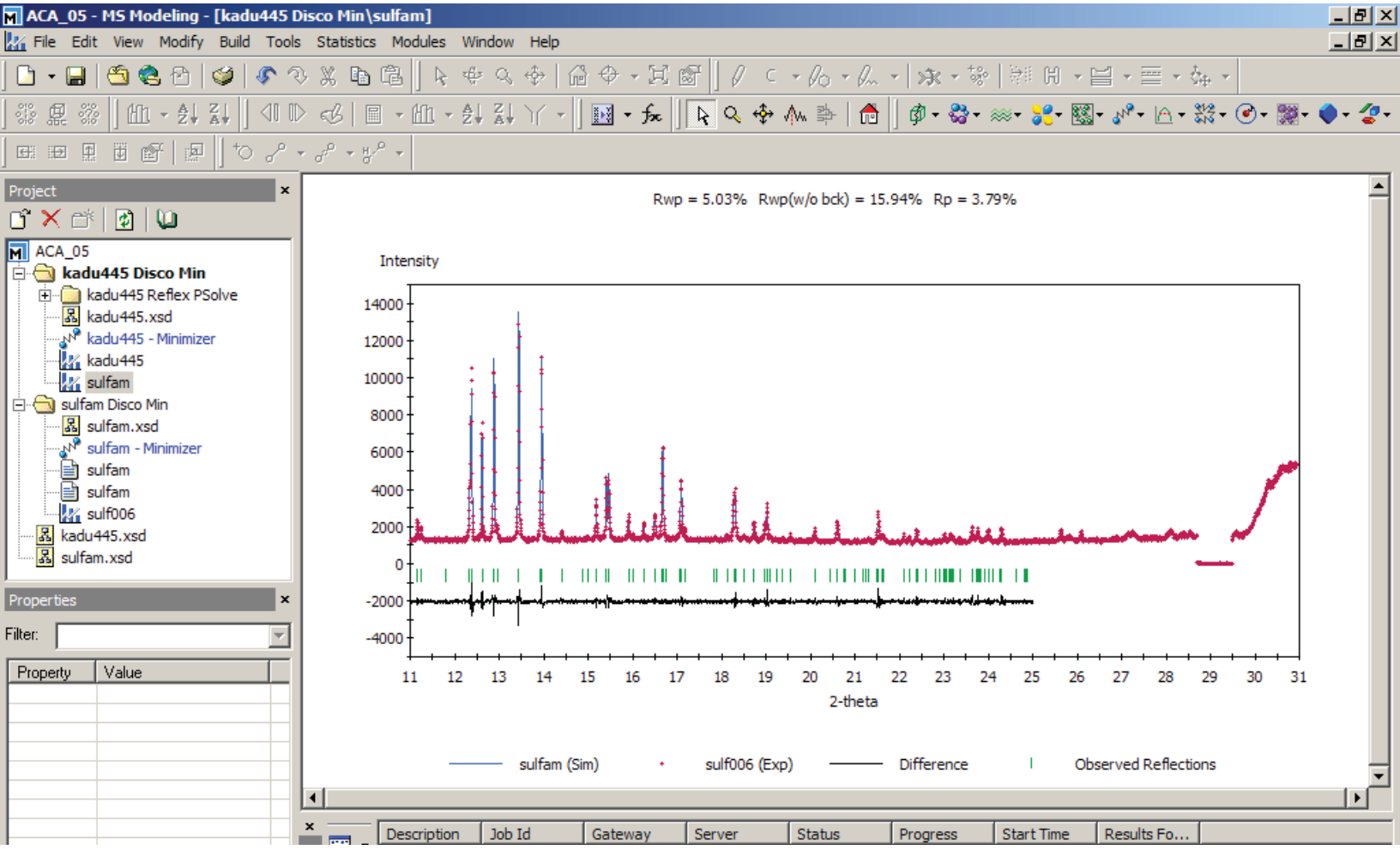
Build the crystal



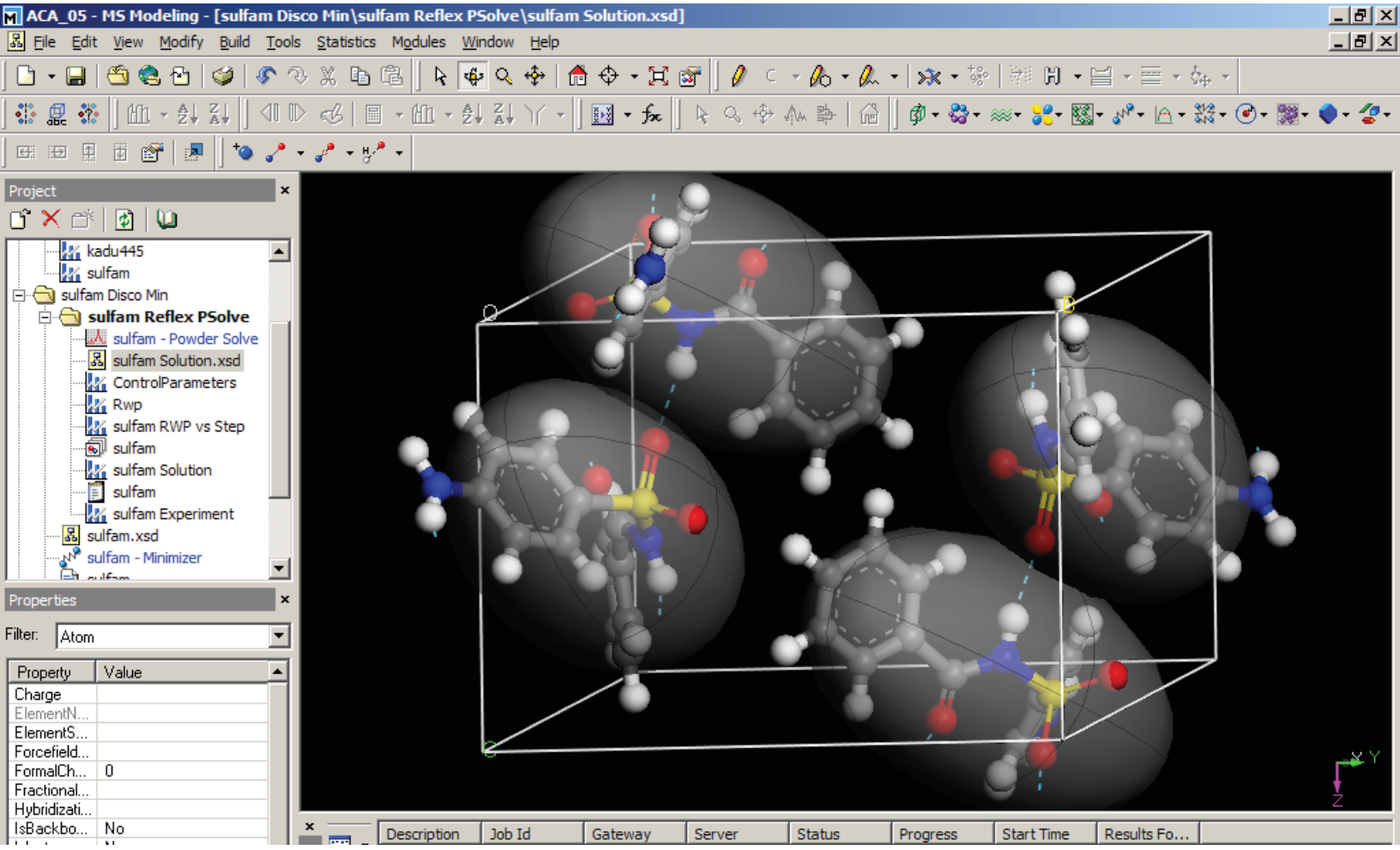
Remove the extra bonds



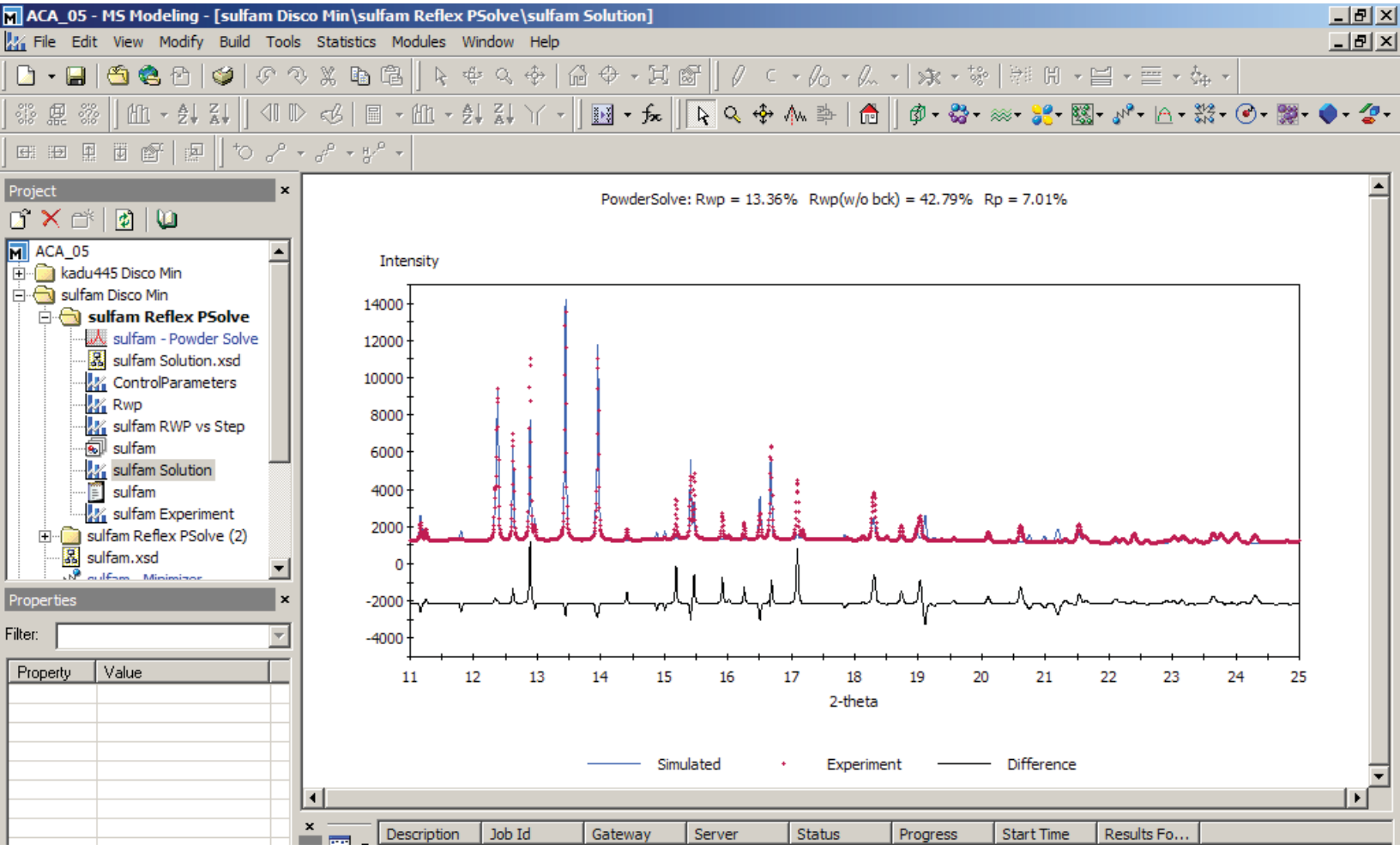
Import data and do Pawley fit



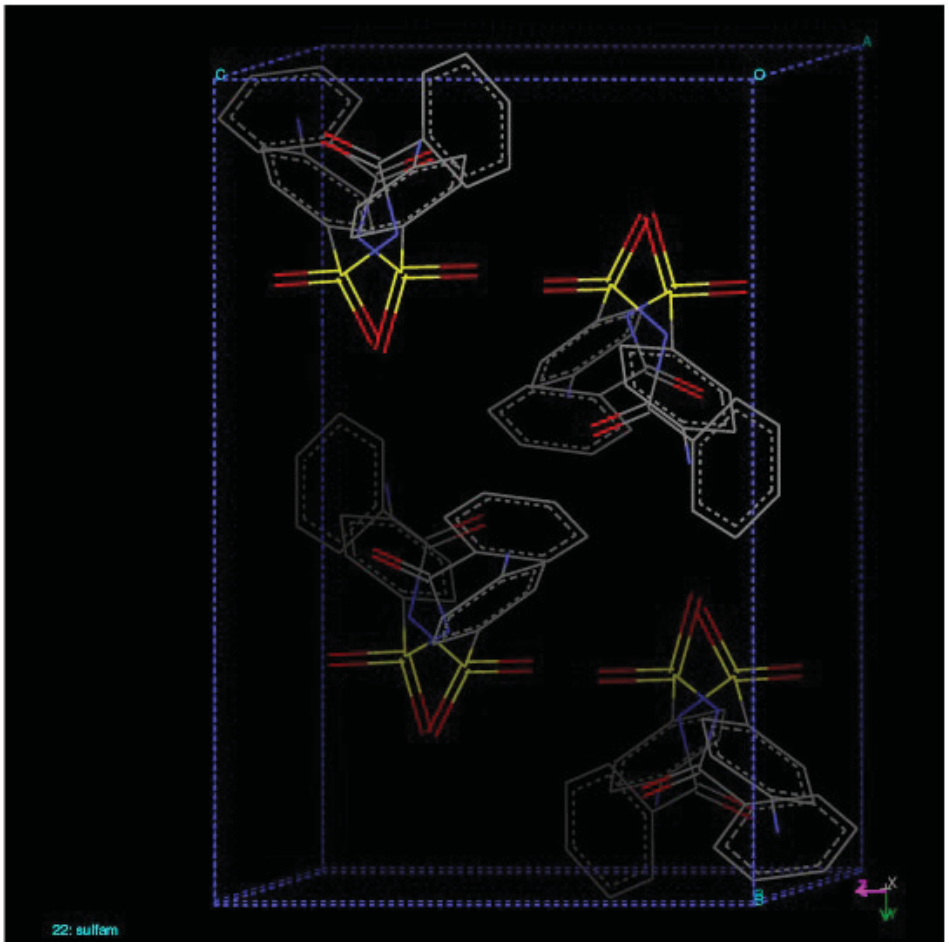
Try a rigid molecule with reasonable torsions



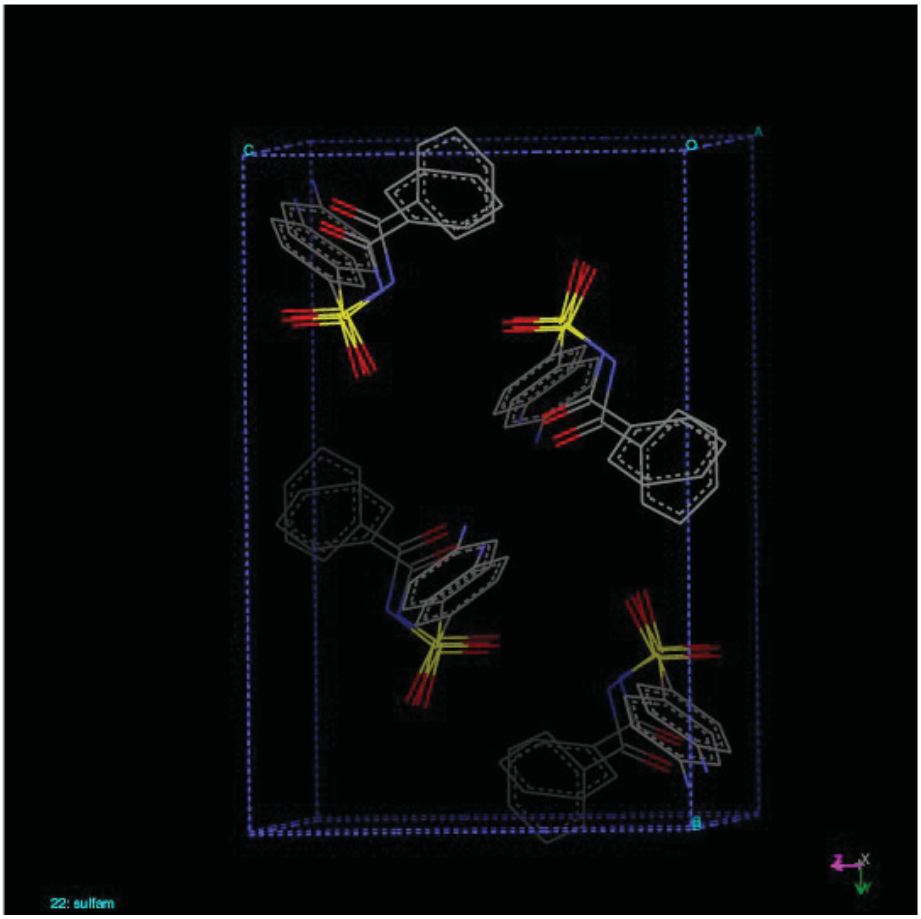
The fit isn’t great…



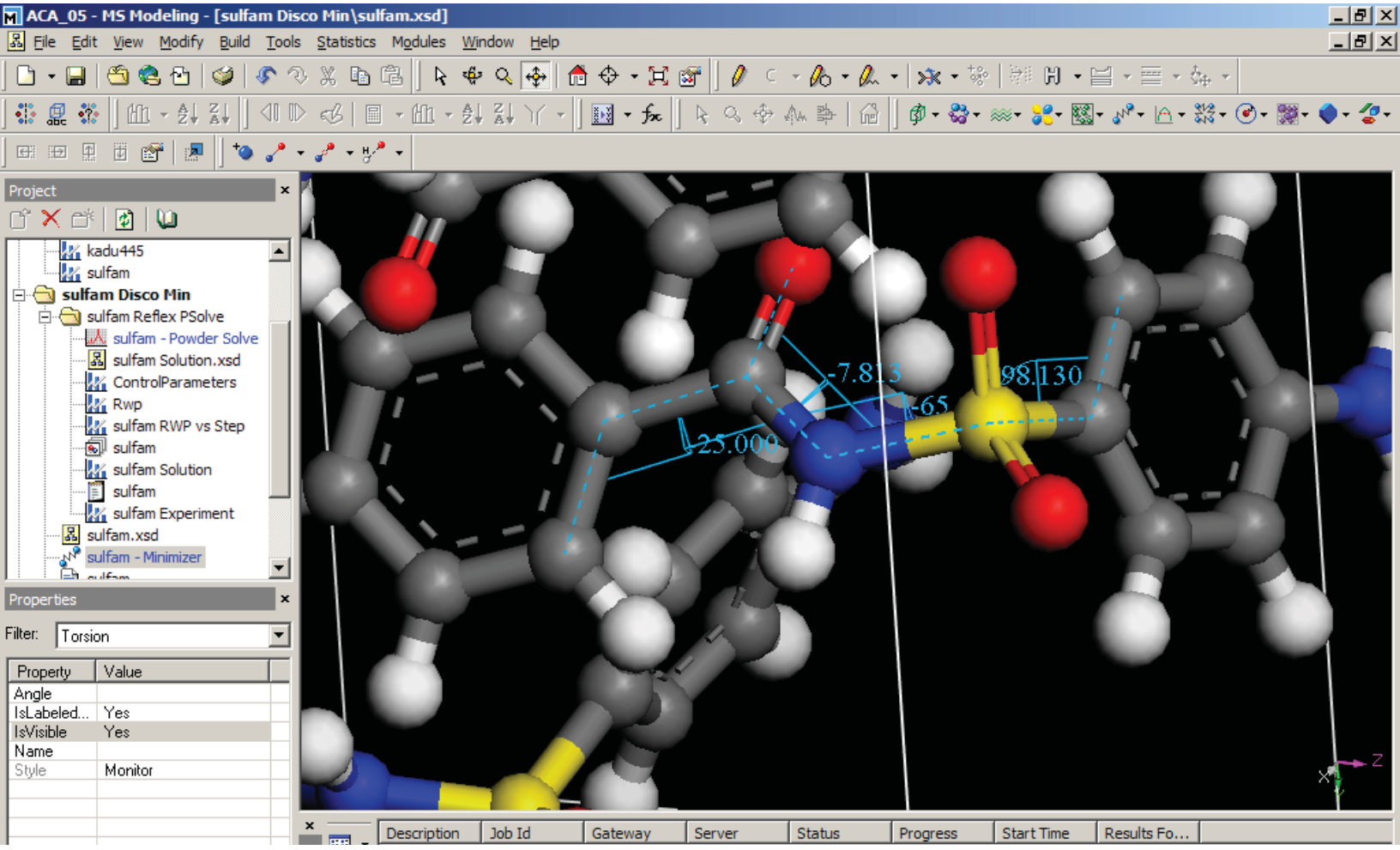
Compare to eventual refined structure



Rotate by 180° around *b*

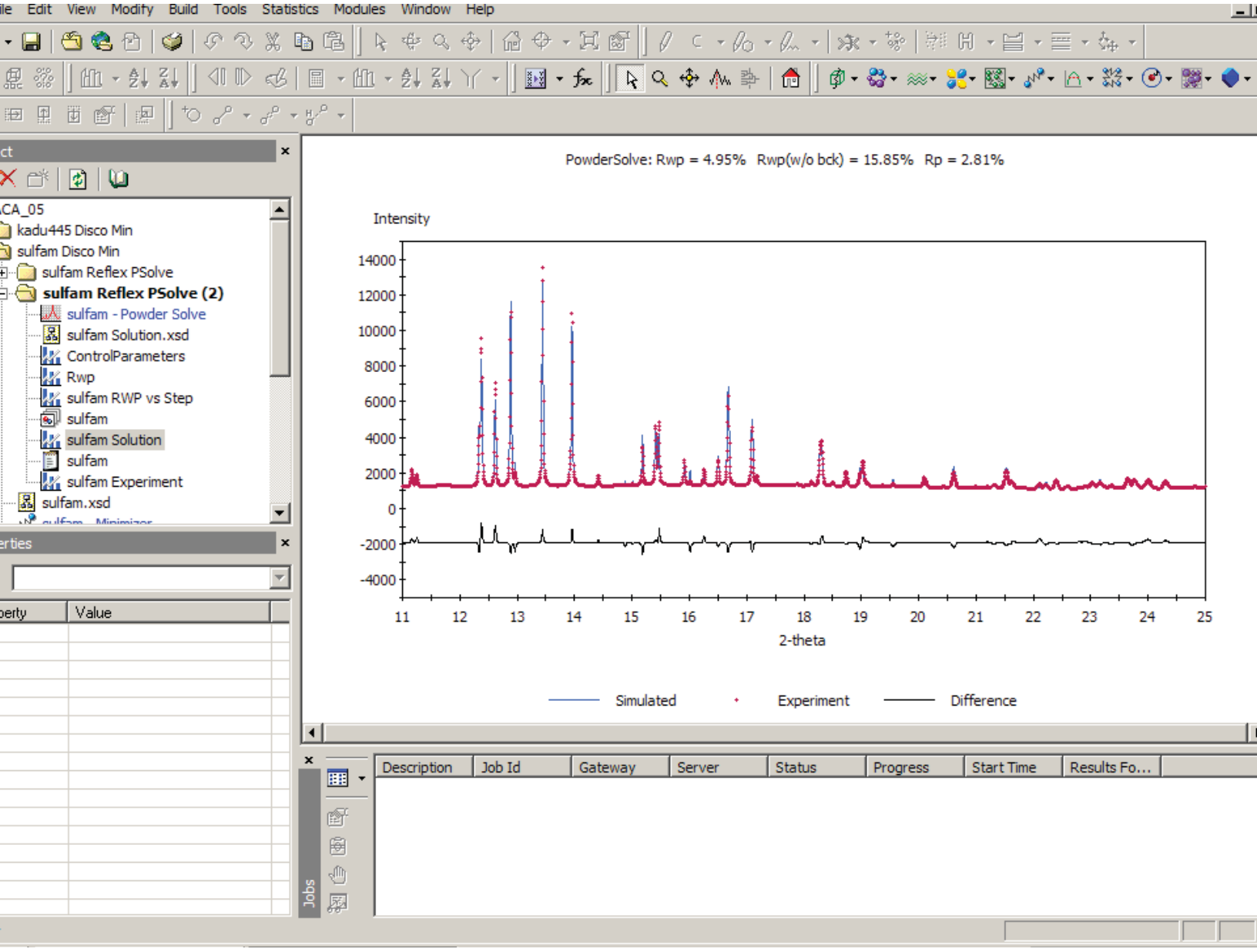


Add four torsions

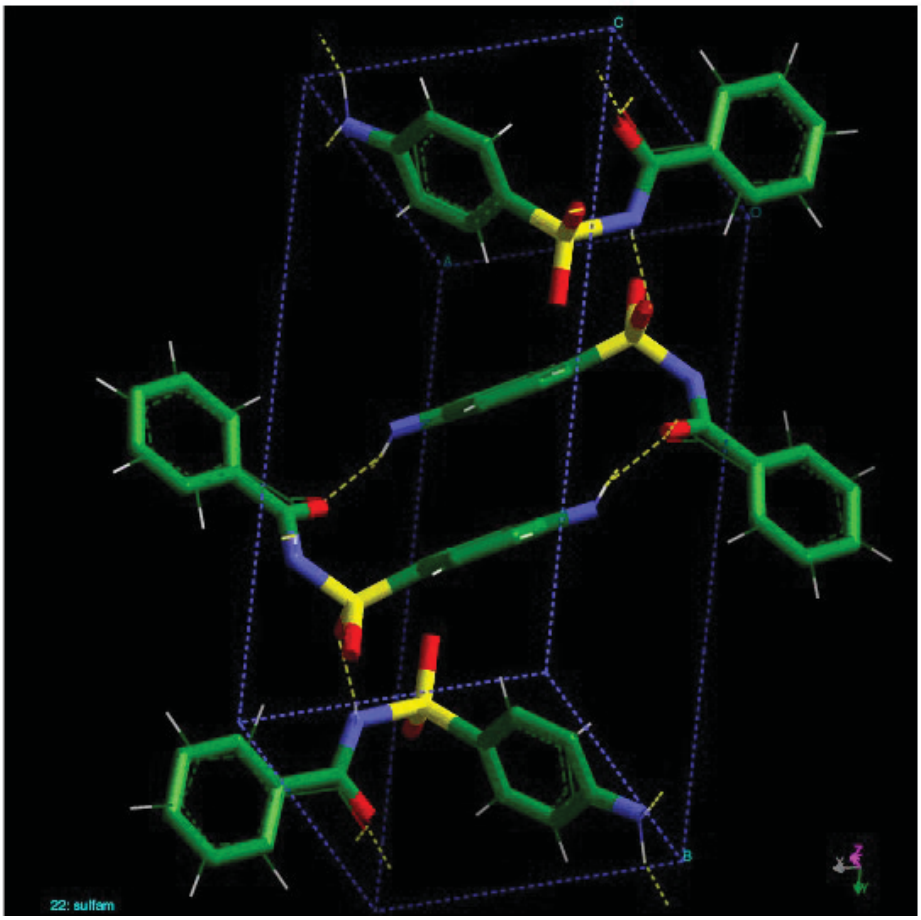


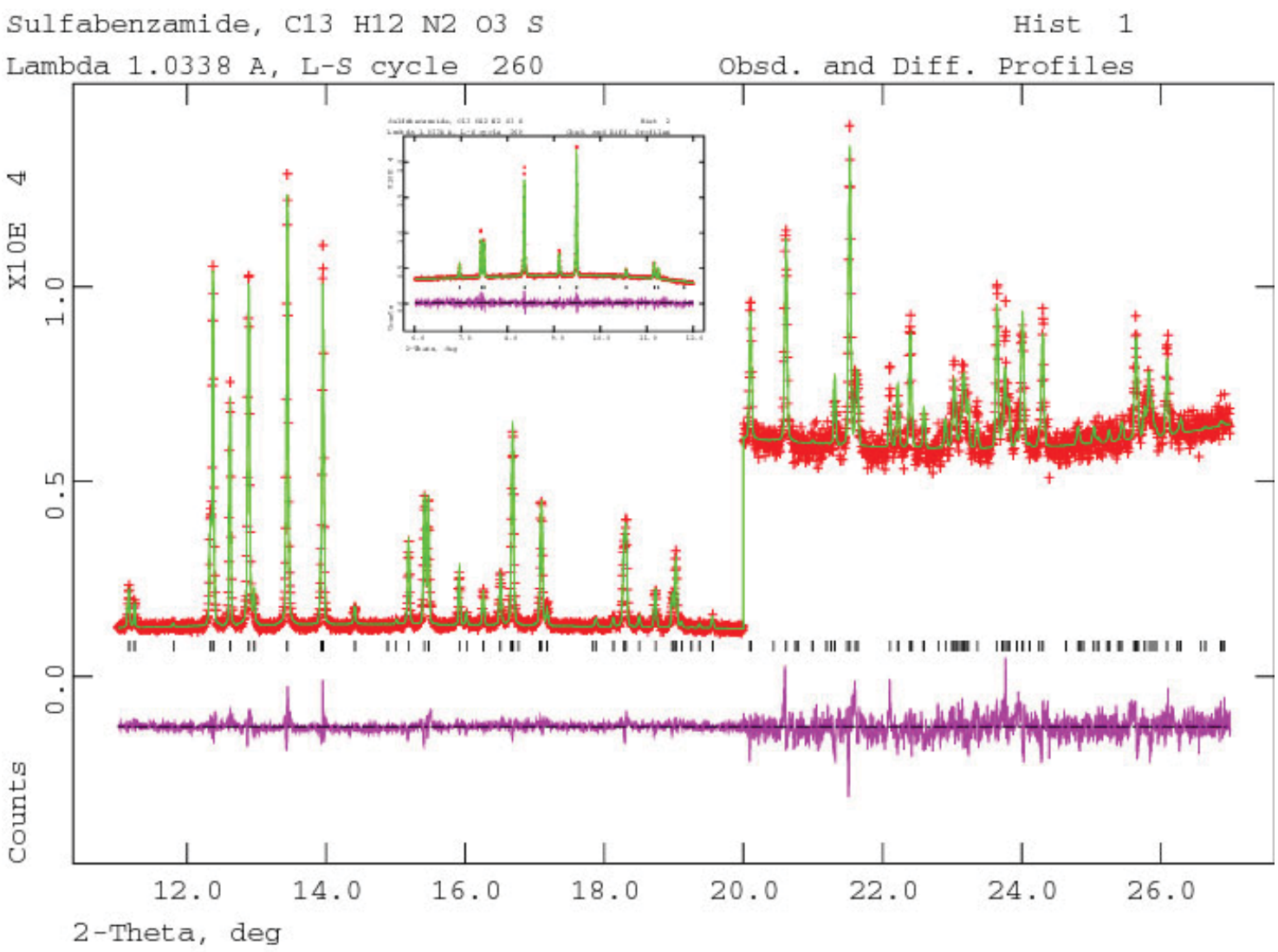
Structure Solution with Torsions

- First try – not good = not enough H-bonds
- Second try – Rwp = 0.0891, but no H-bonds and there were close close contacts
- Third try – add close contact penalty – Rwp = 0.0552 (0.0495), and a good fit:


Edit View Modify Build Tools Statistics Modules Window Help
CA_05
kadu445 Disco Min
sulfam Disco Min
sulfam Reflex PSolve
sulfam Reflex PSolve (2)
sulfam - Powder Solve
sulfam Solution.xsd
ControlParameters
Rwp
sulfam RWP vs Step
sulfam
sulfam Solution
sulfam
sulfam Experiment
sulfam.xsd
Value
PowderSolve: Rwp = 4.95% Rwp(w/o bck) = 15.85% Rp = 2.81%
Intensity
14000
12000
10000
8000
6000
4000
2000
0
-2000
-4000
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
2-theta
Simulated
Experiment
Difference
Description
Job Id
Gateway
Server
Status
Progress
Start Time
Results Fo...
Jobs

Sulfabenzamide Form I





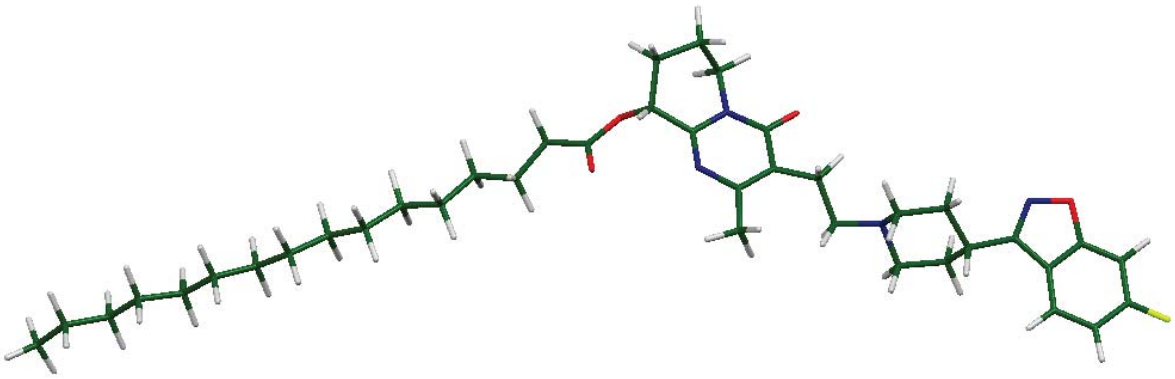
Scaling: 20.0(5.0X)

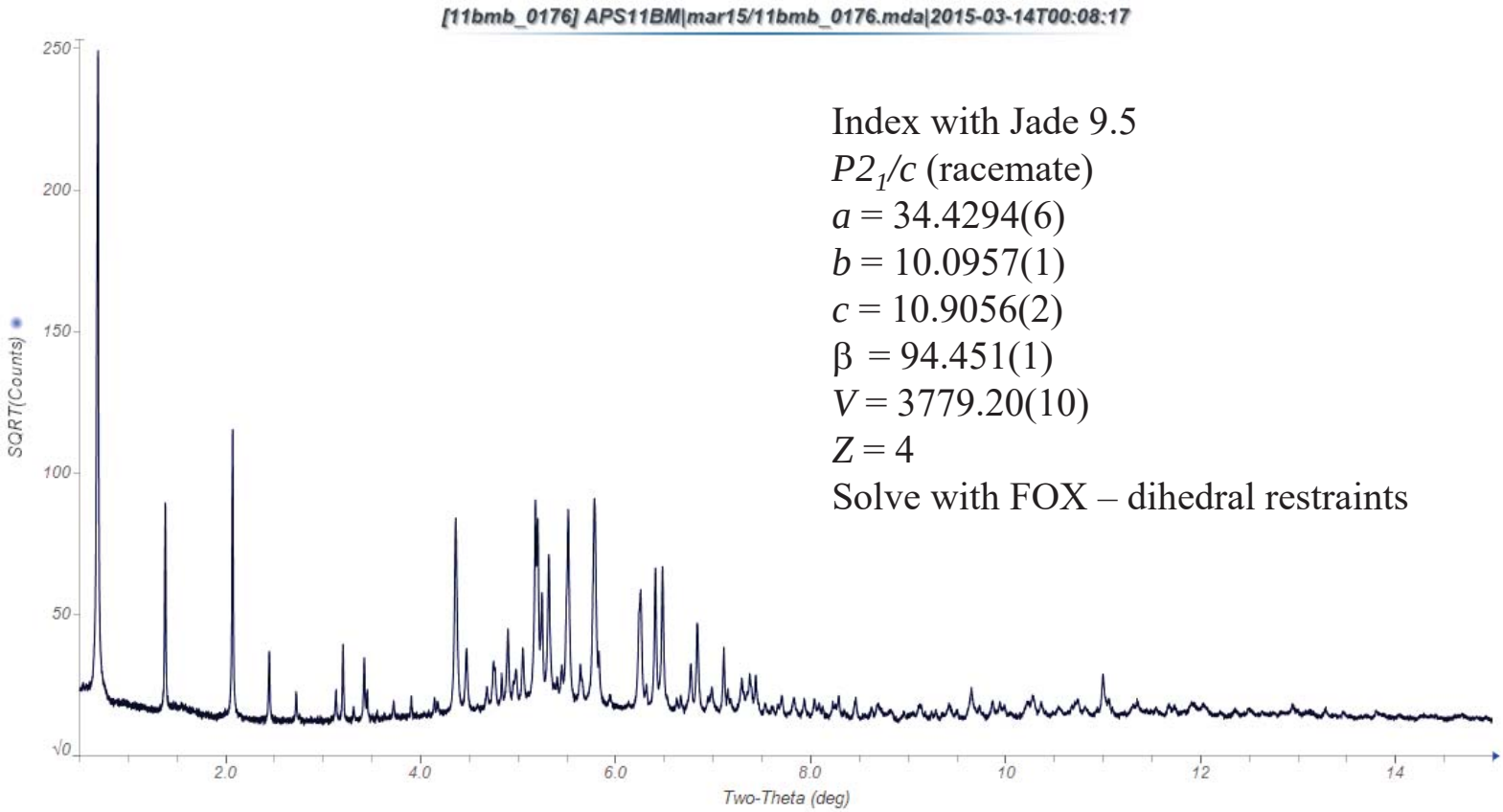
Paliperidone Palmitate
$C_{39}H_{57}FN_4O_4$

Invega® Sustenna®

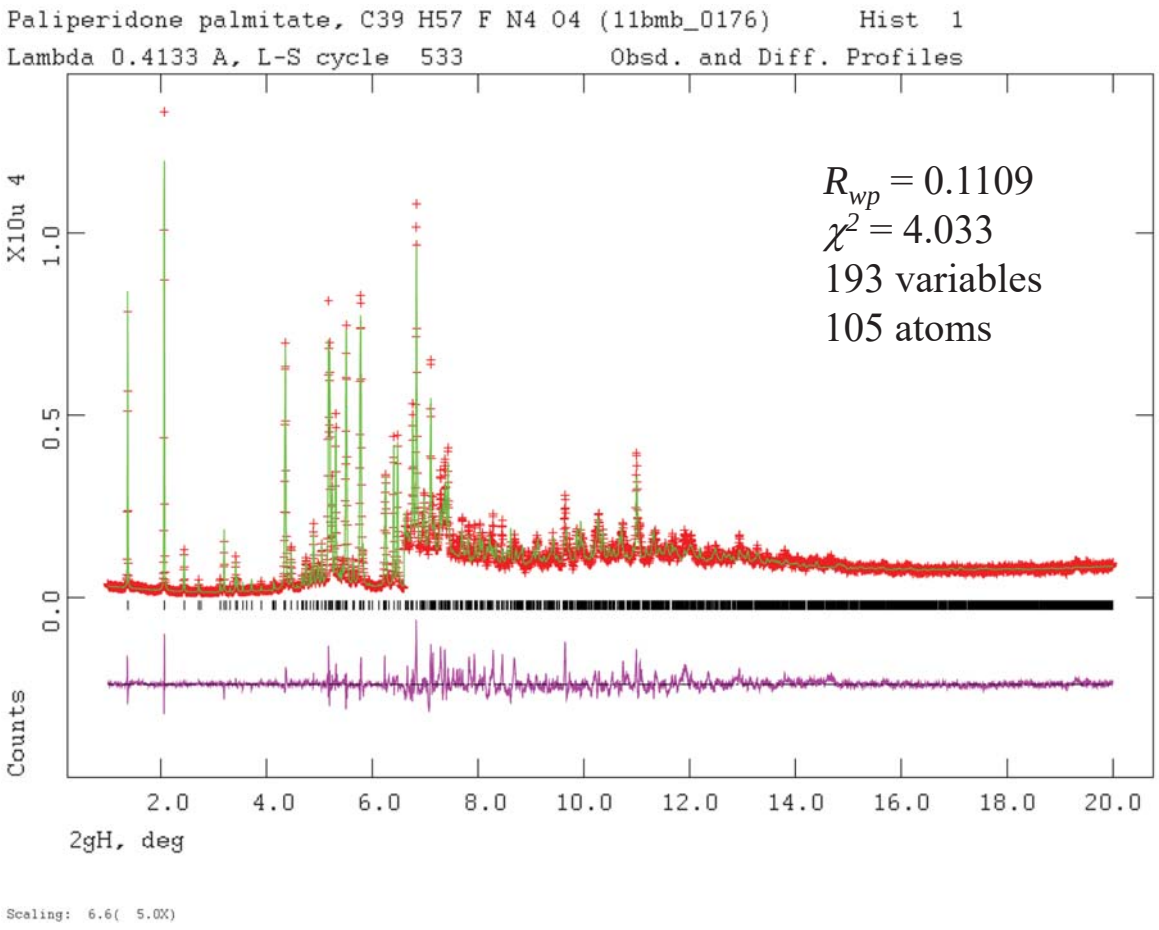
antipsychotic

Paliperidone Palmitate

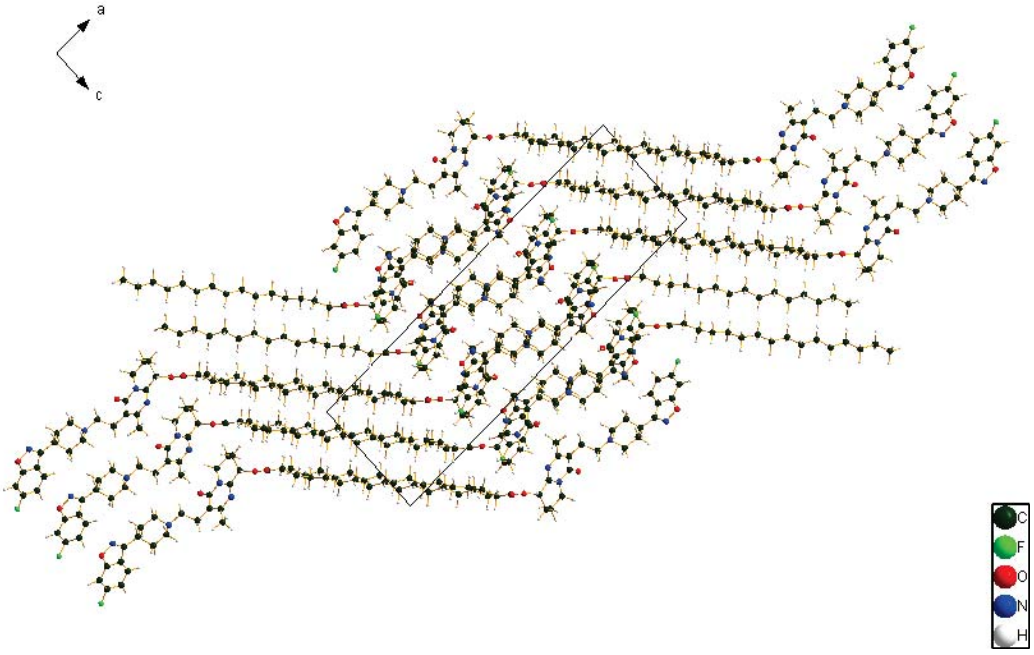




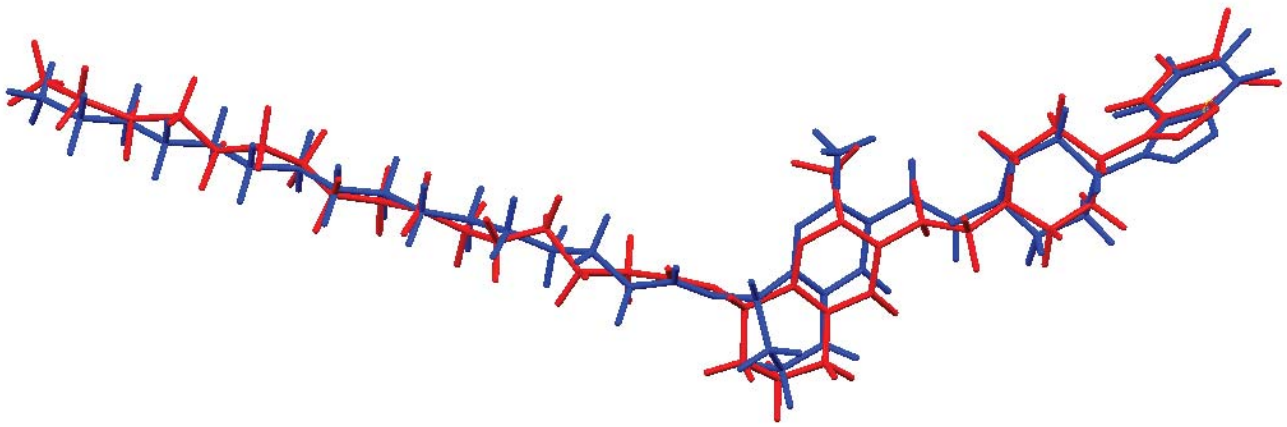
Index with Jade 9.5
$P2_1/c$ (racemate)
a = 34.4294(6)
b = 10.0957(1)
c = 10.9056(2)
β = 94.451(1)
V = 3779.20(10)
Z = 4
Solve with FOX – dihedral restraints


Paliperidone palmitate, C39 H57 F N4 O4 (11bmb_0176) Hist 1
Lambda 0.4133 A, L-S cycle 533 Obsd. and Diff. Profiles
X10u 4
1.0
0.5
0.0
Counts
2.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0
20.0
2gH, deg
R_{wp} = 0.1109
χ^2 = 4.033
193 variables
105 atoms
Scaling: 6.6(5.0X)

Paliperidone Palmitate



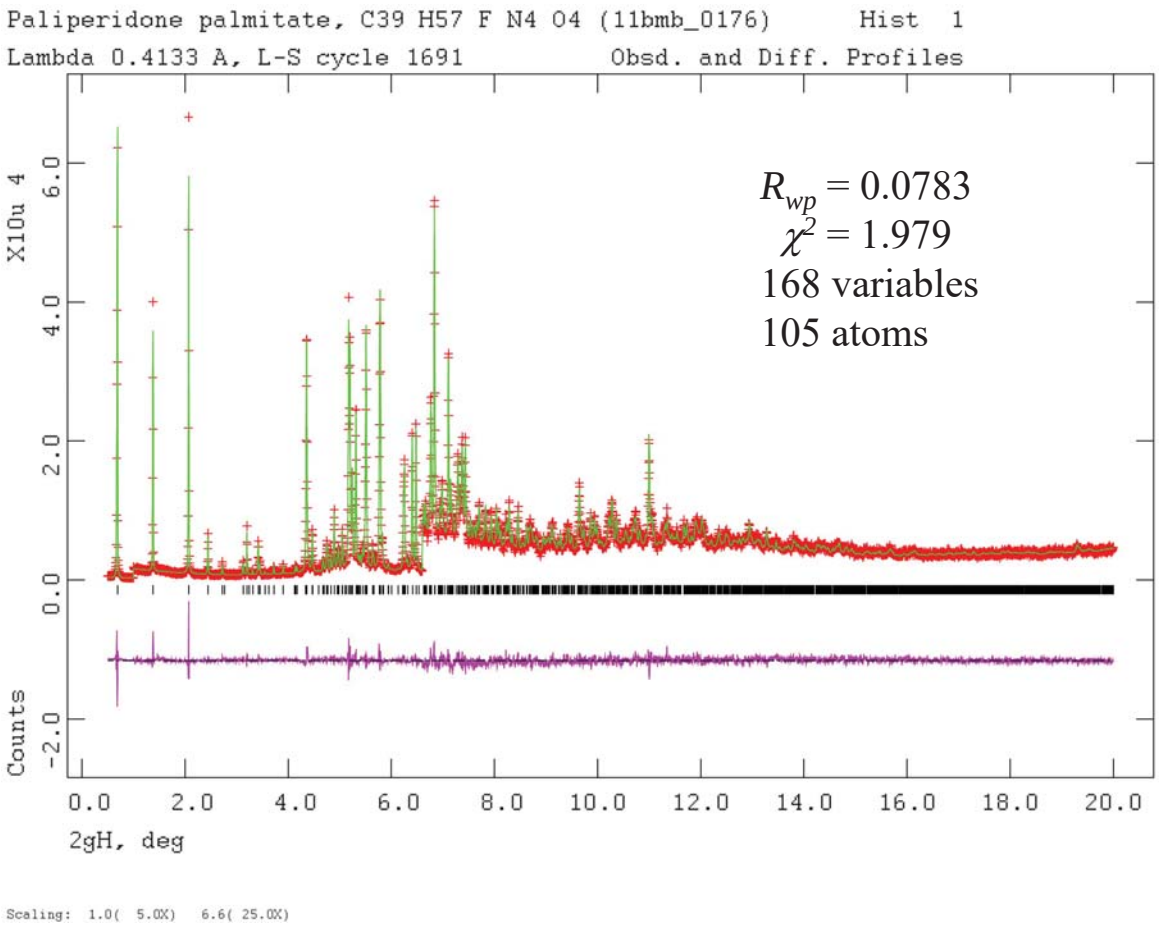
Paliperidone Palmitate (wrong)



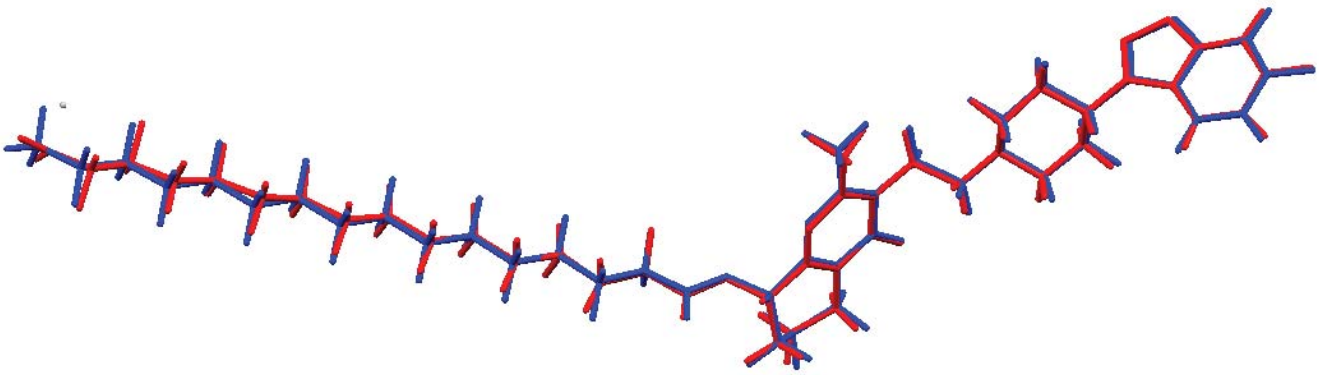
RMS Δ = 0.658 Å; red = Rietveld, blue = DFT

More Simulated Annealing

The 5/6 fused-ring end of the paliperidone rotates by 180°

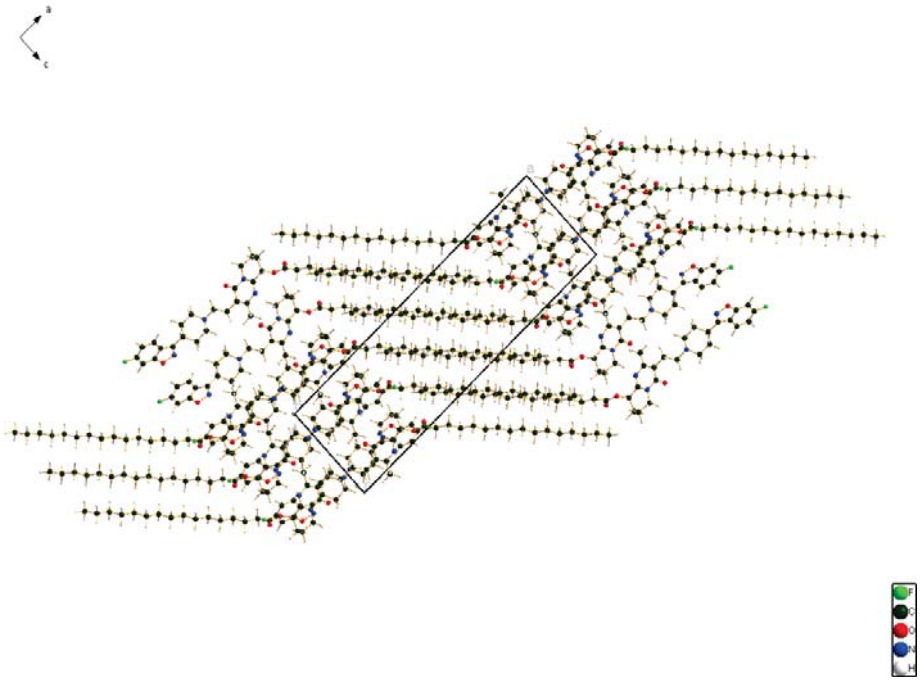

Paliperidone palmitate, C39 H57 F N4 O4 (11bmb_0176) Hist 1
Lambda 0.4133 A, L-S cycle 1691 Obsd. and Diff. Profiles
R_{wp} = 0.0783
χ^2 = 1.979
168 variables
105 atoms
X10u 4
Counts
2gH, deg
Scaling: 1.0(5.0X) 6.6(25.0X)

Paliperidone Palmitate (correct)

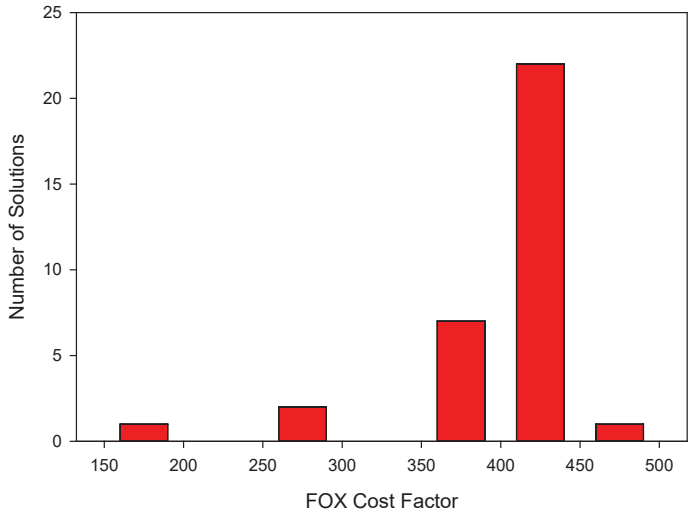


RMS Δ = 0.165 Å; red = Rietveld, blue = DFT

Paliperidone Palmitate (correct)



Eltrombopag Diolamine Structure Solution



Programs for *ab initio* Structure Solution

Program	Source	Price
FOX	Vincent Favre-Nicolin Rodovan Czerny	Fox.vincefn.net SourceForge
EXPO2014	Carmelo Giacovazzo…	Free/1000€/Bari
TOPAS	Alan Coelho	$/$$//Coelho/Bruker
SUPERFLIP	Palatinus & Chapuis	Free http://superspace/epfl.ch/superflip
JANA2006	V. Petříček	Free http://jana.fzu.cz
DASH	W.I.F. David…	With CSD
Reflex Plus	Accelrys	~30k$?
Polymorph Predictor	Accelrys	~70k$?
Endeavour	Crystal Impact	299€/599€/1198€
WinPSSP	Silvina Pagola …	Free http://users.uoi.gr/nkourkou/winpssp
ESPOIR	Armel Le Bail	Free/CCP14
SHELX	George Sheldrick	Free/$$
WinGX	CCP14	Free/$

… and then, once you solve your problem, put the information in the Powder Diffraction File!

Real-Time Example of Monte Carlo Simulated Annealing Using FOX

$Dy(Ti_{0.25}Co_{0.75})O_3$

Pnma

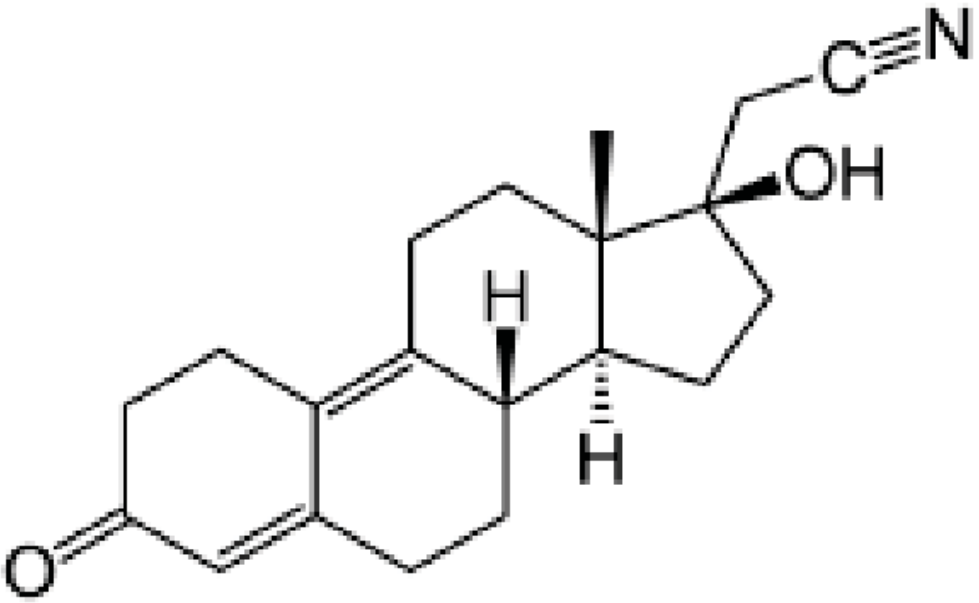
$a = 5.5336$, $b = 7.5008$, $c = 5.2373$

wong764b.dat, 20-130°, $(\sin\theta/\lambda)_{max} = 0.55$

Co-O = 1.96 Å

Real-Time Example of Direct Methods Using EXPO2014

Dienogest, $C_{20}H_{25}NO_2$



11bmb_2406.cif

Real-Time Example of Charge Flipping Using Jana2006 Herbertsmithite, $Cu_3Zn(OH)_6Cl_2$

$R\bar{3}m$, $a = 6.838$, $c = 14.064$, $Z = 3$

wong755.dat, 12-130°