Software Description

Design of experiment, process tracking, and experimental analysis make use of a proprietary software, named InForm, which was developed at TransForm Pharmaceuticals. The software suite was developed using the Java programming language and utilizes several Oracle 8i databases. Images used in this paper were produced using MATLAB.

Table I Solvents Used in 10 K Polymorph Screen that gave Form II

Solvent(s) that gave form II
40% MeOH, 40% THF, 20% Isobutyl acetate
100% 2-Propanol
67% 1-Pentanol, 33% 2-Methyl-1-propanol
67% THF, 33% 2-Propanol
40% 2-Butanol, 40% 2-Methyl-1-propanol, 20% Anisole
40% 2-Ethoxyethanol, 40% 2-Hexanone, 20% 2-Methyl-1-propanol
67% Anisole, 33% Isobutyl acetate
67% 2-Methyl-1-propanol, 33% 1-Butanol
67% EtOH, 33% THF
67% THF, 33% 2-Propanol
100% 1-Butanol
40% EtOH, 40% Toluene, 20% THF
67% 2-Methyl-1-propanol, 33% THF
67% 2-Methyl-1-propanol, 33% 1-Butanol
40% Acetone, 40% THF, 20% 2-Ethoxyethanol
67% 2-Methyl-1-propanol, 33% 2-Ethoxyethanol
40% 2-Methyl-1-propanol, 40% Butyl acetate, 20% THF
67% MeOH, 33% THF
67% 2-Methyl-1-propanol, 33% 2-Butanol
67% MeOH, 33% Isobutyl acetate
67% THF, 33% Acetonitrile
67% MeOH, 33% Acetonitrile
67% Isobutyl acetate, 33% MeOH
67% Isobutyl acetate, 33% 2-Butanol
67% EtOH, 33% 3-Methyl-1-butanol
40% 2-Methyl-1-propanol, 40% Methylethylcetone, 20% Toluene

Table 2. Solvent Boiling Points (source: Merck Index)

Solvent	Boiling Point (°C)
MeOH	64.7
THF	66
Ethanol	78.5
Methylethylcetone/ MEK	79.6
Acetonitrile	81.6
2-Propanol	82.5
2-Butanol	99.5
2-Methyl-1-propanol	108
Toluene	110.6
1-Butanol	117
Isobutyl acetate	118
2-Hexanone	127
3-Methyl-1-butanol	130.5
2-Ethoxyethanol	135
1-Pentanol	137.5
Anisole	155.5

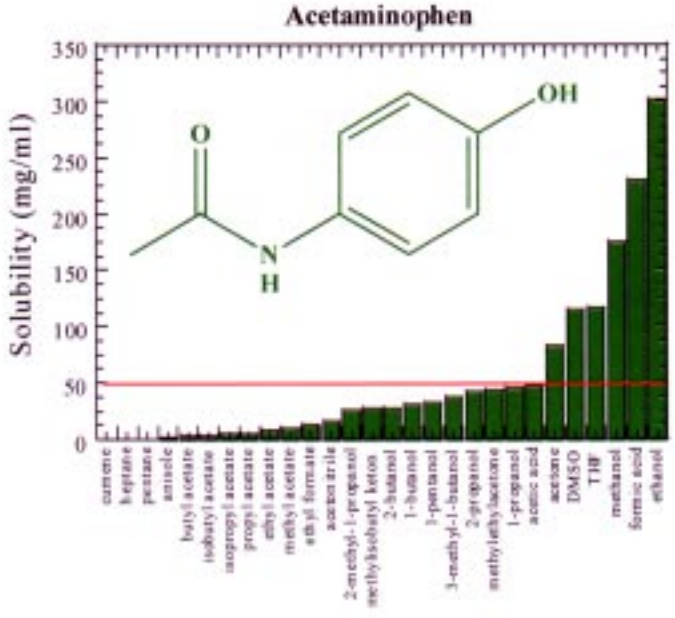


Figure 1. Measured solubilities of acetaminophen in solvents used in the 10 K polymorph screen.

Table 3. Solvent list second experiment

Solvent	Solvent
40% MeOH, 40% THF, 20% Isobutyl acetate	67% MeOH, 33% Isobutyl acetate
100% 2-Propanol	67% THF, 33% Acetonitrile
67% 1-Pentanol, 33% 2-Methyl-1-propanol	67% MeOH, 33% Acetonitrile
67% THF, 33% 2-Propanol	67% Isobutyl acetate, 33% MeOH
40% 2-Butanol, 40% 2-Methyl-1-propanol, 20% Anisole	67% Isobutyl acetate, 33% 2-Butanol
40% 2-Ethoxyethanol, 40% 2-Hexanone, 20% 2-Methyl-1-propanol	67% EtOH, 33% 3-Methyl-1-butanol
67% Anisole, 33% Isobutyl acetate	40% 2-Methyl-1-propanol, 40% Methylethylketone, 20% Toluene
67% 2-Methyl-1-propanol, 33% 1-Butanol	100 % THF
67% EtOH, 33% THF	100 % MEK
67% THF, 33% 2-Propanol	100 % acetonitrile
100% 1-Butanol	100 % toluene
40% EtOH, 40% Toluene, 20% THF	100 % isobutyl acetate
67% 2-Methyl-1-propanol, 33% THF	100 % anisole
67% 2-Methyl-1-propanol, 33% 1-Butanol	67 % THF 33 % anisole
40% Acetone, 40% THF, 20% 2-Ethoxyethanol	67 % THF 33 % isobutyl acetate
67% 2-Methyl-1-propanol, 33% 2-Ethoxyethanol	67 % acetonitrile 33 % anisole
40% 2-Methyl-1-propanol, 40% Butyl acetate, 20% THF	67 % THF 33 % toluene
67% MeOH, 33% THF	67 % toluene 33 % acetonitrile
67% 2-Methyl-1-propanol, 33% 2-Butanol	67 % toluene 33 % anisole

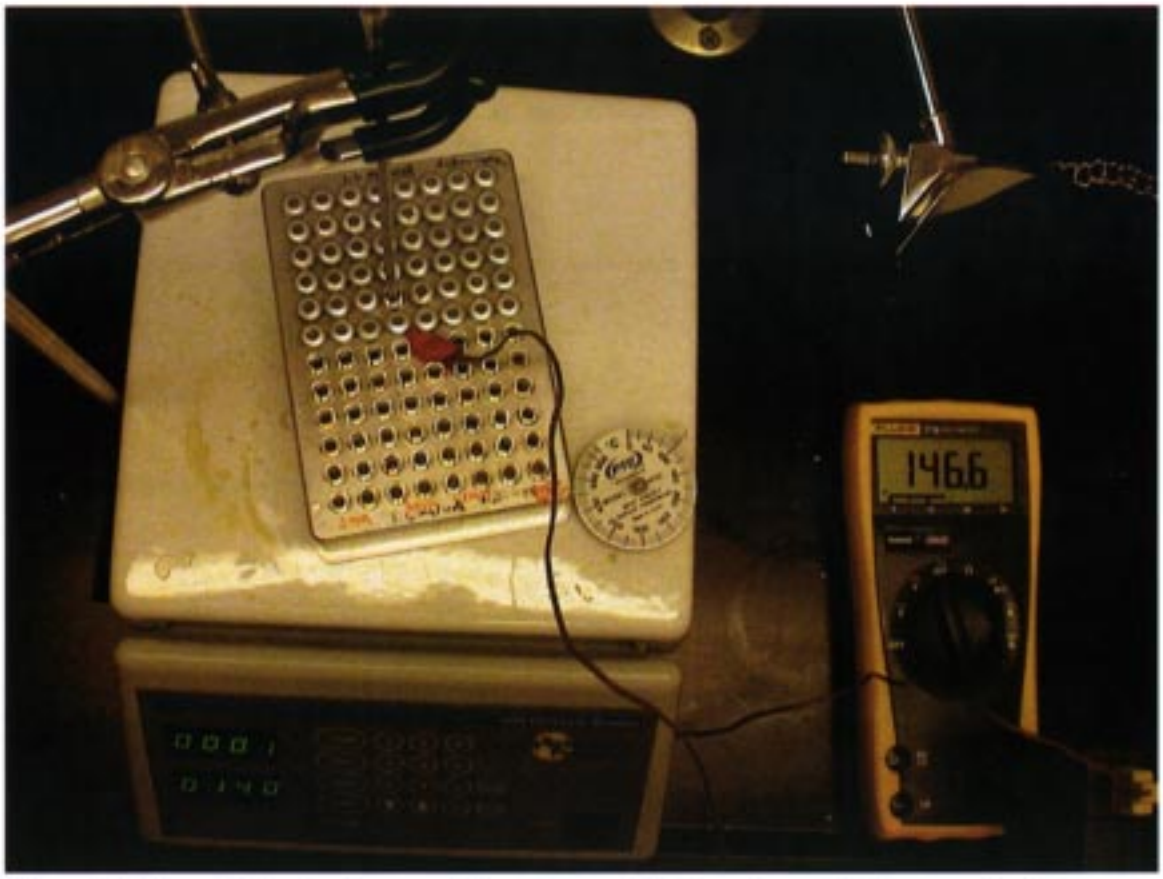


Figure 2. Photograph showing the array of containers used in the melt crystallization experiments.

Description of Tanimot Matricies. Tanimoto matrices are a visual representations of the comparison of Tanimoto coefficients for pairs of spectra and sorts the coefficients into group that are more strongly related (Tanimoto coefficients close to 0). The values represented by colors in the matrices displayed, with red indicating similarity and blue indicating dissimilarity.

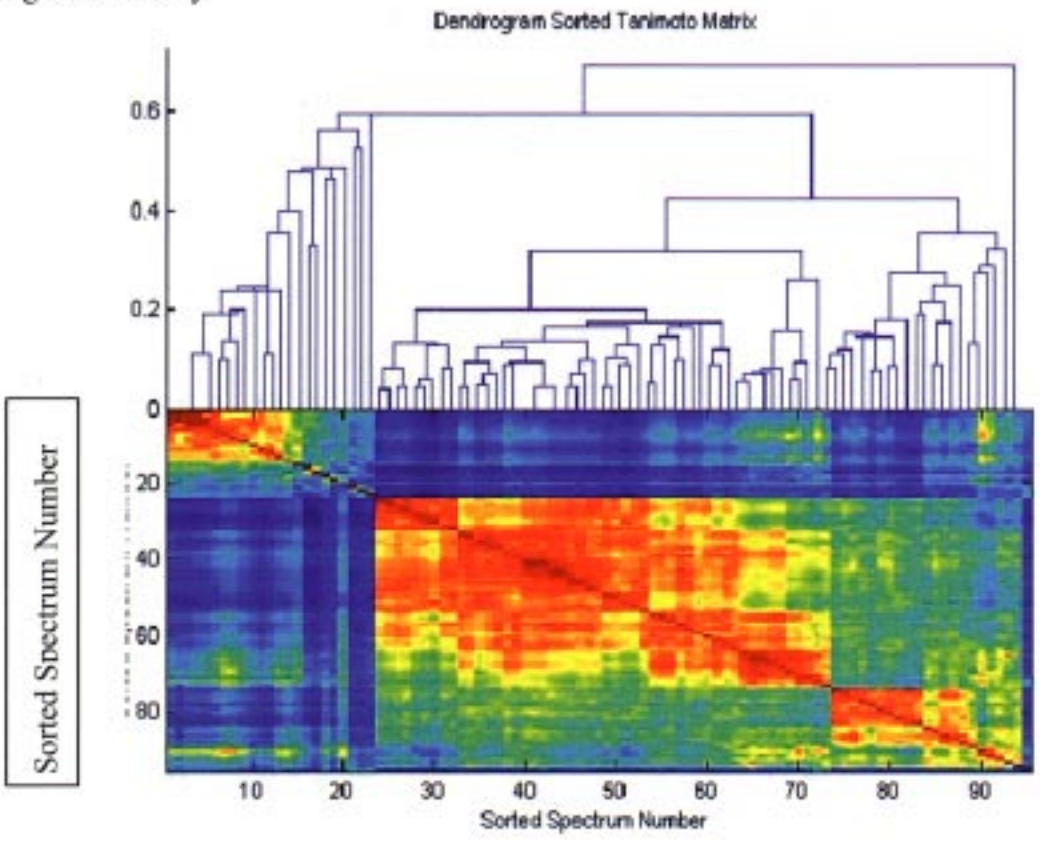


Figure 3. Binning results for 40 deg. C isothermal evaporation experiment.

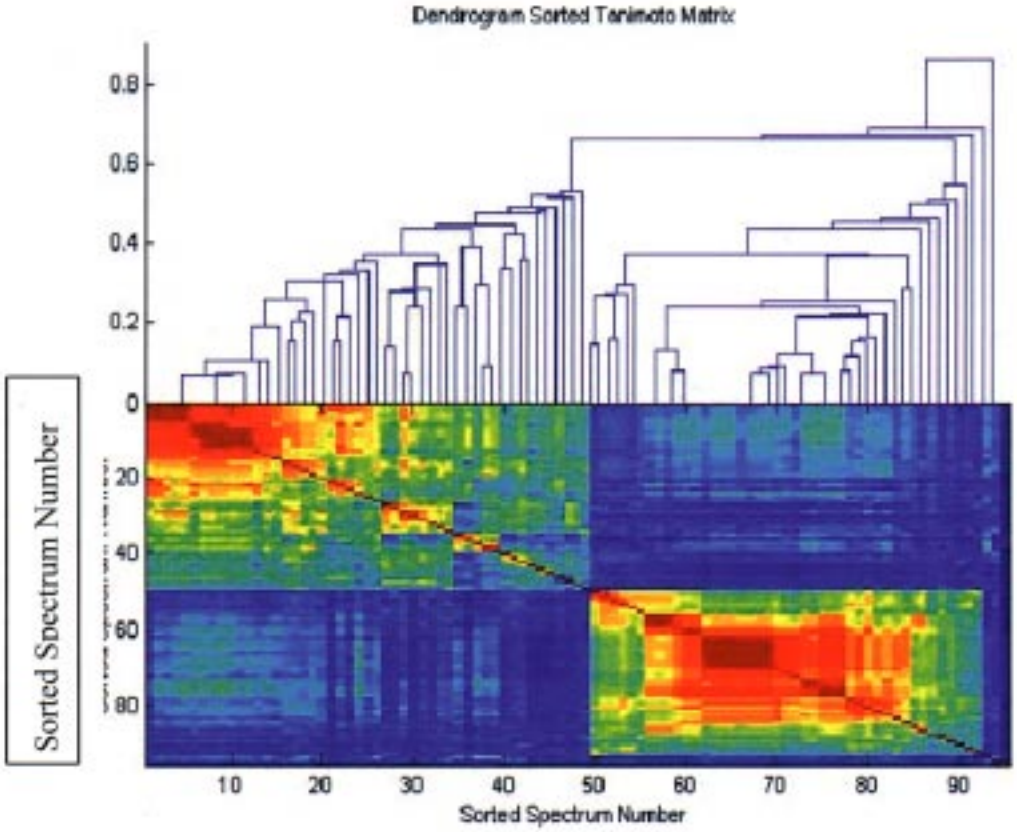


Figure 4. Binning results for 54 deg. C isothermal evaporation experiment.

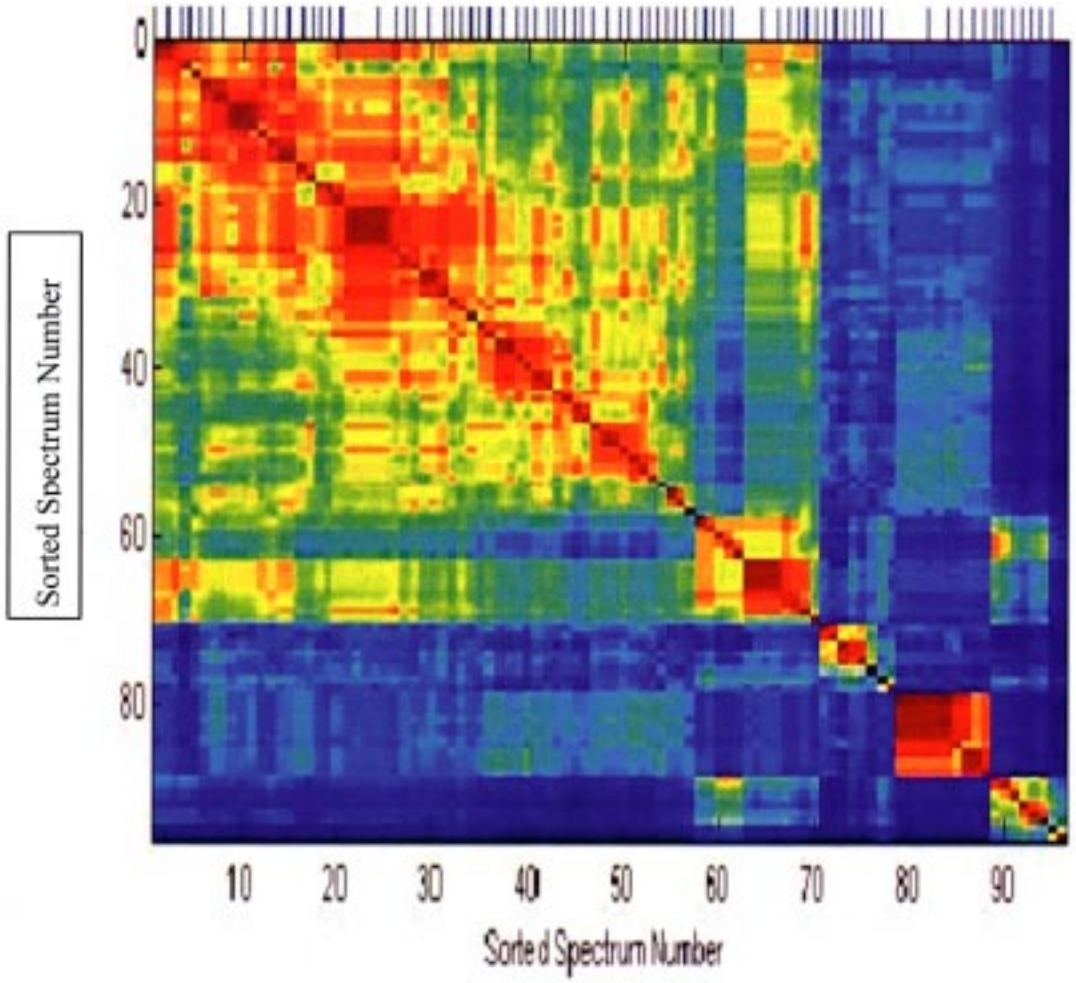


Figure 5. Binning results for 65 deg. C isothermal evaporation experiment.

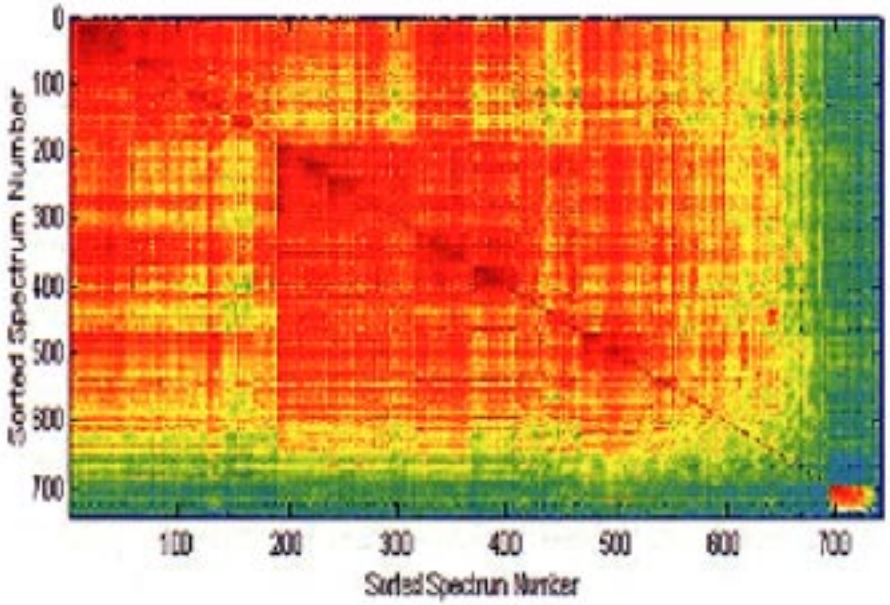
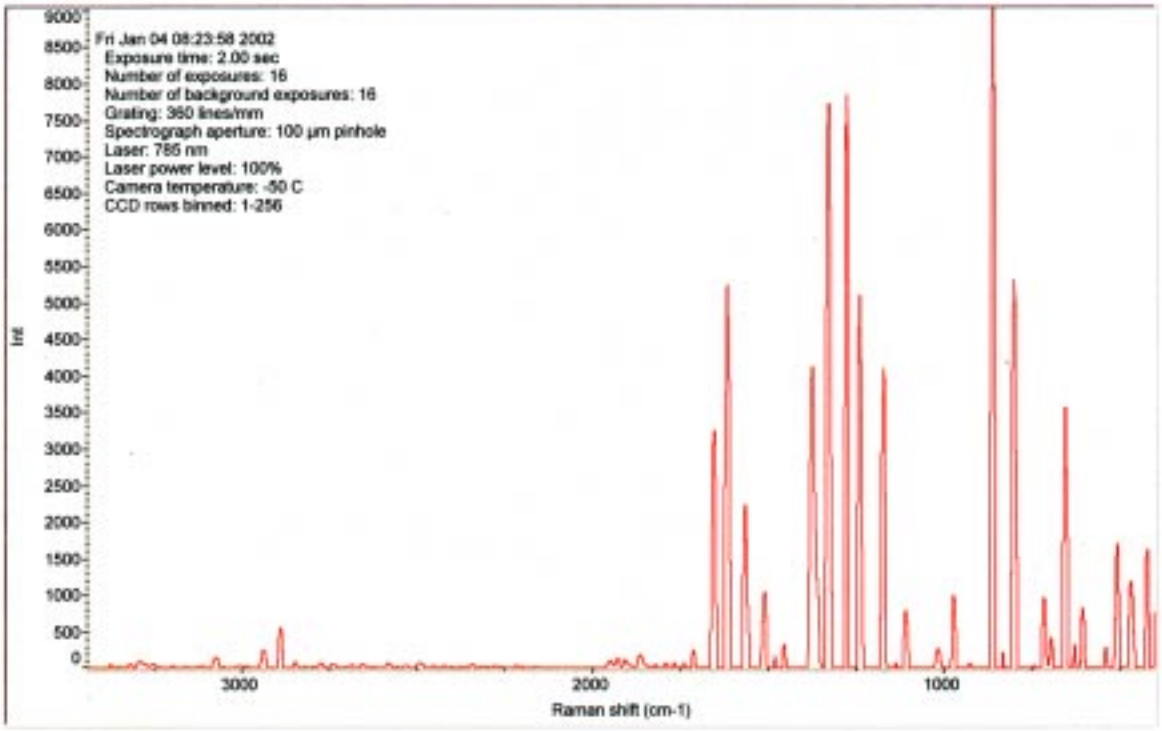
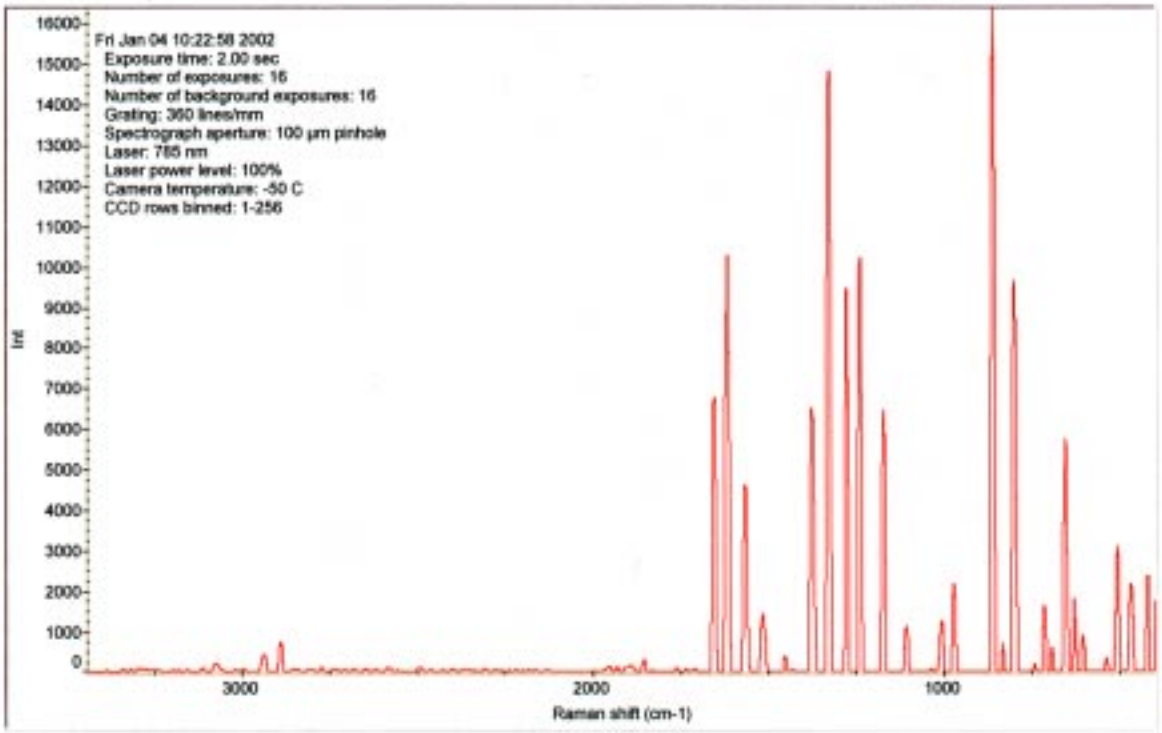


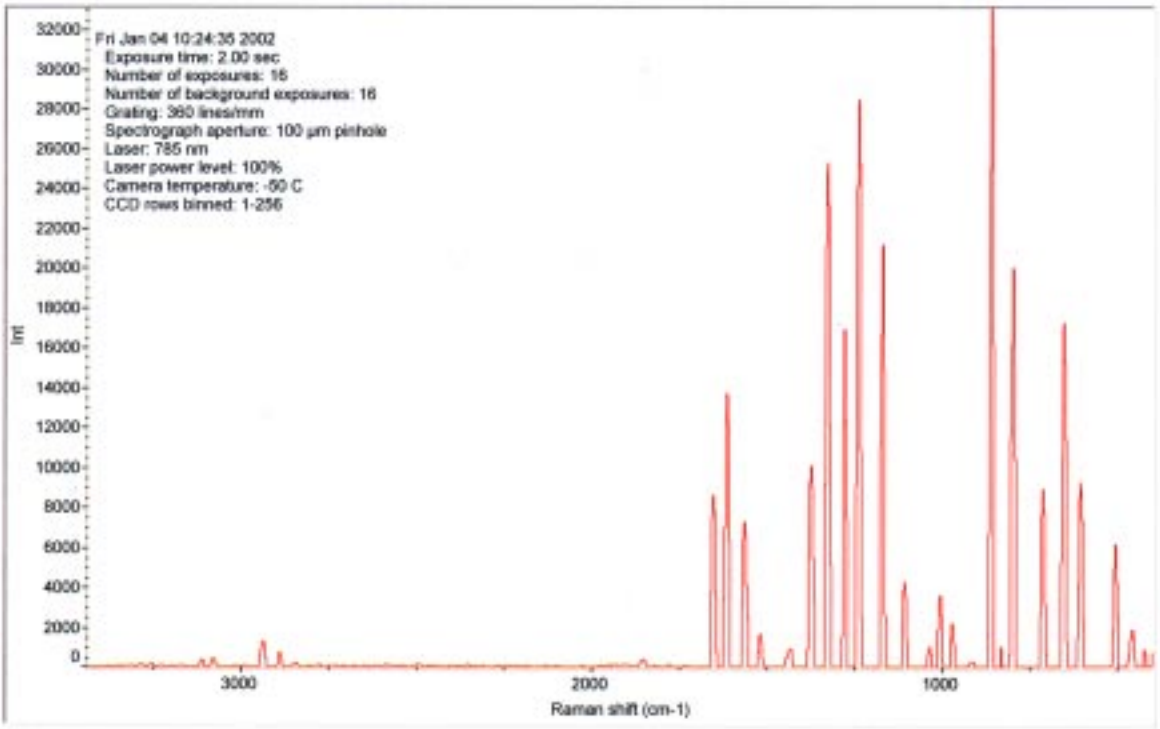
Figure 6. Binning results for 10k polymorph screen.

Representative Raman Spectra for Form I.

Form I



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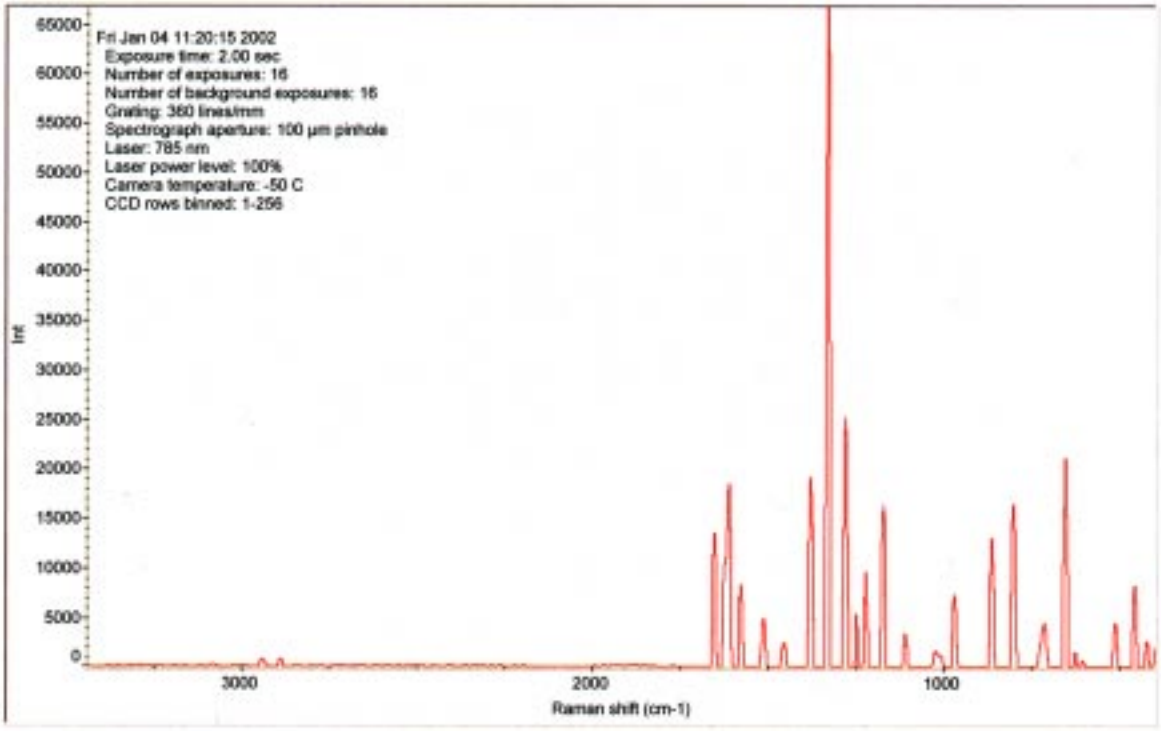
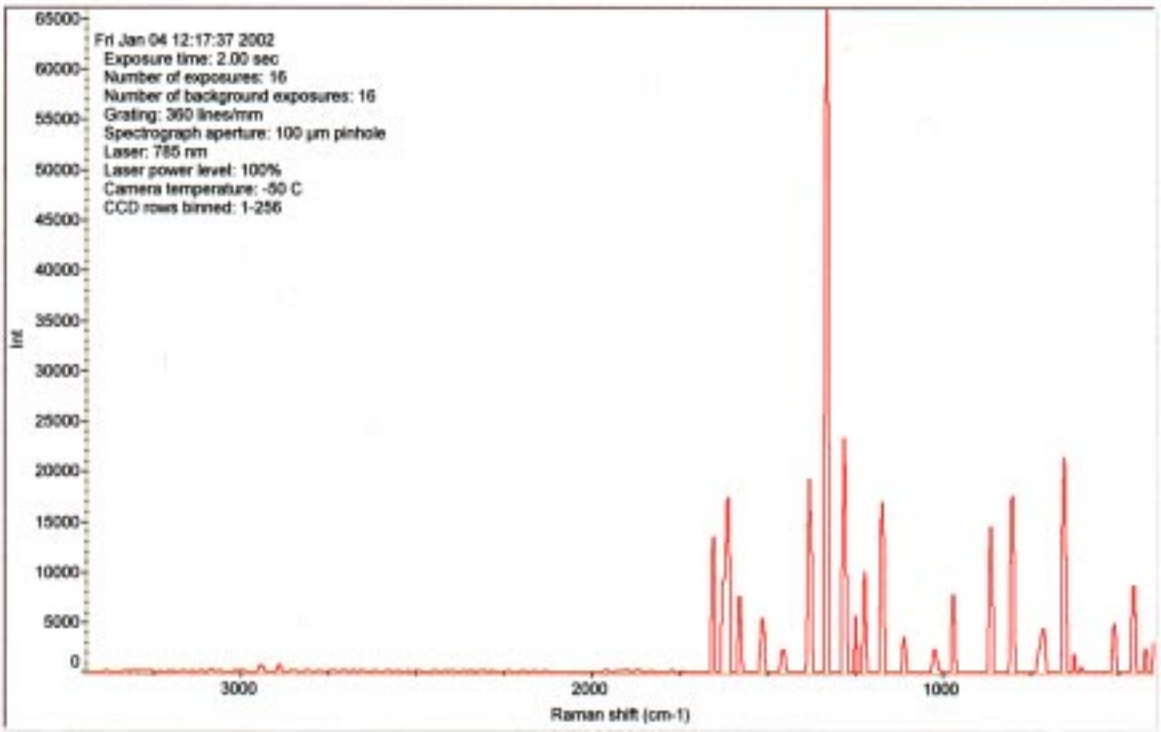
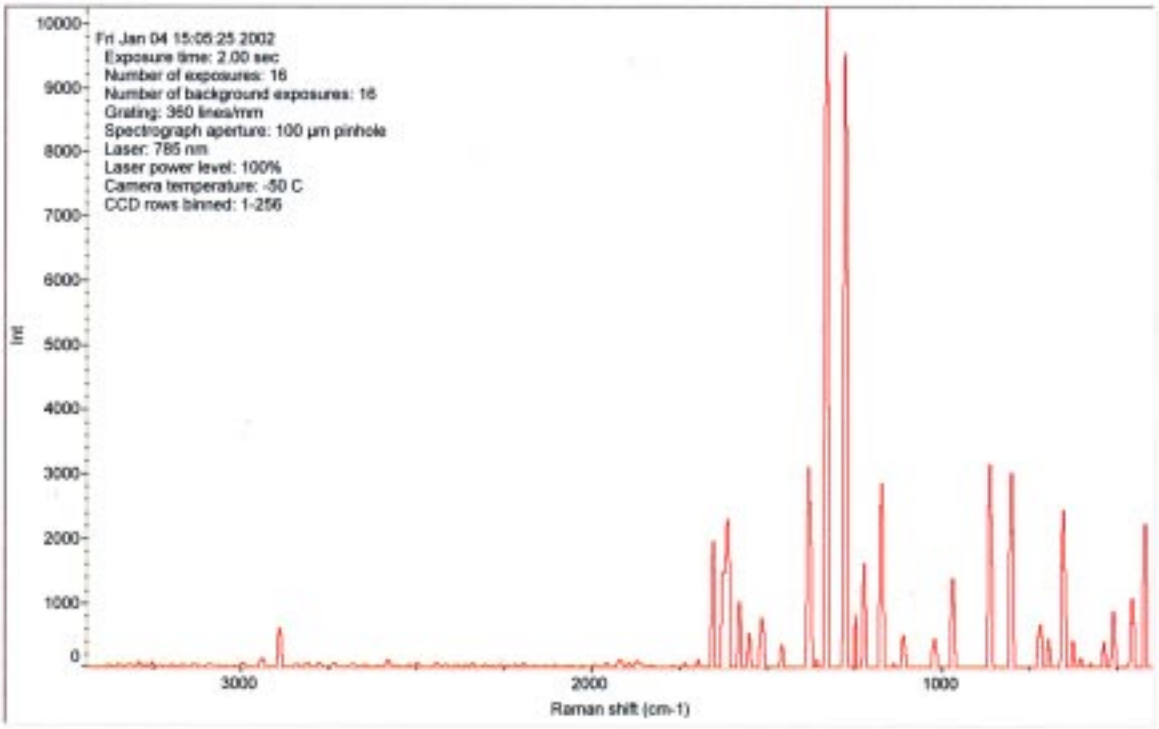
Exposure time: 2.00 sec
Number of exposures: 16
Number of background exposures: 16
Grating: 360 lines/mm
Spectrograph aperture: 100 µm pinhole
Laser: 785 nm
Laser power level: 100%
Camera temperature: -50 C
CCD rows binned: 1-256
Int
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
3000
2000
1000
Raman shift (cm-1)

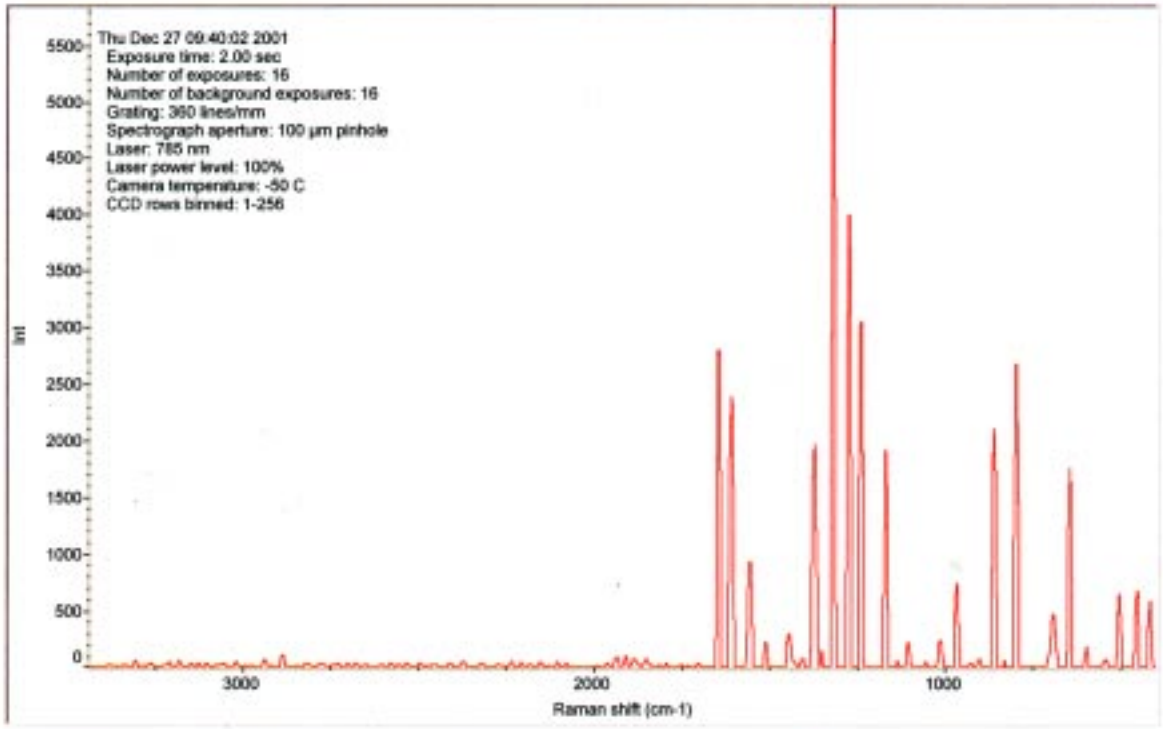
Representative Raman Spectra for Form Form II

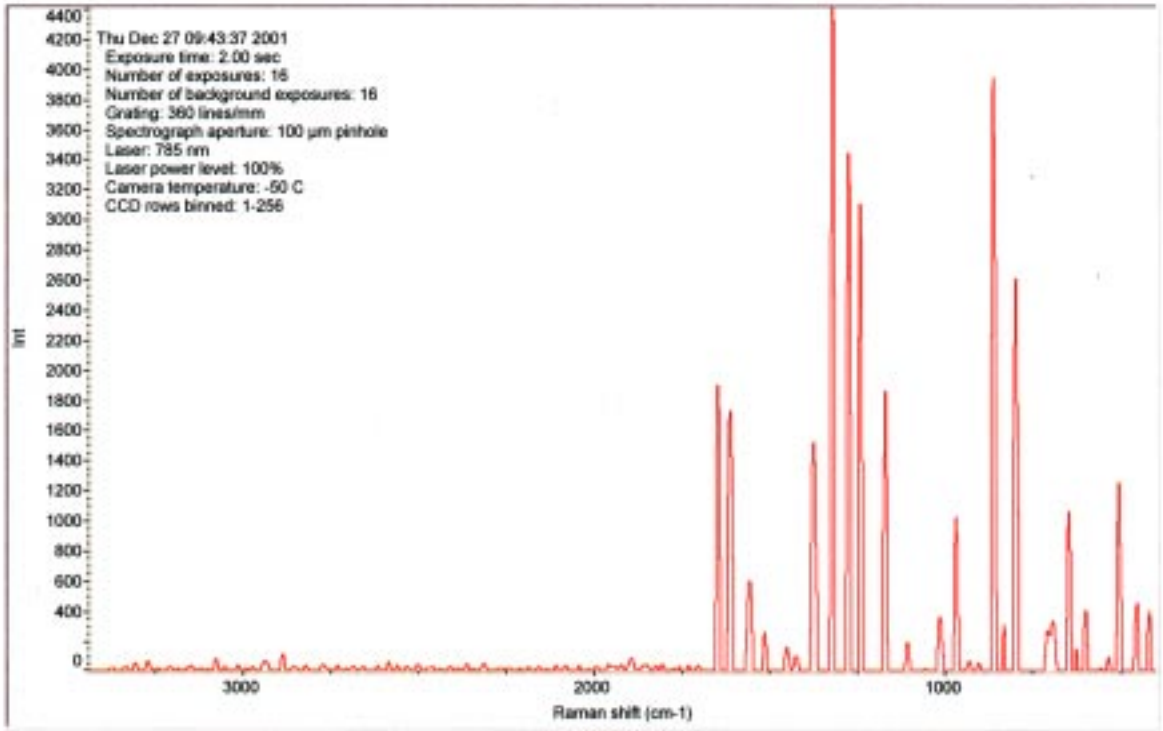


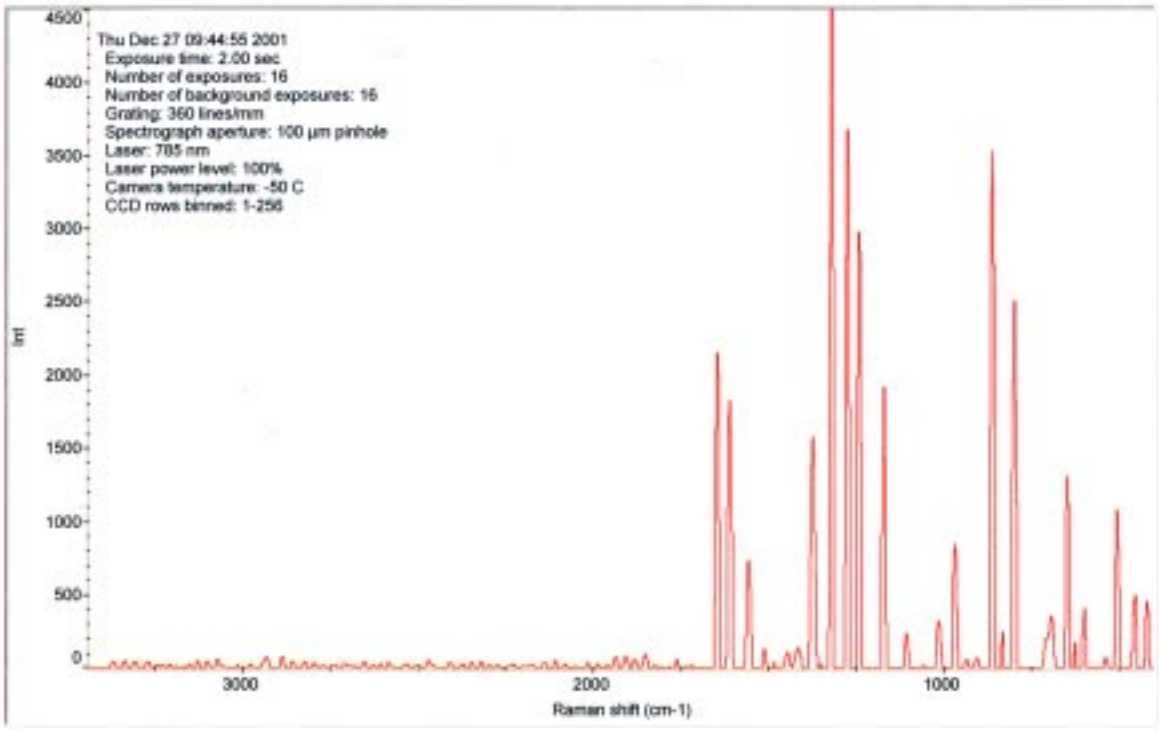



Fri Jan 04 15:05:25 2002
Exposure time: 2.00 sec
Number of exposures: 16
Number of background exposures: 16
Grating: 360 lines/mm
Spectrograph aperture: 100 µm pinhole
Laser: 785 nm
Laser power level: 100%
Camera temperature: -50 C
CCD rows binned: 1-256
Int
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
3000
2000
1000
Raman shift (cm-1)

Representative Raman Spectra for Form Form III



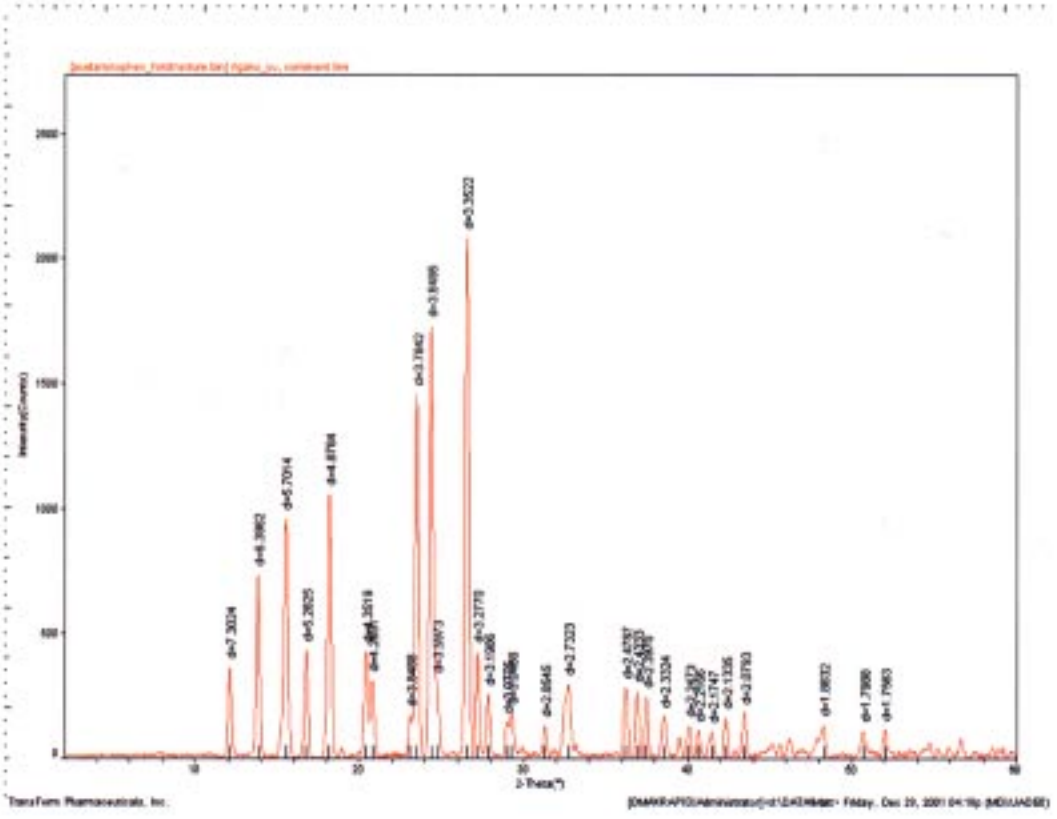



Thu Dec 27 09:44:55 2001
Exposure time: 2.00 sec
Number of exposures: 16
Number of background exposures: 16
Grating: 360 lines/mm
Spectrograph aperture: 100 µm pinhole
Laser: 785 nm
Laser power level: 100%
Camera temperature: -50 C
CCD rows binned: 1-256
Int
4500
4000
3500
3000
2500
2000
1500
1000
500
0
3000
2000
1000
Raman shift (cm-1)

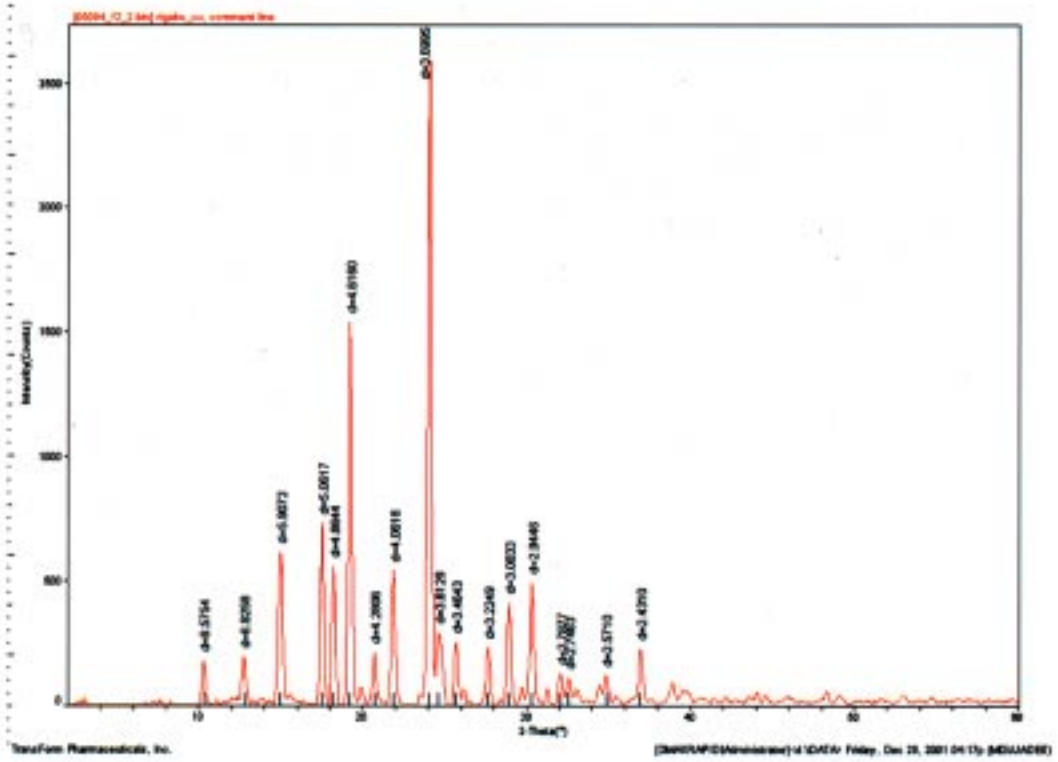
PXRD patterns for Forms I-III.

Diffractometer description. The patterns were recorded on samples in 300 micron-diameter quartz capillaries using a Rigaku D/MAX Rapid microdiffractometer in transmission mode. The goniometer can rotate in phi and omega. Phi is oriented at a 45 degree angle to omega. This is different than the more common theta–2theta powder diffractometer geometry. The samples were rotated in phi and rocked in omega axes. The patterns represent integration results from image plate data from which the Debye ring diffraction was obtained.

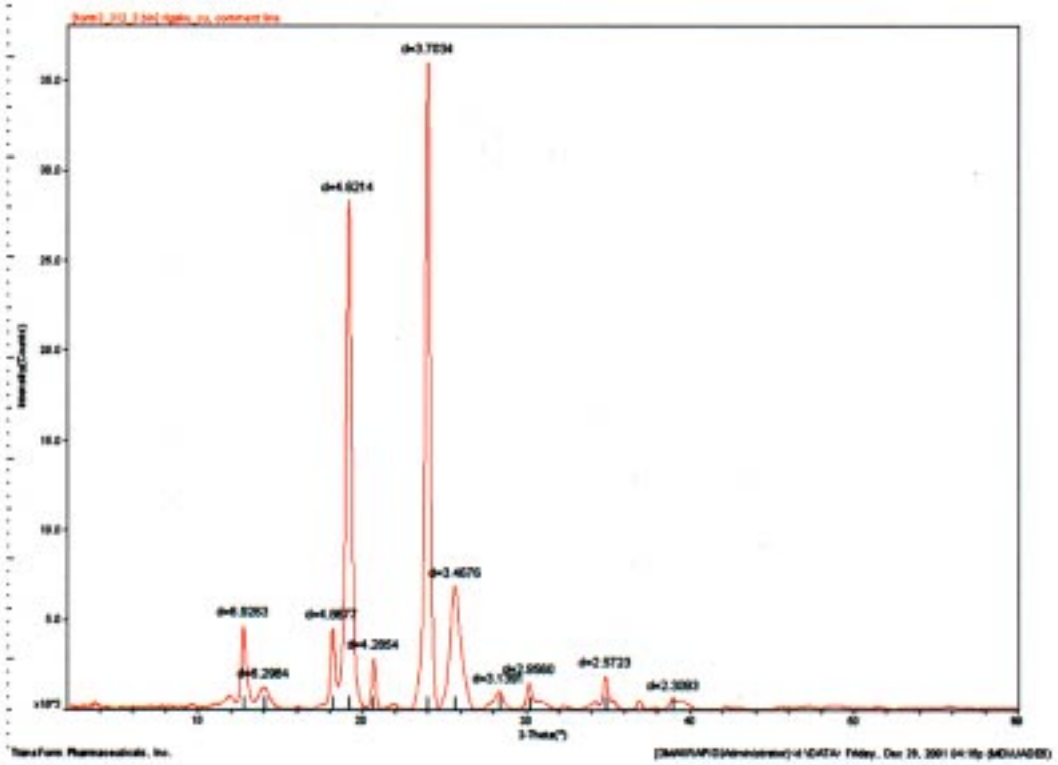
Form I



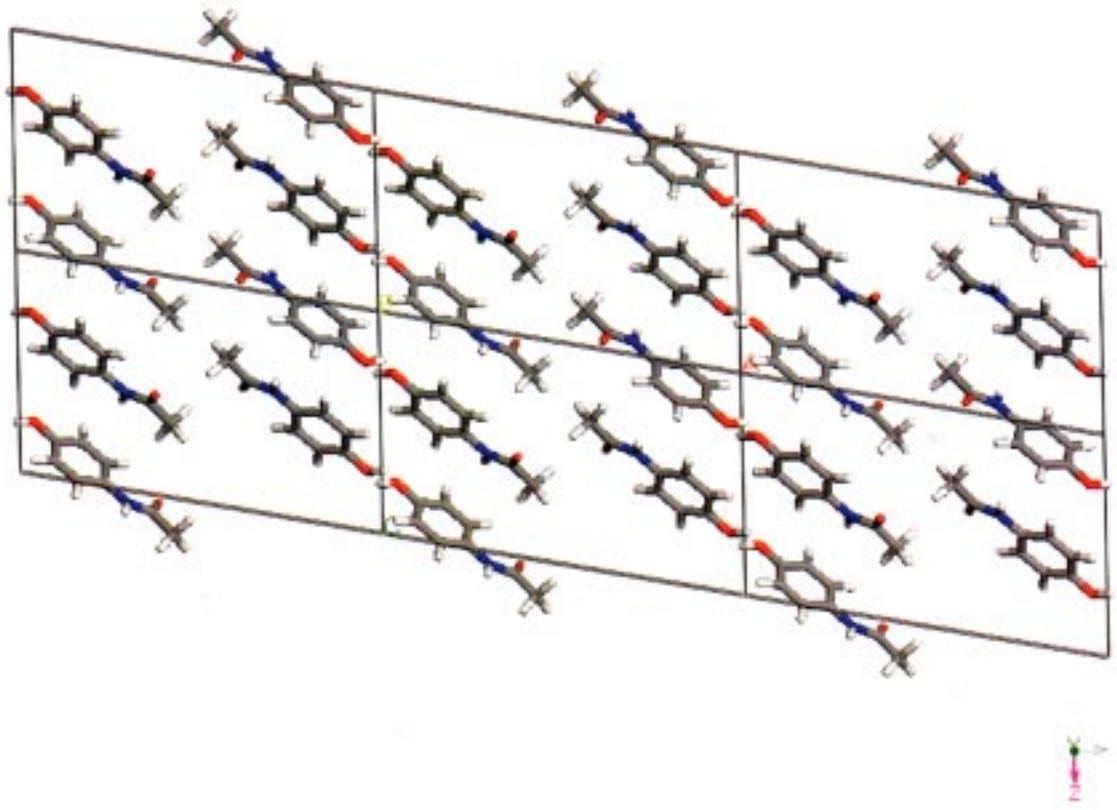
Form II



Form III



Packing diagram for proposed Form III structure



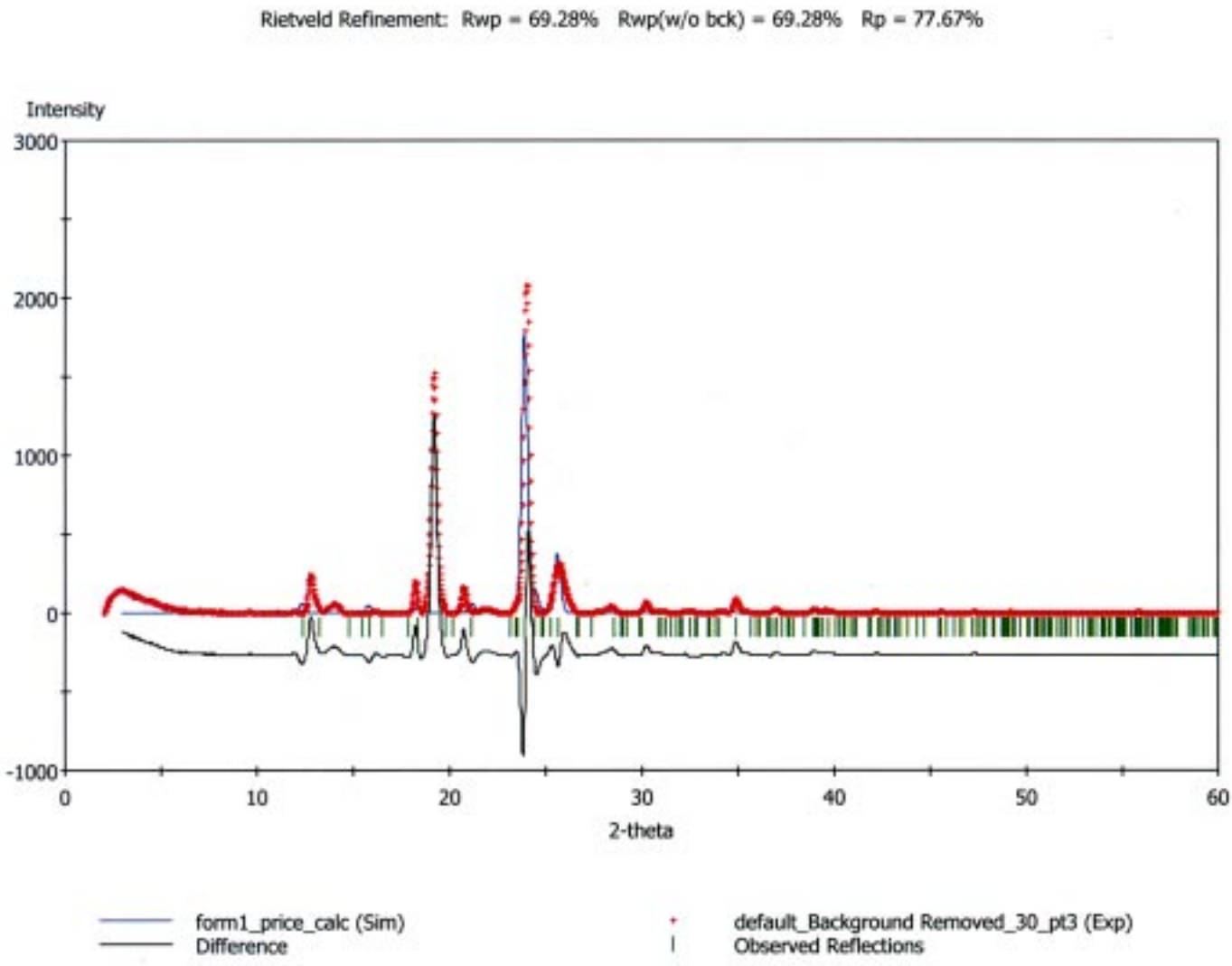


Figure 7. Fitting of the structure of form I with the experimental PXRD data for form III. The unit cell was held rigid while the molec

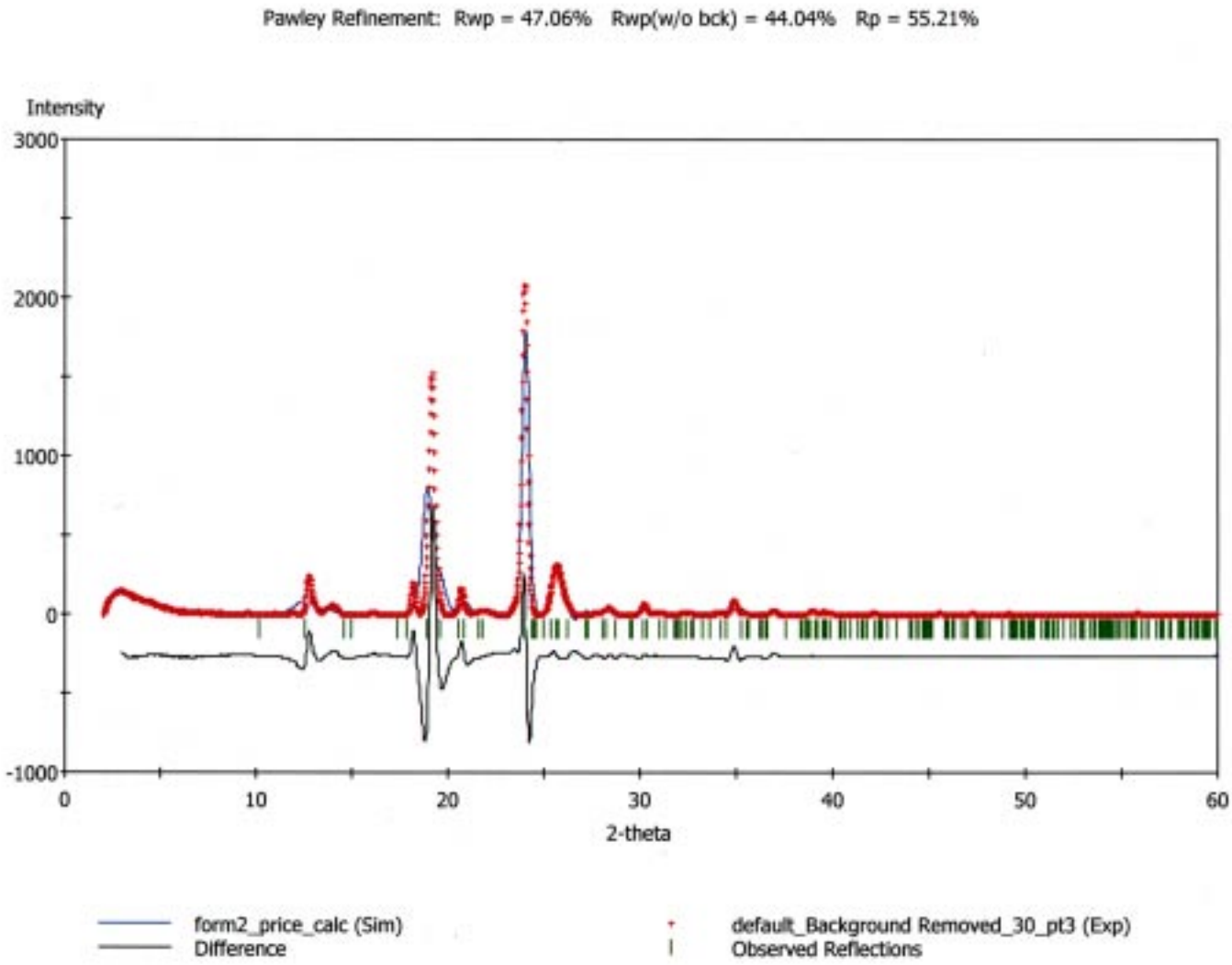


Figure 8. Fitting of the structure of form II with the experimental PXRD data for form III. The unit cell was held rigid while the molec

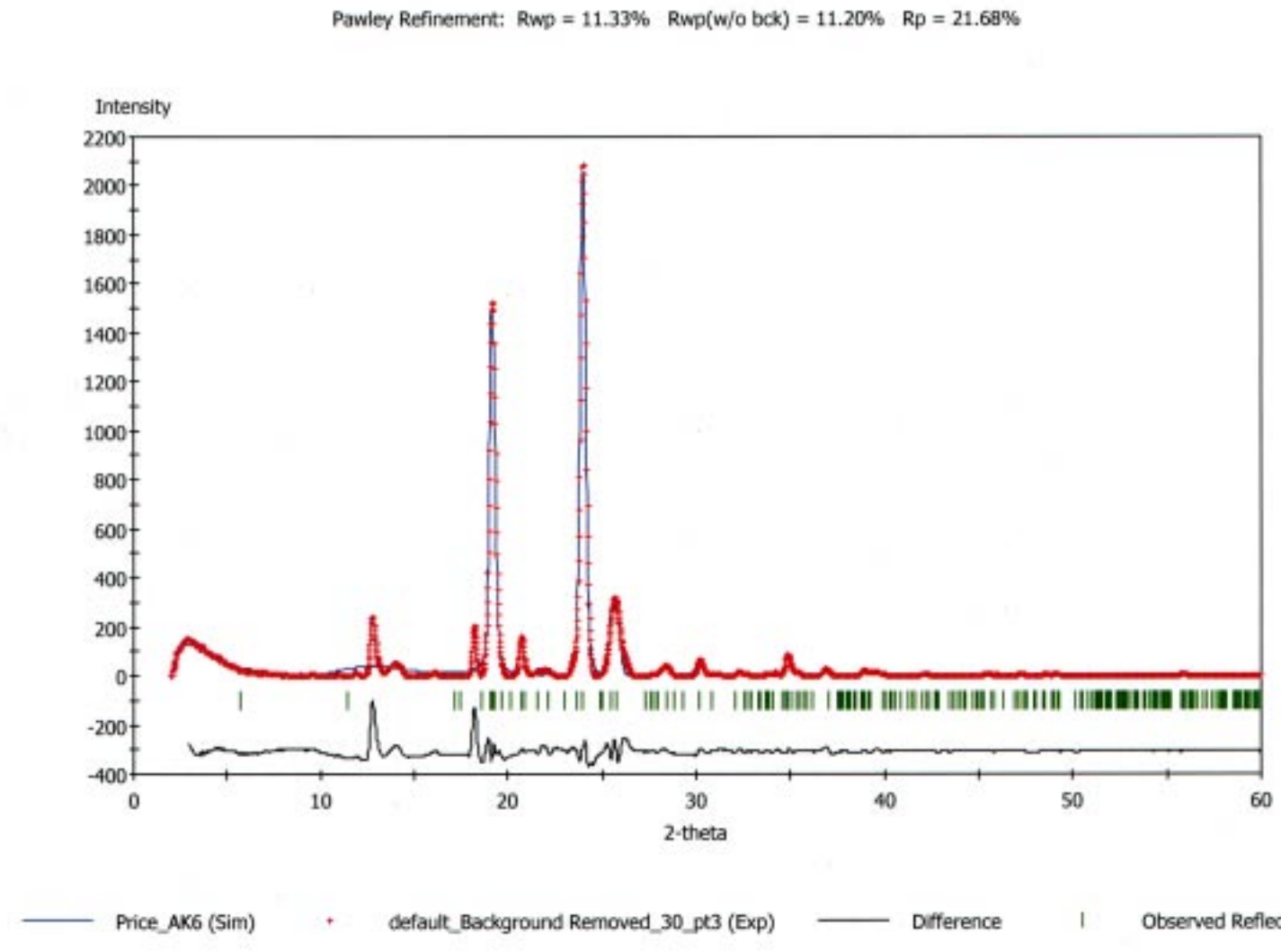


Figure 9. Fitting of the structure of form III with the experimental PXRD data for form III. The unit cell and the molecular position w
starting structure was not experimentally determined.

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[ii] Massachusetts Institute of Technology, Department of Materials Science and Engineering, Room 12-011, 77 Massachusetts Avenue, Cambridge, MA 02139.