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D.K.H.

**ARNOLD & PORTER**

555 TWELFTH STREET, N.W.  
WASHINGTON, D.C. 20004-1206

DONALD O. BEERS  
(202) 942-5012  
INTERNET: Donald\_Beers@aporter.com

(202) 942-5000  
FACSIMILE: (202) 942-5999

NEW YORK  
DENVER  
LOS ANGELES  
LONDON

December 21, 2000

Dockets Management Branch  
Food and Drug Administration  
5630 Fishers Lane  
Room 10-61  
Rockville, MD 20857

Re: Docket No. 00P-1550, Citizen Petition Relating to Cefuroxime Axetil

Dear Sir or Madam:

Enclosed is an additional exhibit relevant to our September 29, 2000 Citizen Petition on behalf of Glaxo Wellcome Inc. (hereafter the "Petition"). The original Petition relied on, among other things, analytical data concerning cefuroxime axetil that were derived from an extensive program of laboratory study conducted by SSCI, Inc. Dr. Stephen Byrn, Chairperson of FDA's Pharmaceutical Science Advisory Committee, directed the SSCI study. He outlined its design and results in a declaration that was attached to the Petition as Exhibit E. He also indicated in his declaration that the formal study report would be forthcoming. Byrn Declaration at ¶ 3. To complete the record, we now enclose the final study report as Exhibit Q.

As we believe FDA will agree on review of the data and arguments provided, the petition is well grounded in science and law and should be, in all aspects, granted.

Respectfully submitted,



Donald O. Beers  
David E. Korn

Enclosure

00P-1550

SUP2

**Exhibit Q**

# CHARACTERIZATION OF CEFUROXIME AXETIL

Glaxo Wellcome

SR-5597.01

11-07-00

Prepared by Aeri Park, Ph.D. 11/7/00

Aeri Park, Ph.D., Senior Research Investigator, Date

Prepared by Leonard J. Chyall Nov-07-2000

Leonard J. Chyall, Ph.D., Research Investigator, Date

Reviewed by Stephen Byrn 11-8-00

Stephen Byrn, Ph.D., Study Director, Date

SSCI, Inc.  
3065 Kent Ave.  
West Lafayette, IN 47906-1076

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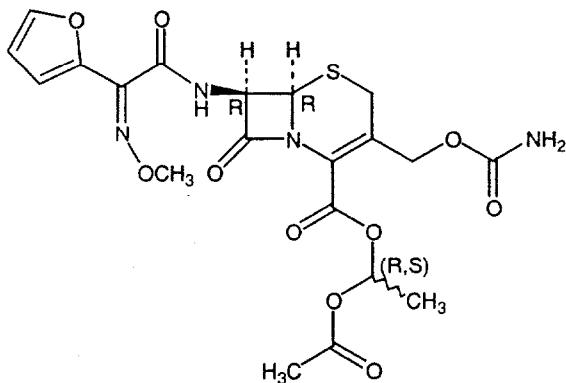
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## I. INTRODUCTION

This report describes solid state characterization studies carried out on cefuroxime axetil. Cefuroxime axetil exists as a mixture of diastereomers, one diastereomer is named isomer A (*R, R, S*) and the other isomer B (*R, R, R*). In addition to the amorphous form, each diastereomer has two known crystalline solid forms, Form I and Form II. Hence, the crystalline solid forms are named AI, AII, BI, and BII. Forms AI, AII and BI are non-solvated forms, and Form BII is a hemihydrate [1]. In this study, the characterization of all solid forms was carried out using X-ray powder diffraction (XRPD), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), infrared (IR) spectroscopy, and Raman spectroscopy. The results of the characterization of each solid form were then used to analyze racemates, and crystalline/amorphous mixtures. In addition to these characterization studies, solubility studies were carried out on each isomer, mixtures of diastereomers, and crystalline/amorphous mixtures.



**Cefuroxime Axetil**

## II. EXPERIMENTAL

### A. Materials

The crystalline racemate, amorphous racemate, and crystalline isomers AI, BI and BII that were used for this study were received from Glaxo Wellcome (Table 1). Crystalline AII and BII, and amorphous forms of isomers A and B used for the study were generated from the received materials.

### B. Preparation of Solid Forms

Amorphous A (391-30-01) was prepared by milling 81.0 mg of SSCI No. 9545 (crystalline AI) for 10 min in a Wig-L-Bug® apparatus.

Amorphous A used for the dissolution experiments was prepared by milling ~ 75 mg portions of SSCI No. 9876 (crystalline AI) for 15-25 min in a Wig-L-Bug® apparatus (Table 9). Some of these samples contained significant quantities of crystalline material after milling. These

samples were subjected to a second milling procedure in order to convert more of the crystalline form.

Crystalline AII (391-11-03) was obtained by slowly cooling a solution of SSCI No. 9545 (crystalline AI) in tetrahydrofuran (THF, 203.3 mg/mL). The solution was prepared at 50 °C and filtered through a 0.2-µm filter.

Amorphous B (385-69-01) was prepared by dissolving 256.9 mg of SSCI No. 9547 (crystalline BI) in 2 mL of tetrahydrofuran. The solution was placed in a refrigerator for 3 days. The solution was filtered through a 0.2-µm filter and added to 60 mL of hexane submerged in a dry ice/acetone bath under a nitrogen atmosphere. The resulting solution was allowed to warm to ambient temperature. The solid formed was collected by filtration and allowed to dry under a vacuum at ambient temperature overnight.

Amorphous B used for dissolution experiments was prepared by milling ~70 mg of SSCI No. 9547 (crystalline BI) in a Wig-L-Bug® apparatus for 10-20 min (Table 9).

Crystalline BII (385-60-01) was prepared by slurring approximately 100-mg portions of SSCI No. 9547 (crystalline BI) in three capped vials that each contained 20 mL of water for 2 weeks. The contents of the three vials were combined and solid material was isolated by filtration. The solid was dried under a vacuum at ambient temperature overnight. Crystalline BII (435-04-01) was also prepared by slurring 524.0 mg of SSCI No. 9875 (crystalline BI) in 100 mL of water at room temperature for 14 days. The solid was collected by filtration and allowed to dry under a vacuum at ambient temperature over a period of 3 days.

Crystalline AI/BII (385-60-05) was prepared by slurring 112.8 mg of SSCI No. 9499 (crystalline AI/BI) in 20 mL of water for 2 weeks. The solid was collected by filtration and allowed to dry under a vacuum at ambient temperature overnight.

Crystalline AII/BII (385-60-03) was prepared by slurring 100.6 mg of SSCI No. 9498 (amorphous A/B) in 20 mL of water for 2 weeks. The solid was collected by filtration and allowed to dry under a vacuum at ambient temperature overnight.

### C. Solubility Measurements

In a typical experiment, a 100-mL three-necked flask equipped with a thermometer and magnetic stirring bar was charged with 60 mL of either water or 0.07 N hydrochloric acid. The flask was immersed in an oil bath that was placed on top of a digital stirrer/hotplate and stirred at a nominal speed of 1100 rpm. Once the dissolution medium had equilibrated to 37 °C, a sample of cefuroxime axetil was added to the flask. For experiments involving single isomers, approximately 168 mg of sample was used. For experiments involving blends of crystalline and amorphous A/B mixtures, 168 mg of amorphous form A/B was used, and an additional amount of crystalline material was added to provide the desired ratio of amorphous and crystalline material.

At various time intervals, approximately 3 mL of the solution was withdrawn from the dissolution flask with a syringe and filtered through a Whatman 0.2- $\mu$ m filter. The first part of the filtered sample (approximately half of the total amount) was returned to the 100-mL flask, while the remainder of the filtered solution was isolated in a separate vial. A sample of this solution (typically 0.50 or 1.00 mL) was withdrawn with a pipette and immediately diluted to a known volume with a fresh sample of the dissolution medium.

The diluted samples that were collected at various time intervals were analyzed by UV spectrophotometry at 280 nm. After correcting for the dilution of the sample, the measured absorbances were converted into solution concentrations using a calibration curve. Dissolution profiles were obtained by plotting solubility (expressed in mg/mL) vs. time.

After the last sample was obtained from the dissolution experiment, the solid material was isolated by suction filtration. The sample was dried then analyzed by XRPD.

### **1. X-Ray Powder Diffraction**

X-ray powder diffraction analyses were carried out on a Shimadzu XRD-6000 X-ray powder diffractometer using Cu K $\alpha$  radiation (1.5406 Å). The instrument was equipped with a fine-focus X-ray tube. The tube voltage and amperage were set at 40 kV and 40 mA, respectively. The divergence and scattering slits were set at 1° and the receiving slit was set at 0.15 mm. A NaI scintillation detector detected diffracted radiation. A theta-two theta continuous scan at 3°/min (0.4 sec/0.02° step) from 2.5 to 40° 2 $\theta$  was used. A silicon standard was analyzed each day to check the instrument alignment.

### **2. Thermal Analyses**

Thermogravimetric (TG) analyses were carried out on a TA Instruments TGA 2050 or 2950. The calibration standards were nickel and Alumel®. The sample was placed in a tared platinum pan, accurately weighed, and inserted into the TG furnace. The samples were heated at a rate of 10 °C/min.

Differential Scanning Calorimetric (DSC) data were obtained on a TA 2920 instrument. The calibration standard was indium. A sample was placed into a tared DSC pan, and the weight accurately recorded. The pans were hermetically sealed and contained a pinhole to allow for pressure release. The samples were heated under nitrogen at a rate of 10 °C min.

### **3. Infrared Spectroscopy**

The mid-IR spectra were acquired on a Nicolet model 860 Fourier-transform IR spectrophotometer equipped with a globar source, Ge/KBr beamsplitter, and deuterated triglycine sulfate (DTGS) detector. A Spectra-Tech, Inc., diffuse reflectance accessory was utilized for sample analysis. Each spectrum represents either 128 or 256 co-added scans at a spectral resolution of 4 cm<sup>-1</sup>. A background data set was acquired with an alignment mirror in place. A single beam sample data set was then acquired. Subsequently, a log 1/R ( $R$  = reflectance) spectrum was acquired by ratioing the two data sets against each other. The spectrophotometer was calibrated (wavelength) with polystyrene at the time of use.

#### **4. Raman Spectroscopy**

Raman spectra were acquired on a Nicolet Fourier-transform (FT) Raman accessory bench interfaced to a Nicolet model 860 FT-infrared spectrophotometer utilizing an excitation wavelength of 1064 nm and approximately 0.5 W of Nd:YAG laser power. A routine spectrum represents either 128 or 256 co-added scans at a spectral resolution of  $4\text{ cm}^{-1}$ . The spectrometer was calibrated (wavelength) with sulfur and cyclohexane at the time of use.

#### **5. Ultraviolet (UV) Spectrophotometry**

Samples were analyzed using a Beckman DU<sup>®</sup> Series 600 UV-VIS single beam spectrophotometer. The wavelength accuracy of this instrument was verified by calibration with a holmium oxide standard. The photometric accuracy of the instrument was verified by measuring the intensity of the light at the detector when filters of known optical density were placed in the path of the beam. Prior to analysis of the samples, the instrument was blanked by placing a cell filled with dissolution medium in the path of the beam and setting the instrument response to read zero absorbance.

### **III. RESULTS AND DISCUSSION**

#### **A. Characterization of Isomer A**

Analyses of the three solid forms of isomer A - amorphous A, AI and AII, are summarized in Table 2.

XRPD patterns of amorphous material and crystalline solid forms (AI and AII) are shown in Figure 1. Amorphous A was prepared by milling crystalline AI using a Wig-L-Bug<sup>®</sup>. Crystalline AII was prepared by slowly cooling a solution of isomer A dissolved in THF. XRPD peaks of AI and AII are distinctive and therefore can easily be identified by comparing the patterns.

DSC analysis of amorphous material showed glass transition at 57 °C, and an exothermic transition maximum at 108.5 °C. This exothermic transition appears to be a crystallization exotherm, since the solid showed onset of melt at 192.7 °C. The crystalline AI and AII each show onset of melt at 201.9 °C and 191.0 °C, respectively.

TG analysis of all three solid forms showed less than 1% of weight loss at 175 °C.

IR and Raman spectroscopy of all three solid forms are shown in Figures 2 and 3, respectively. The amorphous solid shows broader signals in both IR and Raman, where the crystalline solids show more resolved signals. IR and Raman of all three solid forms are unique, and therefore can be used to identify the solid forms.

## B. Characterization of Isomer B

Analyses of the three solid forms of isomer B - amorphous B, BI and BII, are summarized in Table 3.

XRPD patterns of amorphous material and the two crystalline solid forms, BI and BII, are shown in Figure 4. Amorphous B was prepared by precipitation of a THF solution with cold hexane. Crystalline BII was prepared from water slurry of the BI solid. XRPD peaks of BI and BII are distinctive and therefore can easily be identified by comparing the patterns.

DSC analysis of amorphous material showed glass transition at 71.8 °C. No crystallization exothermic event was observed. The crystalline BI and BII show onset of melt at 133.4 °C and 124.3 °C, respectively.

TG analysis of the amorphous solid showed 11.9% weight loss at 175 °C, which is probably due to the residual solvent from the solid preparation. Form BI showed little weight loss at 175 °C. Form BII showed weight loss of 1.6% at 175 °C, which corresponds to a hemihydrate. This is consistent with the findings of Glaxo Wellcome [1].

IR and Raman spectroscopy of all three solid forms are shown in Figures 5 and 6, respectively. The amorphous solid shows broader signals in both IR and Raman, where the crystalline solids show more resolved signals. Form BII shows a crystalline water peak at 3625 cm<sup>-1</sup>, corresponding to its hemihydrate nature. IR and Raman of all three solid forms are unique, and therefore can be used to identify the solid forms.

## C. Characterization of Racemates

A total of four racemates, amorphous A/B, crystalline AI/BI, crystalline AI/BII, and crystalline AII/BII, were analyzed and the results summarized in Table 4. Crystalline AI/BII was prepared from water slurry of crystalline AI/BI. Crystalline AII/BII was prepared from water slurry of amorphous A/B.

XRPD patterns of the crystalline racemates are shown in comparison to their individual isomers in Figures 7 to 9. Figure 7 shows the crystalline AI/BI pattern is a combination of AI and BI patterns. Therefore, the racemate AI/BI is a physical mixture of isomers AI and BI. Figures 8 and 9 show XRPD patterns of crystalline AI/BII and AII/BII racemates, respectively, and each isomer pattern is shown to compare with the pattern of racemates. Since the patterns of racemates are combinations of the patterns of the individual isomers, both racemates are physical mixtures of individual isomers. The XRPD pattern of each racemate clearly shows that XRPD technique can be used to identify individual components in a racemate.

DSC analysis of amorphous A/B showed a glass transition at 71.5 °C, which is the same glass transition temperature of amorphous B. No crystallization exothermic event was observed in amorphous A/B. All crystalline racemates showed two melting events in DSC, each melting event corresponding to each isomer. For example, AI/BI showed two endothermic events, at

118.0 °C (onset of melt) and 170.1 °C (onset of melt), the lower event corresponding to BI (133.4 °C) and the higher to AI (201.9 °C). Note that the melting temperature of each component was depressed due to the presence of the other isomer in the racemate.

TG analysis of amorphous A/B showed 1.1% of weight loss at 175 °C. Crystalline AI/BI showed 2.1% weight loss where AI/BII and AII/BII showed less than 1% weight loss at 175 °C. Most of the weight loss for AI/BI occurred below 100 °C, which is consistent with the presence of atmospheric moisture or residual solvent in this sample.

IR spectra of amorphous A/B is shown in Figure 10 with amorphous A and B for comparison. The IR of amorphous A/B is similar to amorphous A. IR spectra of crystalline racemates are shown in Figures 11 to 13. IR spectra of individual isomers are also shown in the figures for comparison. Individual isomers of the crystalline racemates are visible in the IR spectra. The IR spectrum of AI/BII shows the crystalline water signal at 3625 cm<sup>-1</sup> from the hemihydrate BII. Therefore, IR spectra can be used to identify individual components in a crystalline racemate.

Raman spectra of amorphous A/B, crystalline AI/BI, AI/BII, and AII/BII are shown in Figures 14 to 17. Raman spectra of individual isomers are also shown in the figures for comparison. Individual isomers of the crystalline racemates are visible in the Raman spectra. For example, Raman spectrum of amorphous A/B shows a signal at 1630 cm<sup>-1</sup> that corresponds to amorphous A, and a signal at 1390 cm<sup>-1</sup> that corresponds to amorphous B. For crystalline racemates, the presence of each isomer is very clear in the Raman spectrum.

#### D. Characterization of Crystalline/Amorphous Mixtures

A total of four mixtures, 20% AI in amorphous A/B, 20% BI in amorphous A/B, 20% BII in amorphous A/B, and 25% AII/BII in amorphous A/B, were analyzed. The results are summarized in Table 5. Each sample was prepared by mixing the stated weight percent of the crystalline material with amorphous A/B solid.

XRPD patterns of the mixtures are shown in comparison to their individual components in Figures 18 to 21. The XRPD patterns of the mixtures clearly show the crystalline components. An amorphous halo is visible in the baseline of the pattern. The XRPD patterns of each mixture clearly show that XRPD technique can be used to identify the crystalline components in mixtures of crystalline/amorphous solids.

DSC analysis of 20% AI in amorphous A/B showed glass transition at 76.5 °C, which is similar to the glass transition temperature of amorphous A/B, and a onset of melt at 174.5 °C, which corresponds to AI melt (201.9 °C). Note the melting temperature of AI is depressed due to the presence of amorphous solids in the sample. DSC analysis of 20% BI, and 20% BII mixtures also showed glass transition events and melting events each corresponding to the amorphous A/B and the crystalline component present in the mixture. The 25% AII/BII showed a glass transition as well as two melting events, indicating that both crystalline components can be detected using the DSC technique. The closeness of the melting temperatures of AI and AII make it difficult to identify which crystalline isomer is present in the crystalline/amorphous mixture. However, the difference of melting temperature of A and B isomers are large enough to identify which

diastereomeric crystalline isomers are present. For example, the 20% AI in amorphous A/B shows melting event at 174.5 °C, whereas the 20% BI and 20% BII samples show melting events at 123.4 °C and 122.9 °C, respectively. Likewise, the 25% AII/BII sample shows two melting events at 113.2 and 151.0 °C, corresponding to B and A isomers, respectively.

TG analysis of all four mixtures showed weight loss of about 1% at 175 °C.

IR spectra of the four mixtures are shown in Figures 22 to 25 with IR spectra of each corresponding component for comparison. The IR spectrum of 20% AI sample is similar to amorphous A/B. The IR spectrum of 20% BI sample shows only small differences from that of amorphous A/B. The IR spectrum of 20% BII shows the crystalline water signal at 3650 cm<sup>-1</sup>. The 25% AII/BII sample shows only small differences from that of amorphous A/B. Therefore, IR spectra do not provide a clear identification of individual components in a crystalline/amorphous mixtures except for BII where the crystalline water signal is easily detectable.

Raman spectra of the four mixtures are shown in Figures 26 to 29 with the Raman spectrum of each corresponding component for comparison. The Raman spectra of all four mixtures show clear crystalline signals and amorphous A/B signals. Therefore, Raman spectroscopy provides a clear identification of individual components in a crystalline/amorphous mixtures.

### E. Calibration Curves for Solubility Measurements

Ultraviolet wavelength scans were performed for isomers A and B in order to determine the appropriate wavelengths for sample analysis. Solutions of isomer A and B were prepared by dissolving 75.4 mg of each isomer in 25 mL of methanol and then diluting these solutions to 1000 mL with water in a volumetric flask. SSCI no. 9545 was used to prepare the solution of isomer A, while SSCI no 9547 was used to prepare the solution of isomer B. UV VIS absorbance scans were then obtained from 200 to 400 nm. The solutions were scanned at a rate of 120 nm/min. The spectra obtained for isomers A and B are shown Figure 30 and Figure 31, respectively. As evident from these two spectra, there is an absorbance maximum at ~ 280 nm for each isomer.

Multi-point calibration curves were obtained for isomers A and B. For each isomer, the absorbance at 4 different concentrations was measured. The standard solutions were prepared by dissolving a known amount of each isomer (SSCI no. 9545 and 9547 were used) in 25 mL of methanol and then diluting these solutions to 1000 mL in a volumetric flask. The absorbance measurements at different concentrations for isomers A and B are shown in Table 6 and Table 7, respectively. Linear regression analysis of these two data sets with the intercept forced through zero provided fits with acceptable linearity. The calibration curve for isomer A is shown in Figure 32, and the calibration curve for isomer B is shown in Figure 33.

Single-point calibration curves were obtained for the mixture of isomer A and B in water and 0.07N HCl. SSCI no. 9499 (Crystalline AI/BI) was used to prepare a standard solution in 0.07N hydrochloric acid, while SSCI no. 9498 was used to prepare a standard solution in water. The solutions were prepared and analyzed in the same manner as the solutions listed in Table 6 and

Table 7. The values for the absorbance of the two standard solutions for isomer A/B are listed in Table 8.

#### F. Preparation of Amorphous Single Isomers used for Dissolution

Amorphous samples of isomers A and B that were used for the dissolution experiments were prepared by milling small quantities (~ 70-80 mg) of the corresponding crystalline isomer in a Wig-L-Bug® apparatus. XRPD was used to detect the presence of residual crystalline material after milling (Table 9). Some samples contained peaks in the diffraction patterns that can be attributed to isomer AI or BI. An empirical judgement was made for each sample as to whether the amount of crystalline material was unacceptable for dissolution experiments. The samples with unacceptably high levels of crystallinity were either re-milled or set aside. However, it must be cautioned that even the samples that appear completely amorphous by XRPD are expected to contain trace amounts of crystalline material. This is due to the inability of the milling process to convert all of the crystallinity in a sample.

#### G. Solubility Profiles of the Single Isomers

Because the crystalline forms of isomers A and B must be milled in small batches to ensure adequate conversion to the amorphous form, several samples of amorphous material were combined for each dissolution experiment (Table 10). The dissolution profiles for the three solubility experiments performed on amorphous A are shown in Figure 34, and the kinetic data used to prepare this plot is listed in Table 11. Two of the three profiles (the profiles that contained data points at initial times below 20 min) are characterized by a rapid decrease in the solubility of the material. For all the profiles the solubility remains relatively constant after 20 min. This is indicative of a rapid conversion of amorphous material to a less-soluble crystalline form. XRPD analysis of the isolated material after the dissolution experiments were complete indicated the formation of a mixture of AI/AII in these experiments (Table 10).

SSCI no. 9876 was used for the dissolution experiment for isomer AI. The dissolution profiles for the three experiments performed on this crystal form are shown in Figure 35, and the kinetic data used to prepare this plot is listed in Table 11. Very good precision was obtained for these runs. For each of these experiments, the solubility reaches a maximum value early in the run and remains relatively constant throughout the rest of the experiment. XRPD analysis of the isolated material after the dissolution experiments were complete indicated that the samples did not convert to another crystal form (Table 10).

Only enough sample of amorphous B was on hand to permit one dissolution experiment to be performed. The dissolution profile for amorphous B is shown in Figure 36, and the kinetic data used to prepare this plot is listed in Table 12. As in the case for amorphous isomer A, the profile of amorphous B is characterized by an initially high level of solubility followed by a rapid decrease. The product was isolated after the dissolution experiment and determined to be isomer BII by XRPD analysis (Table 10).

Two separate lots of isomer BI were used to obtain dissolution profiles of this polymorph (Figure 37). The profile for SSCI no. 9875 (isomer BI) was run in duplicate (samples 421-26-01 and

421-38-01). The relative features of the three profiles are similar, however, the absolute values for the dissolution of samples 421-26-01 and 421-38-01 are slightly lower than those obtained for 424-47-01 (Table 12). This may due to minor differences in the two lots of starting material. All experiments provided isomer BII at the end of the run (Table 10), which indicates that isomer BII is less soluble and more stable than isomer BI in water at 37 °C.

The lower solubility of isomer BII relative to isomer BI was confirmed by obtaining dissolution profiles of authentic samples of isomer BII (Figure 38). Three different samples of isomer BII were used for these experiments. As opposed to the profiles obtained for isomer BI, the profiles for isomer BII rapidly attain a solubility of ~ 0.15 – 0.2 mg/mL and remain relatively constant throughout the remainder of the run (Table 12). XRPD analysis of the isolated products indicated that isomer BII did not convert to another form during these dissolution experiments (Table 10).

## H. Solubility Profiles of Mixtures of Isomers A and B in Water

The solubility of mixtures of amorphous and crystalline isomers A and B was also studied in water at 37 °C. These samples were prepared by Glaxo Wellcome and used as received (Table 1). The amorphous material (SSCI no. 9498) was prepared by spray drying technology, and is expected to contain substantially less (if any) crystalline material than the samples prepared by milling [2]. Two separate dissolution profiles for amorphous A/B were collected (Table 14). As shown in Figure 39, good reproducibility was obtained for these two dissolution experiments. The decrease in solubility over time is due to the crystallization of amorphous A/B to isomers AI and BII, as confirmed by XRPD analysis of the material after the dissolution experiment (Table 13).

The dissolution profile for crystalline AI/BI (SSCI no. 9488) is notably different from that for amorphous A/B. As seen in Figure 40 and in Table 14, the maximum solubility of AI/BI is reached early in the run, and with exception of one run, the profiles do not attain the same maximum solubility values that were measured for amorphous A/B. The decrease in solubility over time is indicative of conversion to a less soluble form. This was confirmed by XRPD analysis of the dissolution products (Table 13). The mixture of AI/BI was found to convert to AI/BII under these conditions. This is consistent with the dissolution behavior measured for the single isomers AI and BI, where it was found that isomer AI did not convert to another form under the conditions of the dissolution experiment, while isomer BI converted to BII.

Dissolution experiments were carried out in the presence of the crystalline isomers AI and BI in order to address the effect of crystallinity on the dissolution behavior of mixtures of amorphous isomers A and B. For these experiments the amount of amorphous A/B was held constant at ~ 170 mg, and additional crystalline AI/BI was added to provide the varying ratios of amorphous-to-crystalline material (Table 13). Dissolution profiles were collected for ratios of 70% and 50% amorphous material (Table 15). As shown in Figure 41 and in Figure 42, the dissolution profiles for the 70% and 50% ratios all reach a maximum solubility of ~1.2 mg/mL early in the experiment. However, the presence of crystalline material causes the solubility to decrease earlier in the run than is observed for the 100% amorphous material. For example, it took ~ 3-4

hours for the solubility of two of the amorphous A/B experiments to decrease to near their final values (experiments 395-86-01 and 424-23-01, Figure 39), while it took only 2 hours for the experiments involving the 50% crystalline material to decrease in a similar manner (Figure 42). In the experiments where crystalline AI/BI was initially present, the isolated products were found by XRPD analysis to be A1/BII (Table 13). None of the isomer AII was observed.

In cases where identical lot numbers of starting material were used, it is appropriate to plot the average data so that comparisons in the dissolution profiles can be made. Table 16 contains the average data points for the dissolution profiles of 100% amorphous A/B, 70% amorphous A/B, and 100% crystalline AI/BI where the starting materials were SSCI-9498 and SSCI no. 9499. The averaged data sets for these three ratios are plotted in Figure 43. This figure clearly illustrates the difference in the solubility of amorphous A/B that is caused by the presence of crystalline AI/BI. In addition, the presence of AI/BI leads to the crystallization of the amorphous material into form AI/BII. When the crystalline material is absent, the amorphous product crystallizes to form AII/BII (Table 13).

### I. Solubility Profiles of Mixtures of Isomers A and B in 0.07N HCl

The dissolution experiments involving ratios of amorphous A/B and crystalline AI/BI were repeated in 0.07N HCl (Table 17 and Table 18). The results obtained closely parallel those obtained for the dissolution experiments performed in water. However, for two of the three experiments involving amorphous A/B (samples 424-20-01 and 424-21-01), the isolated product contained isomer AI in addition to isomer AII and BII. The reason for the formation of isomer AI in these two experiments is unknown. All dissolution experiments were performed in triplicate, and very good precision was obtained for each of the three mixtures (Figure 44, Figure 45, and Figure 46). The averaged data for these dissolution experiments is listed in Table 19, and the dissolution profiles are plotted in Figure 47. Although the differences between the 70% amorphous material and the 100% amorphous material are less pronounced in HCl than in water, the solubility of 70% amorphous A/B decreases earlier in the averaged runs than the solubility of the 100% amorphous material (Figure 47). This result provides additional support that the presence of crystalline material affects the solubility of amorphous A/B.

### IV. CONCLUSIONS

Analyses of individual isomers and racemates using XRPD, DSC, IR and Raman spectroscopy demonstrated that these techniques clearly provide identification methods for the presence of individual isomers in racemates. The polymorphic forms can also be identified in racemates using XRPD, IR and Raman spectroscopy.

For mixtures containing crystalline and amorphous A/B solids, XRPD and Raman spectroscopy provide clear identification methods to determine each component present in the mixtures. Both of these techniques can be used to develop quantitative methods to determine crystalline material in the crystalline/amorphous mixtures. DSC also provides glass transition temperature for amorphous components and melting events for the crystalline components. Therefore, DSC can be used to develop a quantitative method to determine amorphous material in the crystalline/amorphous mixtures [3].

The dissolution experiments performed in water at 37 °C show that the amorphous forms of isomers A and B are more soluble than the corresponding crystalline forms. Amorphous A and B convert to crystalline AII and BII, respectively, during dissolution. Experiments on the single isomers BI and BII show that BI is readily converted to form BII, which is less soluble. Isomer AI does not convert to isomer AII, however, isomer AII is produced from amorphous A in water under the dissolution conditions.

Dissolution experiments on mixtures of amorphous A/B and crystalline AI/BI show that the presence of crystalline material affects the time at which the amorphous material begins to crystallize. The presence of isomer AI/BI in the mixture causes amorphous A/B to crystallize to isomer AI/BII in water and in 0.07N HCl. In water, amorphous A/B crystallized to AII/BII, while in HCl, amorphous A/B crystallized to AI/AII/BII in two of the three experiments.

## V. REFERENCES

- 
- [1] Glaxo Wellcome Report, Report No. GCP/83/014.
  - [2] a) Crisp, H. A.; Clayton, J. C.; Elliott, L. G.; Wilson, E. M. US 4,820,833 (1989)  
b) Crisp, H. A.; Clayton, J. C. US 4,562,181 (1985)
  - [3] Glaxo Wellcome Report, Report No. SC0878/DSC/8.

**Table 1. Samples Received**

Sample	Lot No.	SSCI No.	XRPD Pattern	XRPD Filename	Page
Amorphous Cefuroxime A/B	G013528	9498	Amorphous	xr4-1428	71
	G019264	10014	Amorphous	xr4-2220	72
Crystalline Cefuroxime A/B	G014657	9499	AI/BI	xr4-1427	73
	G017837	10015	AI/BI	xr4-2221	74
Crystalline Isomer A (98%)	MRH-0196-111A	9545	AI	xr4-822 <sup>a</sup>	75
Crystalline Isomer B (87%)	MRH-0196-114A	9546	BI	xr4-817	76
Crystalline Isomer B (95%)	MRH-0196-120A	9547	BI	xr4-819	77
Cefuroxime axetil; isomer AI	R5491/90/3 (1 of 2)	9876	AI	-	-
Cefuroxime axetil; isomer AI	R5491/90/3 (2 of 2)	9877	AI	xr4-1960	78
Cefuroxime axetil; isomer BII	R5491/96/4	9874	BII	xr4-2190	79
Cefuroxime axetil; isomer BI	R5007/46/1	9875	BI	xr4-1961	80

a. 356-90-01 is a subsample of SSCI No. 9545

**Table 2. Analyses of Isomer A**

Sample	Amorphous A	AI	AII
Sample No.	391-30-01 <sup>a</sup>	SSCI No. 9545	391-11-03 <sup>b</sup>
XRPD	Result	Amorphous	AI
	Filename	xr4-1091	xr4-822
	Page	81	75
	Figures	1	1
DSC	endotherm <sup>c</sup>	57 °C ( $T_g$ onset) 108.5 °C (exotherm max), 192.7 °C (70)	201.9 °C (106) 191.0 °C (105)
	Filename	ds1-3258	ds1-3259 ds1-3260
TGA	weight loss	0.6% @ 175 °C	0.1% @ 175 °C 0.7% @ 175 °C
	Filename	tg1-731	tg1-715 tg1-730
	DSC/TGA Page	83	84 85
IR	Result	Unique	Unique
	Filename	3913001ir	9545ir 3911103ir
	Page	86	87 88
	Figures	2	2 2
Raman	Result	Unique	Unique
	Filename	3913001rm	9545rm 3911103rm
	Page	89	90 90
	Figures	3	3 3

a. SSCI No. 9545 was milled.

b. Hot solution of SSCI No. 9545 in tetrahydrofuran was cooled, and the solid was formed.

c. Onset temp of endothermic event, °C ( $\delta H$ , J/g)

**Table 3. Analyses of Isomer B**

Sample		Amorphous B	BI	BII
Sample No.		385-69-01 <sup>a</sup>	SSCI No. 9547	385-60-01 <sup>b</sup>
XRPD	Result	Amorphous	BI	BII
	Filename	xr4-1369	xr4-819	xr3-5440
	Page	92	77	93
	Figures	4	4	4
DSC	endotherm <sup>c</sup>	71.8 °C ( $T_g$ Onset)	133.4 °C (58)	124.3 °C (60)
	Filename	ds2-736	ds2-502	ds1-3308
TGA	weight loss	11.9% @ 175 °C	< 0.1% @ 175 °C	1.6% @ 175 °C
	Filename	tg1-770	tg1-705	tg1-763
	DSC/TGA Page	94	95	96
IR	Result	Unique	Unique	Unique
	Filename	3856901ir	9547ir	3856001ir
	Page	97	98	99
	Figures	5	5	5
Raman	Result	Unique	Unique	Unique
	Filename	3856901rm	9547rm	3856001rm
	Page	100	101	102
	Figures	6	6	6

a. A solution of SSCI No. 9547 in tetrahydrofuran was added to cold hexane, and the solid formed was filtered.

b. SSCI No. 9547 was slurried in water.

c. Onset temp of endothermic event, °C (ΔH, J/g)

**Table 4. Analyses of Racemates**

Sample		amorphous A/B	AI/BI	AI/BII	AII/BII
Sample No.		SSCI No. 9498	SSCI No. 9499	385-60-05 <sup>a</sup>	385-60-03 <sup>b</sup>
XRPD	Result	amorphous	AI/BI	AI/BII	AII/BII
	Filename	xr4-1428	xr4-1427	xr3-5444	xr3-5442
	Page	71	73	103	104
	Figures	-	7	8	9
DSC	endotherm <sup>c</sup>	71.5 °C ( $T_g$ onset)	118.0 °C (32) 170.1 °C (29)	123.9 (30) 161.5 (34)	113.2 °C (16) 150.7 °C (15)
	Filename	ds2-494	ds2-492	ds1-3315	ds1-3307
TGA	weight loss	1.1% @ 175 °C	2.1% @ 175 °C	0.8% @ 175 °C	0.8% @ 175 °C
	Filename	tg1-700	tg1-699	tg1-771	tg1-762
	DSC/TGA Page	105	106	107	108
IR	Result	Similar to amorphous A	AI/BI	AI/BII	AII/BII
	Filename	9498ir	9499ir	3856005ir	3856003ir
	Page	109	110	111	112
	Figures	10	11	12	13
Raman	Result	amorphous A/B	AI/BI	AI/BII	AII/BII
	Filename	9498rm	9499rm	3856005rm	3856003rm
	Page	113	114	115	116
	Figures	14	15	16	17

a. SSCI No. 9499 was slurried in water.

b. SSCI No. 9498 was slurried in water.

c. Onset temp of endothermic event, °C (ΔH, J/g)

**Table 5. Analyses of Crystalline/Amorphous Mixtures**

Sample		20% AI in amorphous A/B	20% BI in amorphous A/B	20% BII in amorphous A/B	25% AII/BII in amorphous A/B
Sample No.		391-87-01 <sup>a</sup>	391-90-03 <sup>b</sup>	391-94-01 <sup>c</sup>	395-69-01 <sup>d</sup>
XRPD	Result	AI	BI	BII	AII/BII
	Filename	xr4-1400	xr4-1480	xr4-1481	xr3-5561
	Page	117	118	119	120
	Figures	18	19	20	21
DSC	endotherm <sup>e</sup>	76.5 °C ( $T_g$ onset) 174.5 °C (18)	75.7 °C ( $T_g$ onset) 123.4 °C (12)	73.9 °C ( $T_g$ onset) 122.9 °C (15)	84.6 °C ( $T_g$ onset) 113.2 (7), 151.0 (15)
	Filename	ds1-3306	ds1-3312	ds1-3313	ds1-3305
TGA	weight loss	1.3% @ 175 °C	1.3% @ 175 °C	1.5% @ 175 °C	1.1% @ 175 °C
	Filename	tg1-764	tg1-765	tg1-766	tg1-761
	DSC/TGA Page	121	122	123	124
IR	Result	similar to amorphous A/B	Small differences from amorphous A/B	crystalline H <sub>2</sub> O peak of BII is visible	Small differences from amorphous A/B
	Filename	3918701ir	3919003ir	3919401ir	3956901ir
	Page	125	126	127	128
	Figures	22	23	24	25
Raman	Result	clear AI peaks	clear BI peaks	clear BII peaks	clear AII/BII peaks
	Filename	3918701rm	3919003rm	3919401rm	3956901rm
	Page	129	130	131	132
	Figures	26	27	28	29

a. Mixture of SSCI No. 9545 and SSCI No. 9498.

b. Mixture of SSCI No. 9547 and SSCI No. 9498.

c. Mixture of 385-60-01 and SSCI No. 9498.

d. Mixture of 385-60-03 and SSCI No. 9498.

e. Onset temp of endothermic event, °C (ΔH, J/g)

**Table 6. Calibration Curve Data for Isomer A (Standards File 4245201)**

Sample No.	Concentration (mg/mL)	Absorbance (280 nm)
424-27-01	0.0754	2.6983
424-30-01	0.0569	2.1068
424-30-02	0.0401	1.4929
424-30-03	0.0194	0.7576

**Table 7. Calibration Curve Data for Isomer B (Standards file 4244803)**

Sample No.	Concentration (mg/mL)	Absorbance (280 nm)
424-27-02	0.0754	2.7438
424-30-04	0.0562	2.1084
424-30-05	0.0375	1.3681
424-30-06	0.0196	0.7252

**Table 8. Calibration Curve Data for Isomer A/B**

Sample No.	Concentration (mg/mL)	Dissolution Medium	Absorbance (280 nm)	Slope	Standards File
395-47-02	0.0752	0.07N HCl	2.8484	37.88	3954702
395-81-01	0.0749	Water	3.0559	40.80	3958102

**Table 9. Amorphous Isomers of A and B Used in Dissolution Experiments**

Sample no.	Starting Isomer (Sample no.)	Milling Time (min)	XRPD Filename	XRPD on page
332-87-01	AI (SSCI no. 9876)	15	xr3-6256	133
332-87-02	AI (SSCI no. 9876)	15	xr3-6257	134
332-87-03	AI (SSCI no. 9876)	15	xr3-6258	135
332-87-04	AI (SSCI no. 9876)	15	xr3-6259	136
332-88-02	AI (SSCI no. 9876)	15	xr3-6264	137
332-88-05	AI (SSCI no. 9876)	15	xr3-6267	138
332-95-02	AI (332-87-05) <sup>a</sup>	20	xr3-6383	139
332-95-03	AI (332-88-01) <sup>a</sup>	20	xr3-6384	140
332-95-04	AI (332-88-03) <sup>a</sup>	20	xr3-6385	141
332-95-05	AI (332-88-04) <sup>a</sup>	20	xr3-6386	142
332-96-01	AI (SSCI no. 9876)	25	xr3-6450	143
332-96-02	AI (SSCI no. 9876)	25	xr3-6451	144
385-95-01	BI (SSCI no. 9547)	10	xr4-1933	145
385-95-02	BI (SSCI no. 9547)	15	xr4-1934	146
385-95-03	BI (SSCI no. 9547)	20	xr4-1935	147

a. Prepared by milling SSCI no. 9876 for 15 min

**Table 10. Dissolution Experiments for the Individual Isomers**

Dissolution Experiment <sup>a</sup> Sample No.	Isomer Form	Isomer Sample No.	Sample No. after dissolution	Crystal Form after dissolution	XRPD Filename	XRPD on page
424-53-01	Amorphous A	332-87-01, 332-87-03, 332-87-04, 332-88-02	424-53-02	AI/AII	xr4-2148	148
421-21-01	Amorphous A	332-95-02, 332-95-03, 332-95-04, 332-95-05, 332-96-02	421-21-02	AI/AII	xr3-6471	149
421-24-01	Amorphous A	332-88-05, 332-96-01, 332-88-02, 332-87-02, 332-95-05	421-24-02	AI/AII	xr3-6501	150
424-57-01	AI	SSCI no. 9876	424-57-02	AI	xr4-2159	151
424-59-01	AI	SSCI no. 9876	424-59-02	AI	xr4-2165	152
425-73-01	AI	SSCI no. 9876	425-73-02	AI	xr3-6613	153
424-42-01	Amorphous B	385-95-01, 385-95-02, 385-95-03	424-43-01	BII	xr4-2025	154
424-47-01	BI	SSCI no. 9547	424-47-02	BII	xr4-2147	155
421-26-01	BI	SSCI no. 9875	421-26-02	BII	xr3-6502	156
421-38-01	BI	SSCI no. 9875	421-38-02	BII	xr3-6614	157
424-45-01	BII	385-60-01	424-45-02	BII	xr4-2023	158
424-62-03	BII	435-04-01	424-63-01	BII	xr3-6558	159
421-39-01	BII	SSCI-9874	421-39-02	BII	xr4-2313	160

a. Dissolution was carried out in water at 37 °C.

**Table 11. Dissolution Profile Data for Isomer A**

time (min)	Amorphous A Concentration (mg/mL)			AI Concentration (mg/mL)		
	424-53-01	421-21-01	421-24-01	424-57-01	424-59-01	425-73-01
0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
1	0.2772	-	-	0.0373	0.0410	0.0264
5	0.1114	-	0.1527	0.0406	0.0401	0.0390
10	0.0724	-	0.1269	0.0416	0.0417	0.0429
15	0.0789	0.0846	0.0955	0.0416	0.0423	0.0462
20	0.0784	0.0827	0.0909	0.0418	0.0425	0.0471
30	0.0773	0.0784	0.0843	0.0431	0.0429	0.0522
40	0.0641	0.0819	0.0831	0.0424	0.0433	0.0540
60	0.0699	0.0758	0.0828	0.0429	0.0432	0.0503
90	0.0660	0.0721	0.0844	0.0426	0.0433	0.0497
120	0.0633	0.0699	0.0840	0.0410	0.0439	0.0552
160	-	0.0677	-	-	-	-

**Table 12. Dissolution Profile Data for Isomer B**

time (min)	Amorphous B Concentration (mg/mL)	BI Concentration (mg/mL)			BII Concentration (mg/mL)		
		424-42-01	424-47-01	421-26-01	421-38-01	424-45-01	424-62-03
0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
1	0.9522	0.5469	0.4053	0.3610	0.1951	0.0677	0.0641
5	1.3293	0.5922	0.4212	0.4697	0.2140	0.0843	0.1339
10	0.6717	0.6129	0.4464	0.4925	0.2145	0.1217	0.1409
15	0.4565	0.6084	0.4344	0.4933	0.2195	0.1240	0.1345
20	0.3944	0.6109	0.4557	0.4749	0.2263	0.1290	0.1442
30	0.3479	0.6183	0.4397	0.4032	0.2217	0.1356	0.1550
40	0.3162	0.5271	0.4044	0.3110	0.2199	0.1399	0.1472
60	0.2840	0.4204	0.3263	0.2741	0.2119	0.1406	0.1661
90	0.2815	0.3500	0.2346	0.2122	0.2032	0.1444	0.1661
120	0.2762	0.3178	0.1853	0.1789	0.2007	0.1514	0.1666
150	0.2769	0.2870	-	0.1867	-	0.1597	0.1698
180	-	0.2847	-	0.1753	-	-	0.1643
210	-	0.2864	0.1664	0.1719	-	-	0.1665

**Table 13. Dissolution Experiments for the Mixtures of Isomers A and B in Water**

Dissolution Experiment <sup>a</sup> Sample No.	Isomer Form	Isomer Sample No. (amount used, mg)	Sample No. after dissolution	Crystal Form after dissolution	XRPD Filename	XRPD on page
395-86-01	100% Amorphous A/B	SSCI No. 9498 (172.1)	395-86-02	AII/BII	xr3-5787	162
424-23-01	100% Amorphous A/B	SSCI No. 9498 (169.8)	424-24-01	AII/BII	xr4-1987	163
424-15-01	70% Amorphous A/B 30% AI/BI	SSCI No. 9498 (170.3) SSCI No. 9499 (73.4)	424-15-02	AI/BII	xr4-1923	164
424-16-01	70% Amorphous A/B 30% AI/BI	SSCI No. 9498 (170.6) SSCI No. 9499 (72.9)	424-16-02	AI/BII	xr4-1924	165
421-35-01	70% Amorphous A/B 30% AI/BI	SSCI No. 10014 (168.1) SSCI No. 9499 (71.3)	421-35-02	AI/BII	xr4-2273	166
425-70-01	50% Amorphous A/B 50% AI/BI	SSCI No. 10014 (168.8) SSCI No. 9499 (169.0)	425-70-02	AI/BII	xr4-2274	167
421-31-01	50% Amorphous A/B 50% AI/BI	SSCI No. 10014 (167.3) SSCI No. 9499 (167.9)	421-31-02	AI/BII	xr4-2272	168
421-32-01	50% Amorphous A/B 50% AI/BI	SSCI No. 10014 (168.2) SSCI No. 9499 (168.7)	421-32-02	AI/BII	xr3-6565	169
395-89-01	100% Crystalline AI/BI	SSCI No. 9499 (171.9)	395-92-01	AI/BII	xr3-5788	170
424-23-02	100% Crystalline AI/BI	SSCI No. 9499 (172.1)	424-24-02	AI/BII	xr4-1988	171
425-65-01	100% Crystalline AI/BI	SSCI No. 9499 (167.8)	425-65-02	AI/BII	xr4-2234	172

a. Dissolution was carried out in water at 37 °C.

**Table 14. Dissolution Profile Data for Amorphous A/B and AI/BI in Water**

time (min)	100% Amorphous A/B Concentration (mg/mL)		100% Crystalline AI/BI Concentration (mg/mL)		
	395-86-01	424-23-01	395-89-01	424-23-02	425-65-01
0	0.0000	0.0000	0.0000	0.0000	0.0000
20	1.0800	1.2120	0.5200	0.6100	0.6473
40	1.1320	1.2460	0.5540	0.6100	0.6504
60	1.1060	1.1680	0.5620	0.5480	1.0665
90	1.0900	1.0920	0.4280	0.3540	0.6415
120	1.0700	0.9060	0.3220	0.3340	0.4094
180	0.8100	0.4560	0.3000	0.2980	0.3205
240	0.4640	0.3980	0.2920	0.2780	0.3163
300	0.3620	0.3760	0.2880	0.2760	0.4432
360	0.3220	0.3620	0.2700	0.2680	0.2974

**Table 15. Dissolution Profile Data for Mixtures of Amorphous A/B and Crystalline AI/BI in Water**

time (min)	30% Crystalline AI/BI Concentration (mg/mL)			50% Crystalline AI/BI Concentration (mg/mL)		
	424-15-01	424-16-01	421-35-01	425-70-01	421-31-01	421-32-01
0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
20	1.2940	1.2300	0.9978	0.9508	0.6840	0.7809
40	1.1940	1.1380	1.1782	0.7274	0.7379	1.1961
60	1.1340	1.1120	1.2686	0.5064	0.5800	0.9652
90	1.1060	0.7400	1.3816	0.6866	0.4025	0.5471
120	0.6480	0.5060	1.2106	0.3510	0.4118	0.4137
180	0.4140	0.3840	0.5485	0.3200	0.3659	0.3520
240	0.3620	0.3460	0.3889	0.2952	0.3413	0.3446
300	0.3300	0.3000	0.3887	0.3161	0.3245	0.3279
360	0.3100	0.2820	0.3618	0.3022	0.3172	0.3378

**Table 16. Averaged Profile Data for Amorphous and Crystalline A/B Mixtures in Water**

time (min)	Average of 395-86-01 and 424-23-01 (100% Amorphous A/B)	Average of 424-15-01 and 424-16-01 (30% AI/BI)	Average of 395-89-01, 424-23-02 and 425-65-01 (100% AI/BI)
0	0.0000	0.0000	0.0000
20	1.1460	1.2620	0.5924
40	1.1890	1.1660	0.6048
60	1.1370	1.1230	0.7255
90	1.0910	0.9230	0.4745
120	0.9880	0.5770	0.3551
180	0.6330	0.3990	0.3062
240	0.4310	0.3540	0.2954
300	0.3690	0.3150	0.3357
360	0.3420	0.2960	0.2785

**Table 17. Dissolution Experiments for the Mixtures of Isomers A and B in 0.07N HCl**

Dissolution Experiment <sup>a</sup> Sample No.	Isomer Form	Isomer Sample No. (amount used, mg)	Sample No. after dissolution	Crystal Form after dissolution	XRPD Filename	XRPD on page
395-94-02	100% Amorphous A/B	SSCI No. 9498 (169.9)	395-94-03	AII/BII	xr3-5804	173
424-20-01	100% Amorphous A/B	SSCI No. 9498 (171.6)	385-94-02	AI/AII/BII	xr4-1931	174
424-21-01	100% Amorphous A/B	SSCI No. 9498 (170.6)	385-94-03	AI/AII/BII	xr4-1932	175
424-10-02	70% Amorphous A/B 30% AI/BI	SSCI No. 9498 (170.0) SSCI No. 9499 (72.9)	424-11-03	AI/BII	xr4-1876	176
424-11-01	70% Amorphous A/B 30% AI/BI	SSCI No. 9498 (170.5) SSCI No. 9499 (73.3)	424-11-04	AI/BII	xr4-1877	177
421-34-01	70% Amorphous A/B 30% AI/BI	SSCI No. 10014 (169.0) SSCI No. 9499 (72.0)	421-34-02	AI/BII	xr4-2312	178
424-07-01	100% Crystalline A I/BI	SSCI No. 9499 (173.0)	424-07-02	AI/BII	xr4-1826	179
395-96-02	100% Crystalline A I/BI	SSCI No. 9499 (170.3)	395-97-02	AI/BII	xr3-5803	180
424-06-01	100% Crystalline A I/BI	SSCI No. 9499 (171.1)	424-06-02	AI/BII	xr4-1825	181

a. Dissolution was carried out in 0.07N HCl at 37 °C.

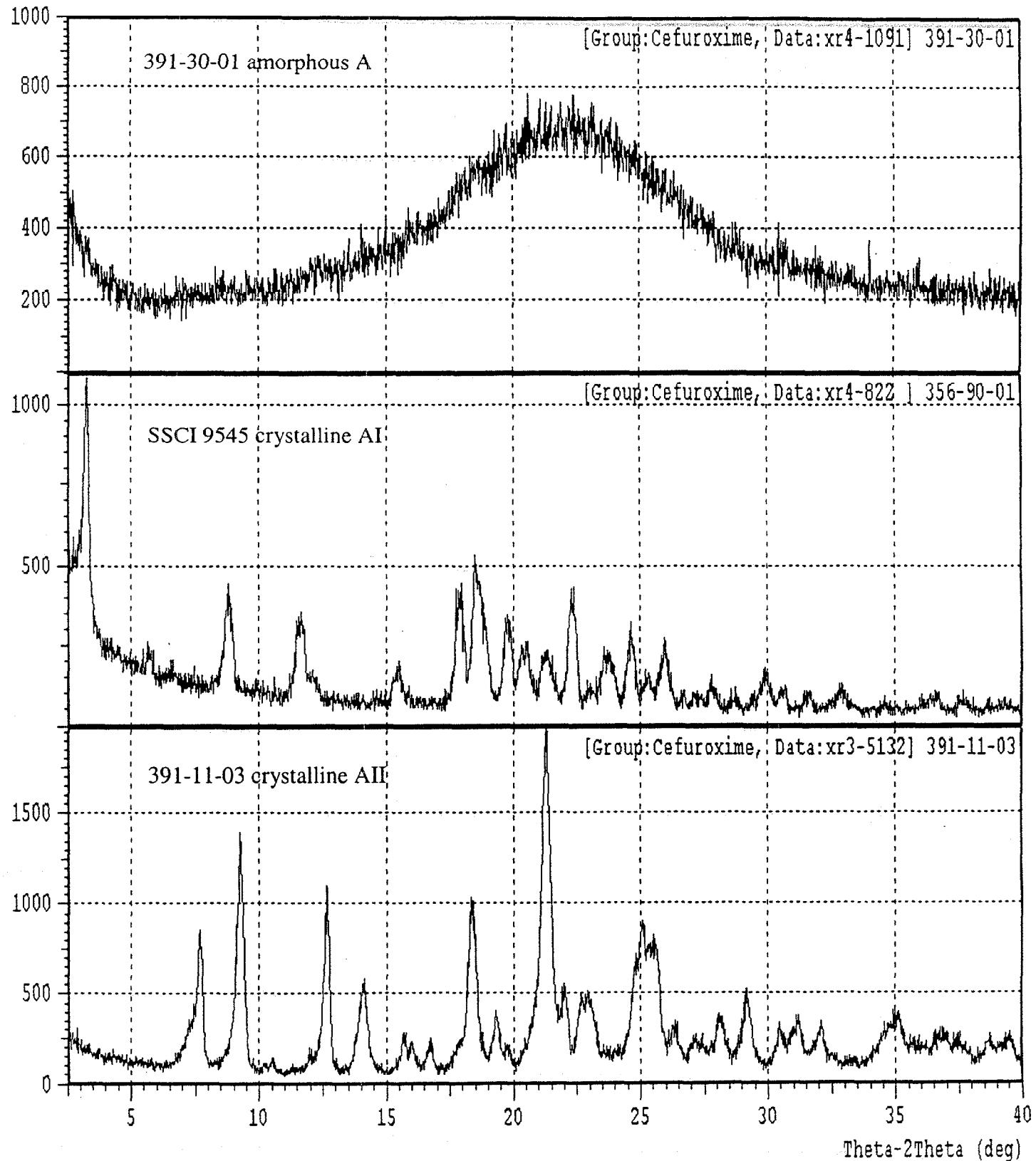
**Table 18. Dissolution Profile Data for Amorphous A/B and AI/BI in 0.07N HCl**

time (min)	100% Amorphous A/B Concentration (mg/mL)			30% Crystalline Concentration (mg/mL) in HCl			100% Crystalline Concentration (mg/mL) in HCl		
	395-94-02	424-20-01	424-21-01	424-10-02	424-11-01	421-34-01	424-07-01	395-96-02	424-06-01
0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
20	1.2280	1.2420	1.2160	1.2200	1.1960	1.1009	0.6820	0.5920	0.6300
40	1.1600	1.1720	1.1780	1.1420	1.1520	1.2751	0.5520	0.6300	0.6380
60	1.1460	1.1640	1.1780	1.1240	0.8700	1.2751	0.3640	0.5740	0.7020
90	0.8640	1.1400	0.9740	0.7140	0.5820	1.2667	0.3100	0.3480	0.3340
120	0.6200	0.7720	0.6560	0.5160	0.4780	0.8259	0.3140	0.3280	0.3220
180	0.5120	0.5320	0.5000	0.4200	0.4040	0.4918	0.3200	0.3280	0.3160
240	0.4600	0.5040	0.4760	0.3920	0.3920	0.4515	0.3200	0.3320	0.3160
300	0.4540	0.4900	0.4620	0.3740	0.1640	0.4497	0.3160	0.3220	0.3100
360	0.4460	0.4660	0.4460	0.3680	0.3700	0.4426	0.3200	0.3280	0.3140

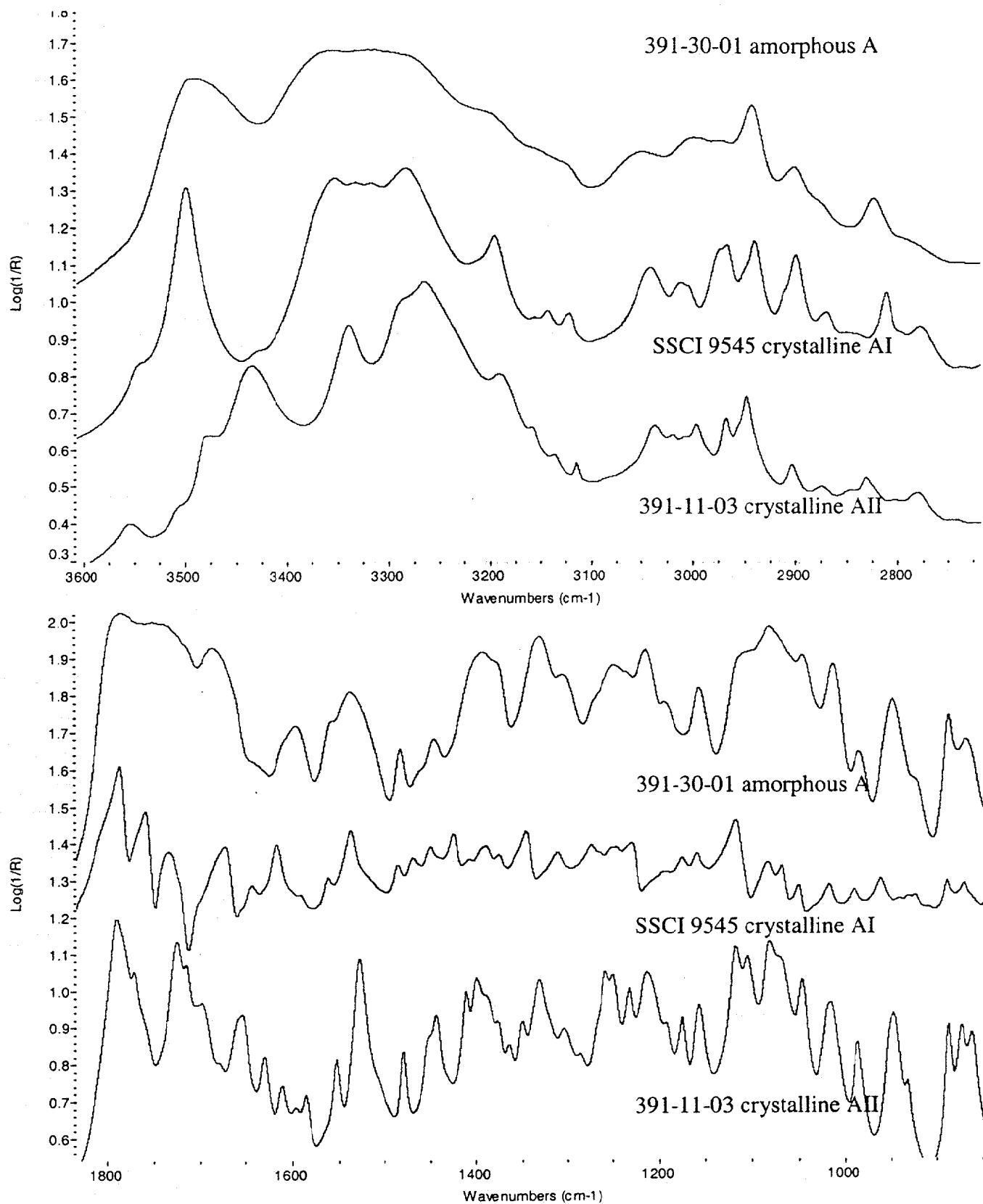
**Table 19. Averaged Dissolution Profile Data for Amorphous and Crystalline A/B Mixtures in 0.07N HCl**

time (min)	Average of 395-94-02, 424-20-01 and 424-21-01 (100% Amorphous A/B)	Average of 424-10-02, 424-11-01 and 421-34-01 (30% AI/BI)	Average of 424-07-01, 395-96-02, and 424-06-01 (100% AI/BI)
0	0.0000	0.0000	0.0000
20	1.2287	1.1723	0.6347
40	1.1700	1.1897	0.6067
60	1.1627	1.0897	0.5467
90	0.9927	0.8542	0.3307
120	0.6827	0.6066	0.3213
180	0.5147	0.4386	0.3213
240	0.4800	0.4118	0.3227
300	0.4687	0.3292	0.3160
360	0.4527	0.3935	0.3207

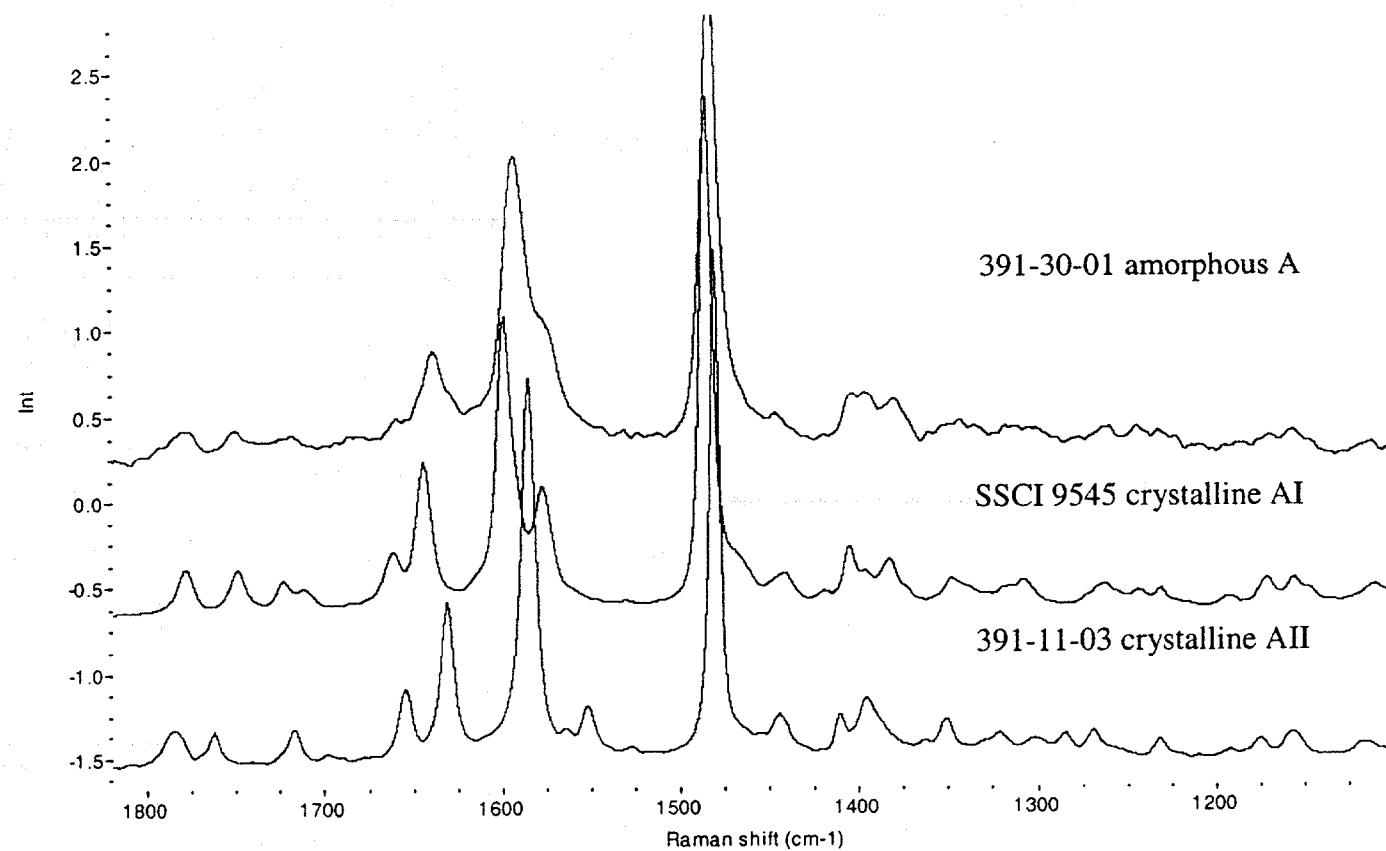
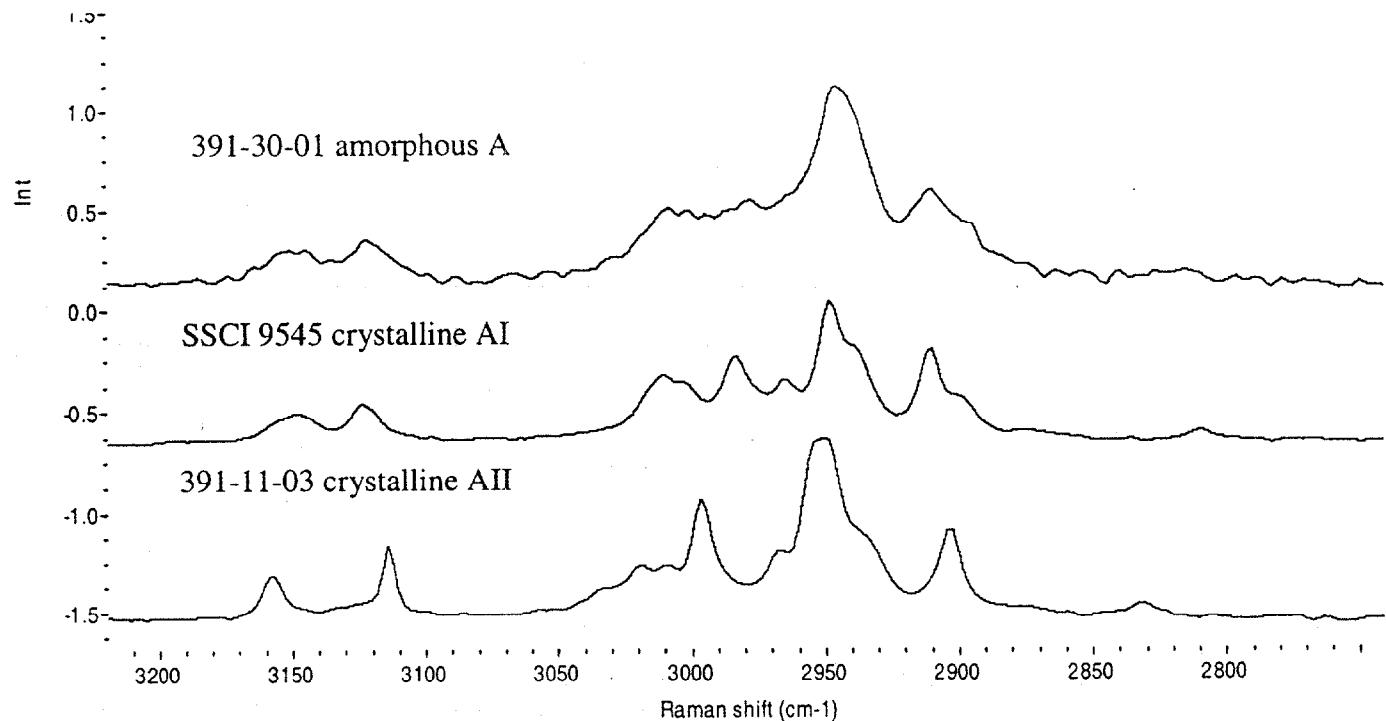
**Figure 1. XRPD Patterns of Amorphous A, Crystalline AI and AII**



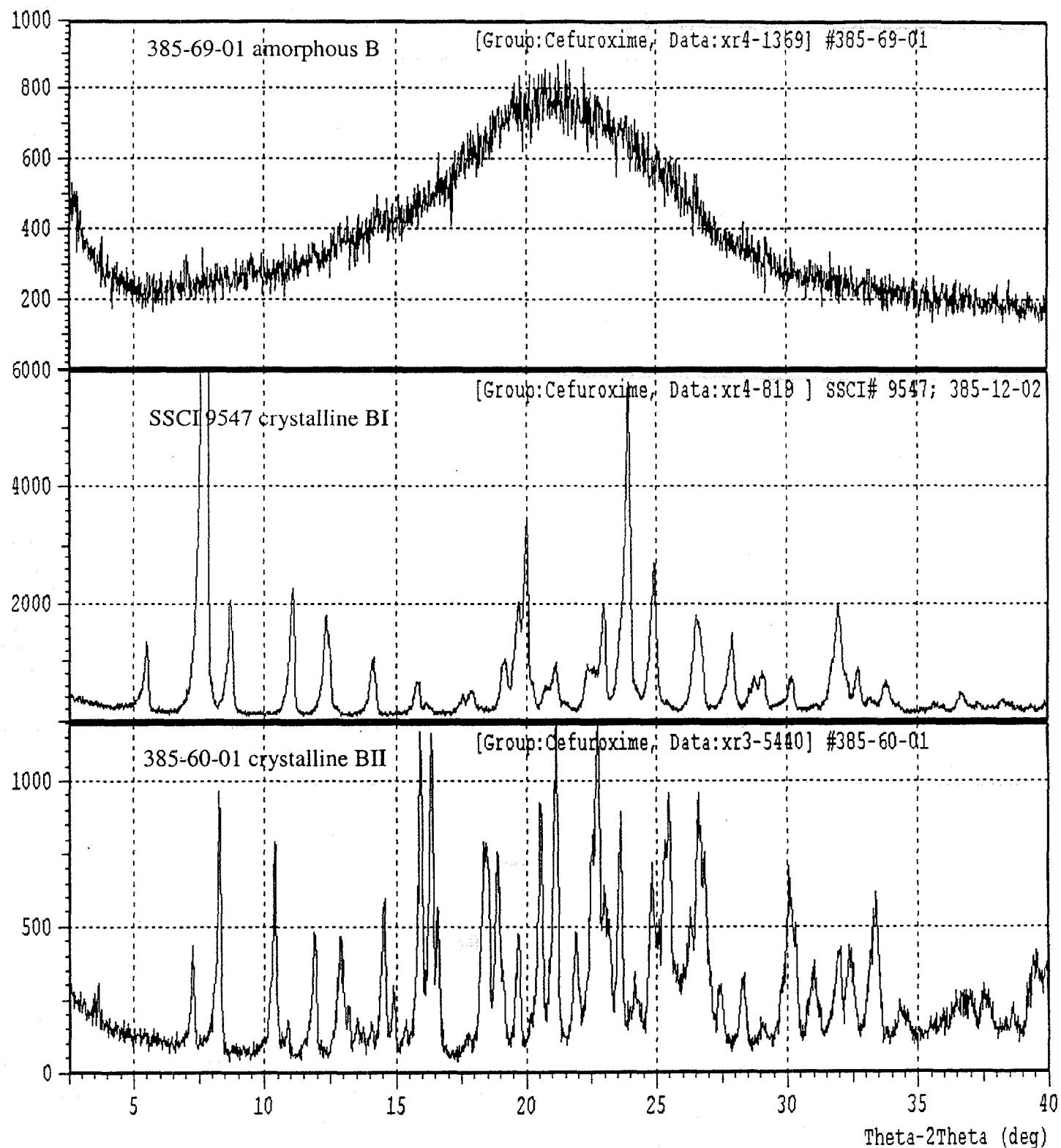
**Figure 2. IR Spectra of Amorphous A, Crystalline AI and AII**



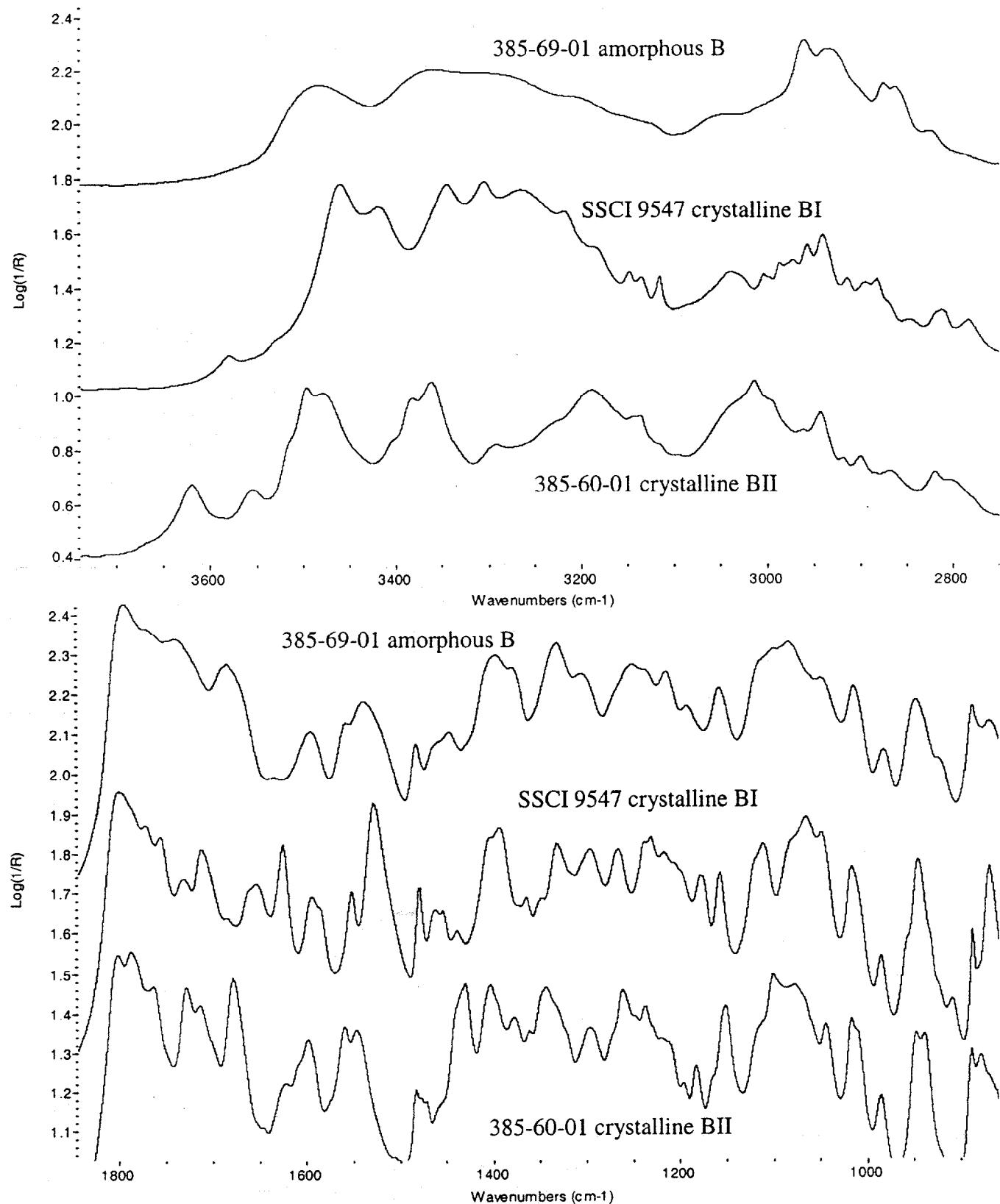
**Figure 3. Raman Spectra of Amorphous A, Crystalline AI and AII**



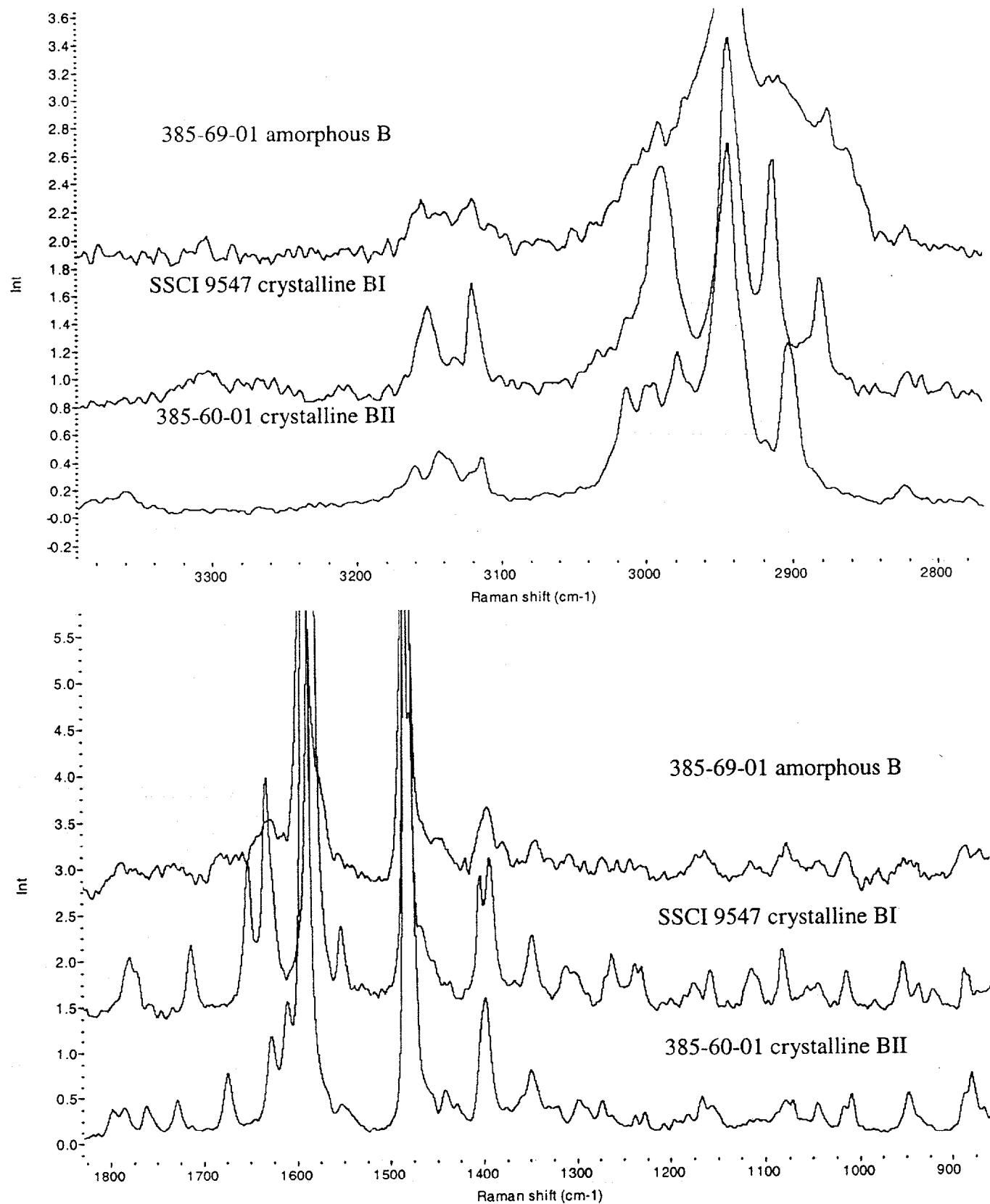
**Figure 4. XRPD Patterns of Amorphous B, Crystalline BI and BII**



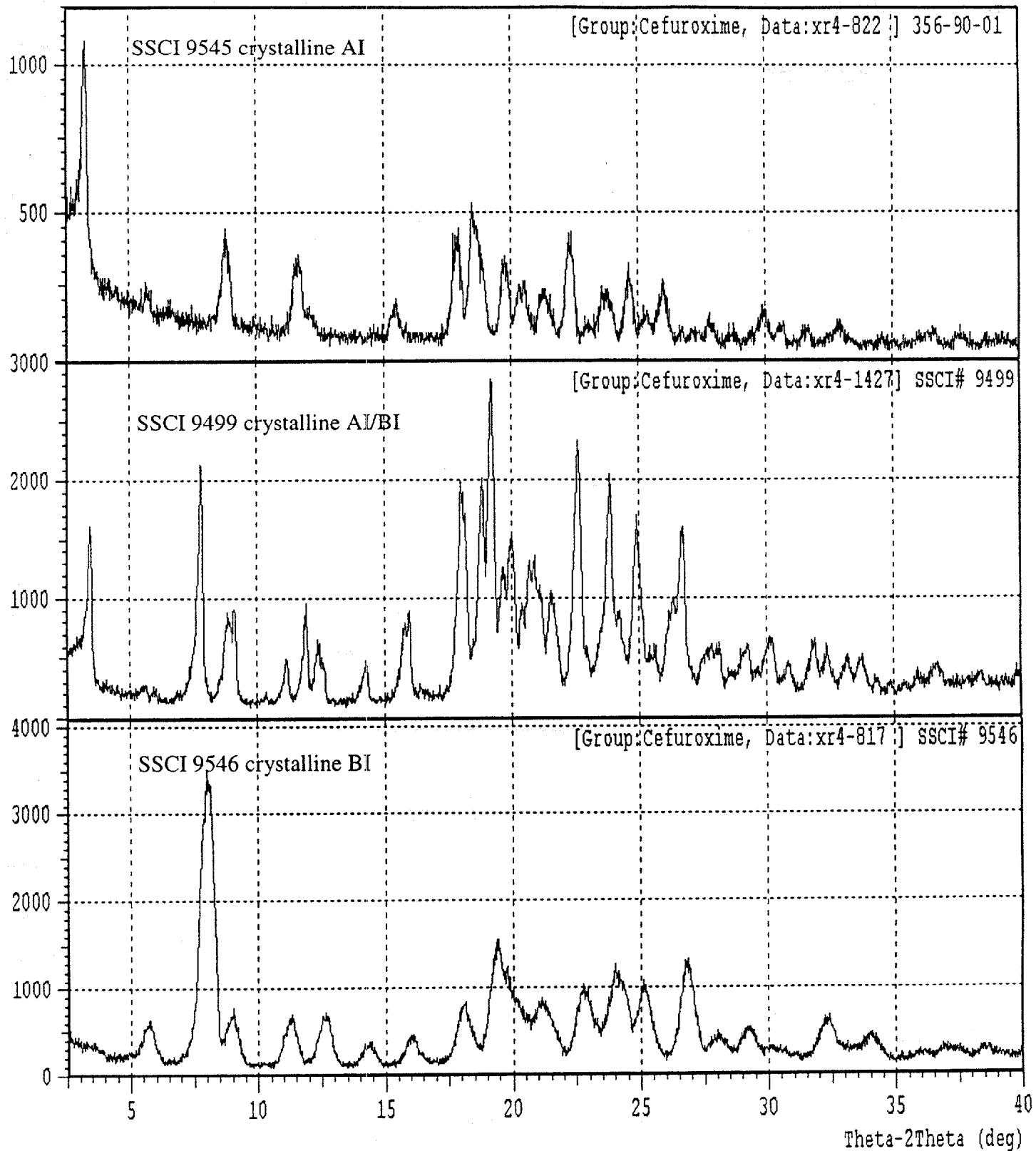
**Figure 5. IR Spectra of Amorphous B, Crystalline BI and BII**



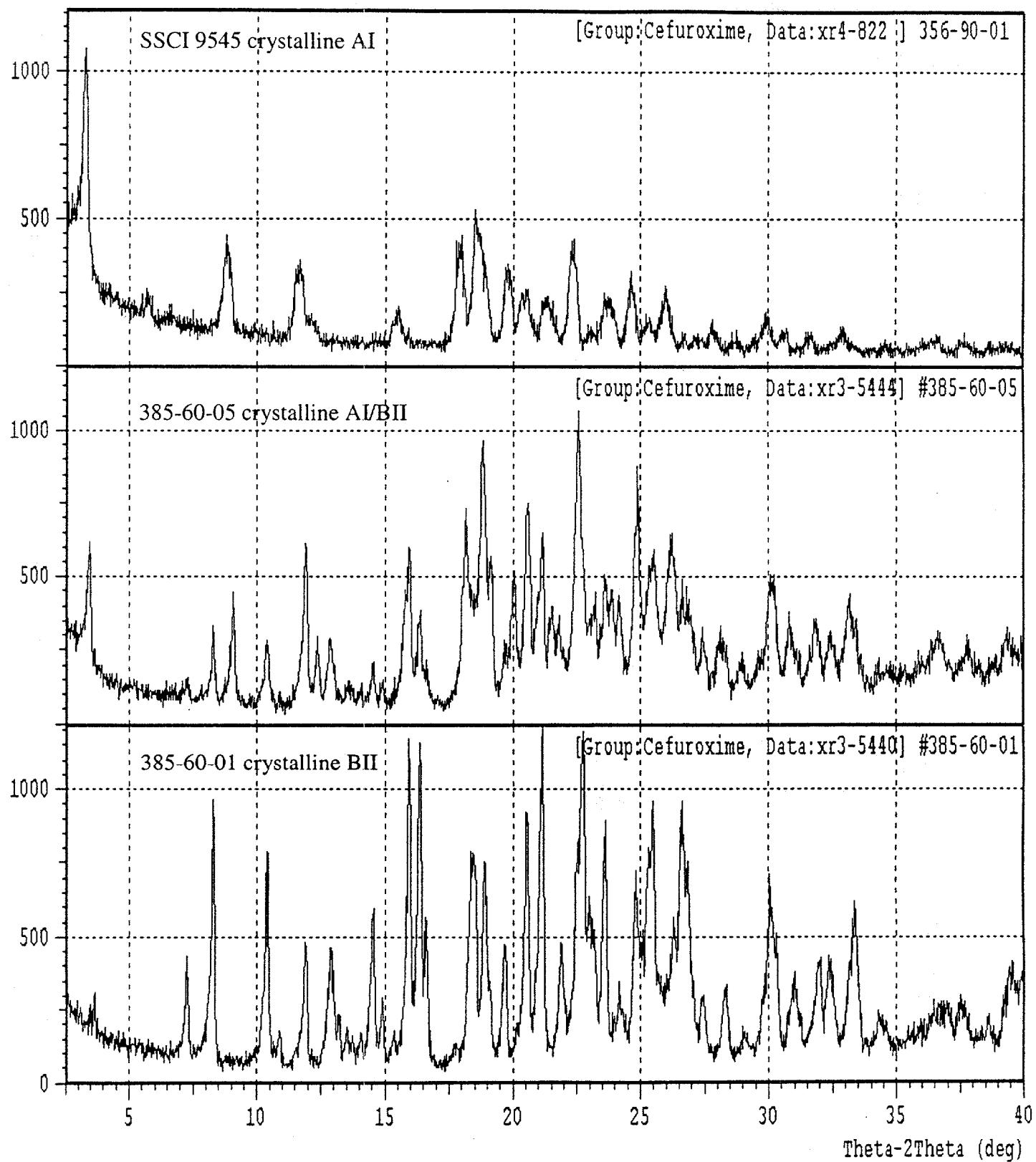
**Figure 6. Raman Spectra of Amorphous B, Crystalline BI and BII**



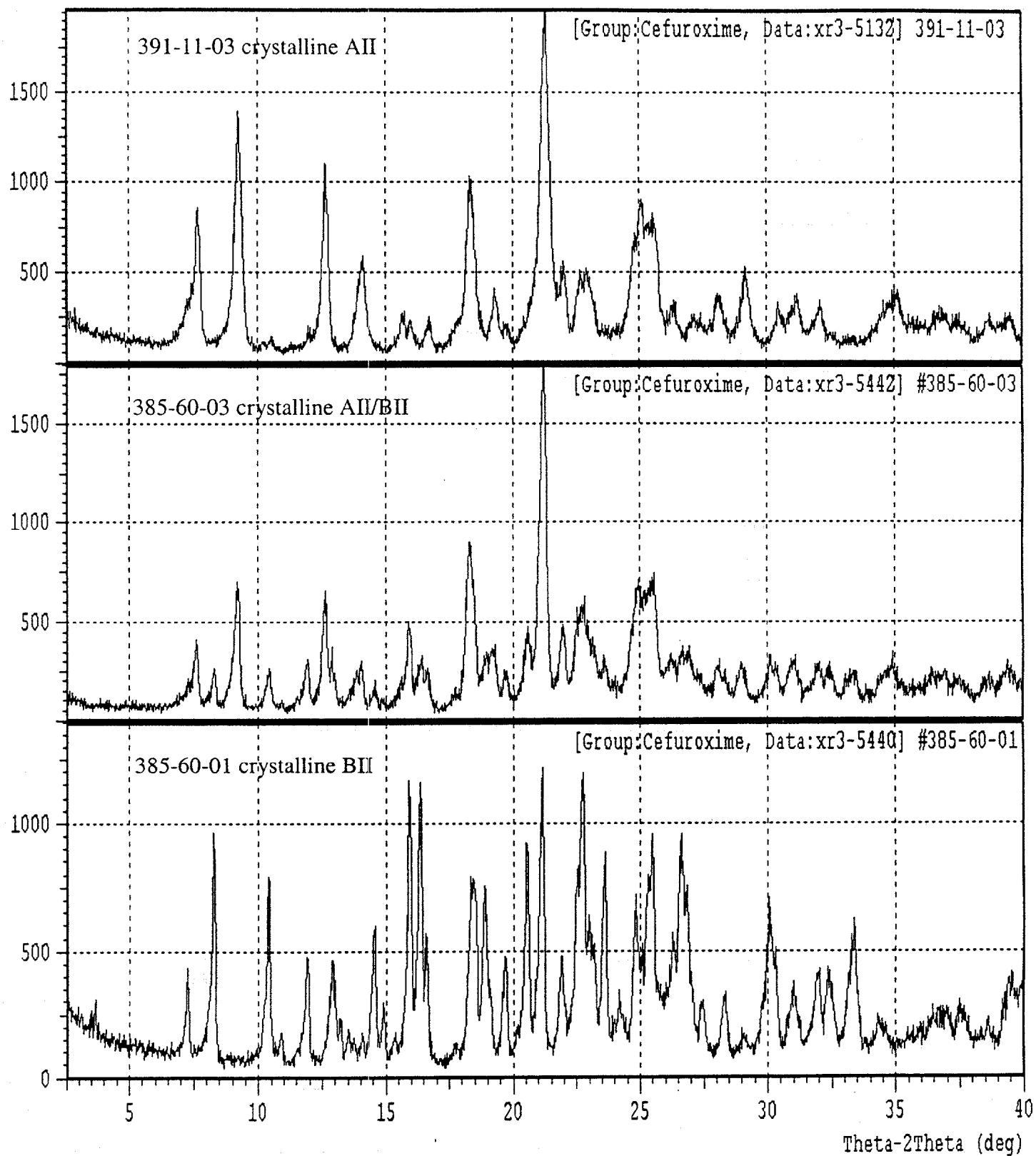
**Figure 7. XRPD Patterns of AI, AI/BI, and BI**



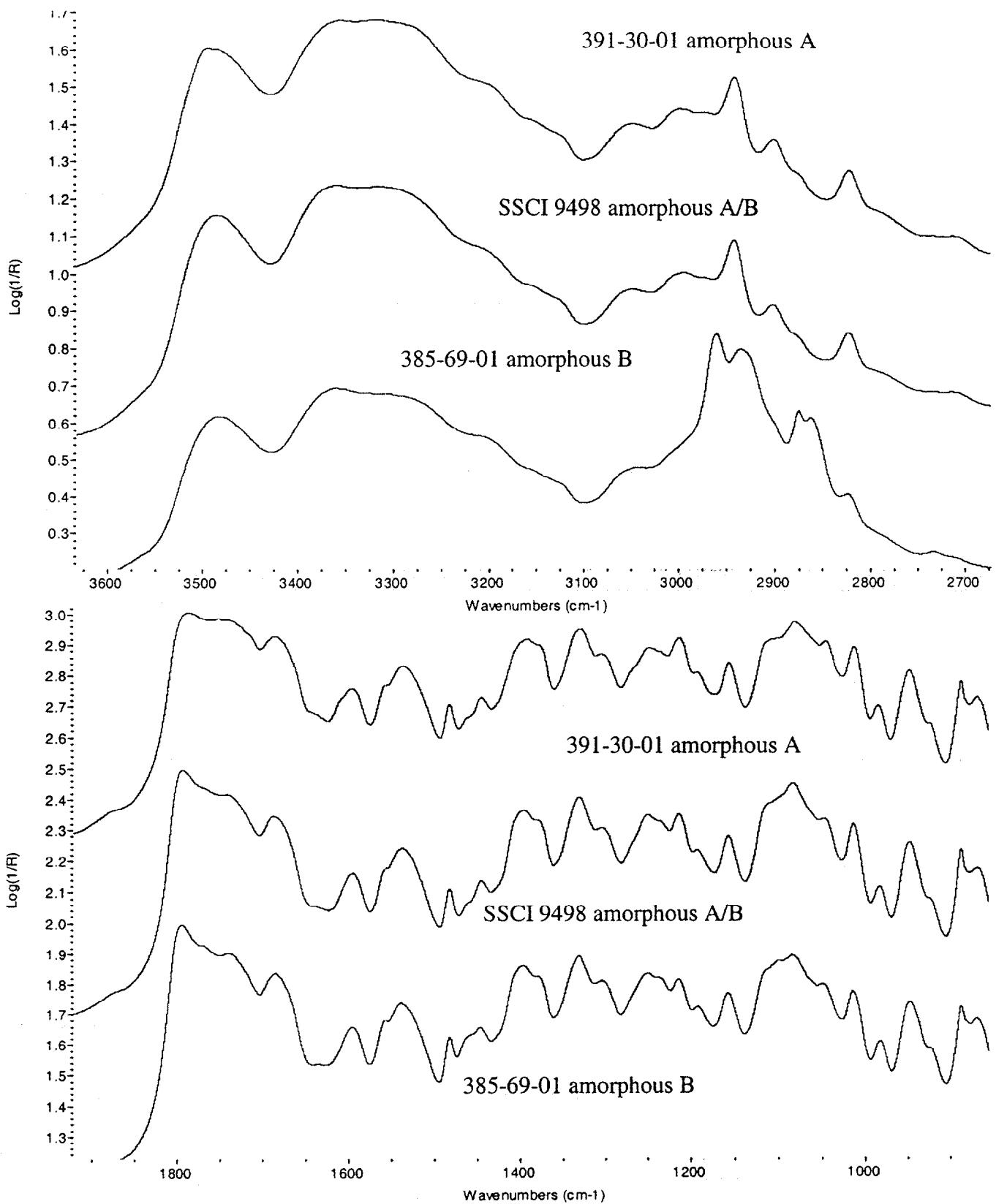
**Figure 8. XRPD Patterns of AI, AI/BII, and BII**



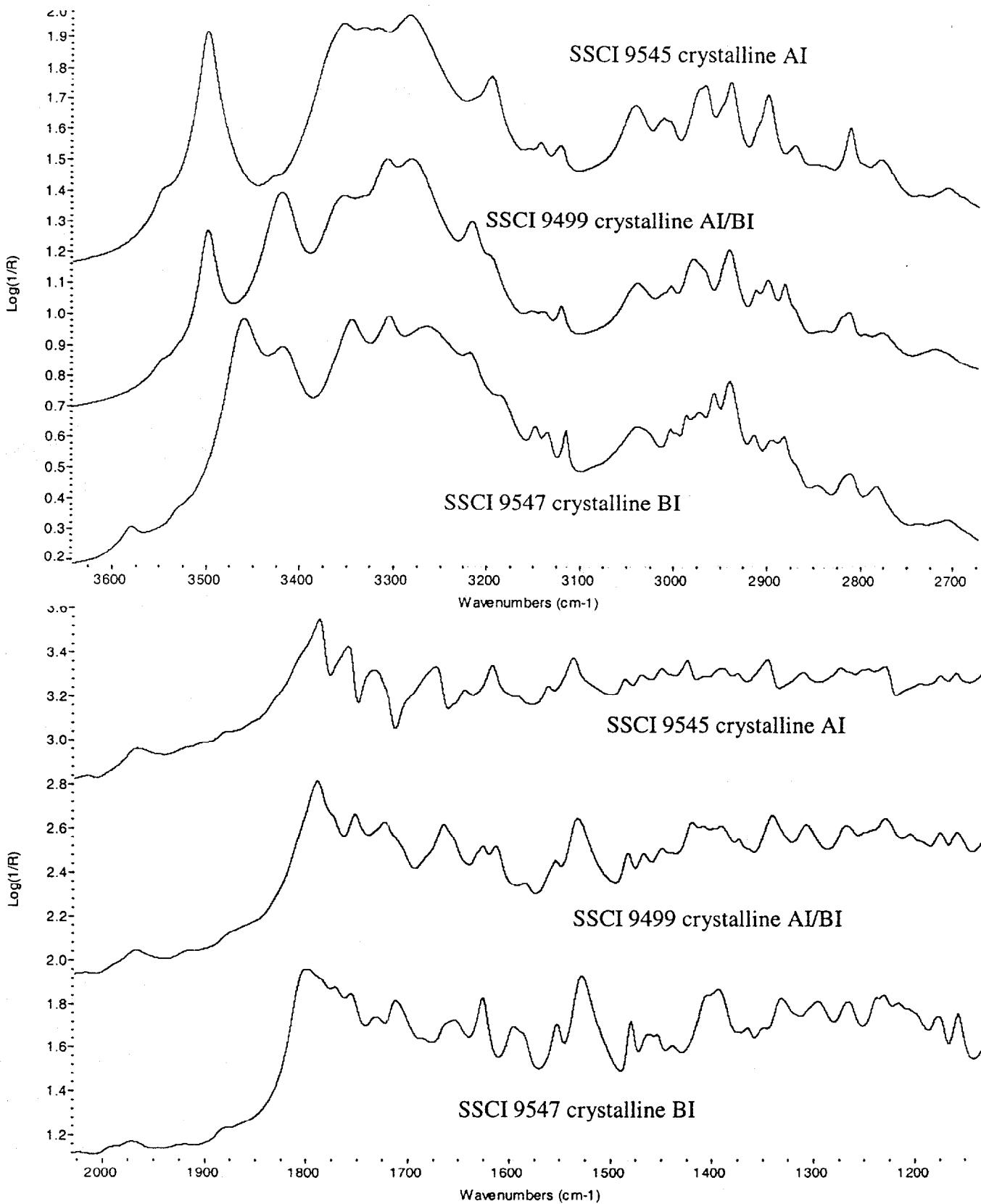
**Figure 9. XRPD Patterns of AII, AII/BII, and BII**



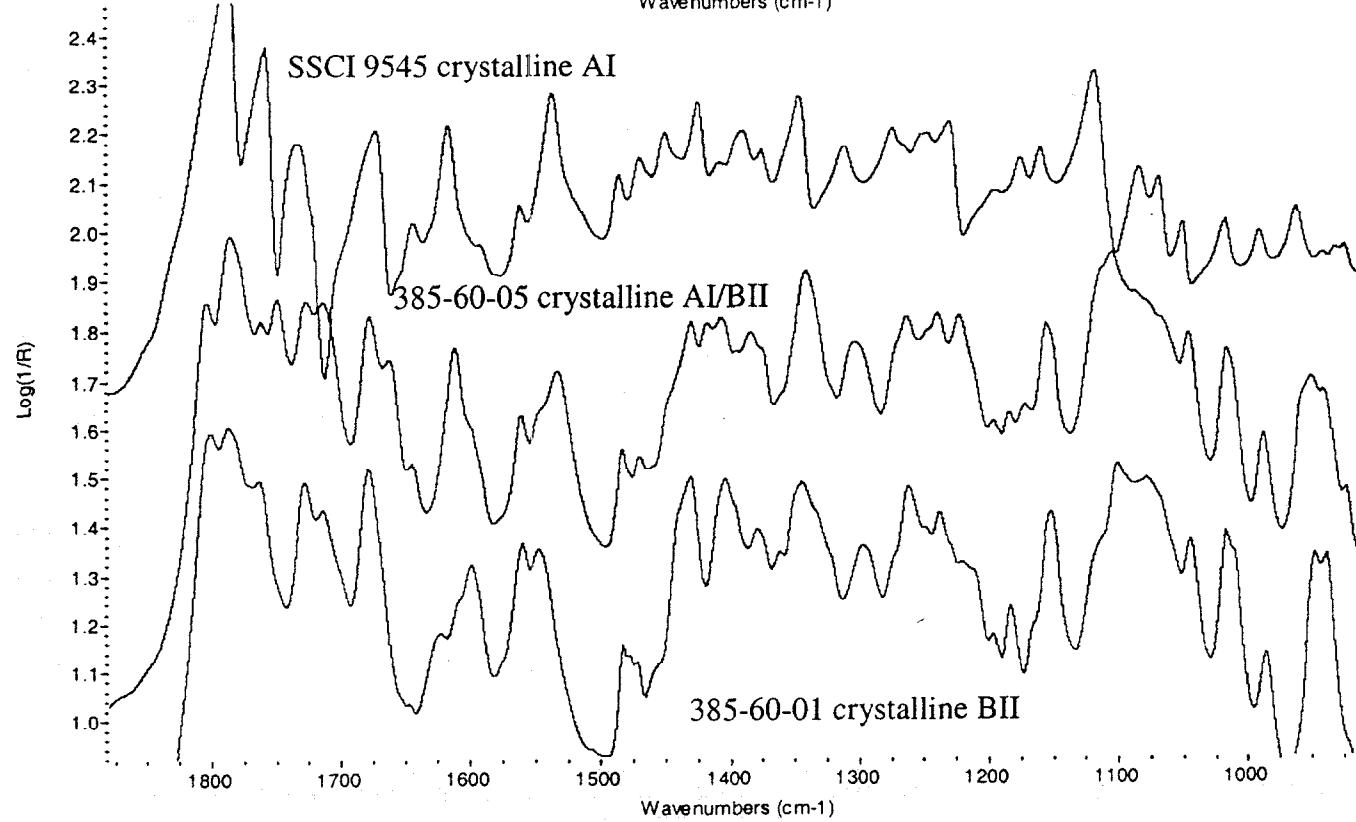
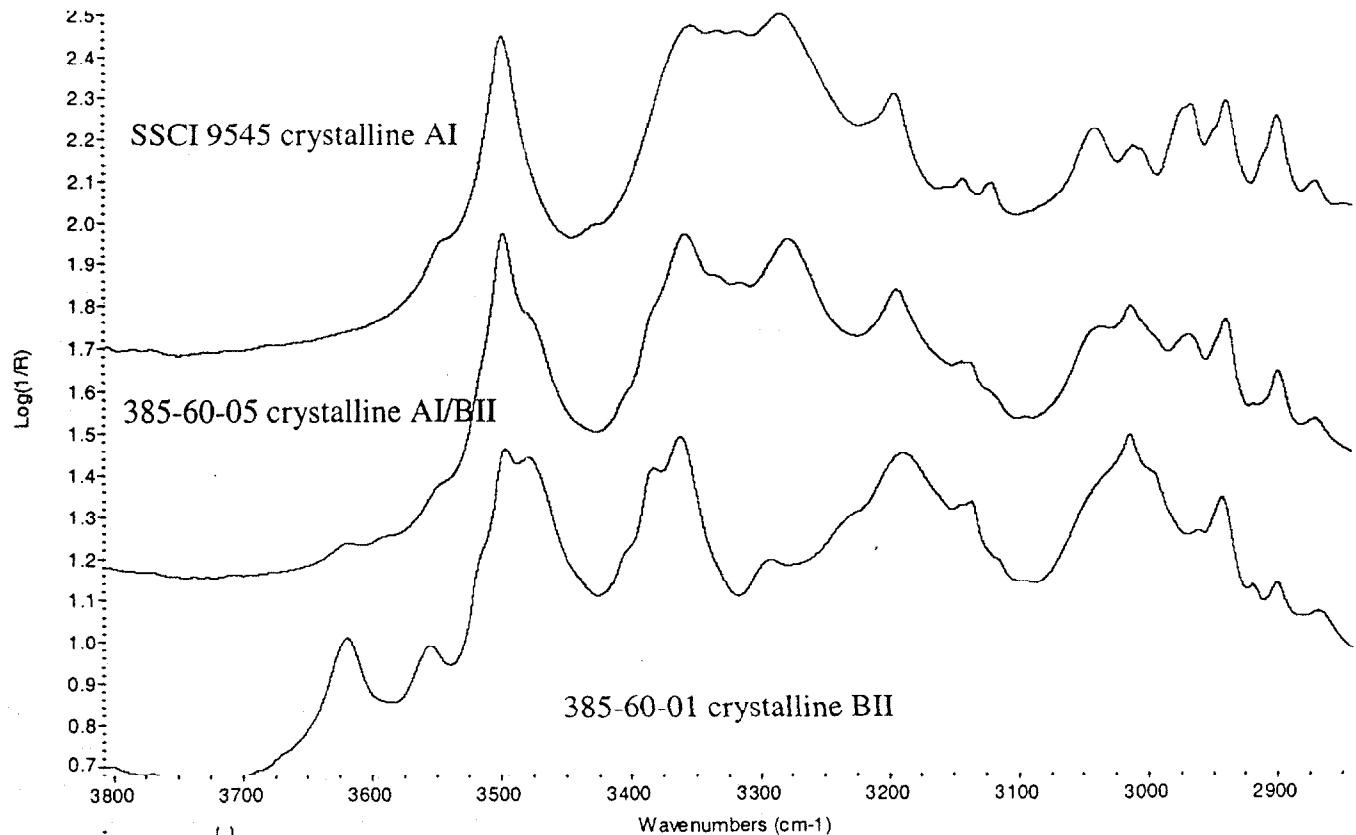
**Figure 10. IR Spectra of Amorphous A, A/B and B**



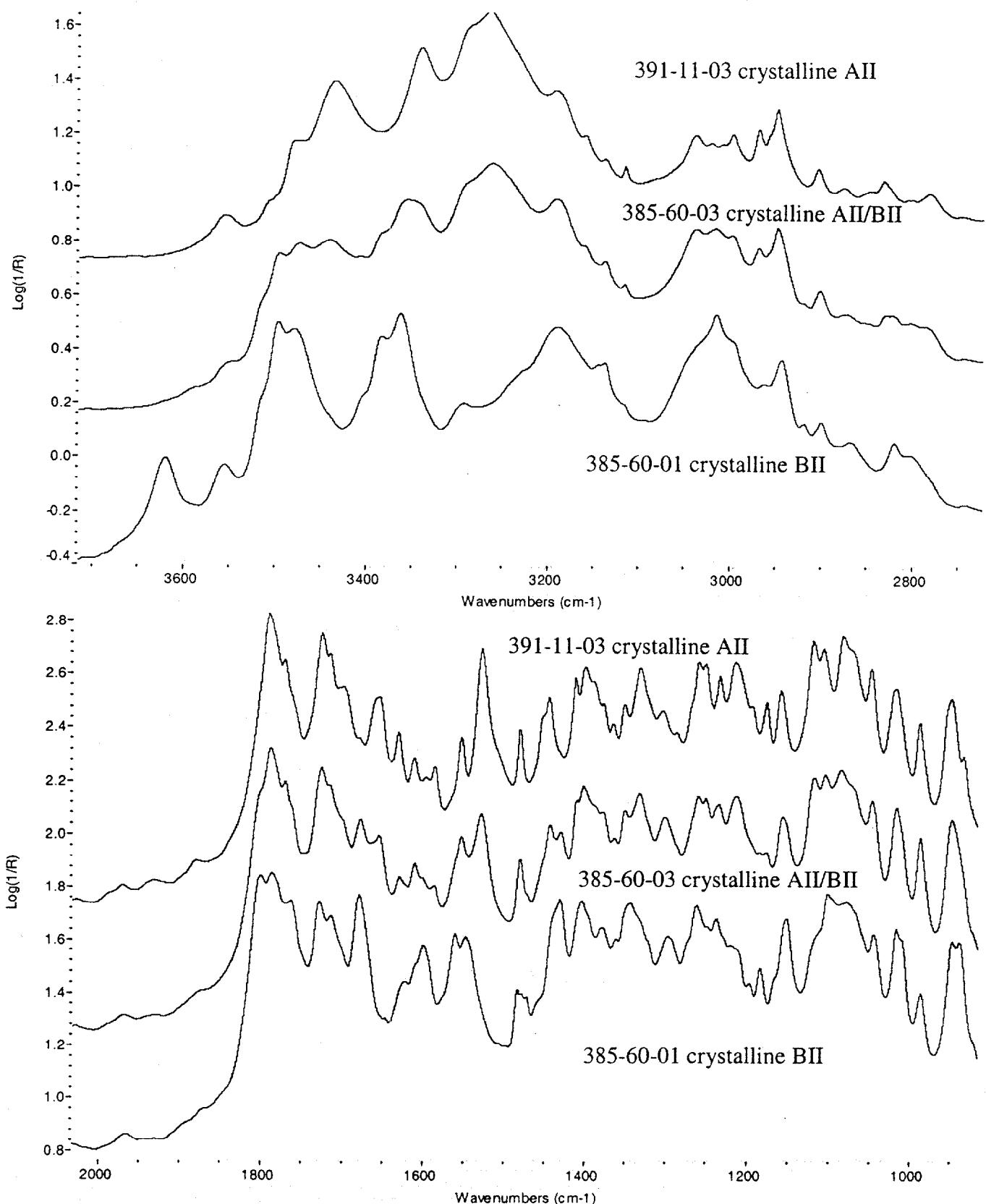
**Figure 11. IR Spectra of Crystalline AI, AI/BI and BI**



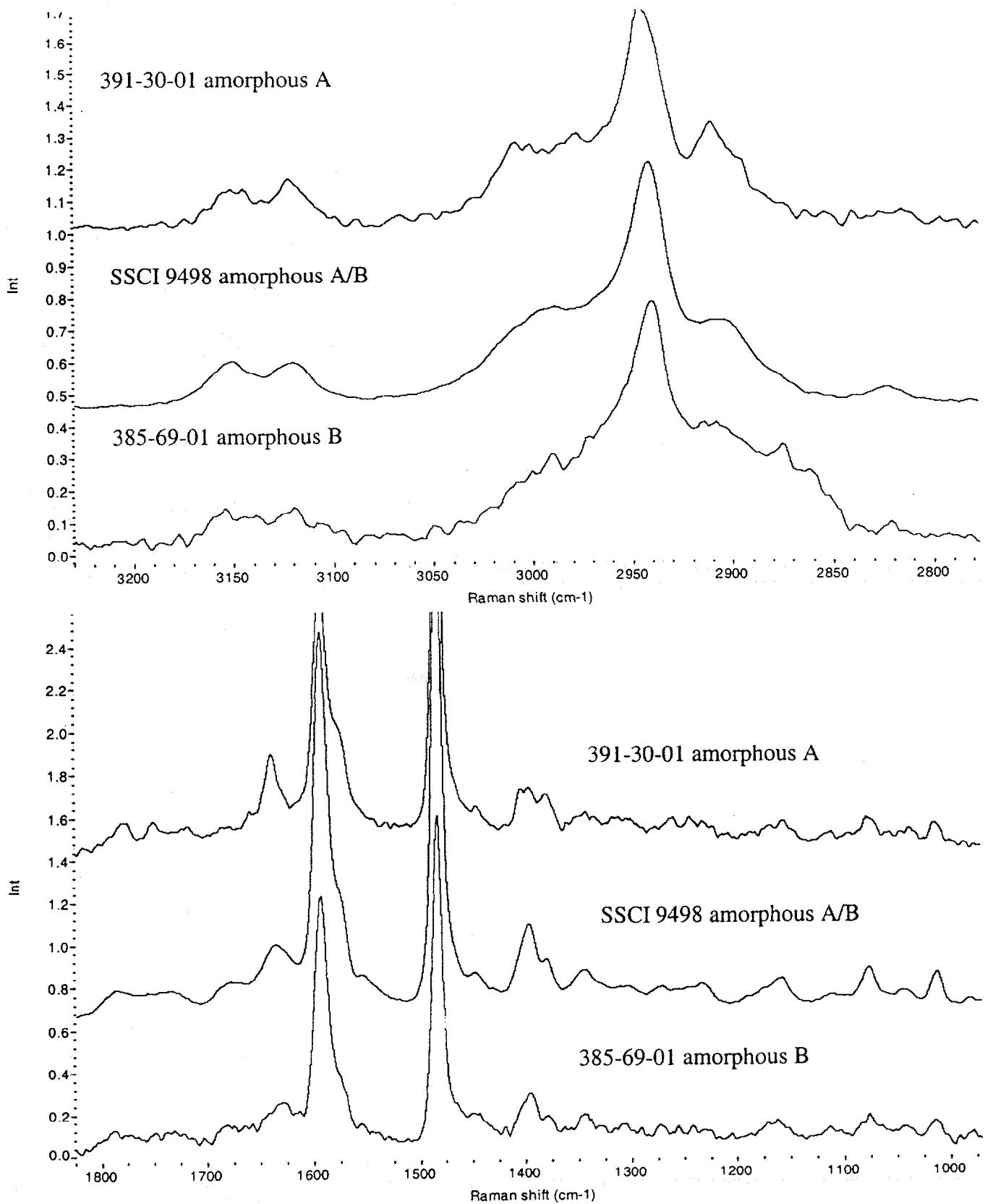
**Figure 12. IR Spectra of Crystalline AI, AI/BII and BII**



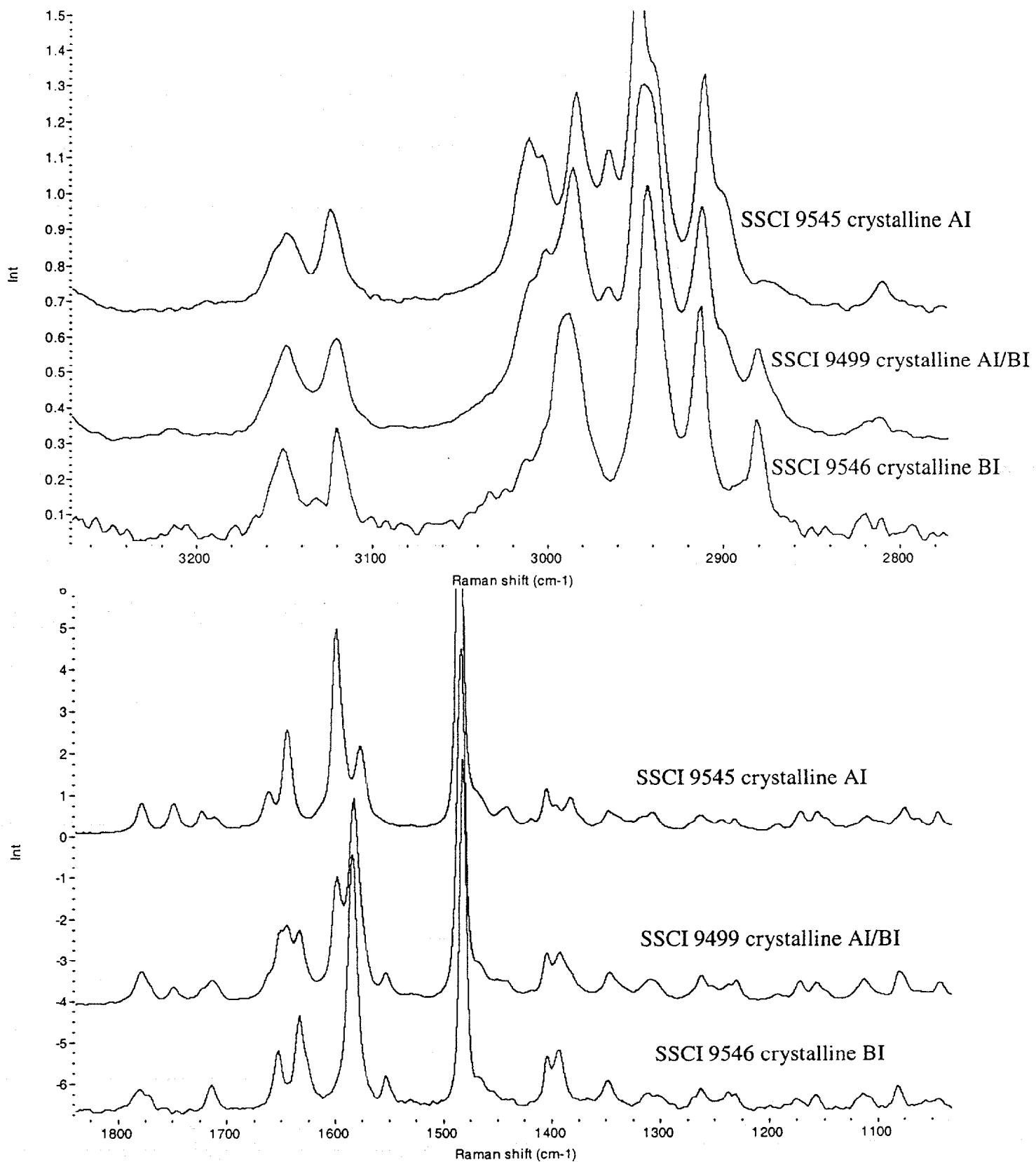
**Figure 13. IR Spectra of Crystalline AII, AII/BII and BII**



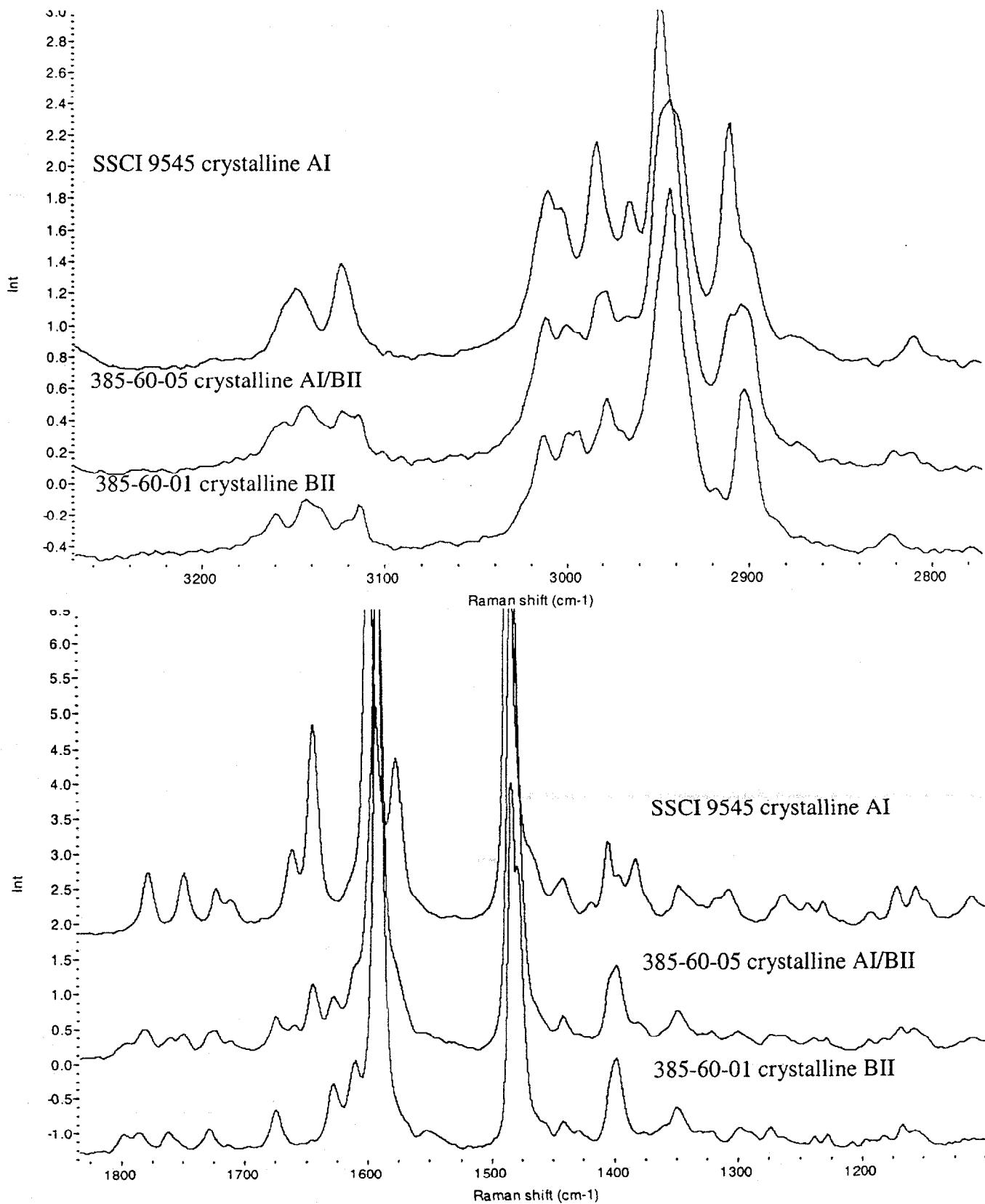
**Figure 14. Raman Spectra of Amorphous A, A/B and B**



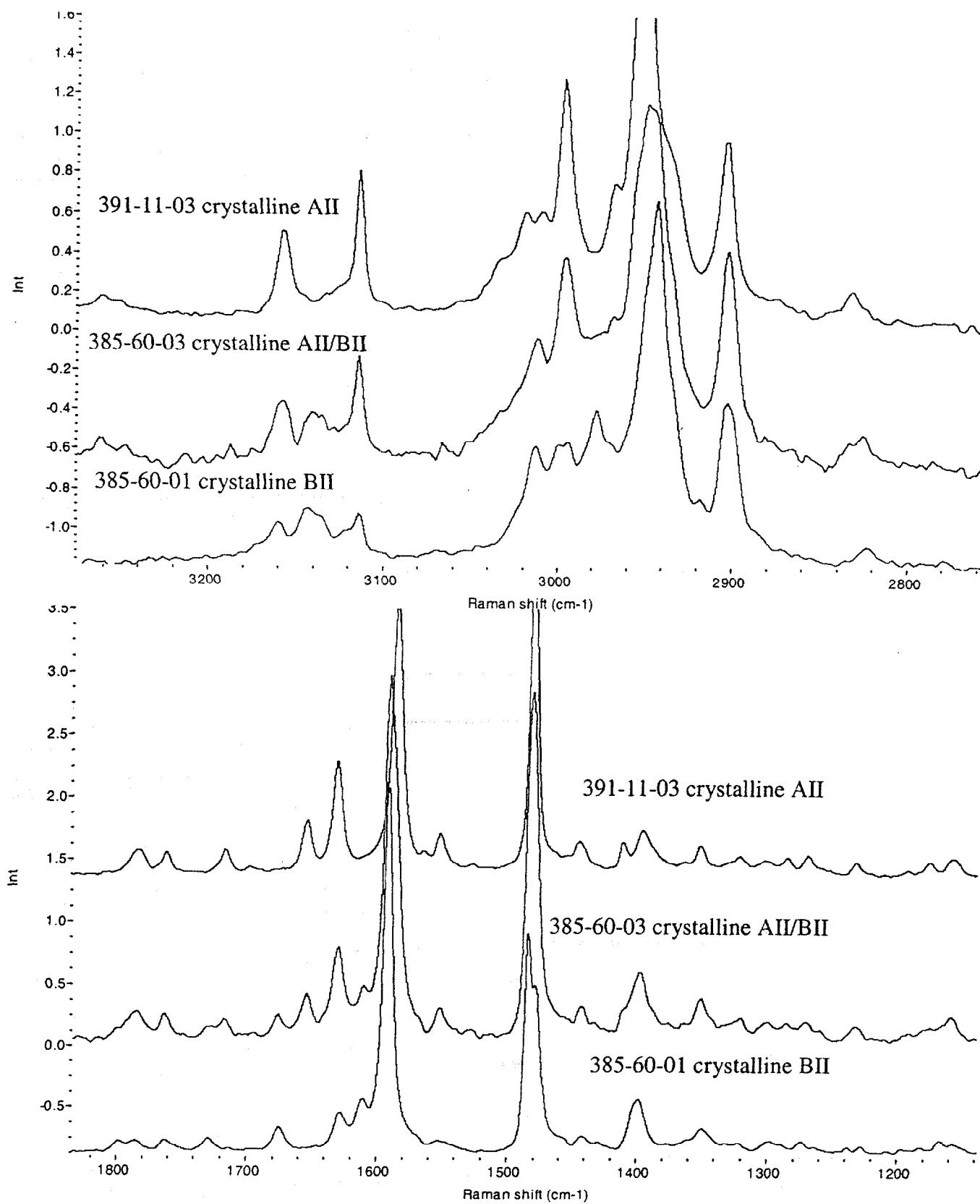
**Figure 15. Raman Spectra of Crystalline AI, AI/BI and BI**



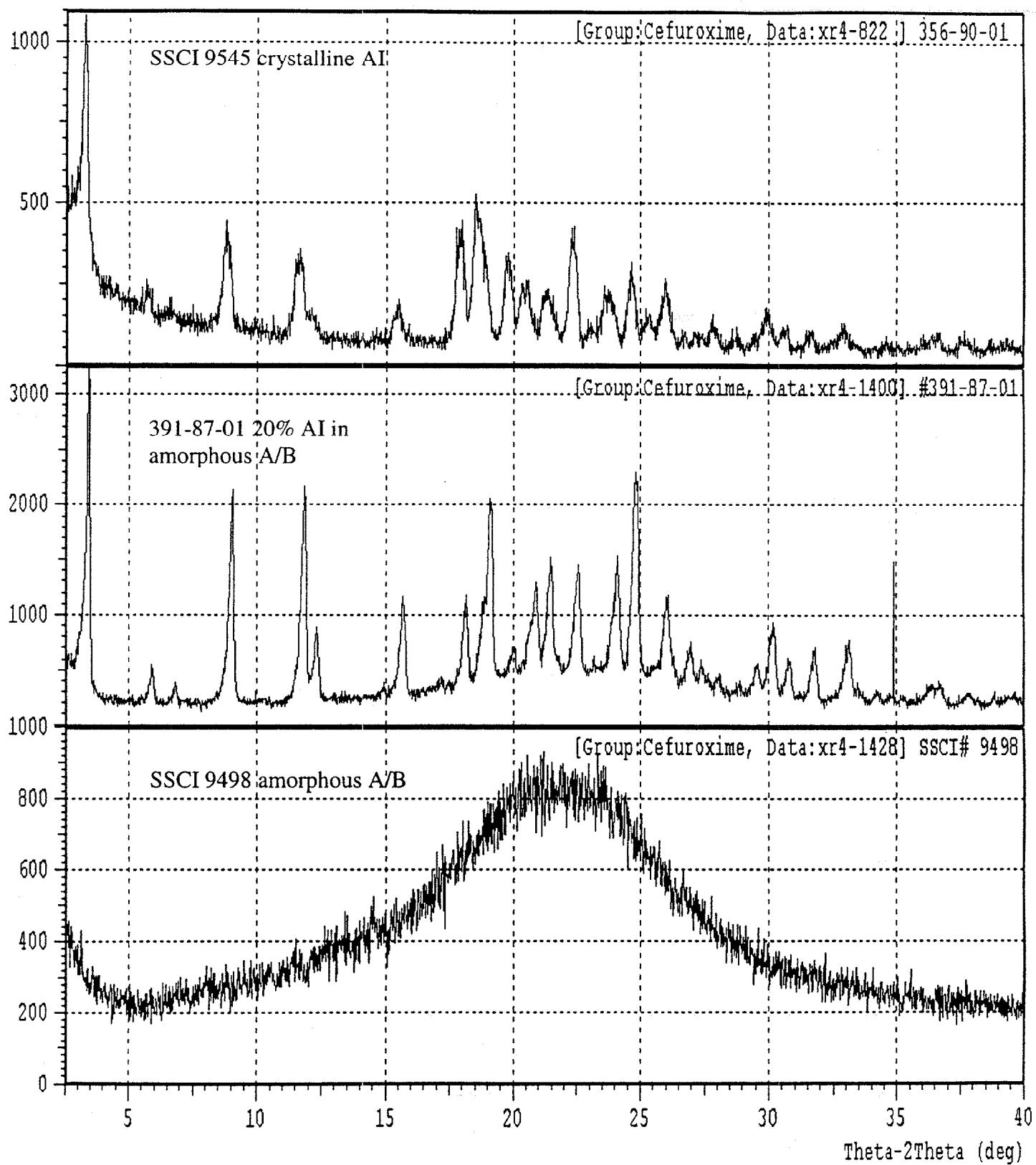
**Figure 16. Raman Spectra of Crystalline AI, AI/BII and BII**



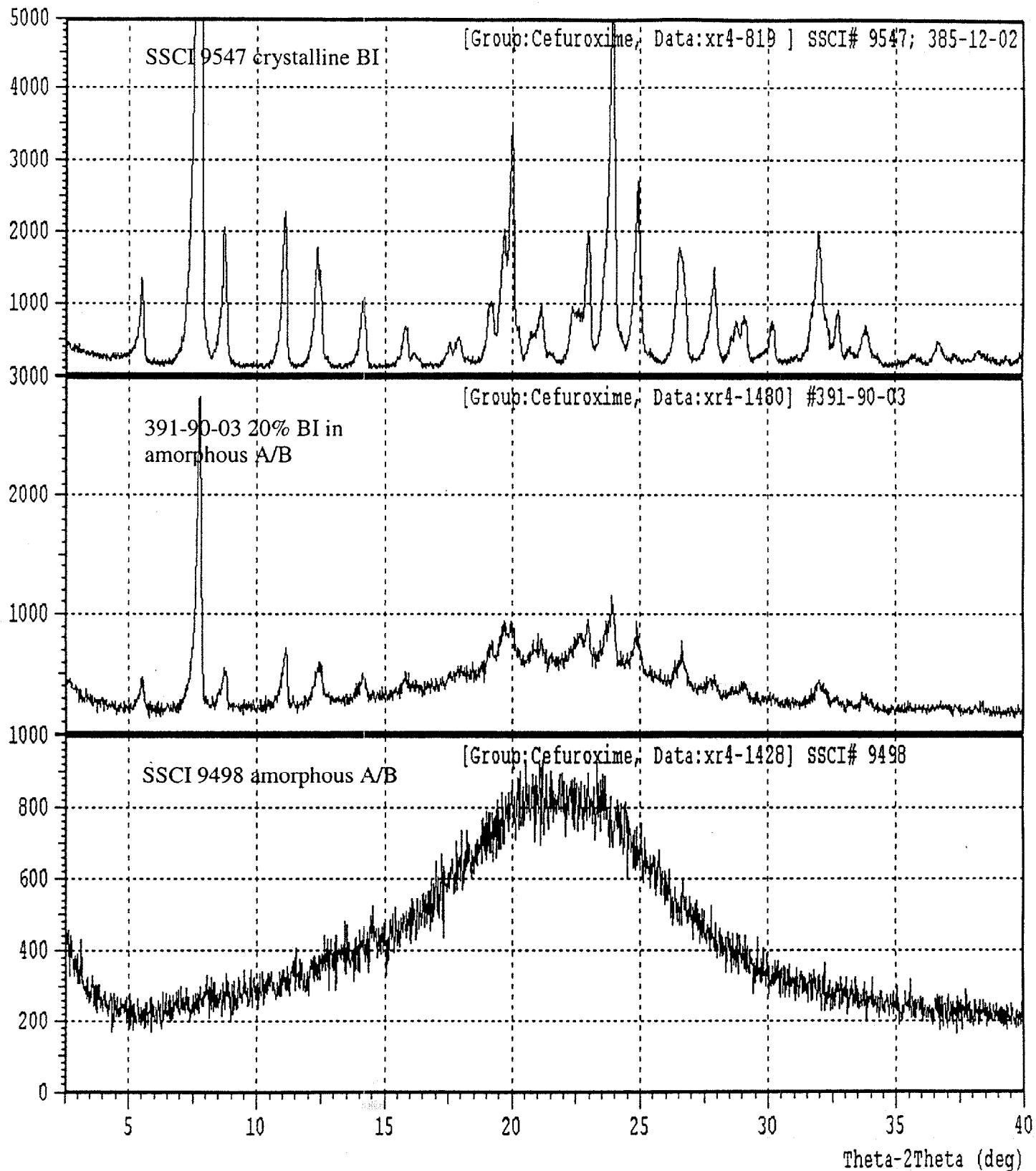
**Figure 17. Raman Spectra of Crystalline AII, AII/BII and BII**



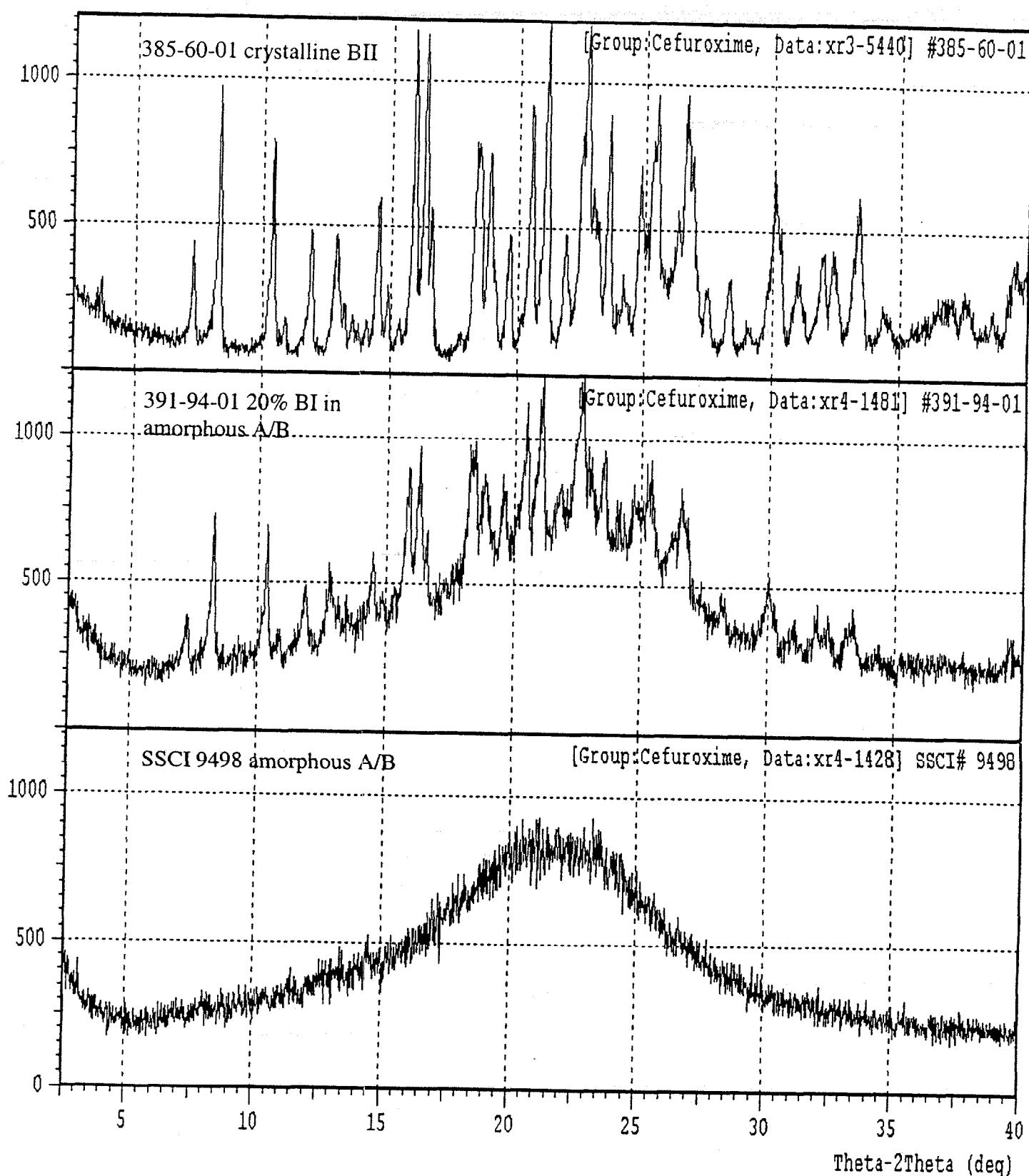
**Figure 18. XRPD Patterns of AI, and 20% AI in Amorphous A/B**



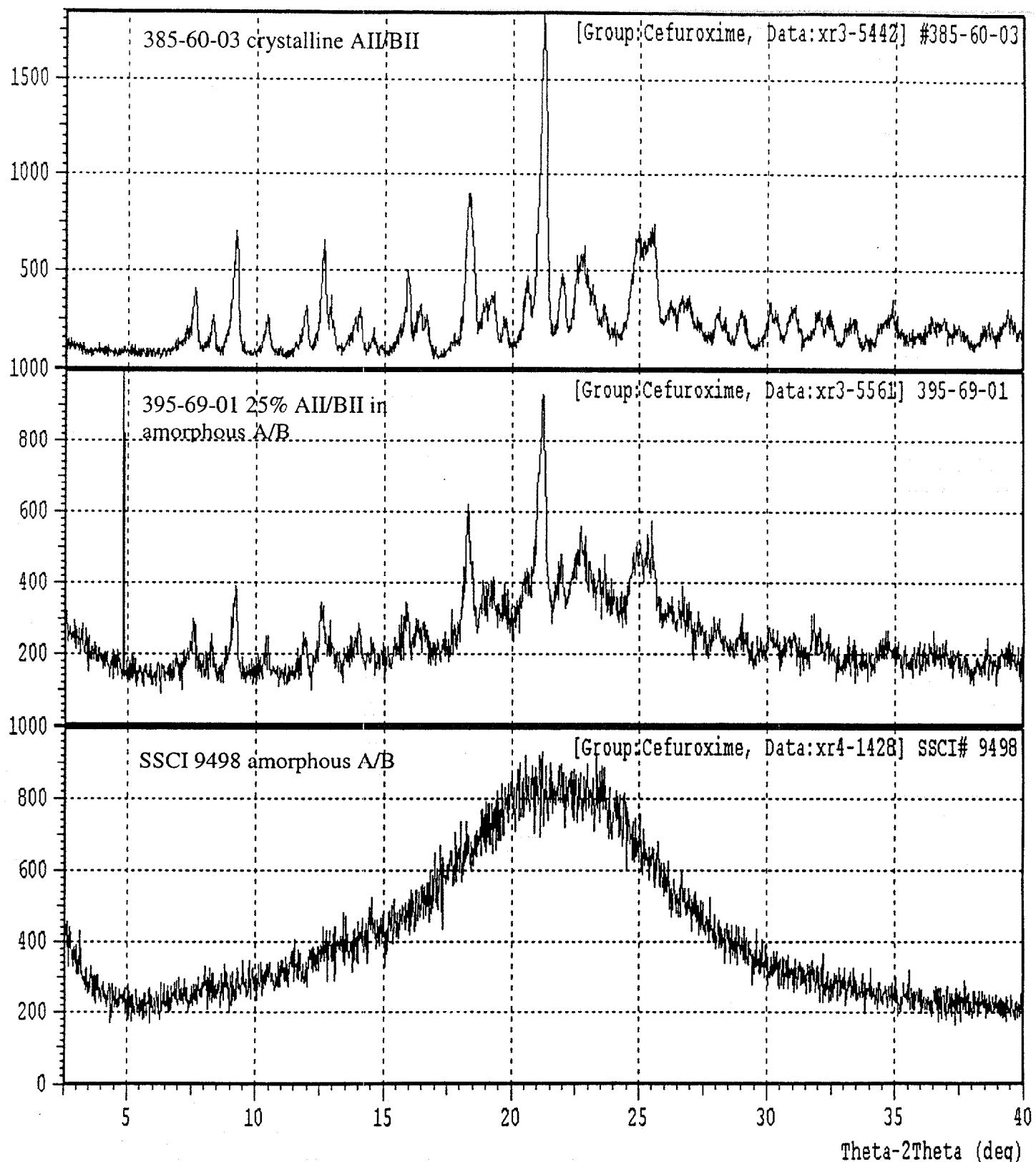
**Figure 19. XRPD Patterns of BI, and 20% BI in Amorphous A/B**



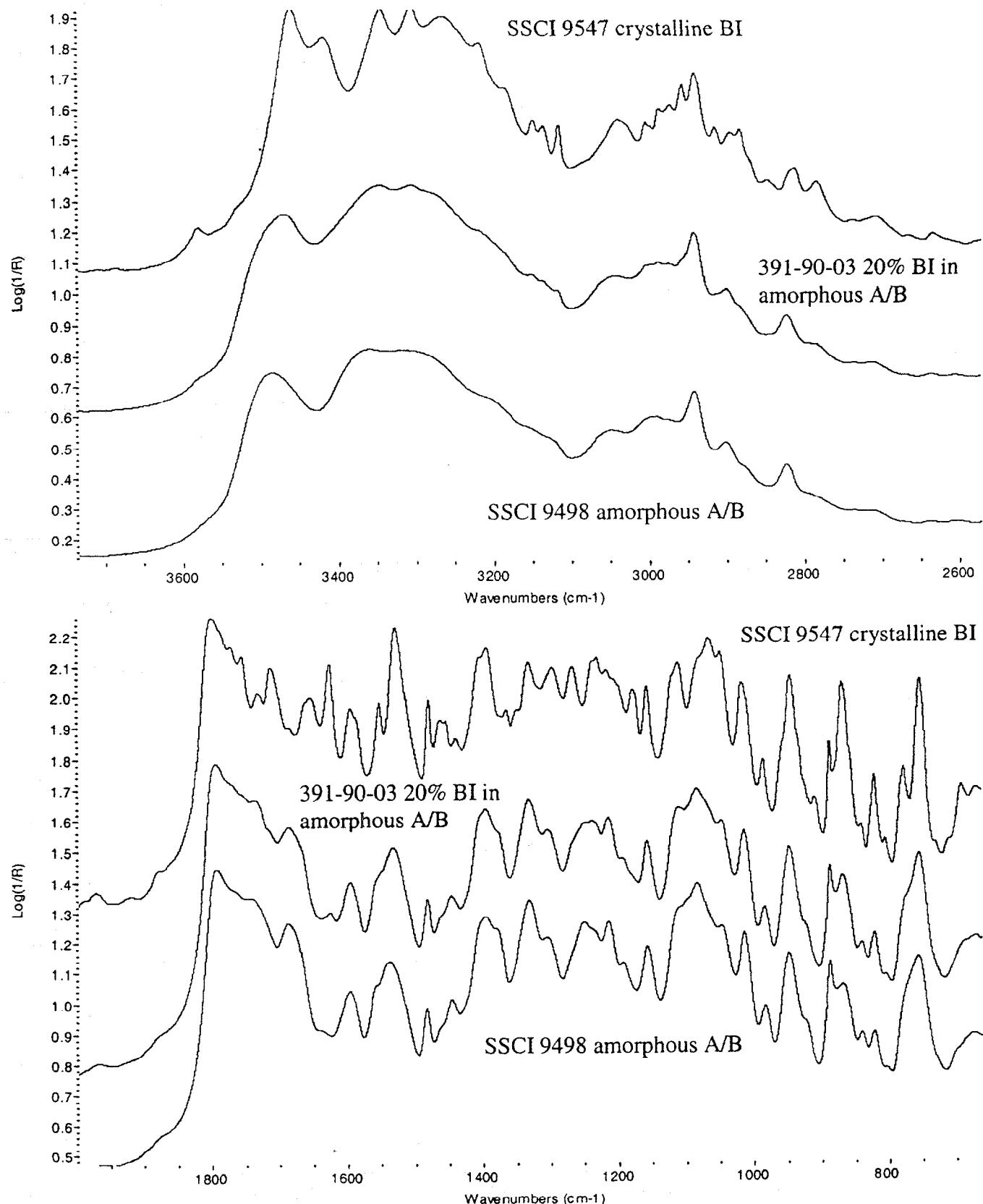
**Figure 20. XRPD Patterns of BII, and 20% BII in Amorphous A/B**



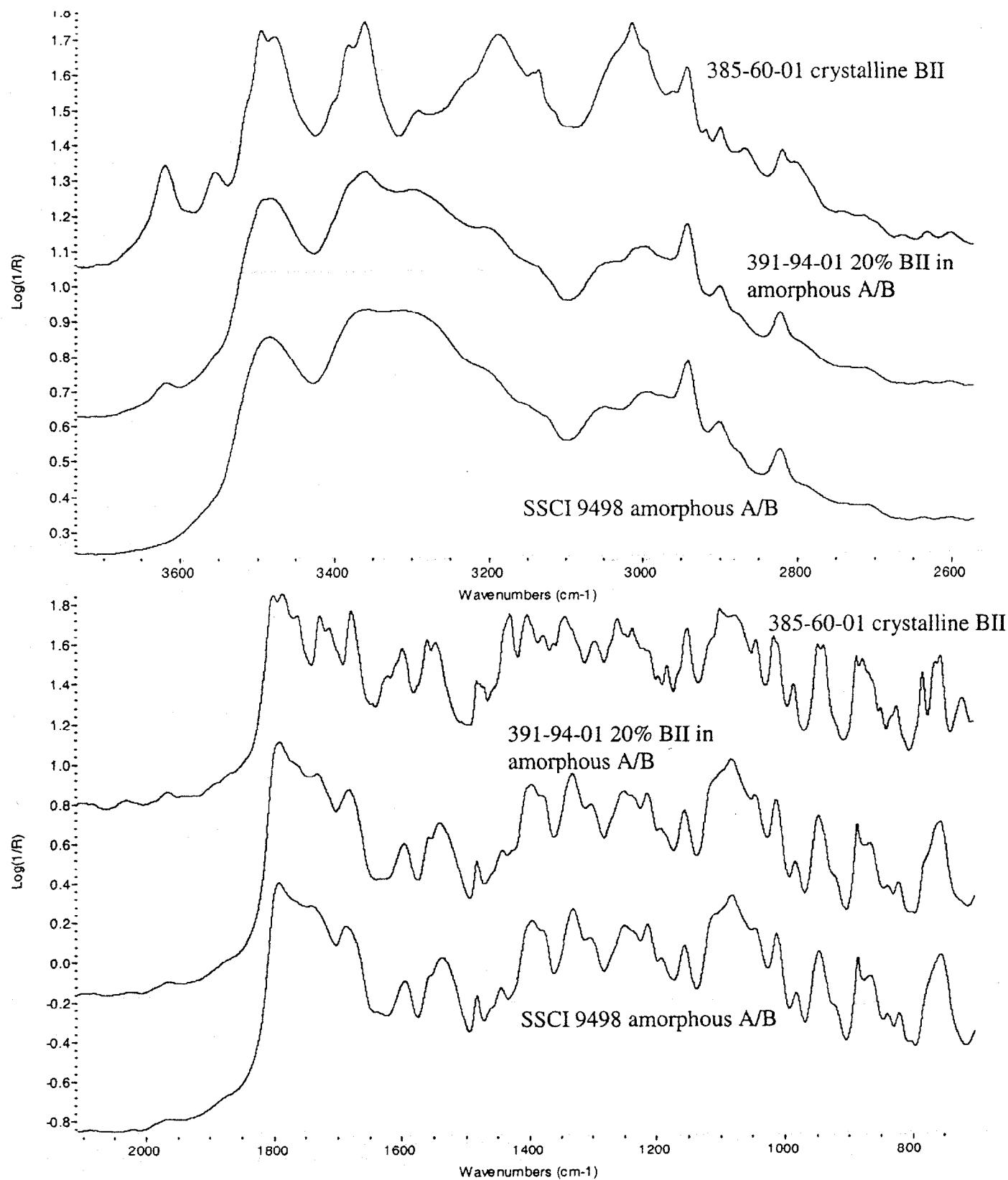
**Figure 21. XRPD Patterns of AII/BII, and 25% AII/BII in Amorphous A/B**



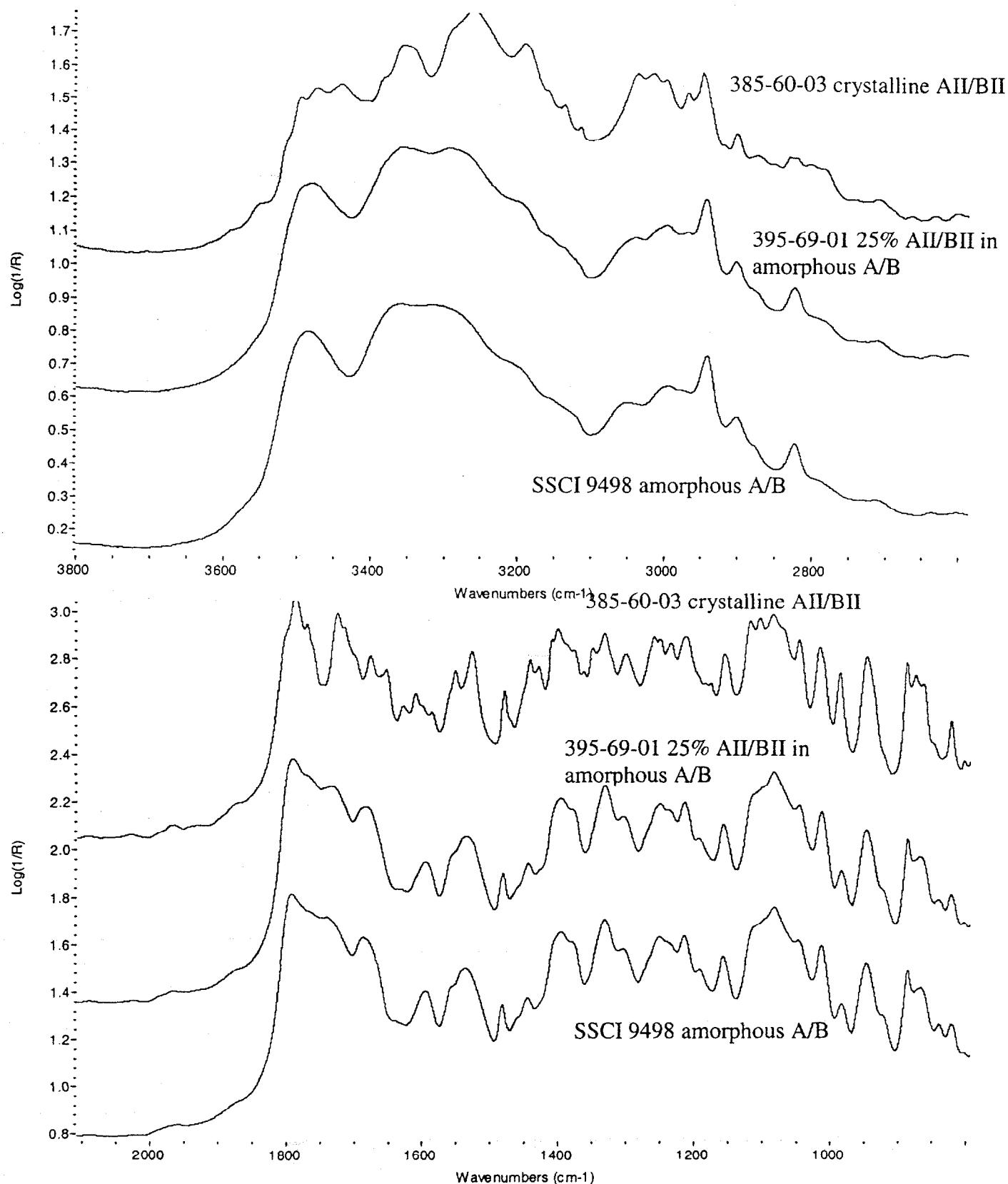
**Figure 23. IR Spectra of BI, 20% BI in Amorphous A/B, and Amorphous A/B**



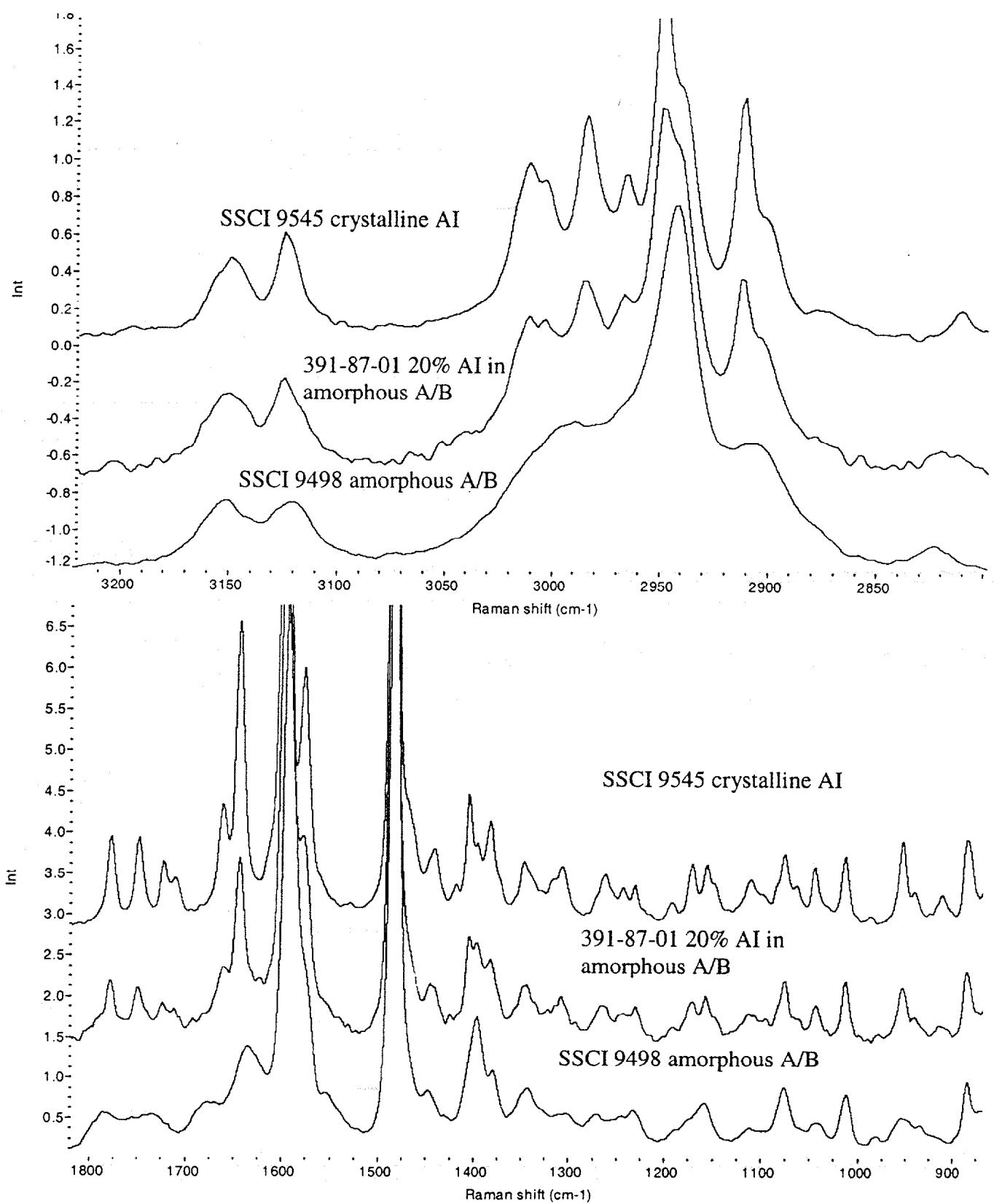
**Figure 24. IR Spectra of BII, 20% BII in Amorphous A/B, and Amorphous A/B**



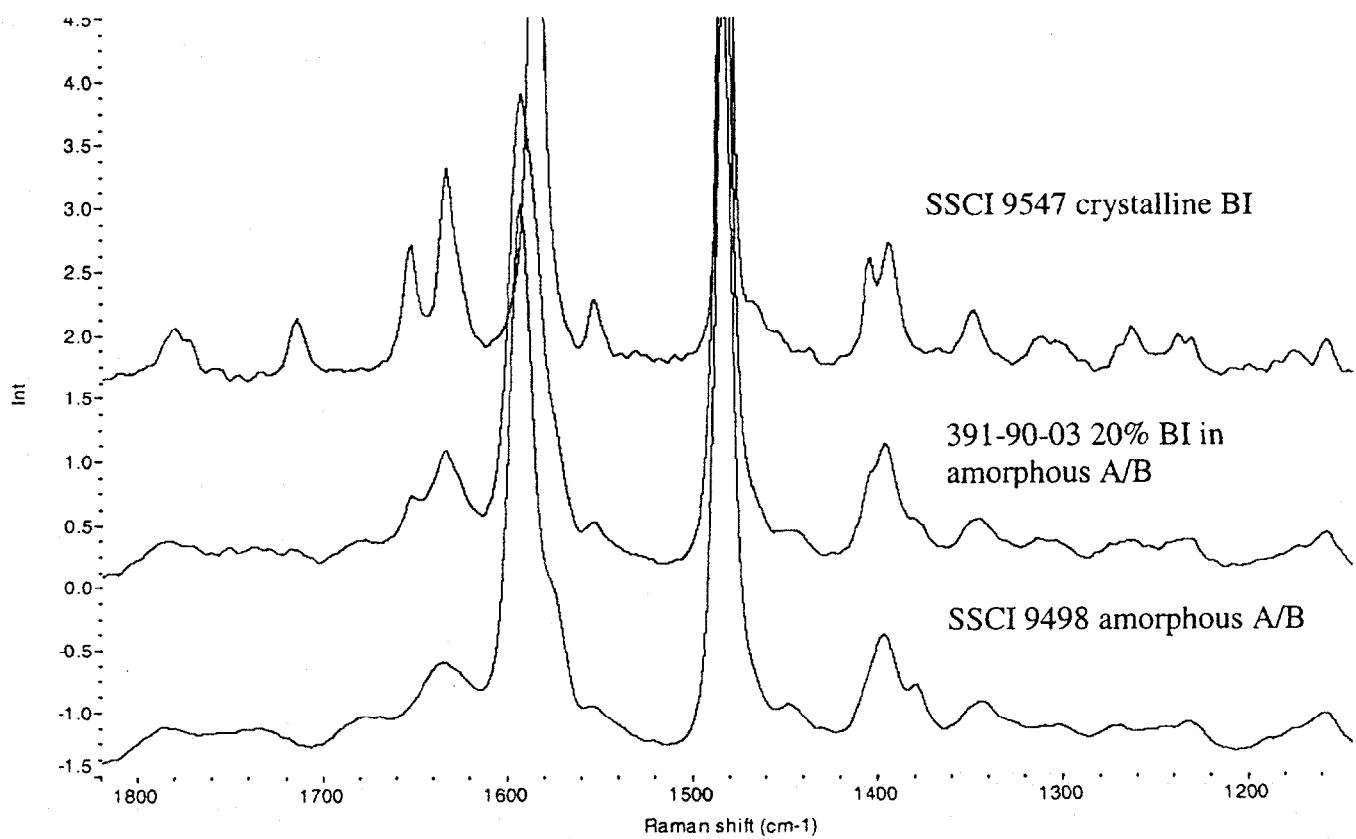
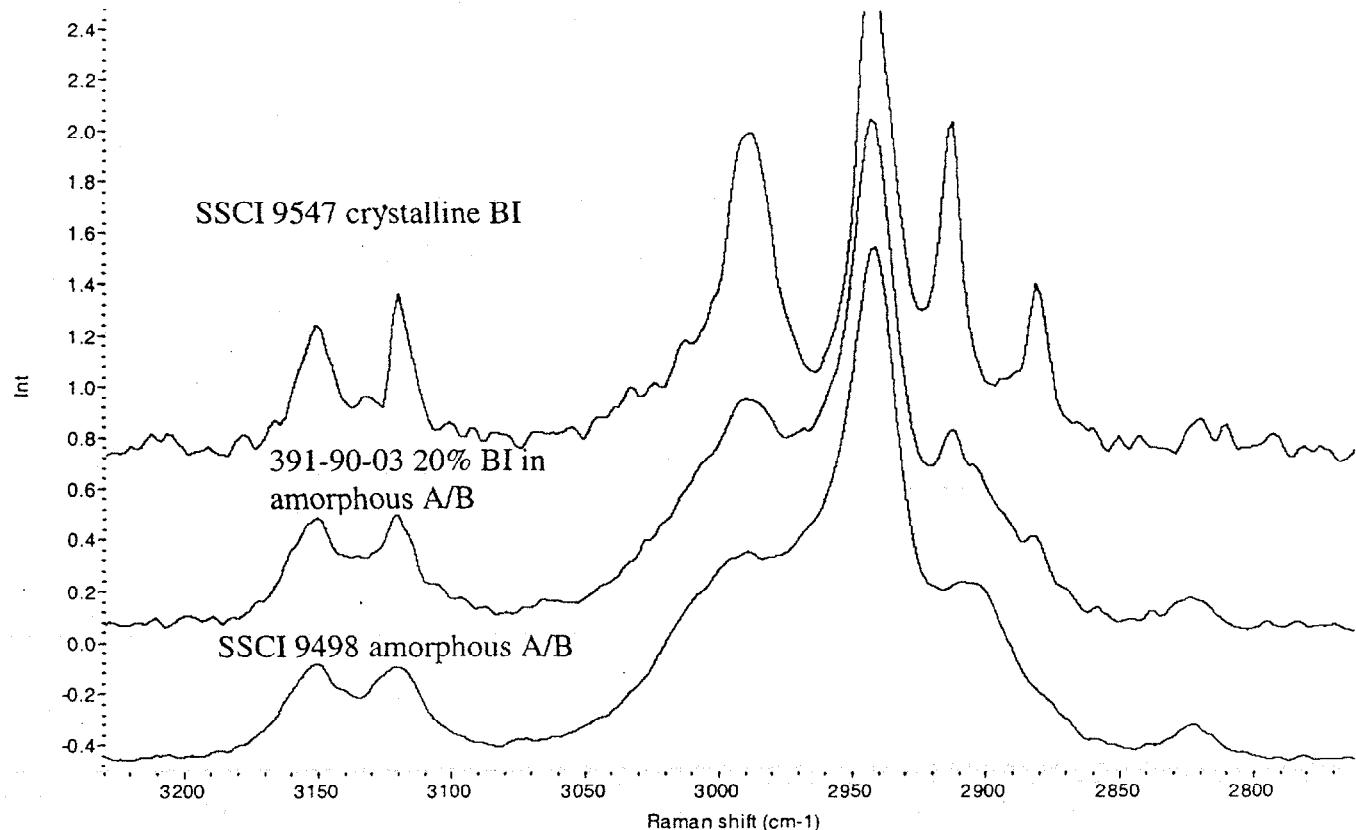
**Figure 25. IR Spectra of AII/BII, 25% AII/BII in Amorphous A/B, and Amorphous A/B**



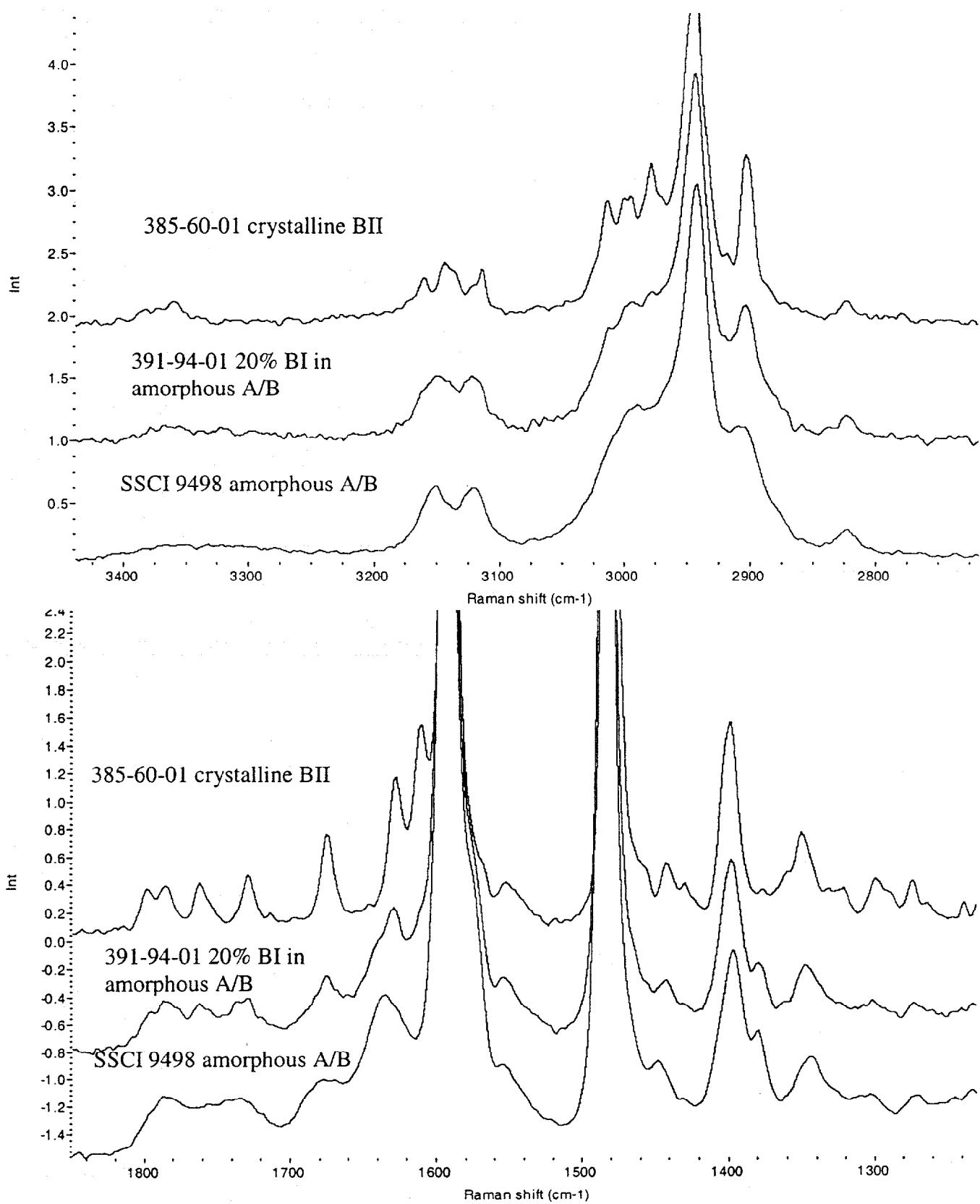
**Figure 26. Raman Spectra of AI, 20% AI in Amorphous A/B, Amorphous A/B**



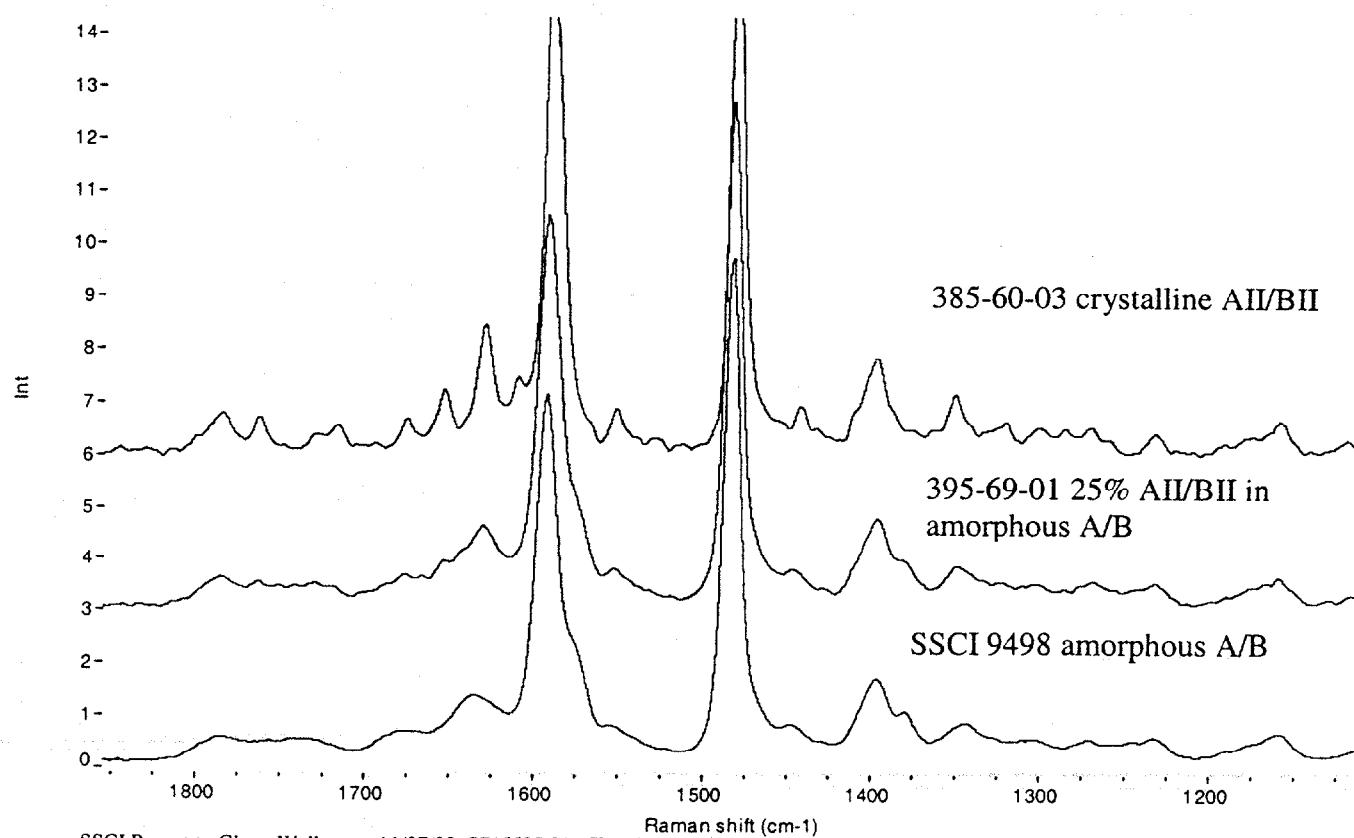
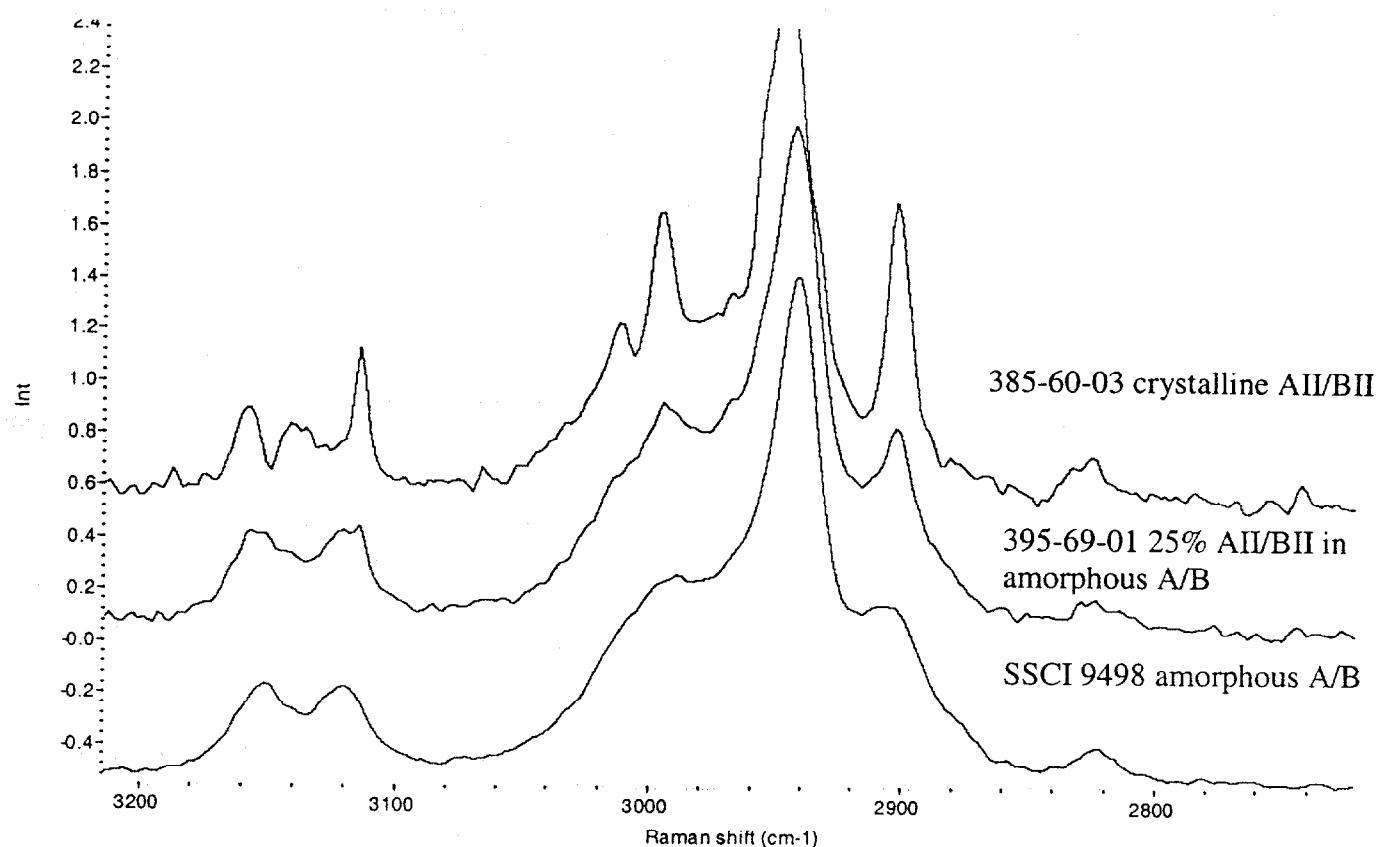
**Figure 27. Raman Spectra of BI, 20% BI in Amorphous A/B, and Amorphous A/B**



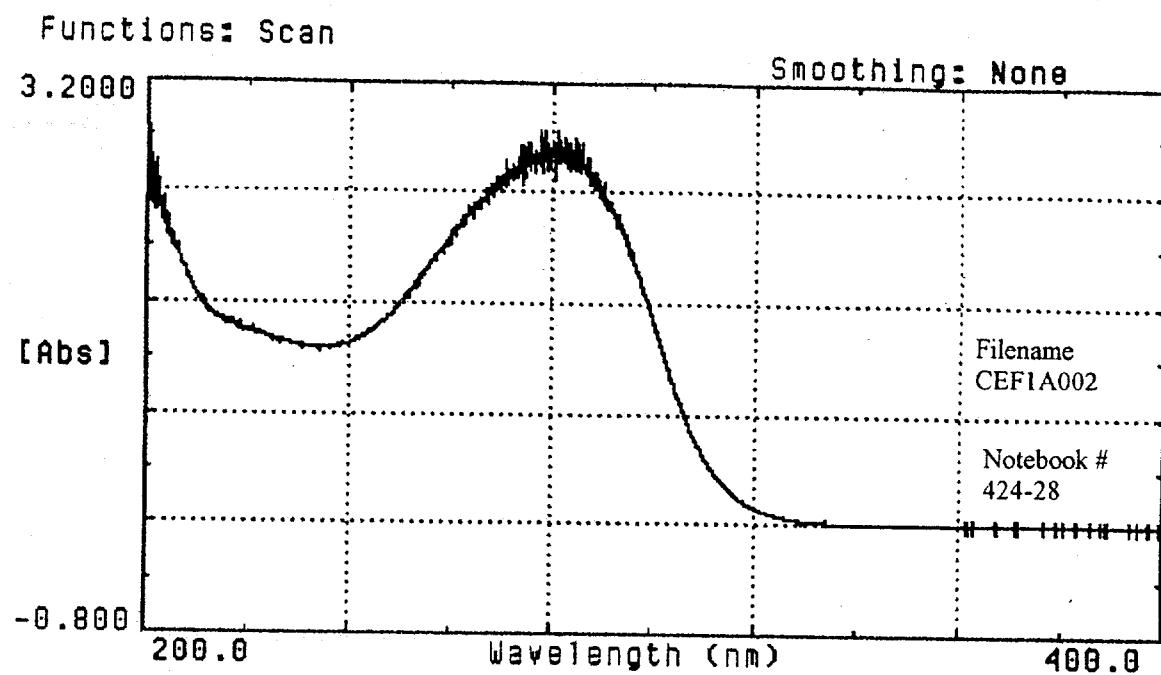
**Figure 28. Raman Spectra of BII, 20% BII in Amorphous A/B, and Amorphous A/B**



**Figure 29. Raman Spectra of AII/BII, 25% AII/BII in Amorphous A/B, and Amorphous A/B**



**Figure 30. Wavelength Scan of Isomer A**



**Figure 31. Wavelength Scan of Isomer B**

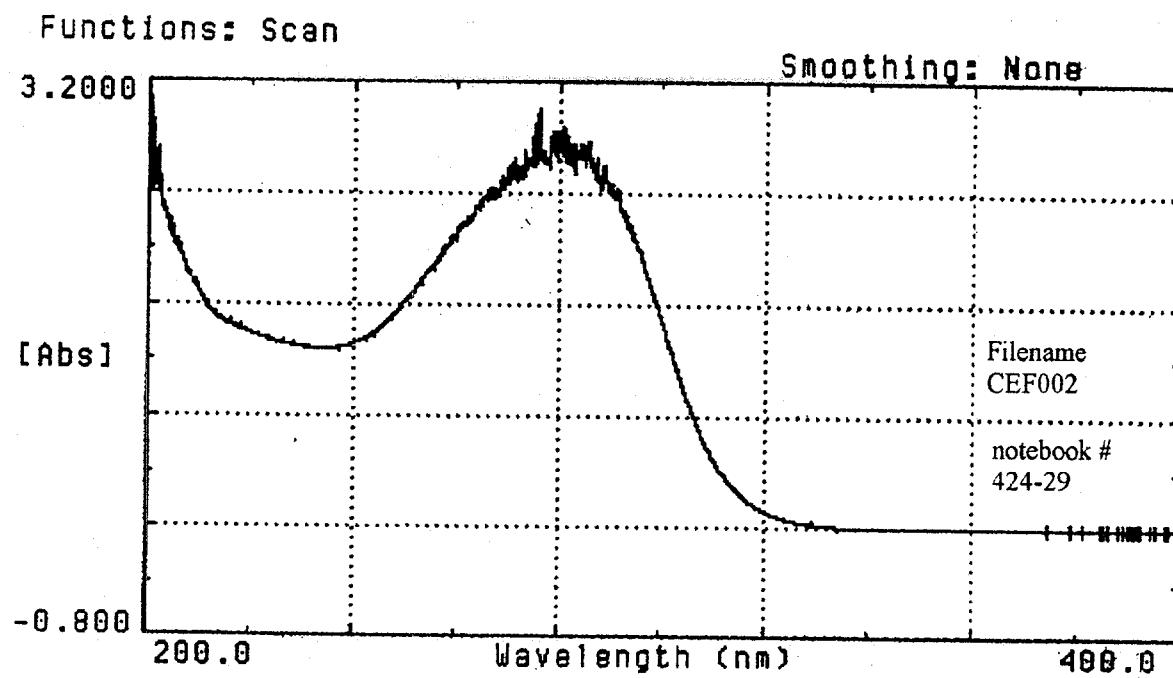


Figure 32. Calibration Curve for Isomer A (Standards File 4245201)

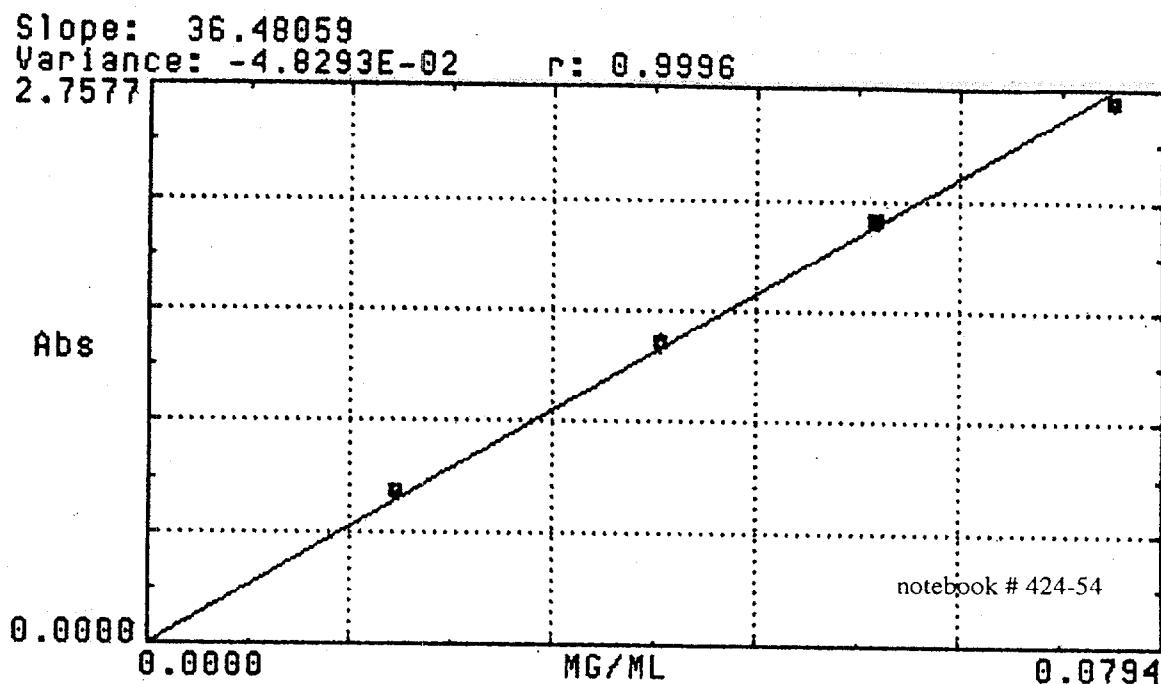
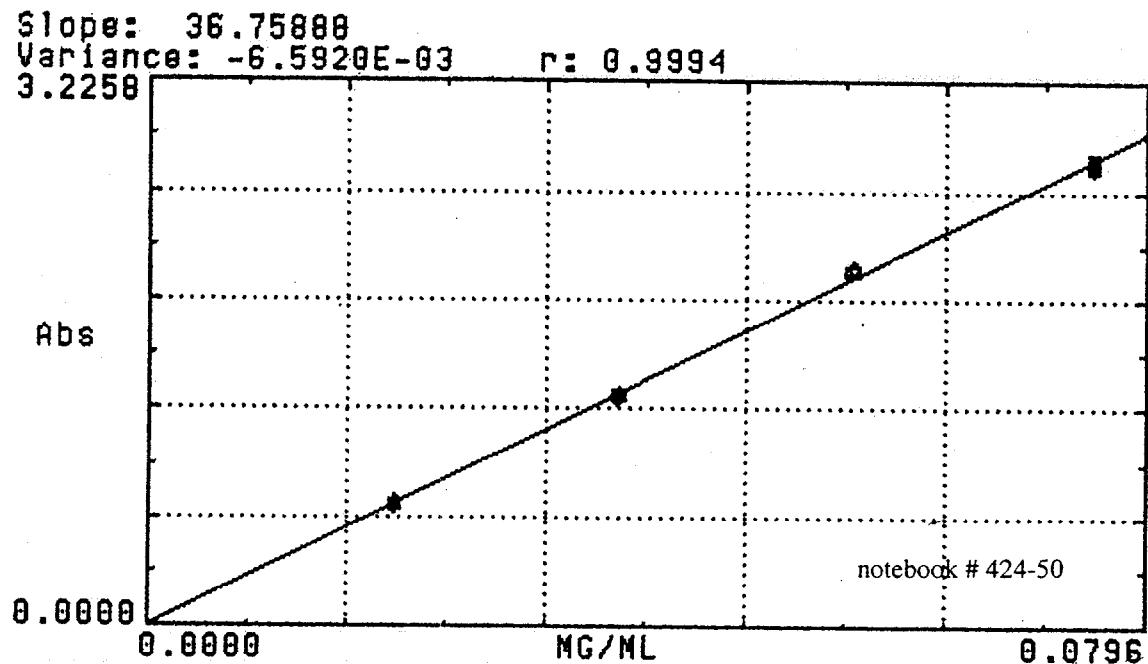
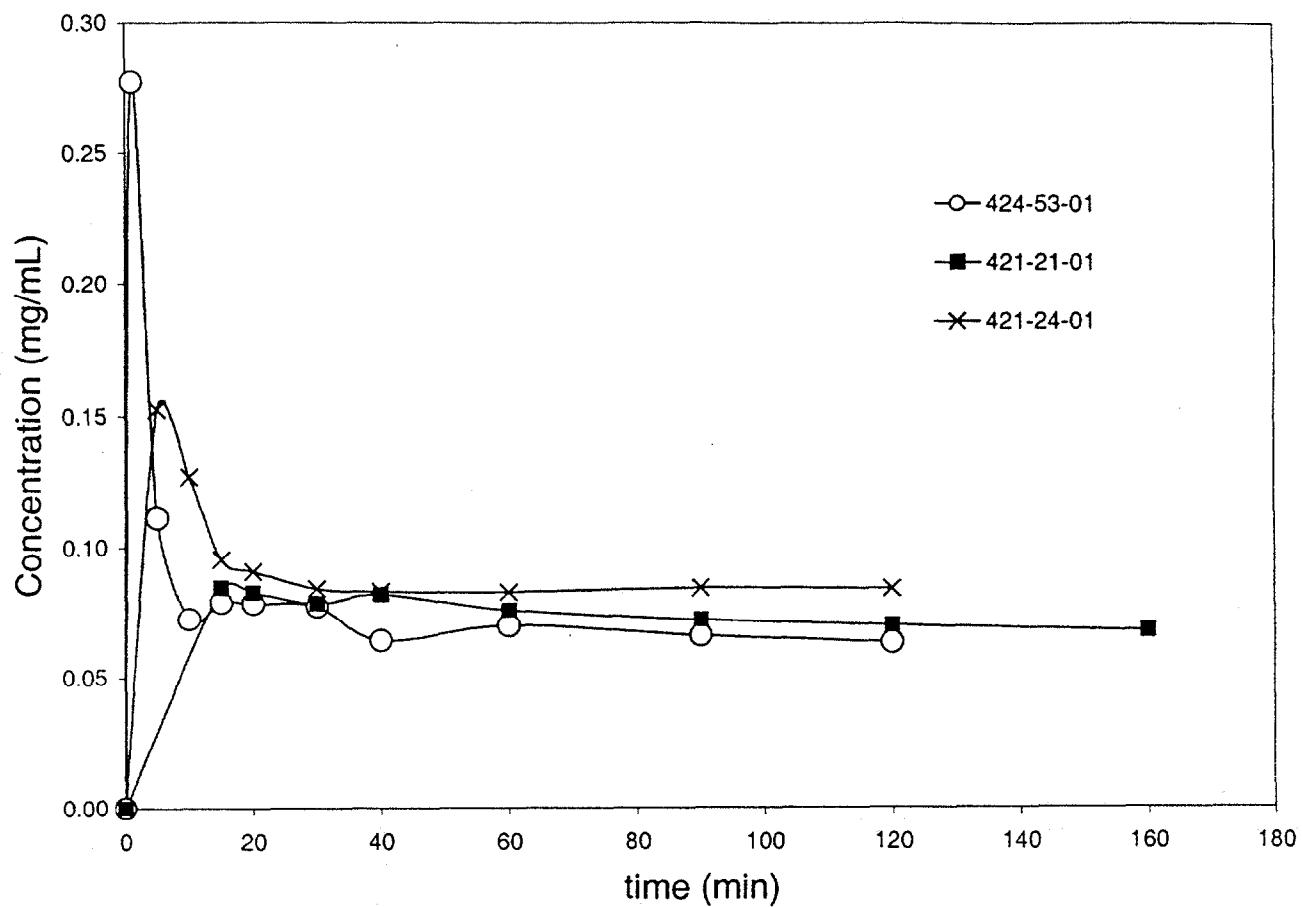


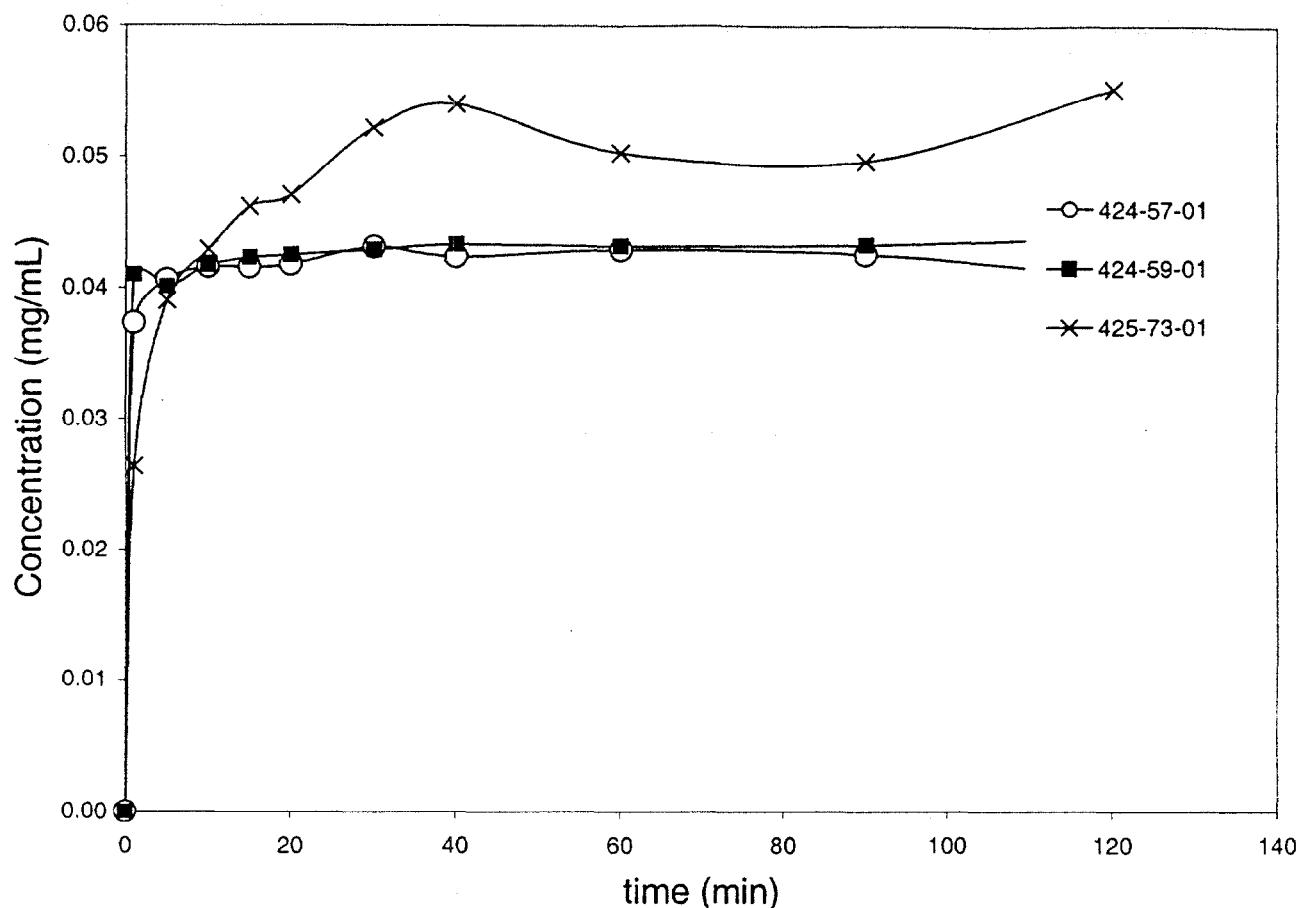
Figure 33. Calibration Curve for Isomer B (Standards file 4244803)



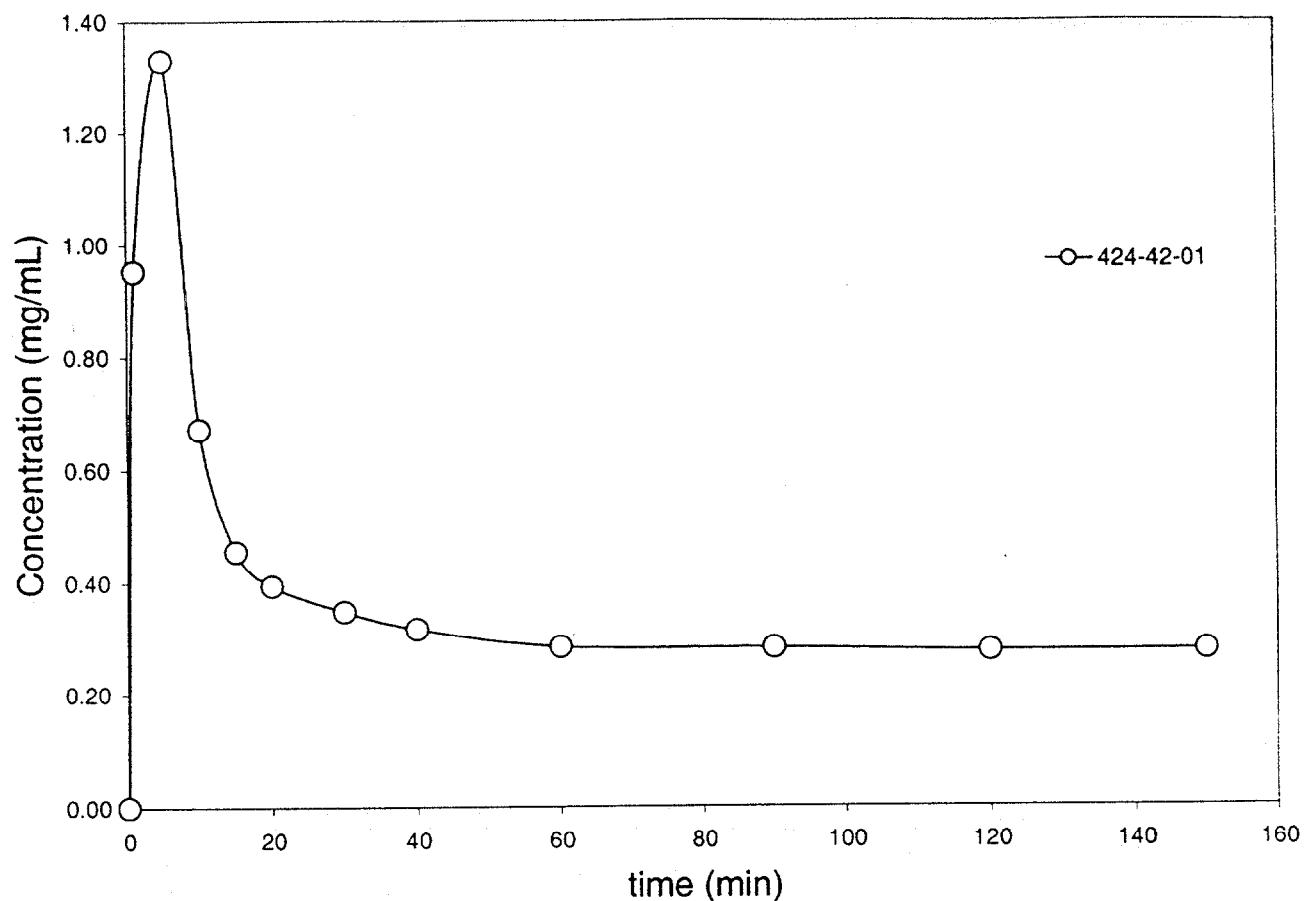
**Figure 34. Dissolution Profile of Amorphous Isomer A**



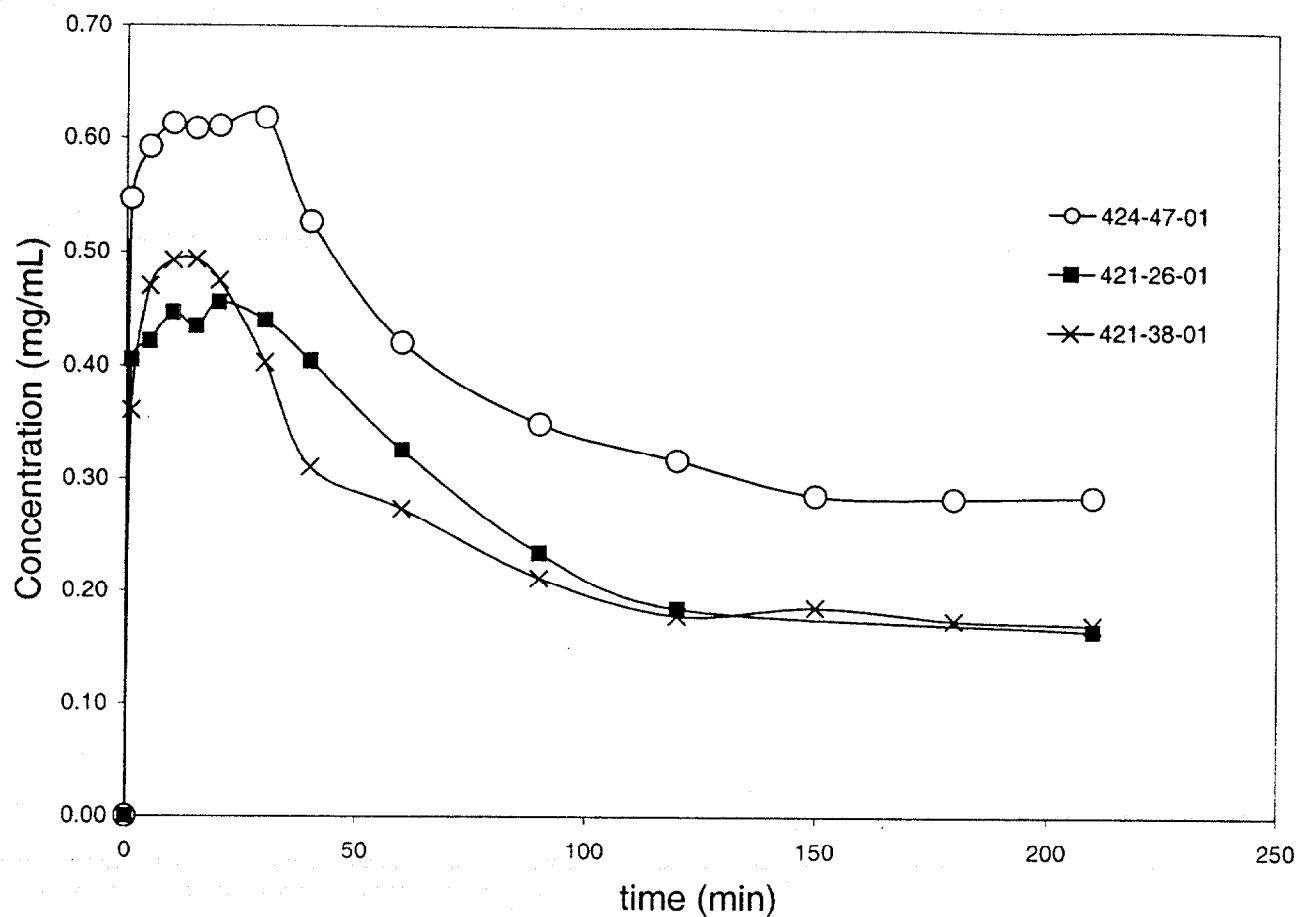
**Figure 35. Dissolution Profile of Isomer AI**



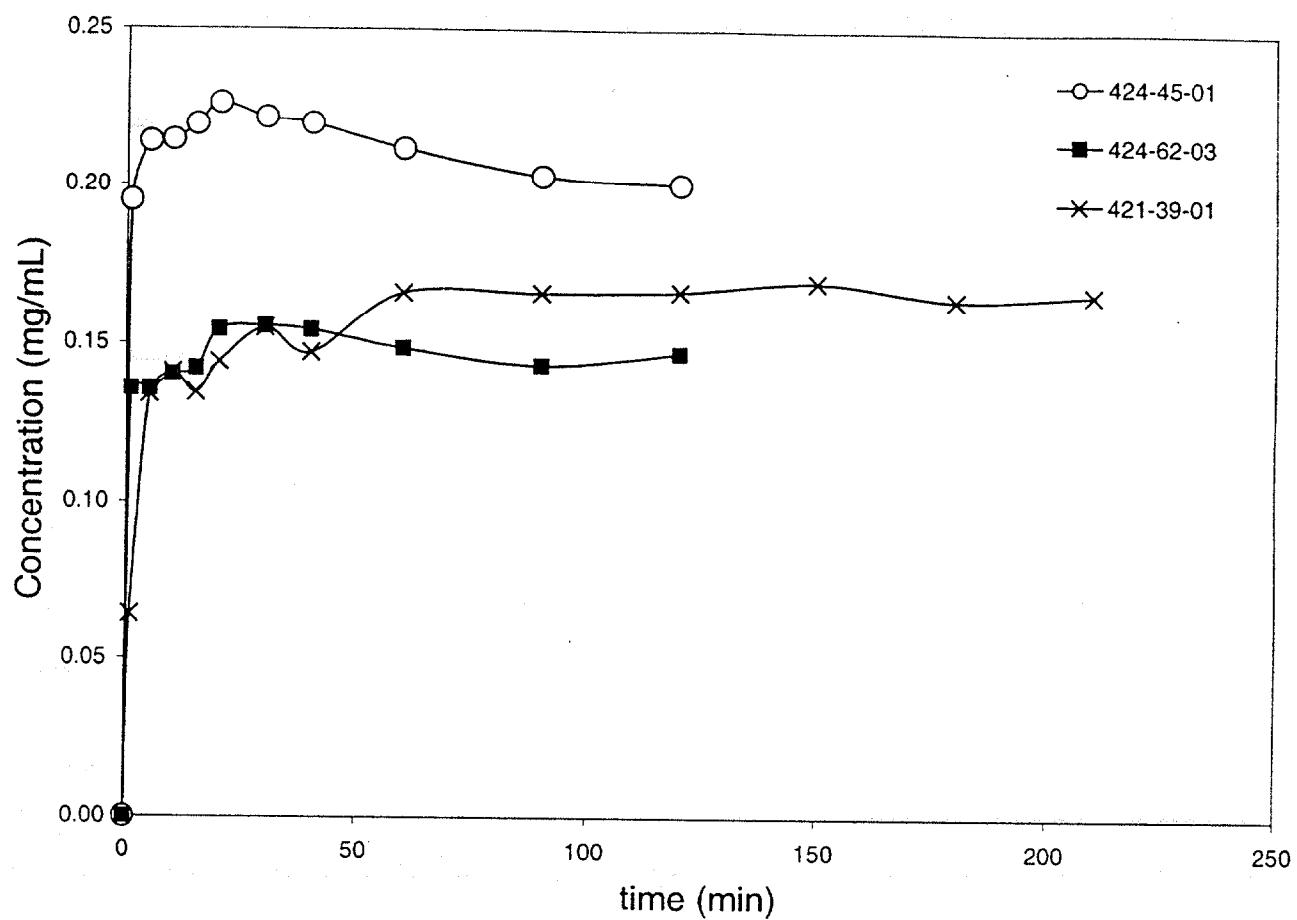
**Figure 36. Dissolution Profile of Amorphous Isomer B**



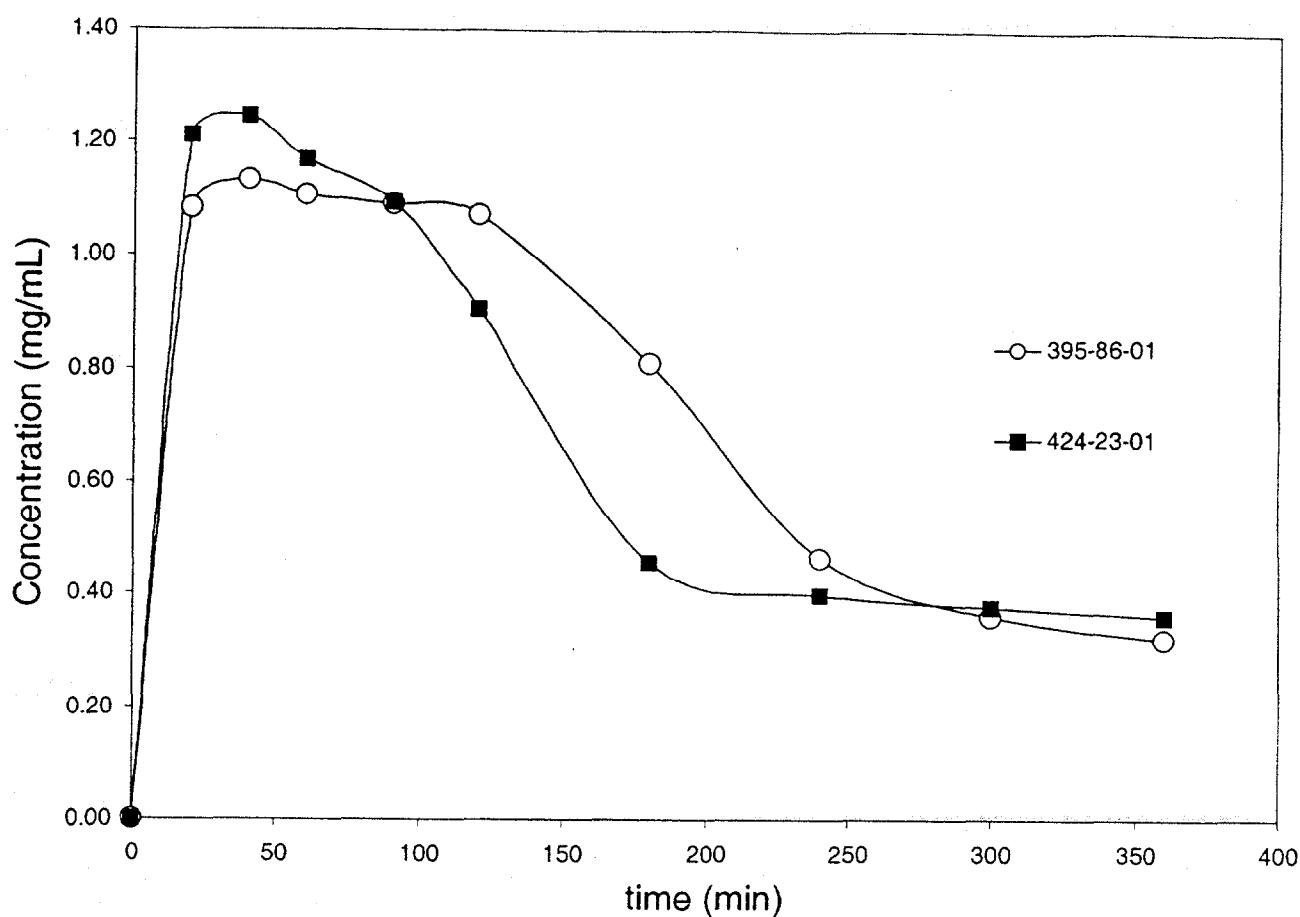
**Figure 37. Dissolution Profile of Isomer BI**



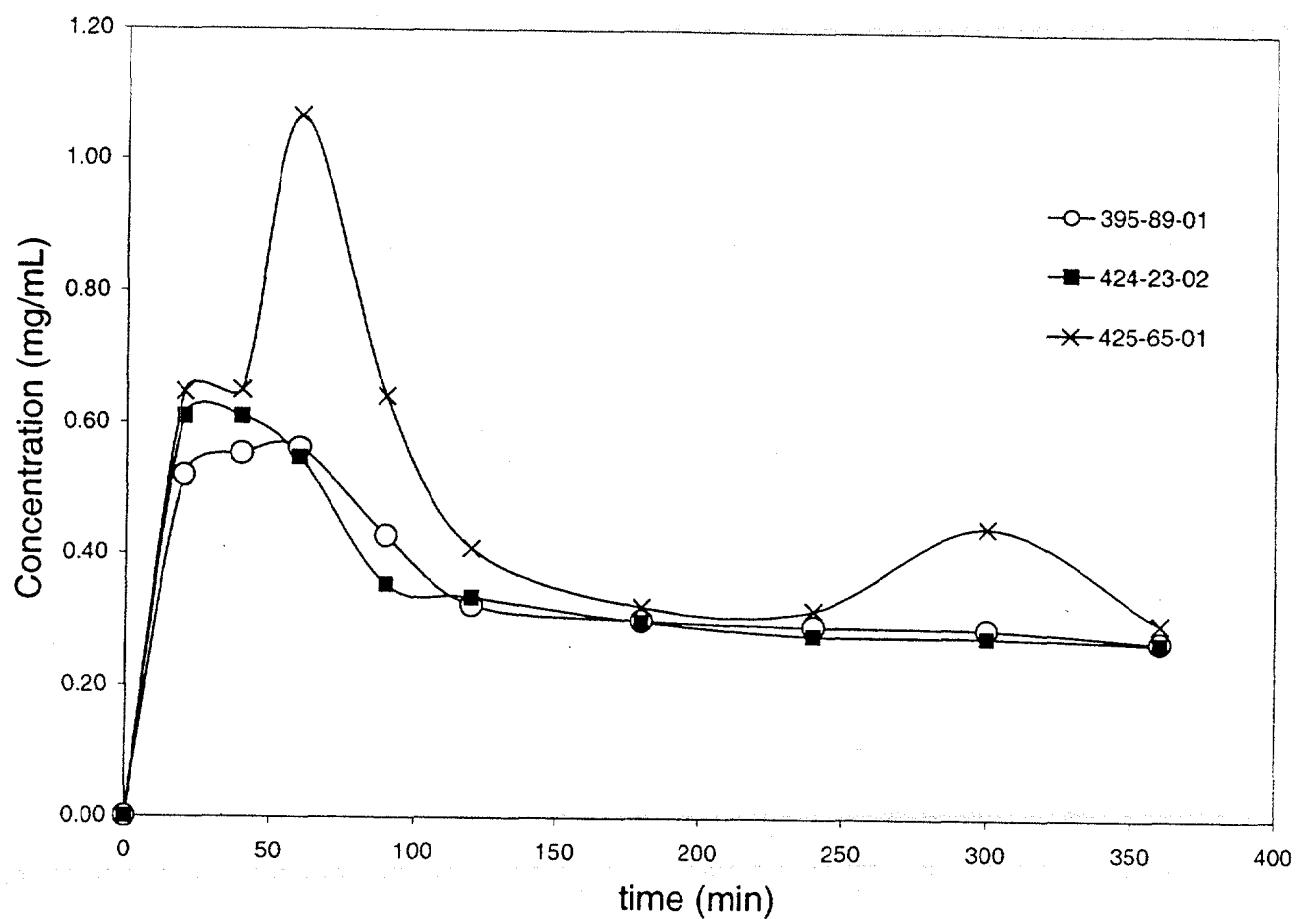
**Figure 38. Dissolution Profile of Isomer BII**



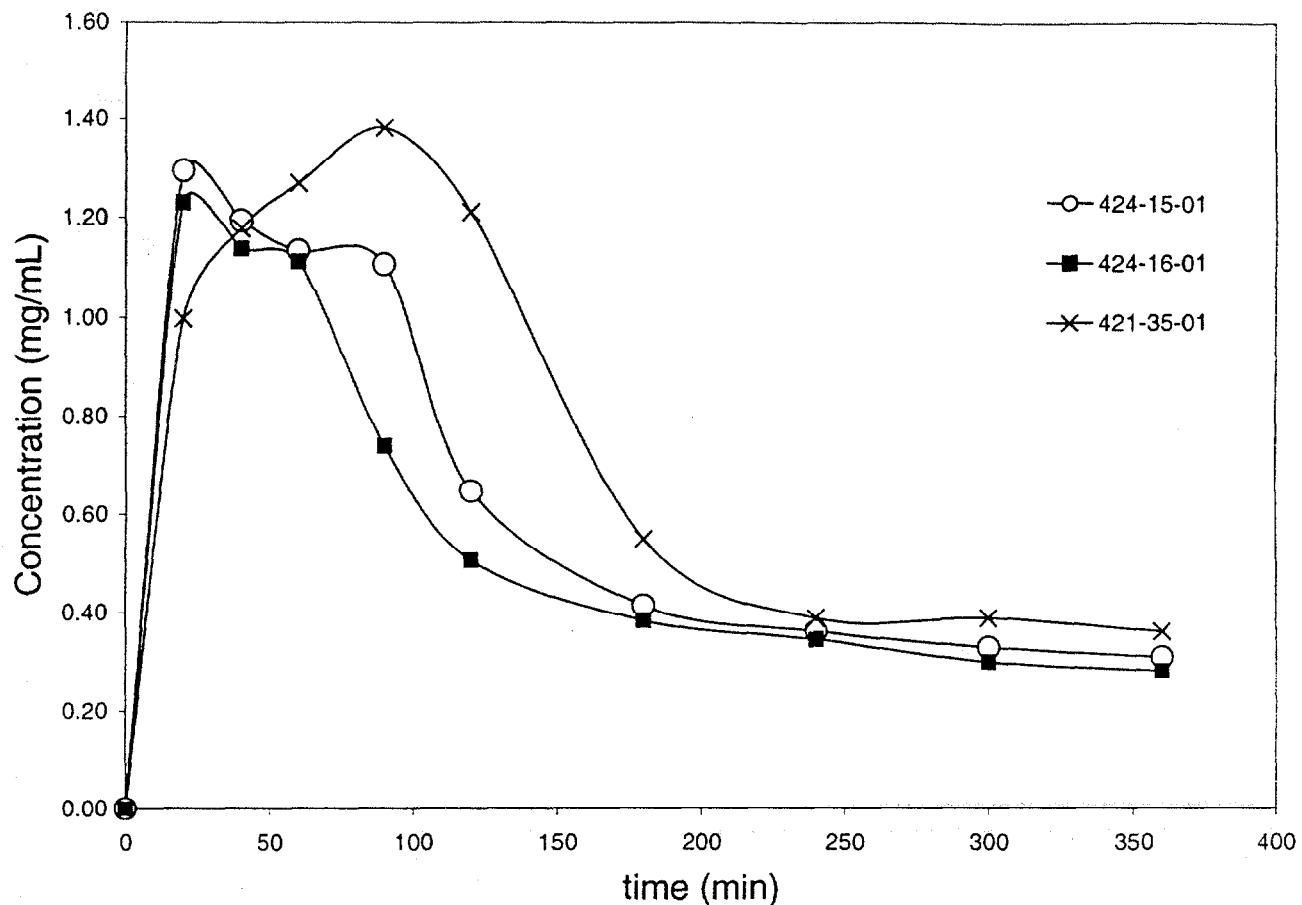
**Figure 39. Dissolution Profile of 100% Amorphous A/B in Water**



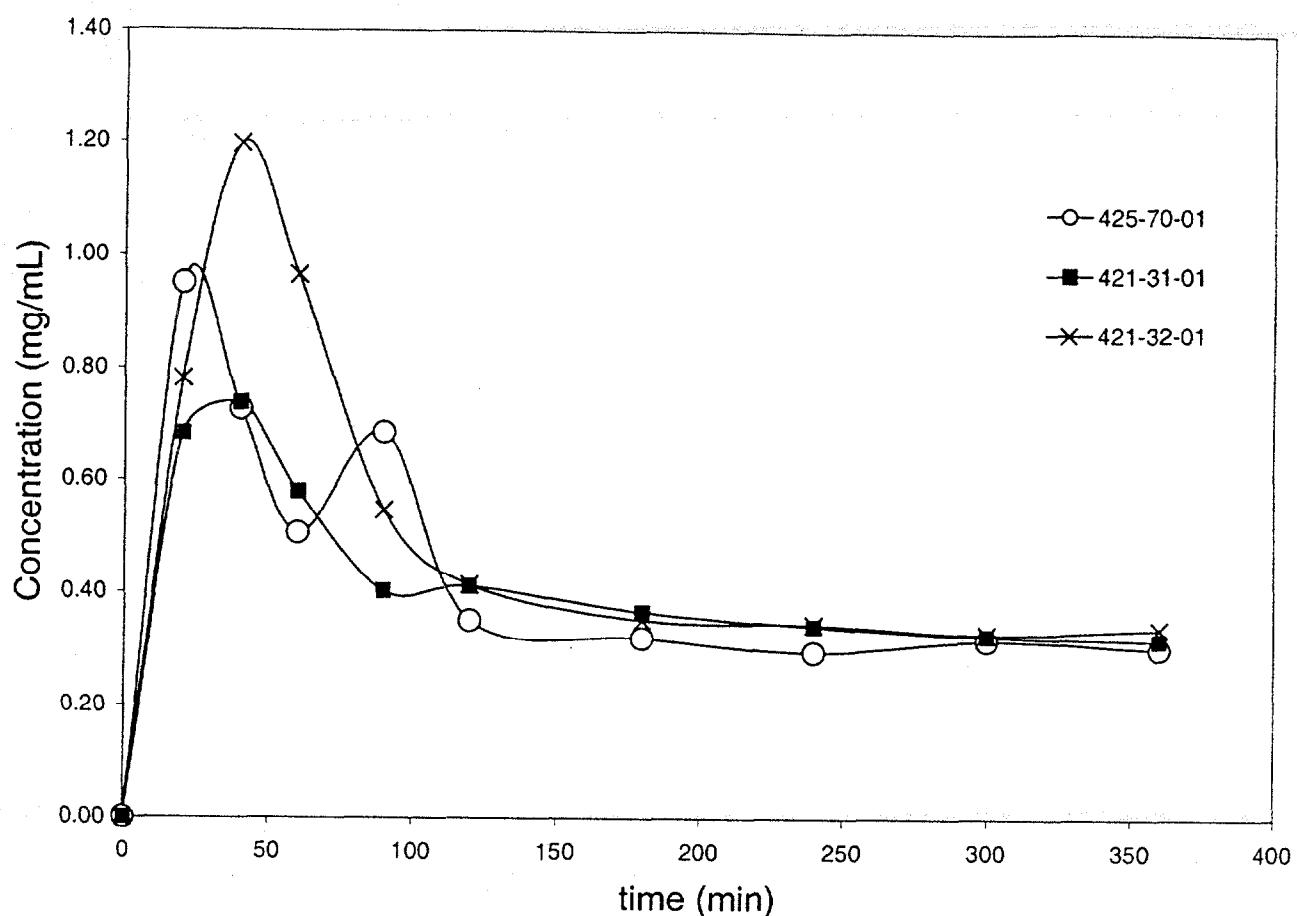
**Figure 40. Dissolution Profile of 100% AI/BI in Water**



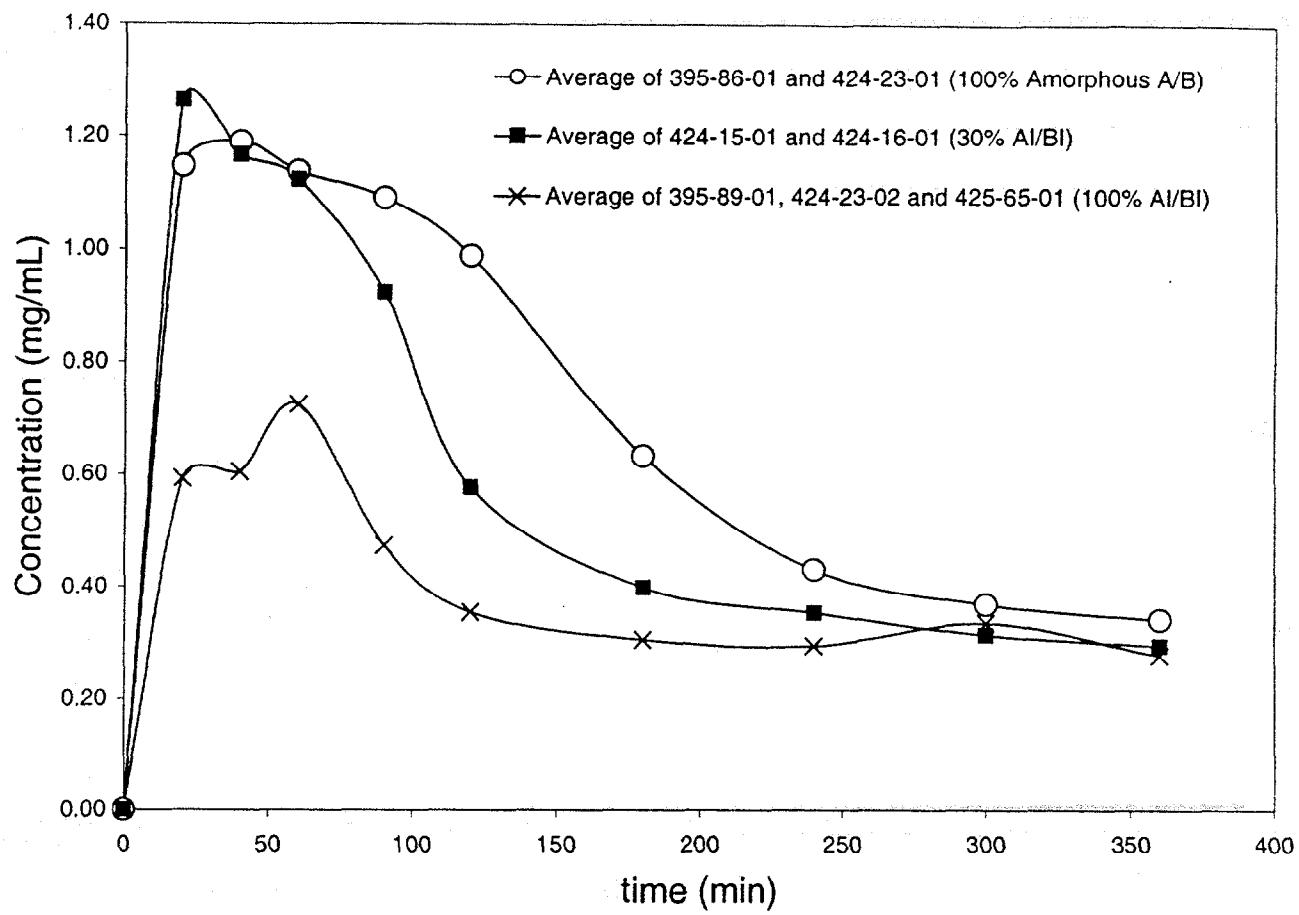
**Figure 41. Dissolution Profile of 70% Amorphous A/B - 30% AI/BI in Water**



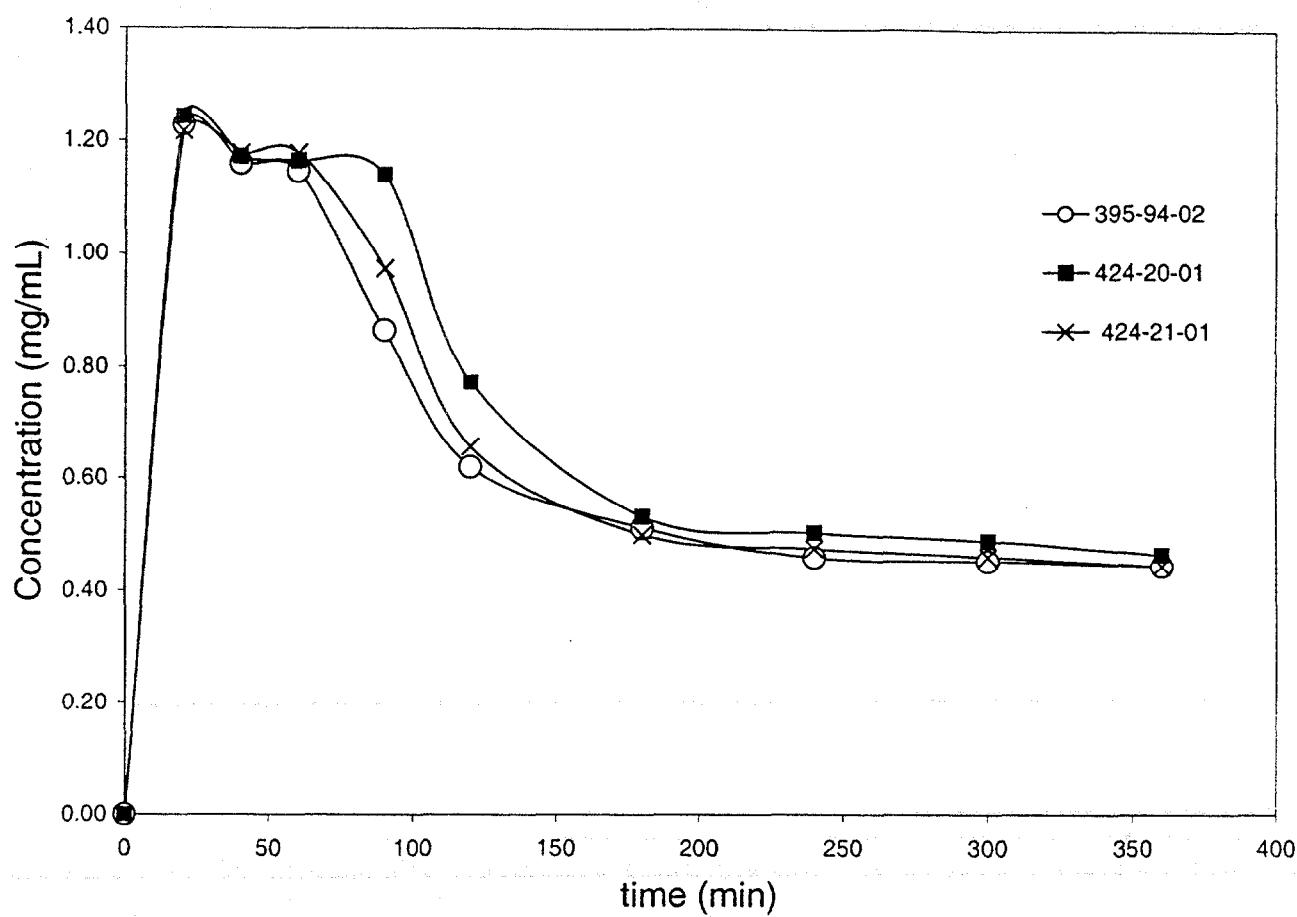
**Figure 42. Dissolution Profile of 50% Amorphous A/B - 50% AI/BI in Water**



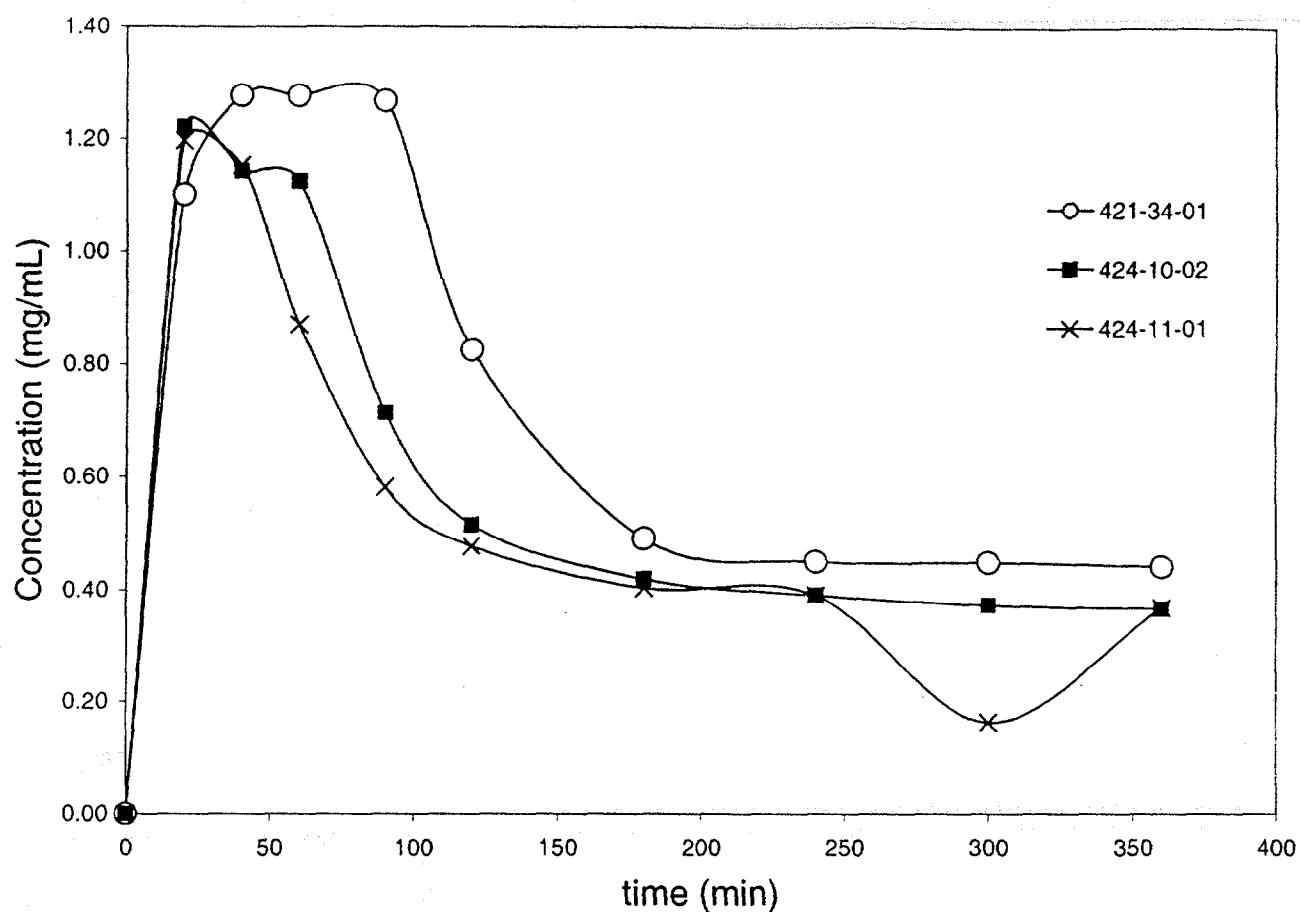
**Figure 43. Profiles of Averaged Dissolution Runs of Isomer A/B Mixtures in Water**



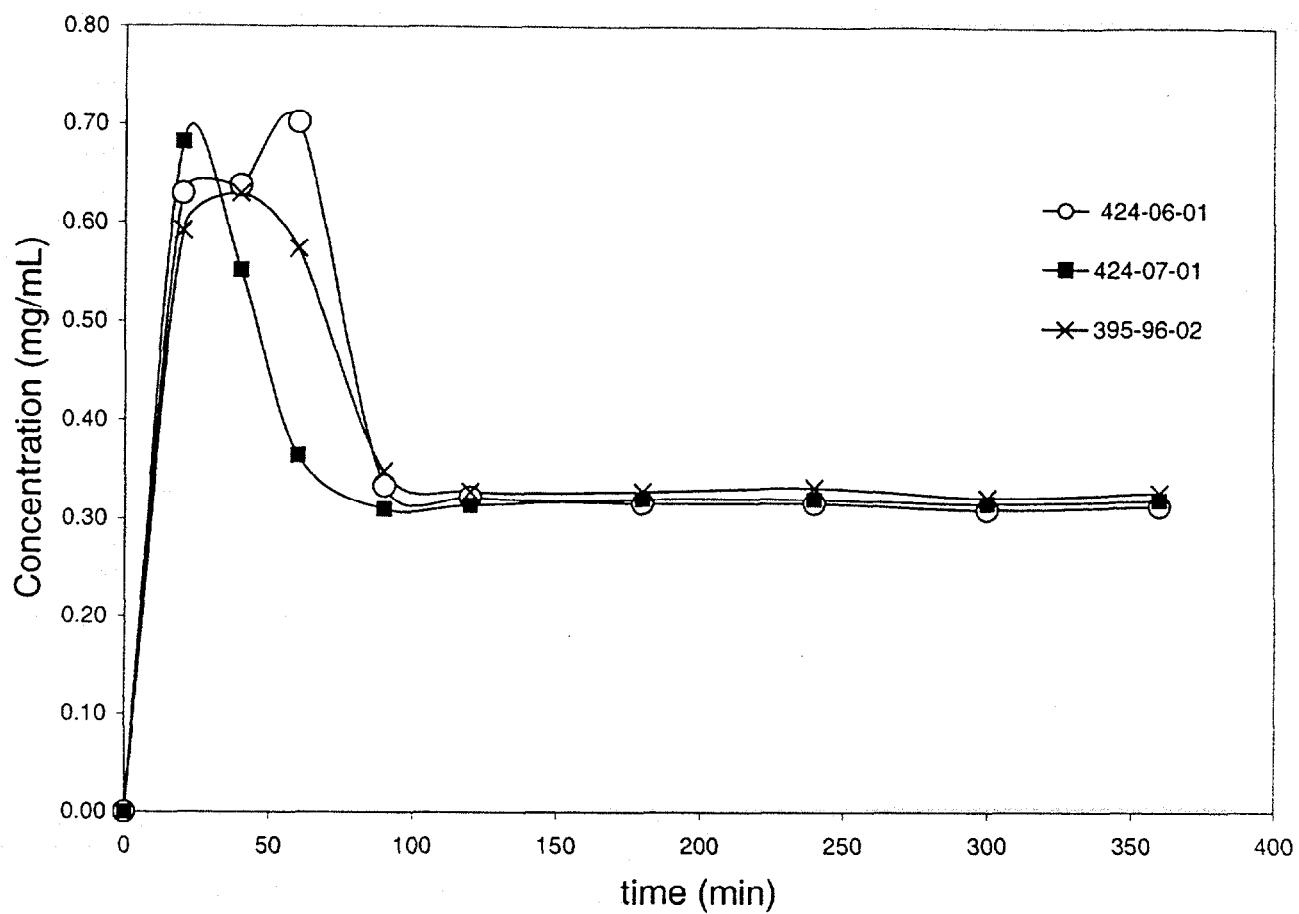
**Figure 44. Dissolution Profile of 100% Amorphous A/B in HCl**



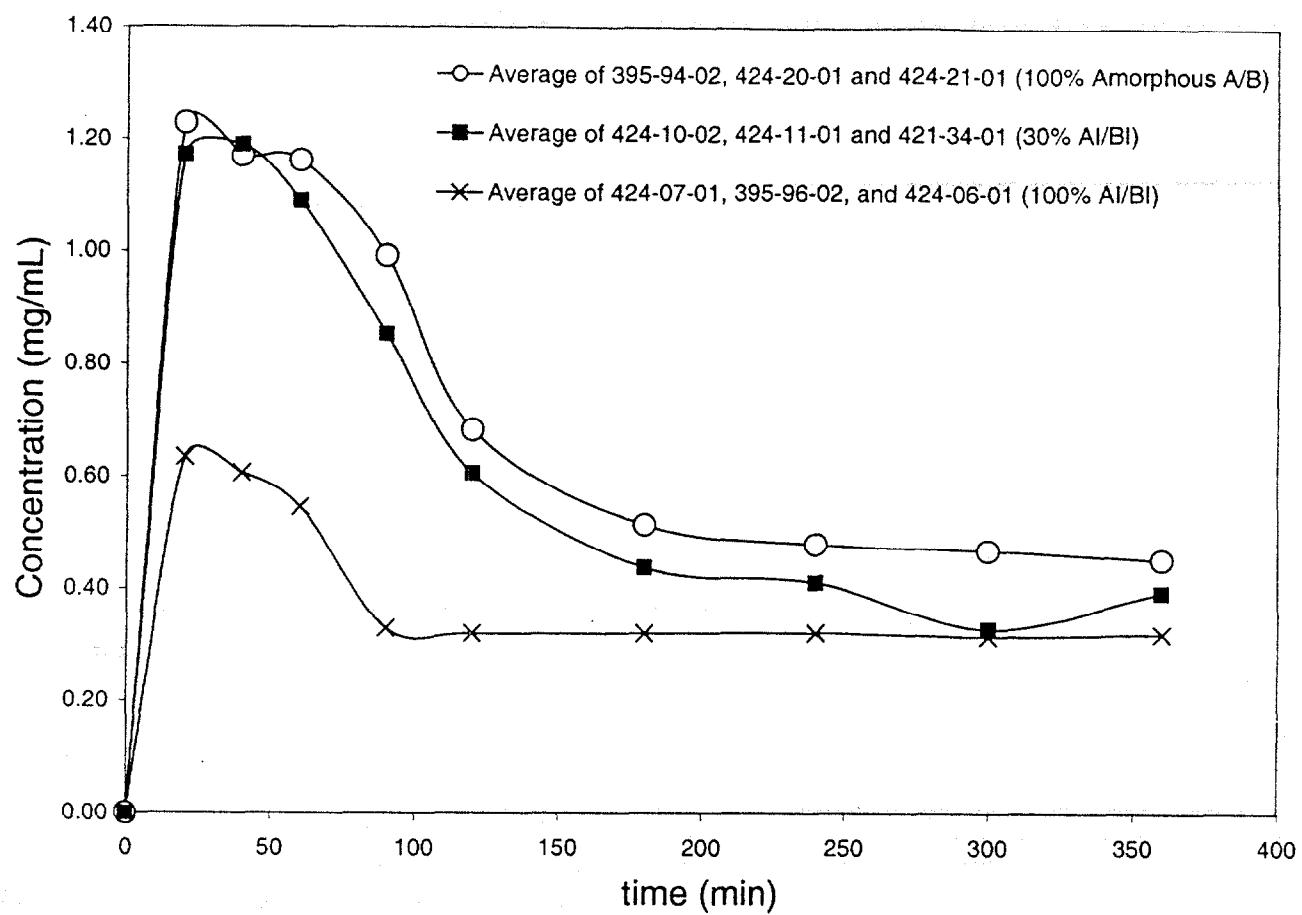
**Figure 45. Dissolution Profile of 70% Amorphous A/B - 30% AI/BI in HCl**



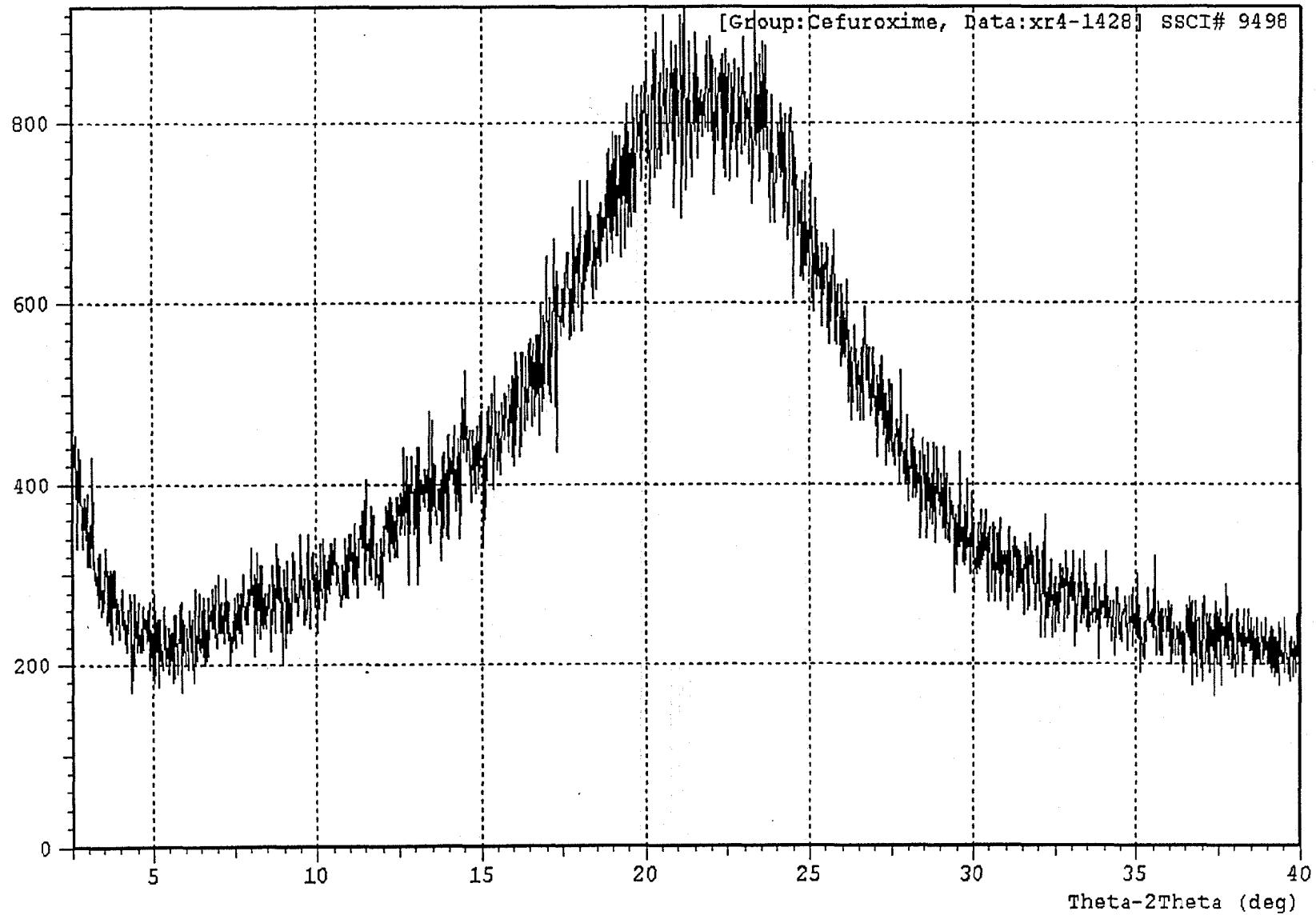
**Figure 46. Dissolution Profile of 100% AI/BI in HCl**

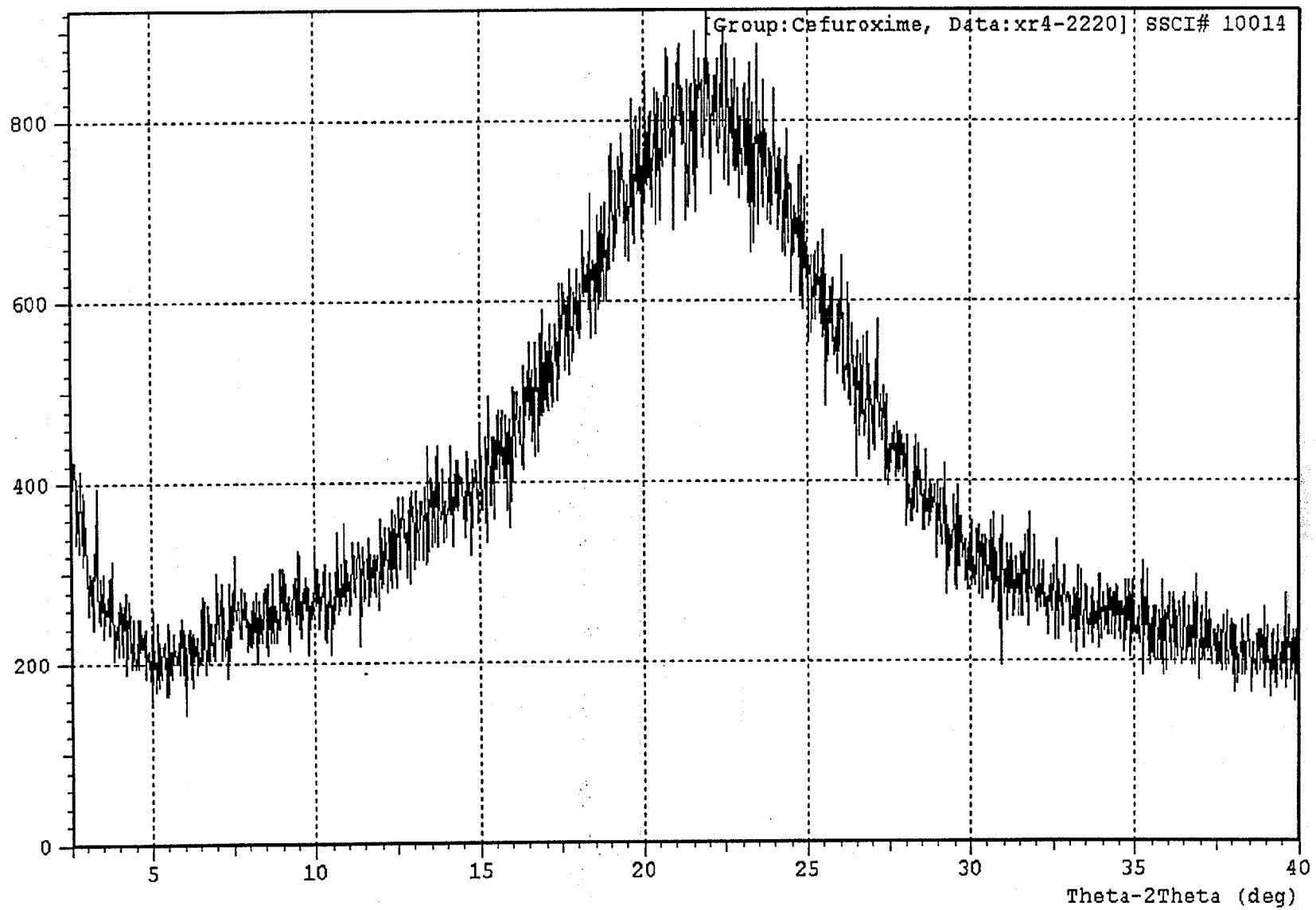


**Figure 47. Profiles of Averaged Dissolution Runs of Isomer A/B Mixtures in HCl**

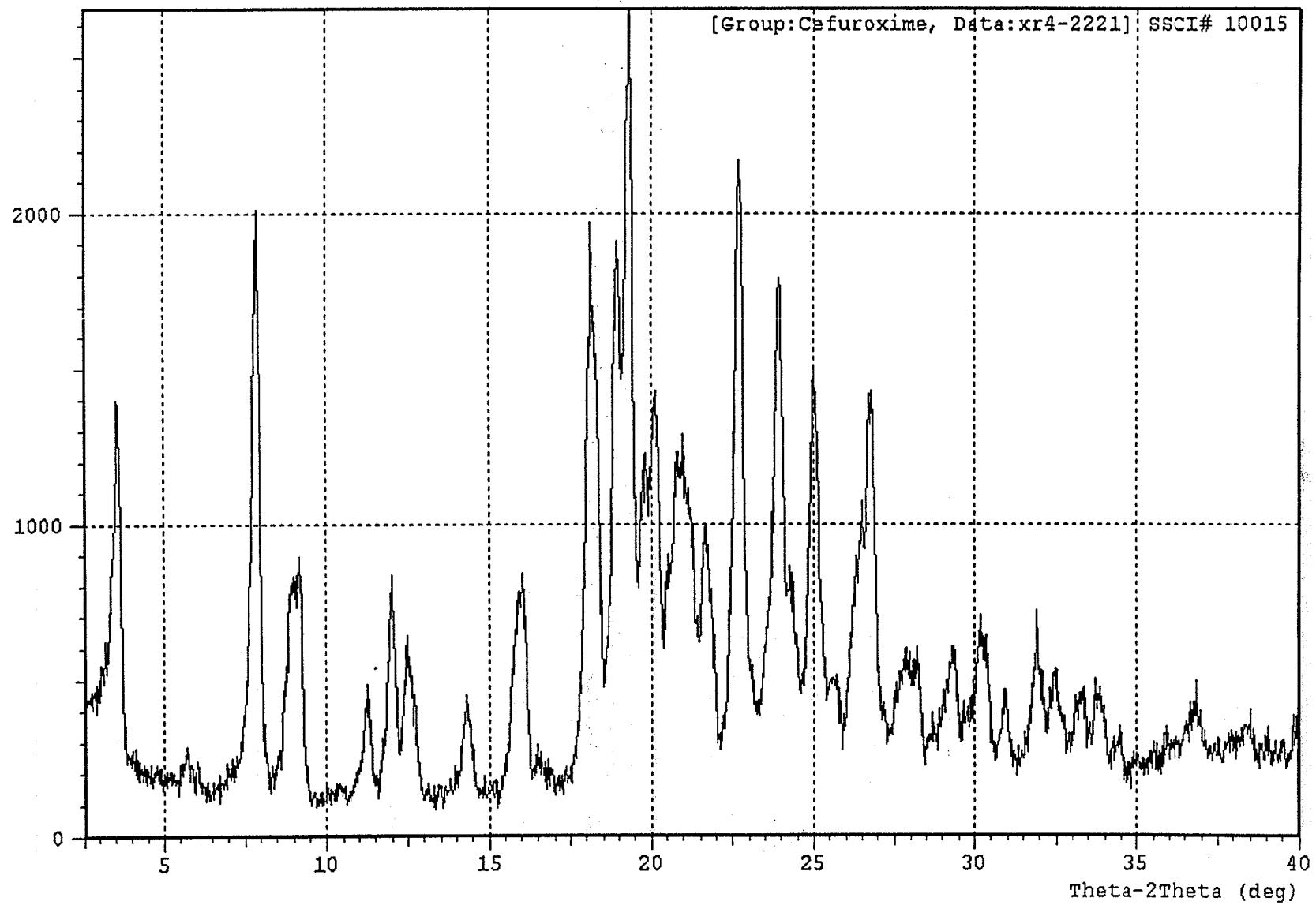


[Group:Cefuroxime, Data:xr4-1428] SSCI# 9498

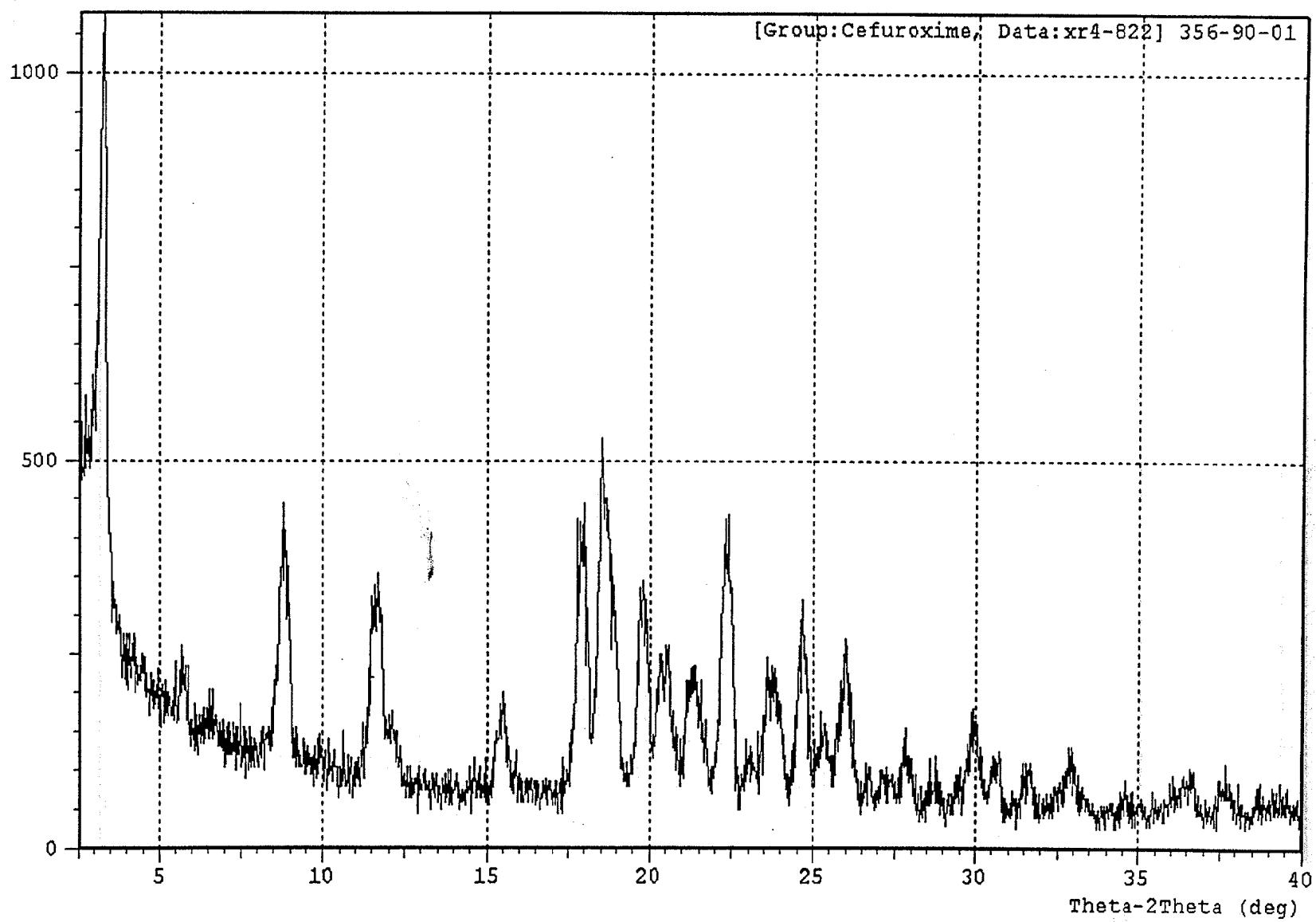




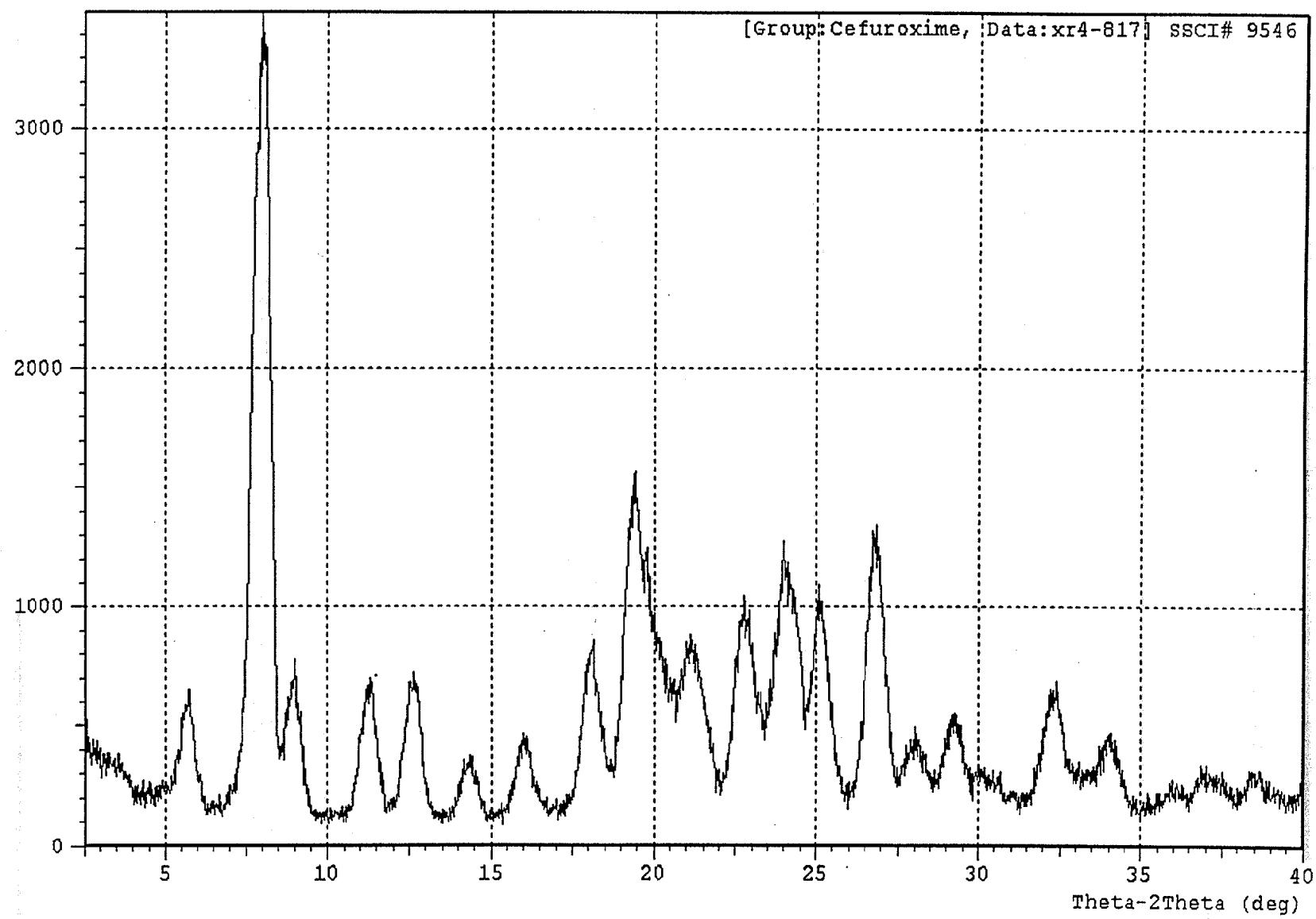
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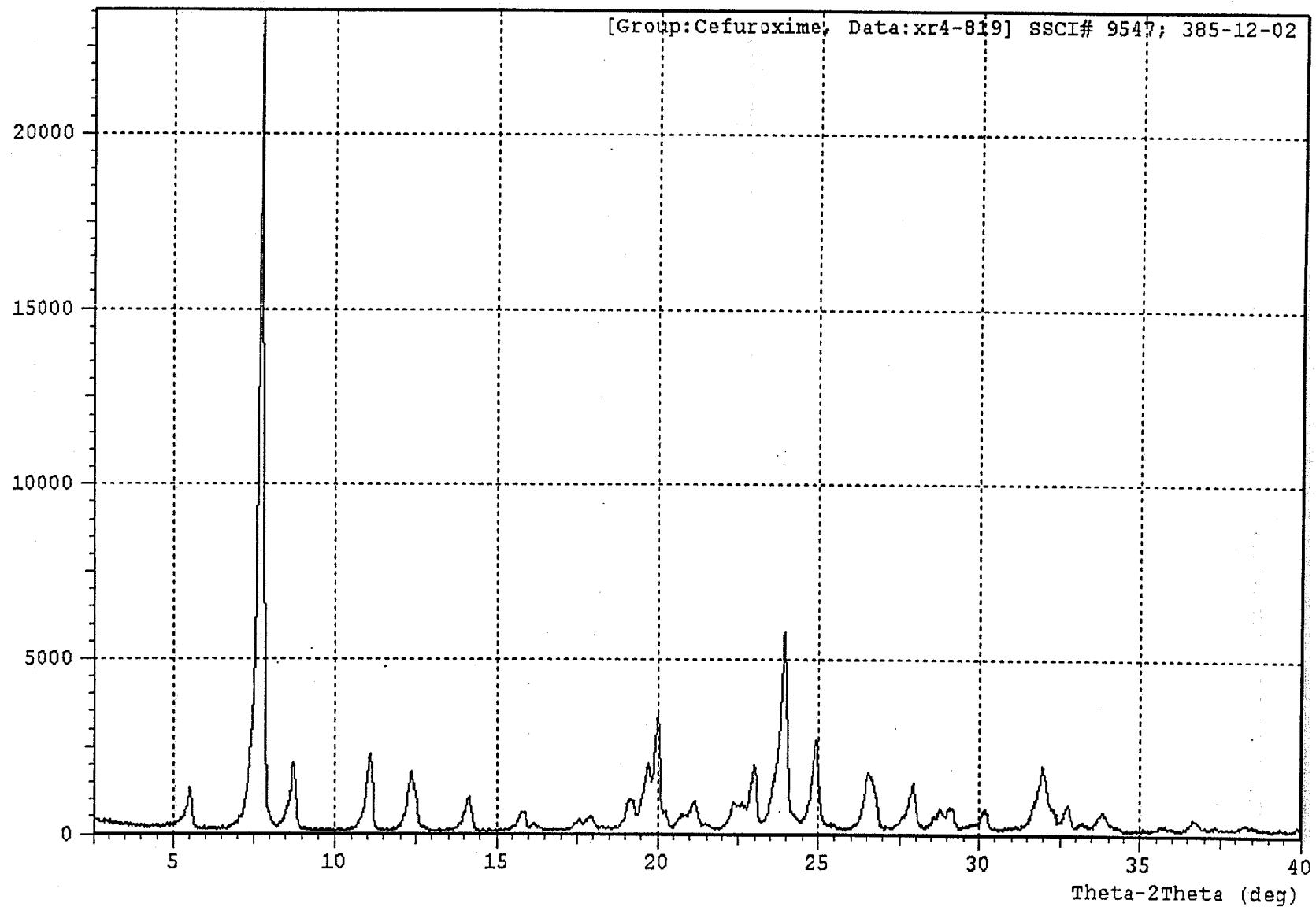
[Group:Cefuroxime, Data:xr4-822] 356-90-01



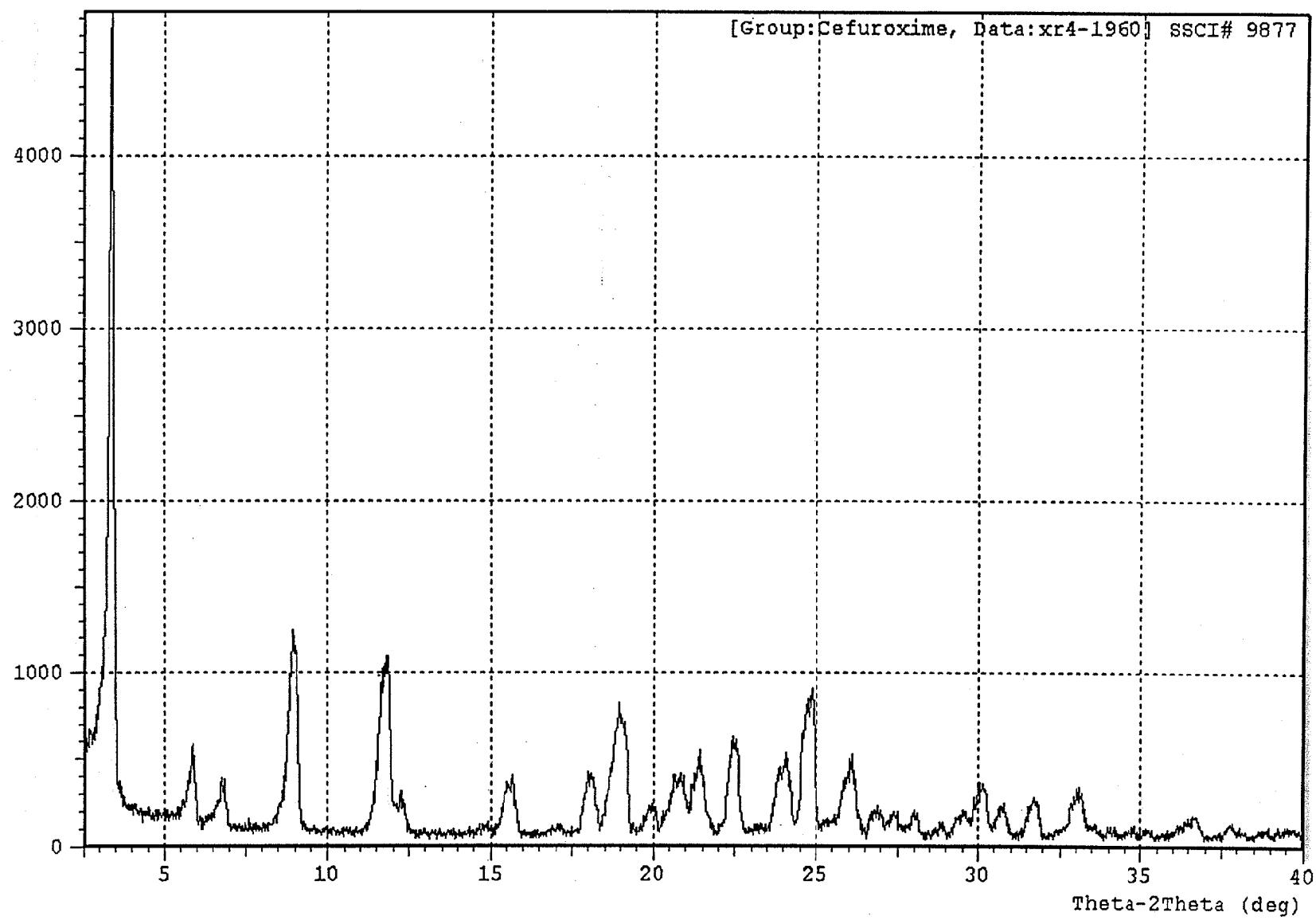
[Group:Cefuroxime, Data:xr4-817] SSCI# 9546



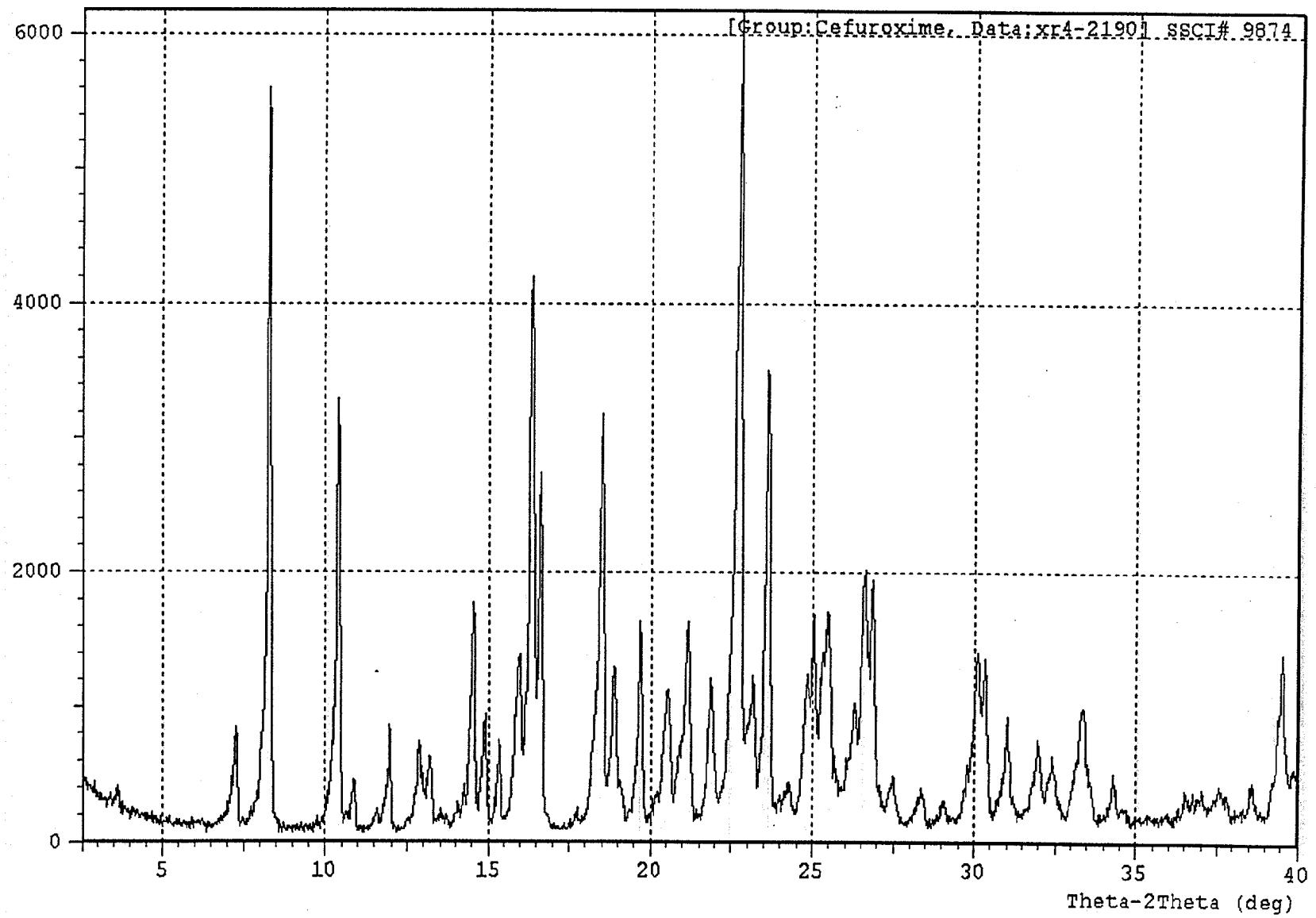
[Group:Cefuroxime, Data:xr4-819] SSCI# 9547; 385-12-02

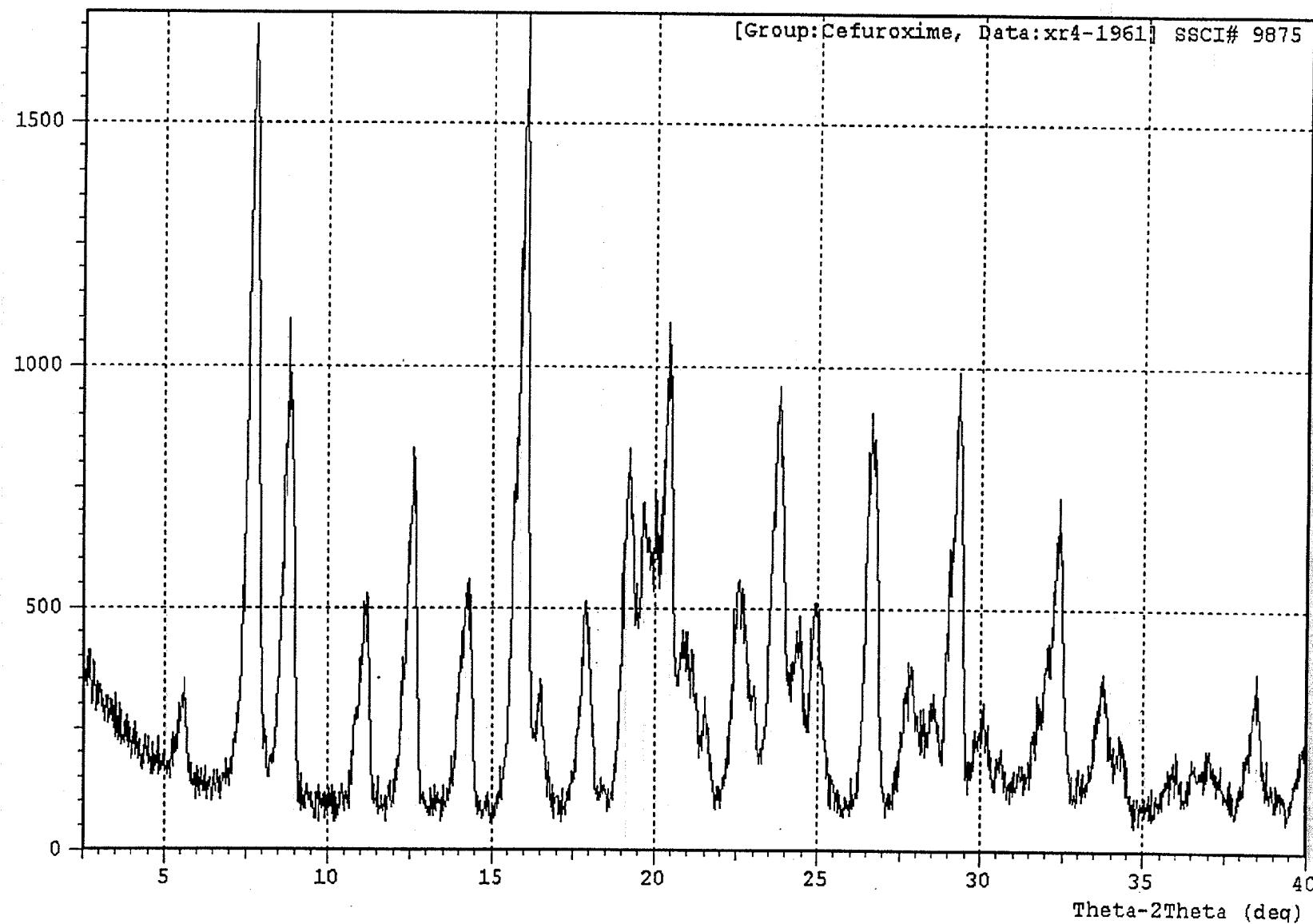


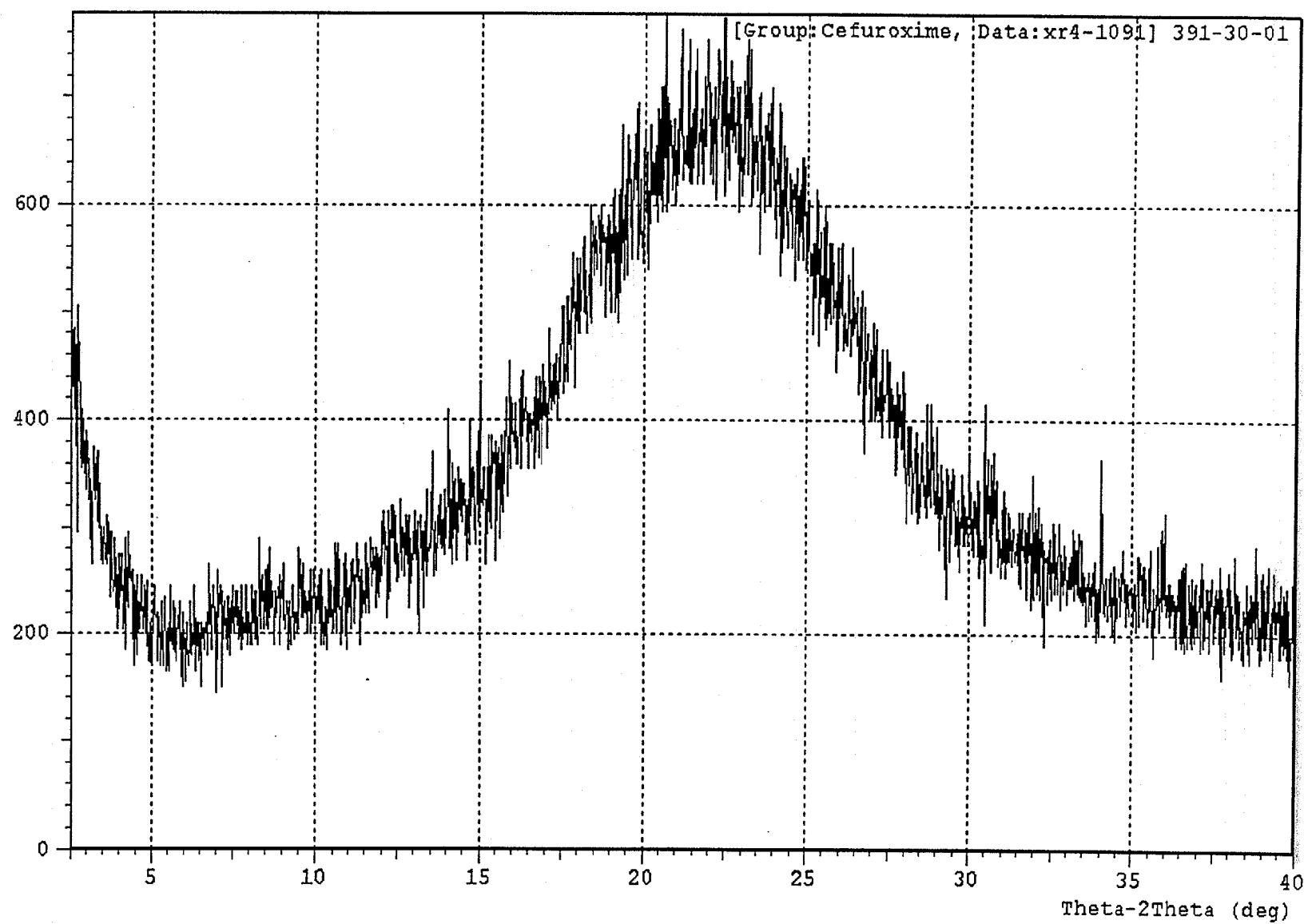
[Group:Cefuroxime, Data:xr4-1960] SSCI# 9877

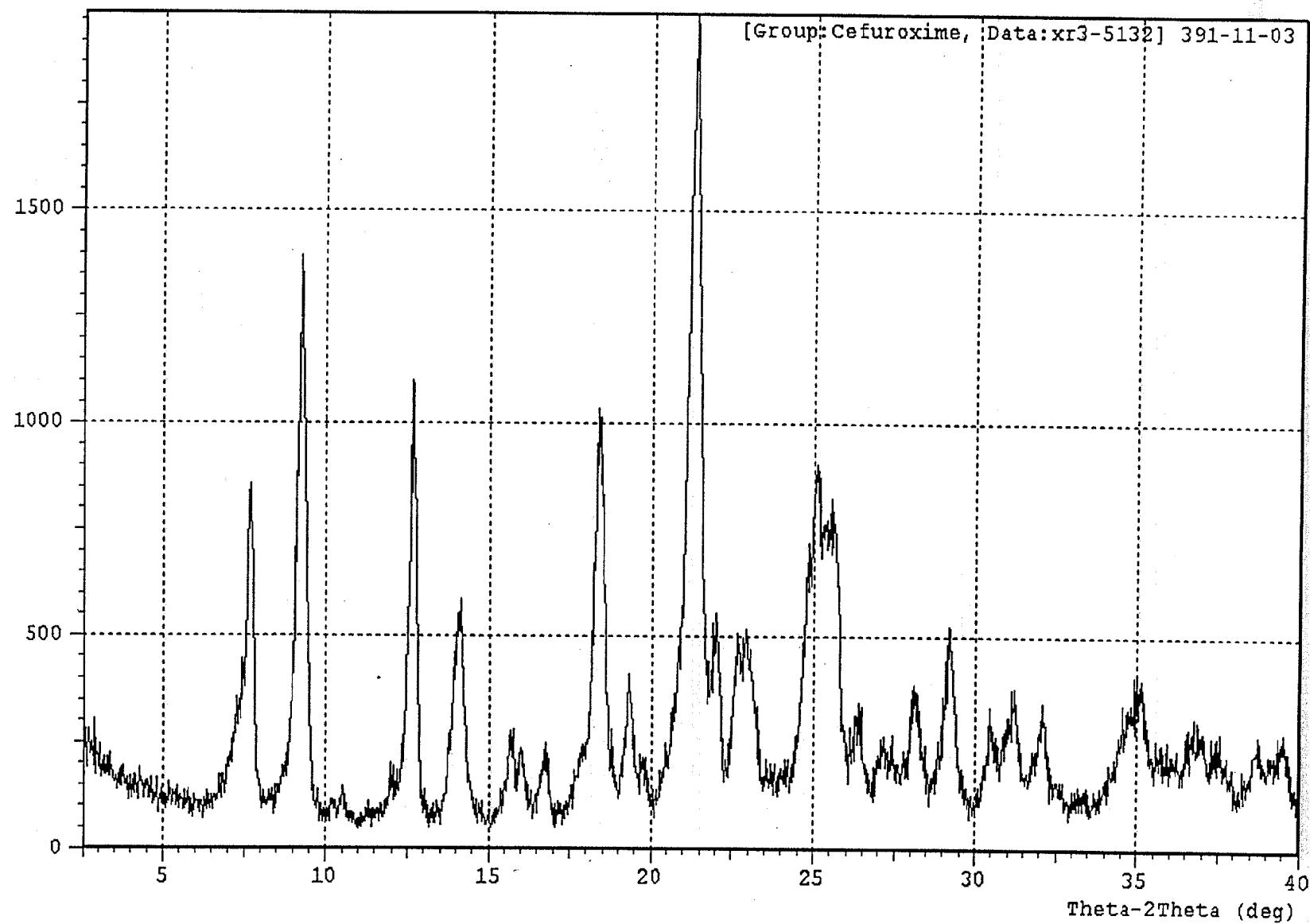


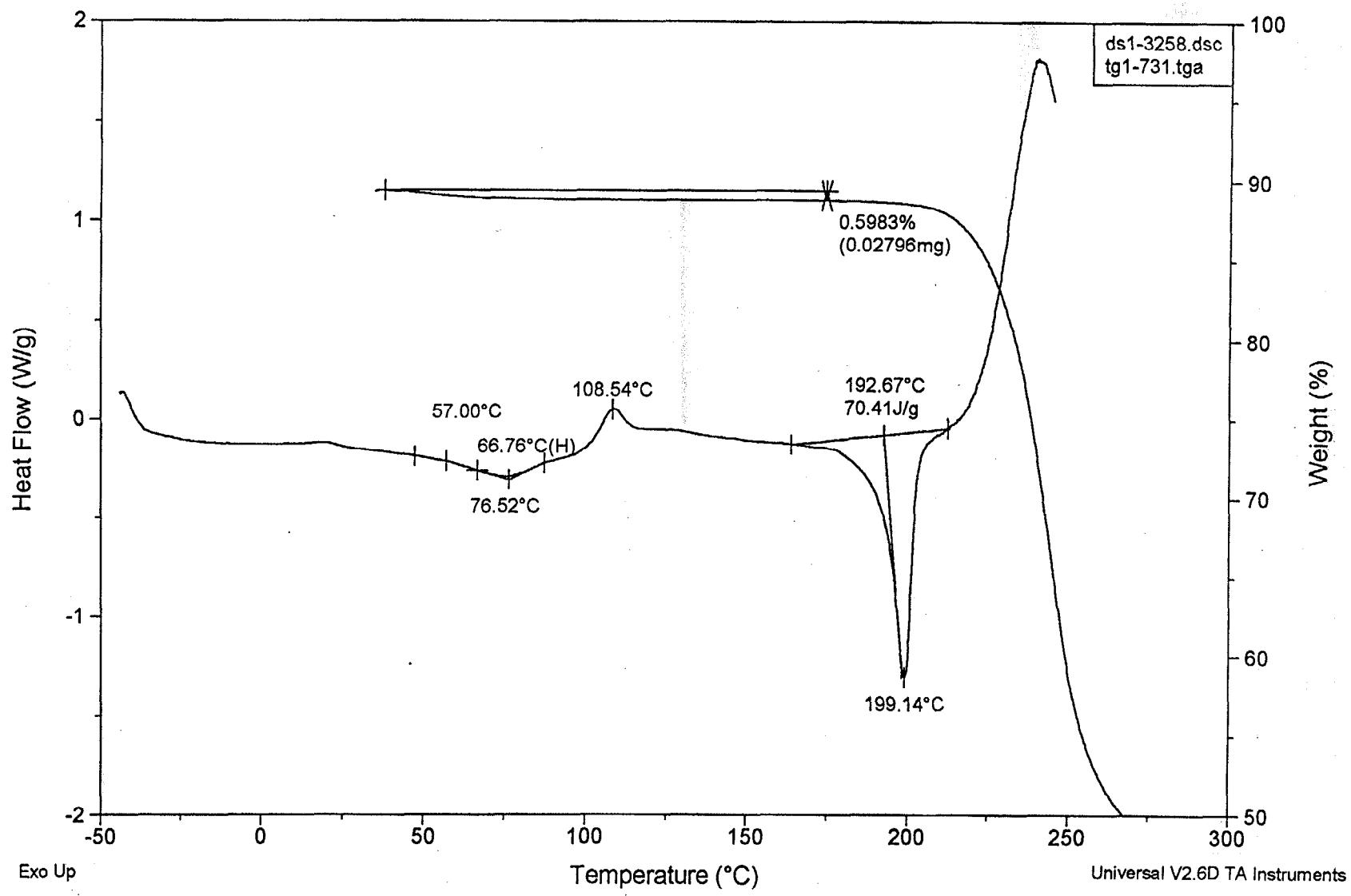
[Group:Cefuroxime, Data:xr4-21901, SSCI# 9874]

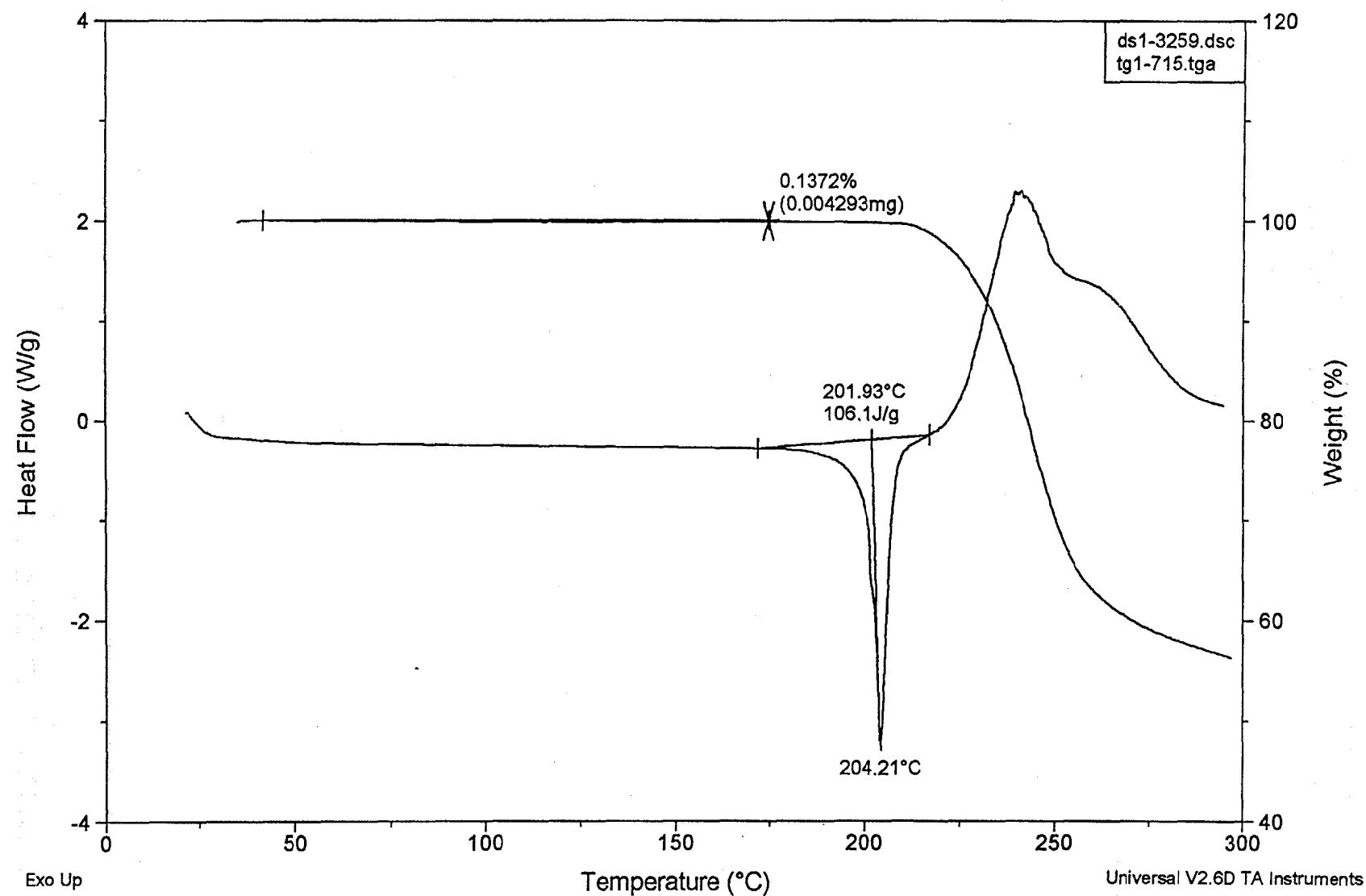


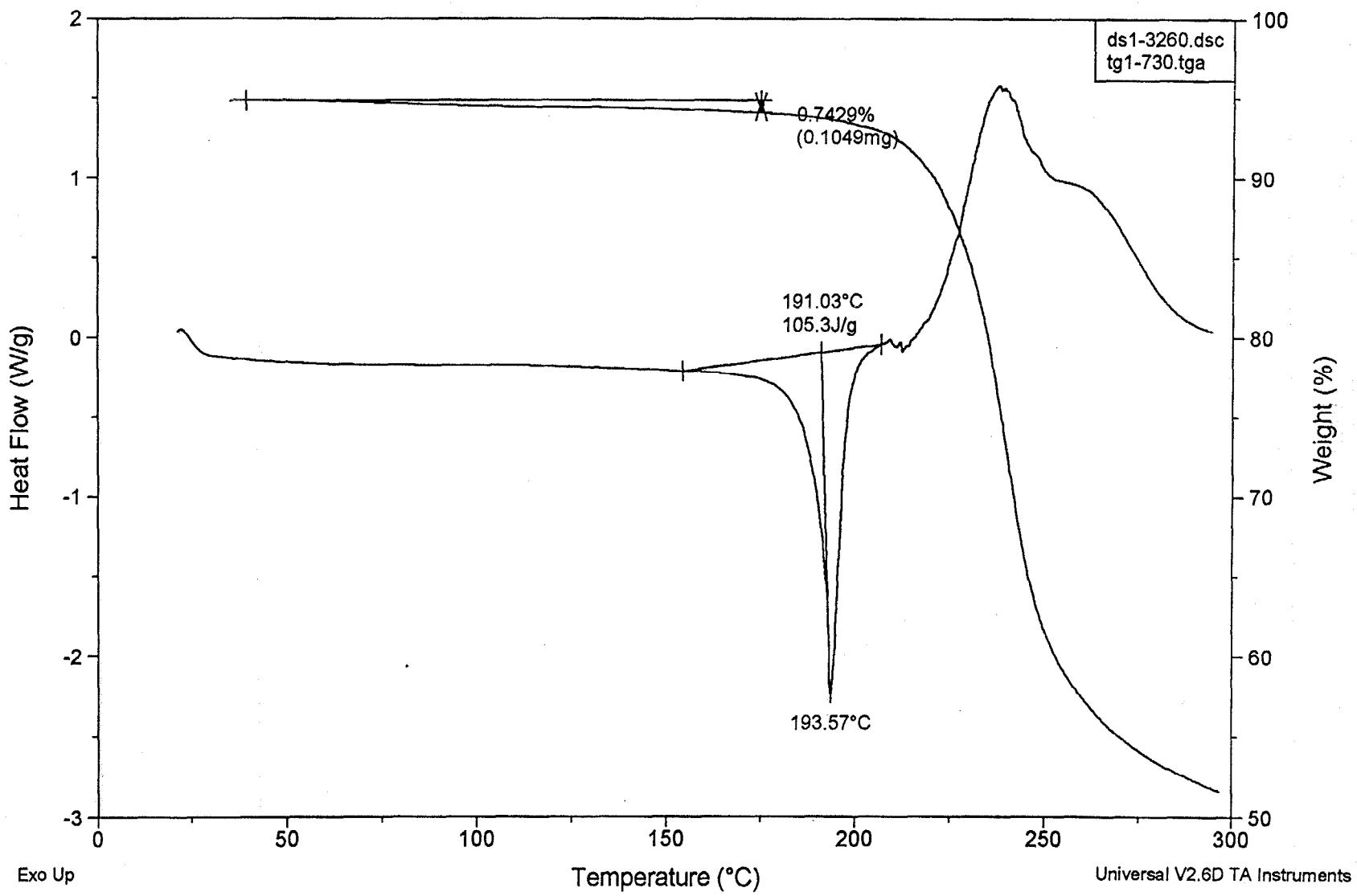












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## Sample Name: cefuroxime

Sample ID: 391-30-01

Lot #:

Notebook Reference: 424-03

Operator: SL

Sample Preparation: micro cup

Notes: amorphous A

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\rramni1\1D\1Data\Spectral\Cefuroxime\3913001ir.SPA

## Acquisition Parameters

Collection time: Wed Aug 30 17:40:15 2000

Number of sample scans: 128

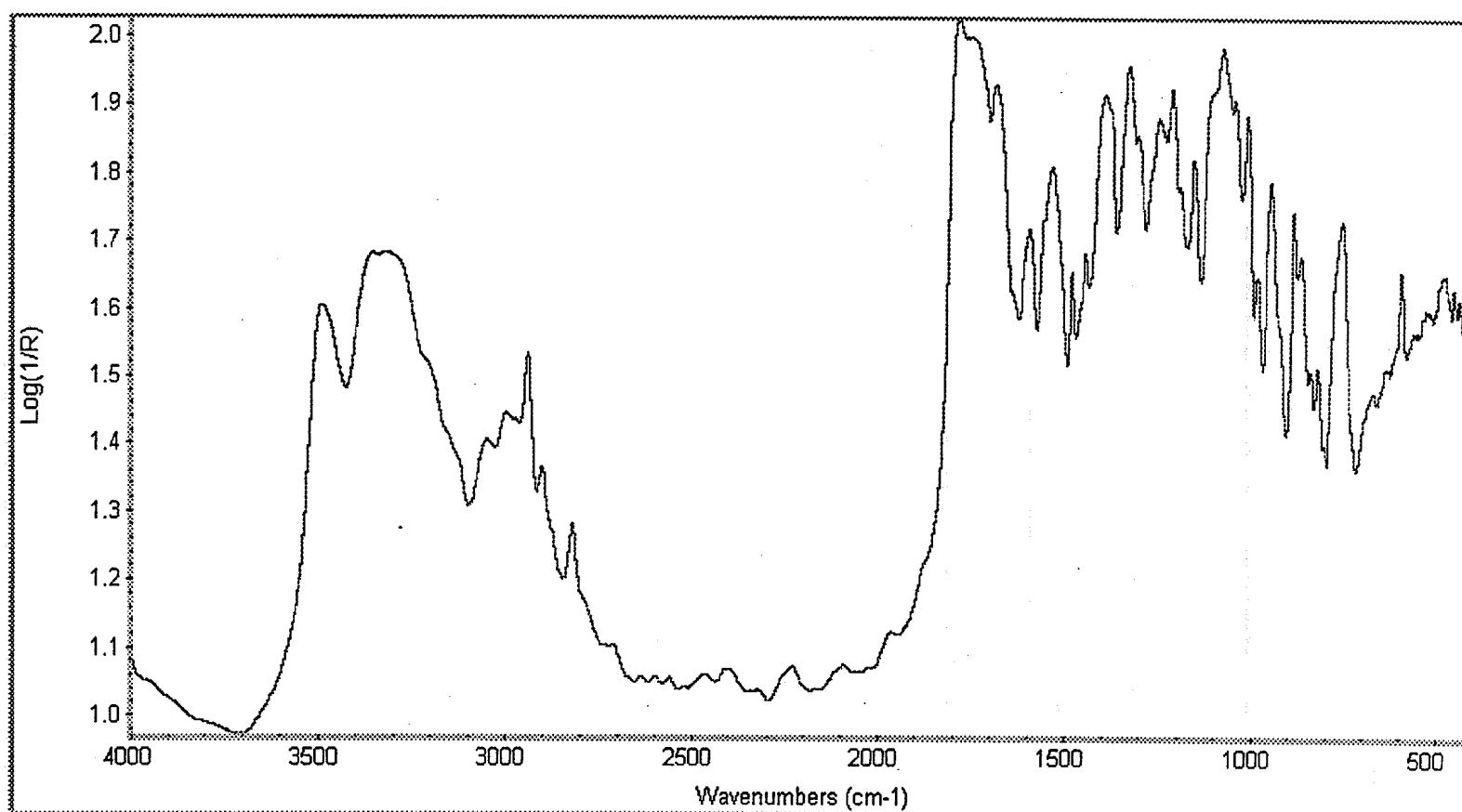
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

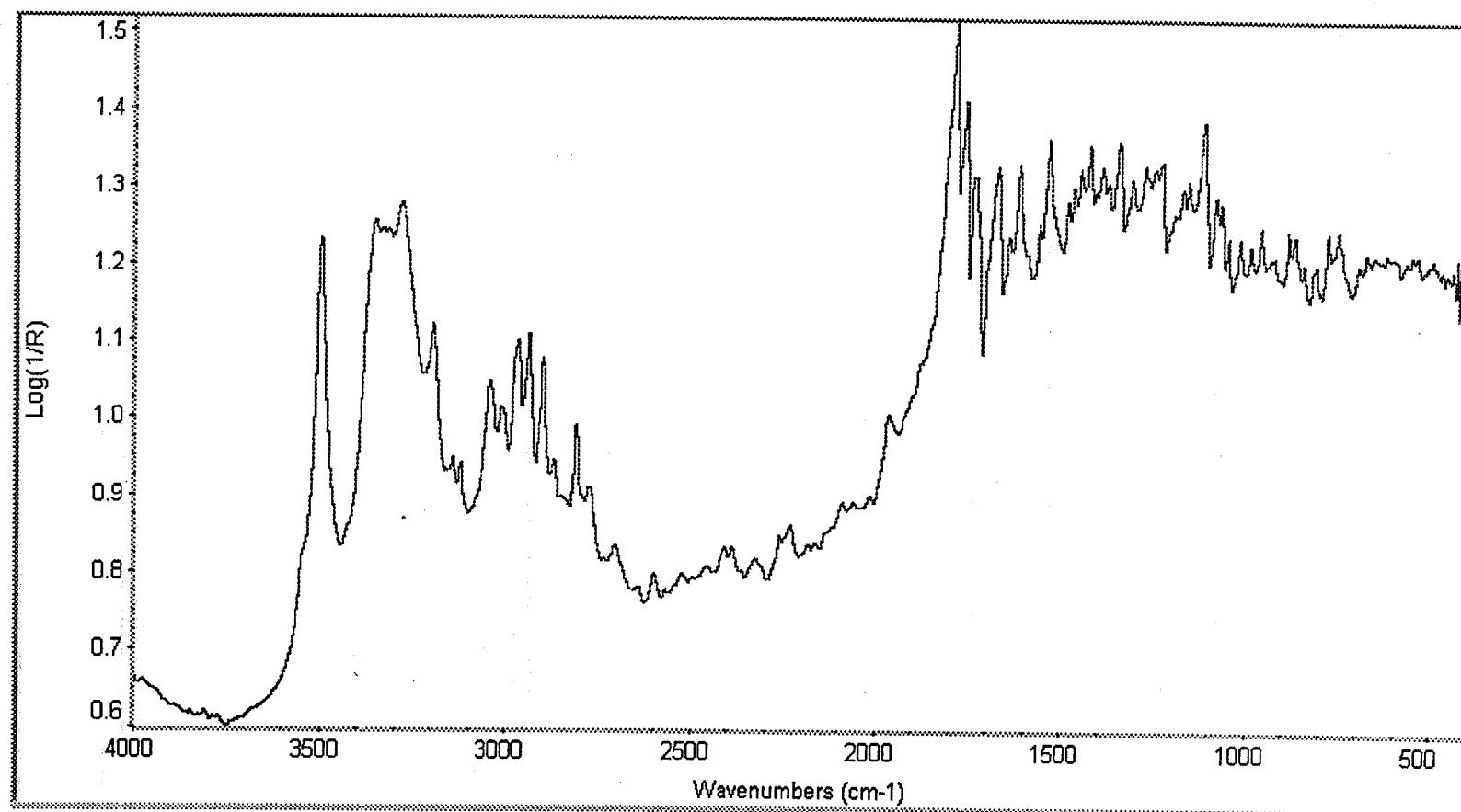
cefuroxime axetil Isomer A SSCI#9545

**IR Spectrum, Nicolet model 860 FT-IR**

Filename: \\rramni11D\\Data\\Spectral\\Cefuroxime9545ir.SPA

**Acquisition Parameters**

Collection time: Wed Jul 05 08:50:21 2000  
Number of sample scans: 256  
Number of background scans: 256  
Resolution: 4.000  
Sample gain: 8.0  
Mirror velocity: 0.6329  
Aperture: 100.00



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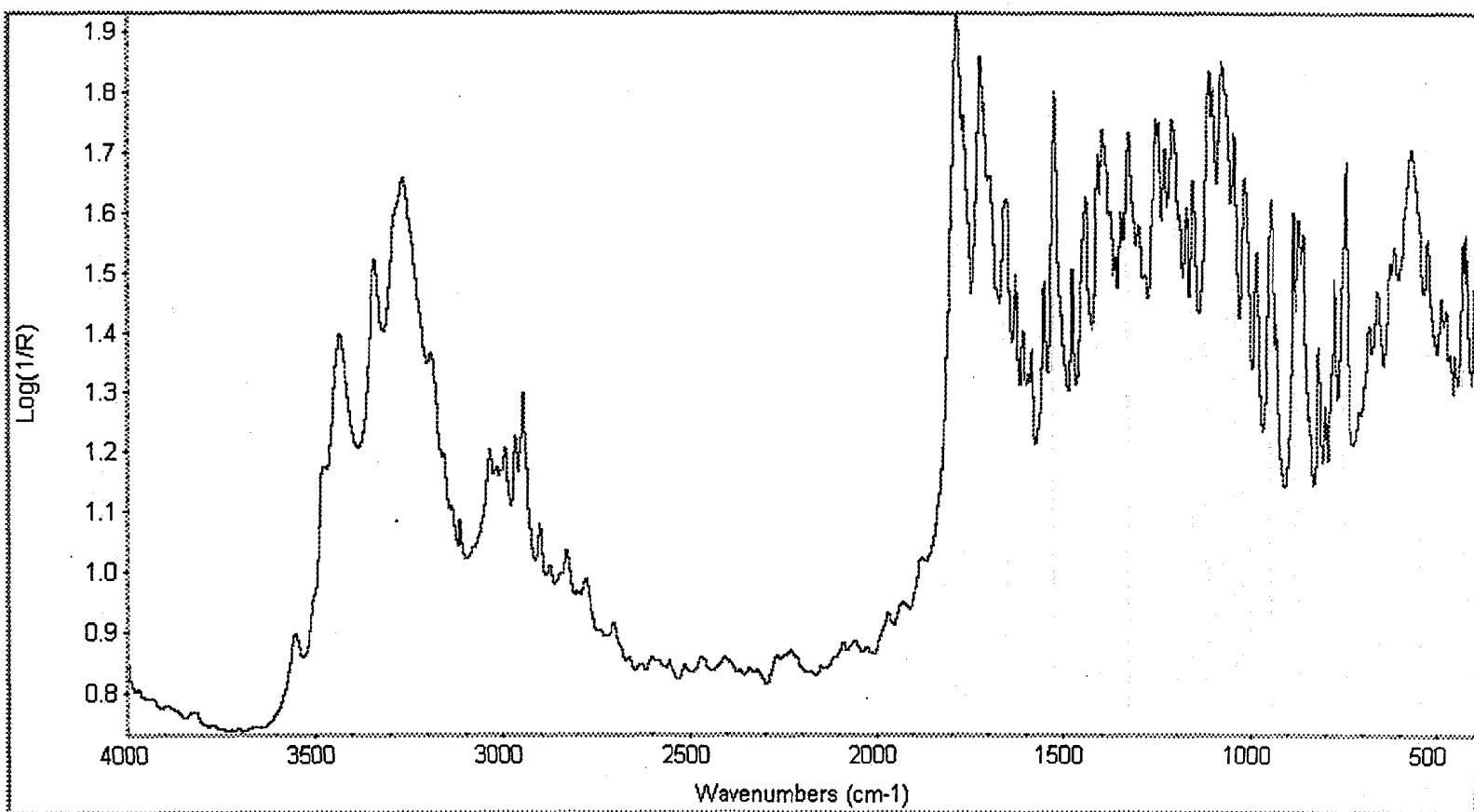
Cefuroxime Axetil Isomer A, THF SC

**IR Spectrum, Nicolet model 860 FT-IR**

Filename: \\rramni1\1D\1Data\Spectra\Cefuroxime\3911103ir.spa

**Acquisition Parameters**

Collection time: Fri Jul 28 11:42:00 2000  
Number of sample scans: 256  
Number of background scans: 256  
Resolution: 4.000  
Sample gain: 8.0  
Mirror velocity: 0.6329  
Aperture: 100.00



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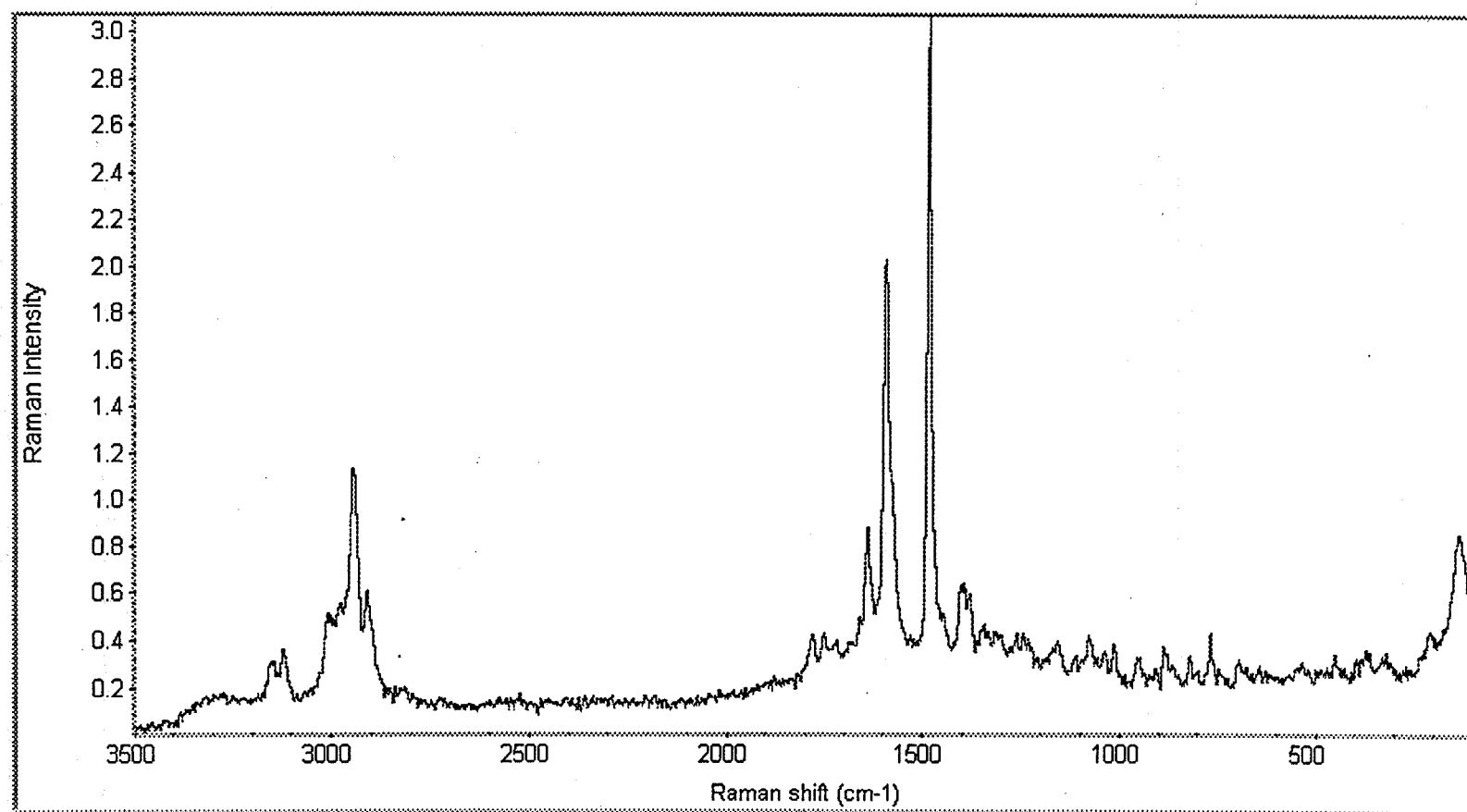
39130-01 amorph A In Wig-L-Bug

**Raman Spectrum, Nicolet model 860 FT-Raman**

Filename: \\rramn\\1D\\Data\\Spectral\\Cefuroxime\\3913001rm.SPA

**Acquisition Parameters**

Collection time: Wed Aug 30 16:17:37 2000  
Number of sample scans: 128  
Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3165  
Aperture: 59.00



**SSCI, Inc.**

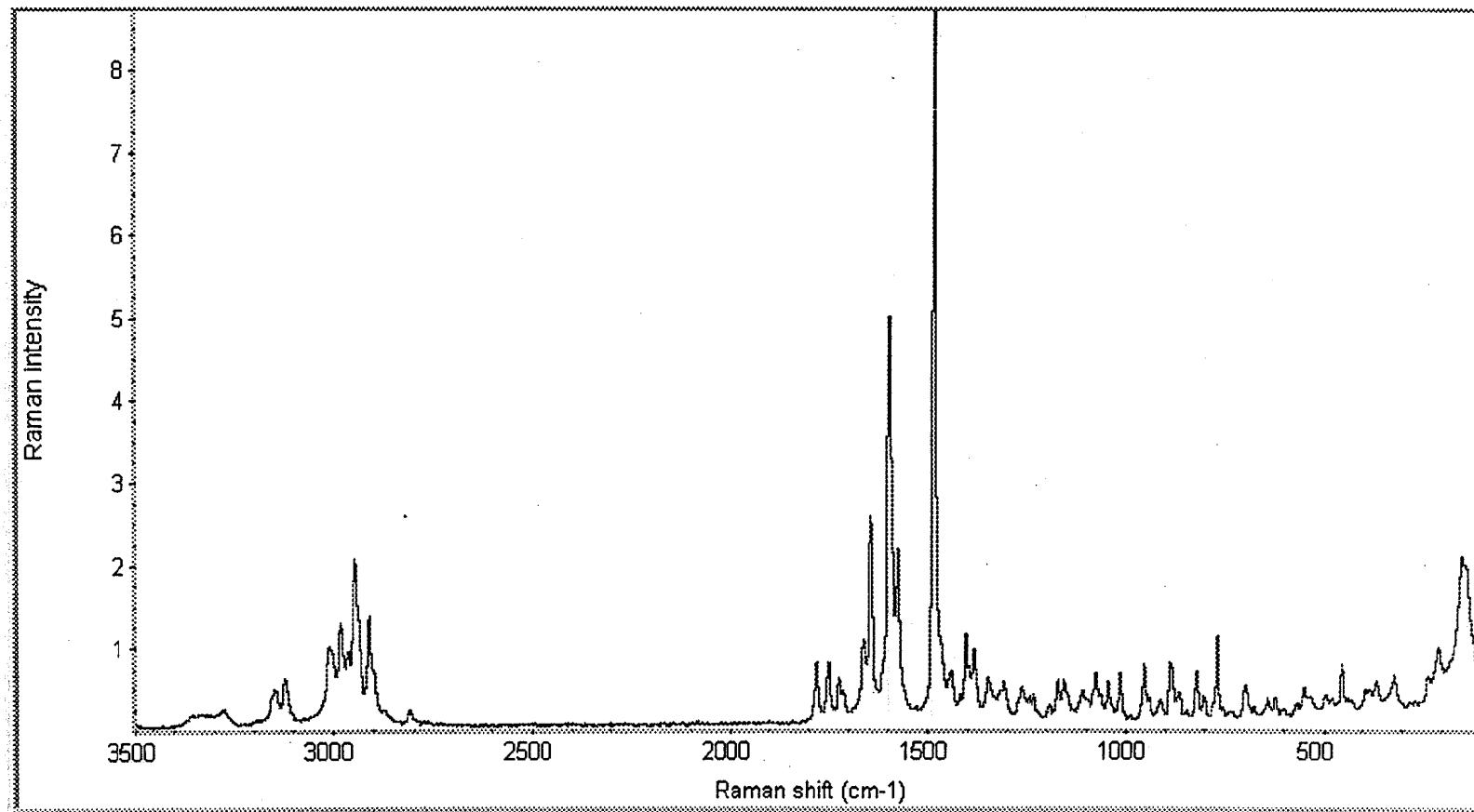
1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

**Raman Spectrum, Nicolet model 860 FT-Raman  
cefuroxime axetil isomer A SSCI#954J**

Filename: \\rramni1\1D\Data\Spectra\Cefuroxime9545rm.SPA

**Acquisition Parameters**

Collection time: Wed Jul 05 17:33:21 2000  
Number of sample scans: 256  
Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3166  
Aperture: 59.00



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Cefuroxime Axetil Isomer A, THF SC

Raman Spectrum, Nicolet model 860 FT-Raman

Filename: \\rramni1\1D\Data\Spectra\Cefuroxime\3911103rm.spa

Acquisition Parameters

Collection time: Fri Jul 28 15:29:45 2000

Number of sample scans: 256

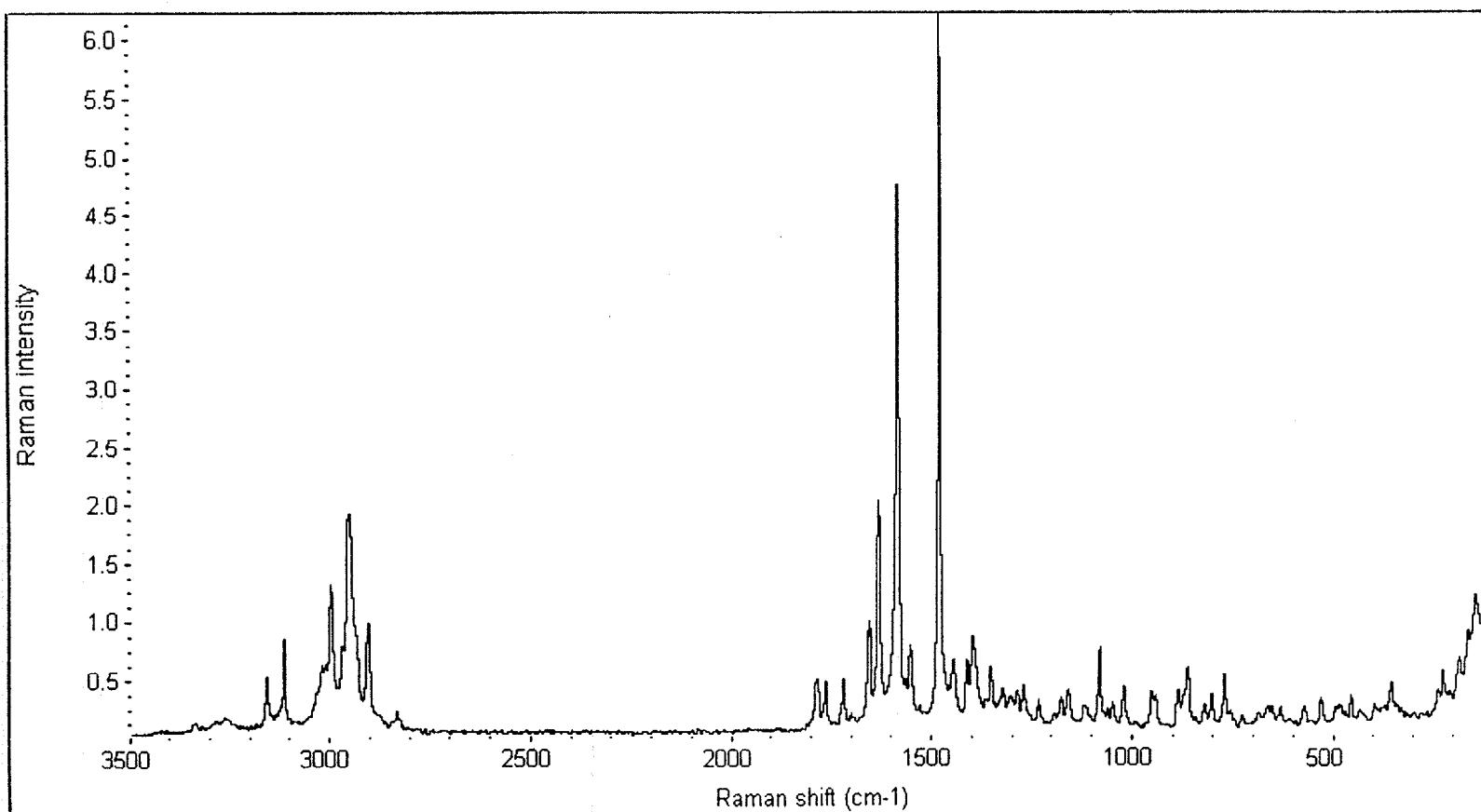
Number of background scans: 0

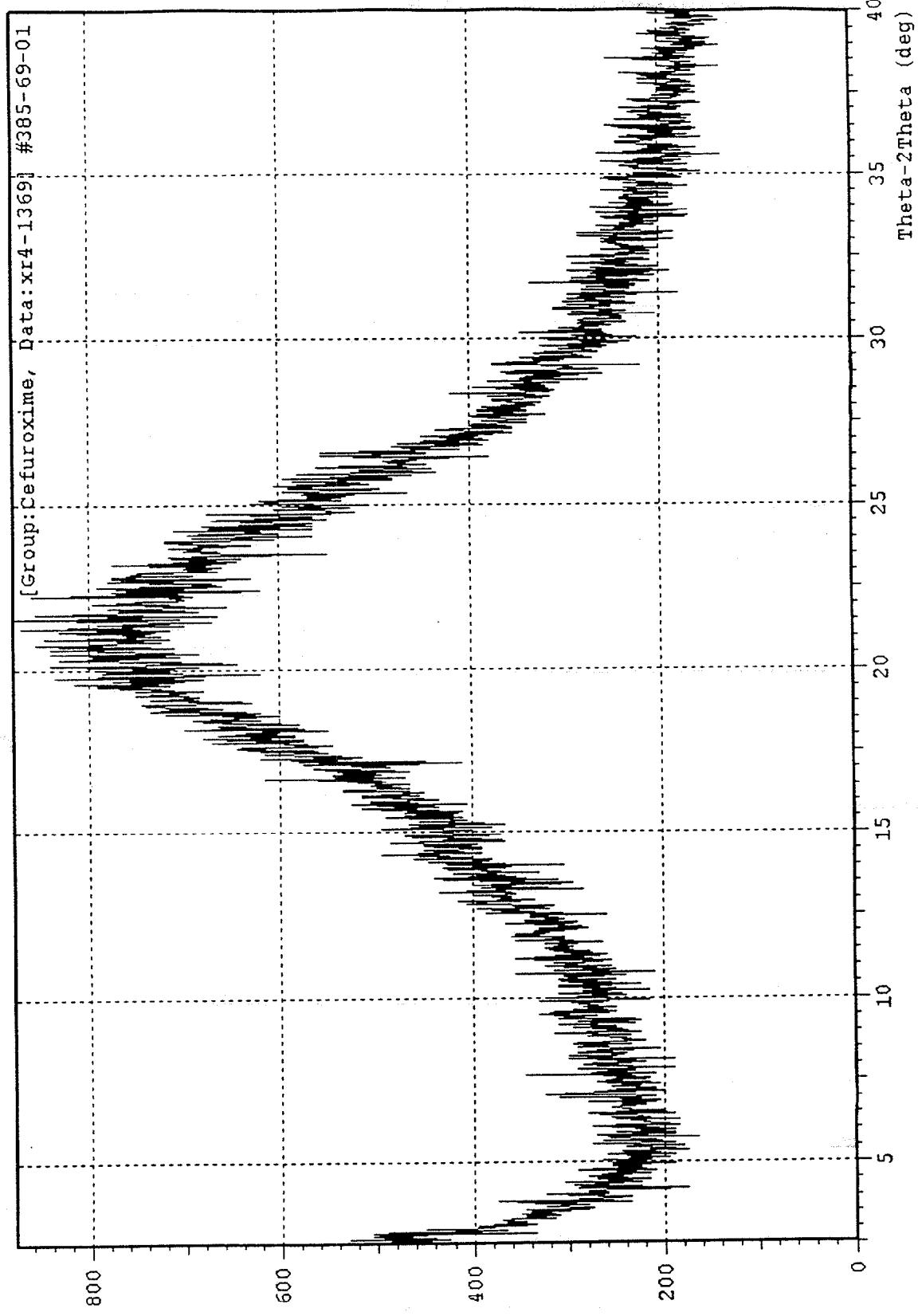
Resolution: 4.000

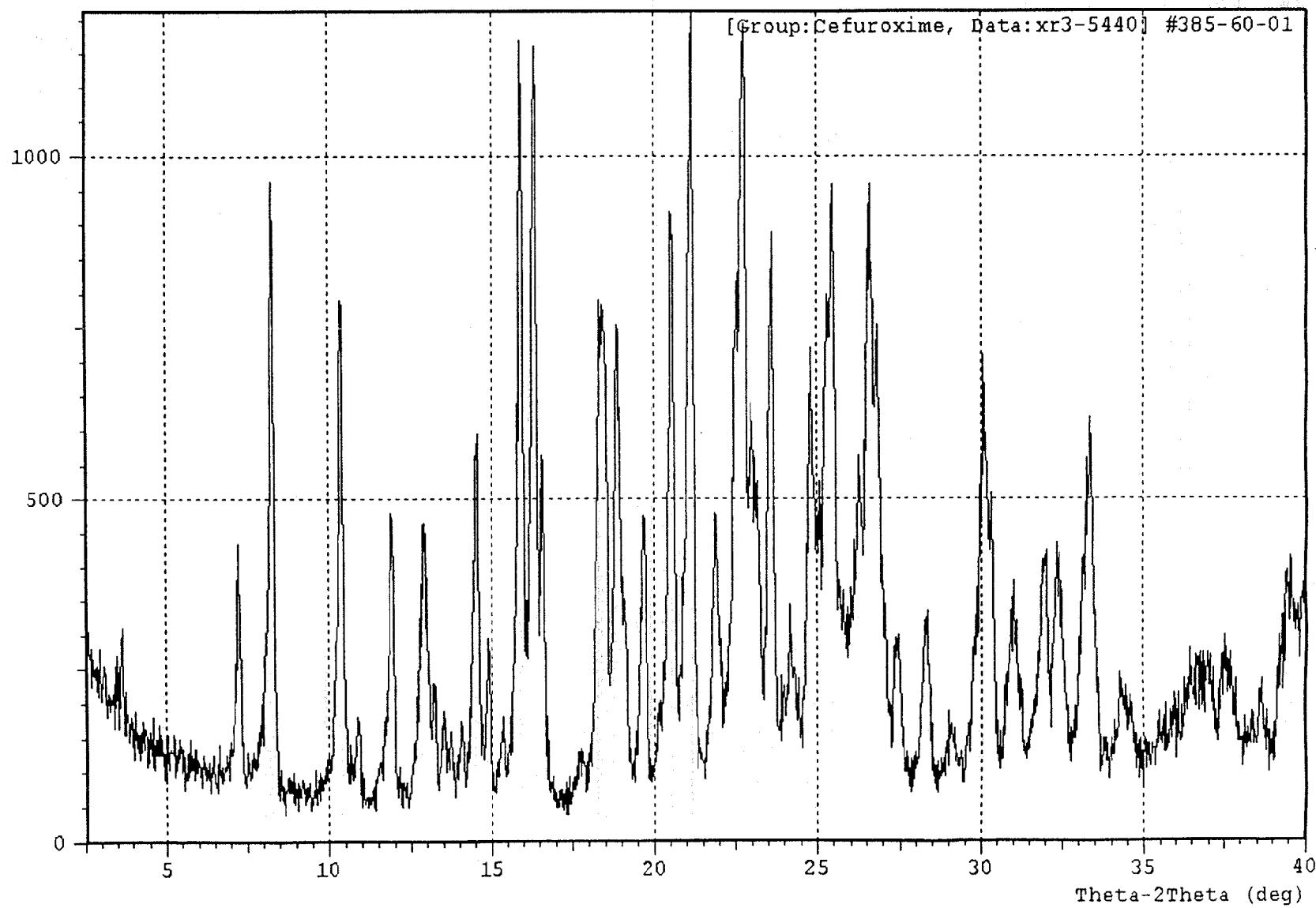
Sample gain: 64.0

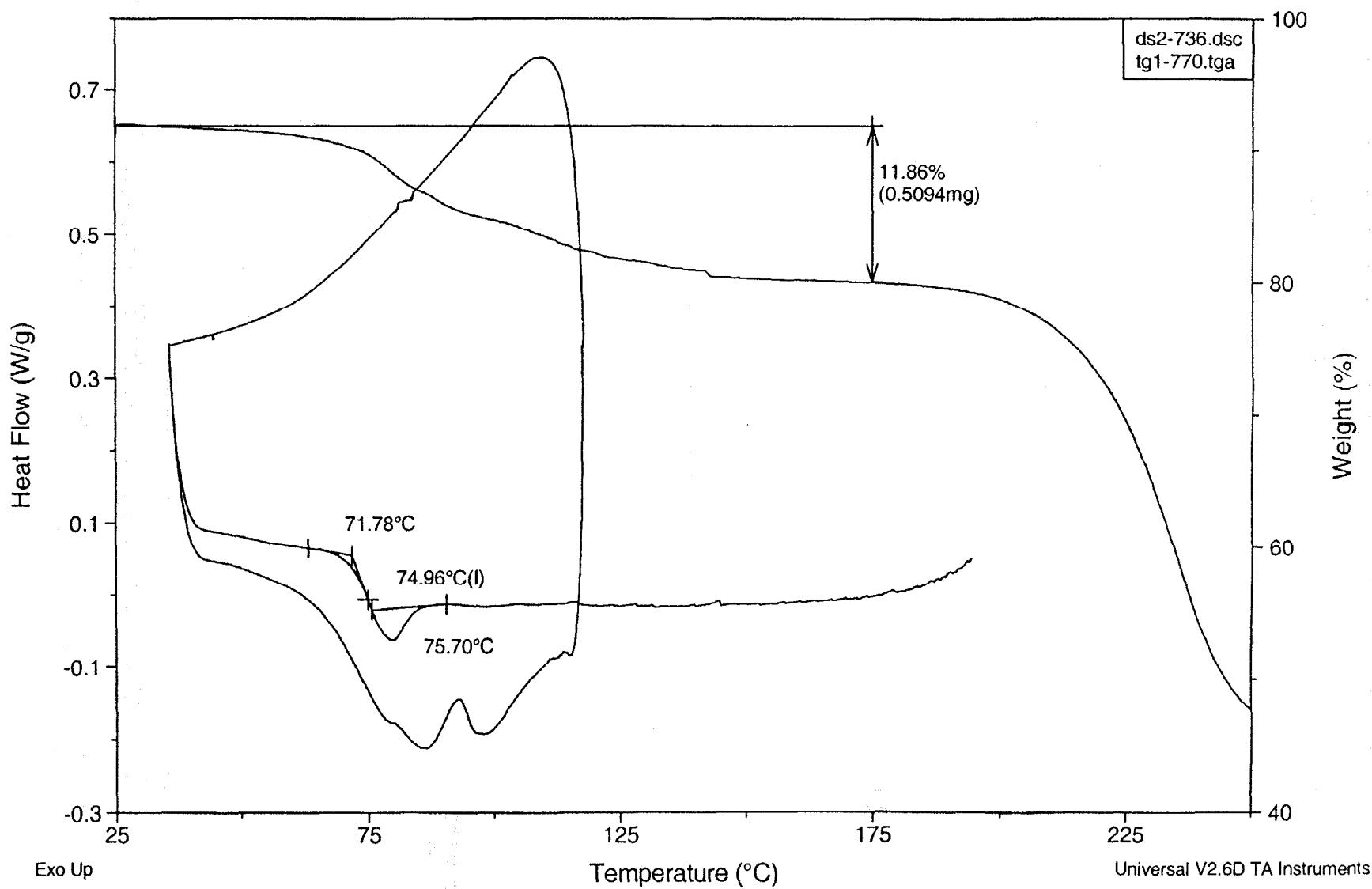
Mirror velocity: 0.3165

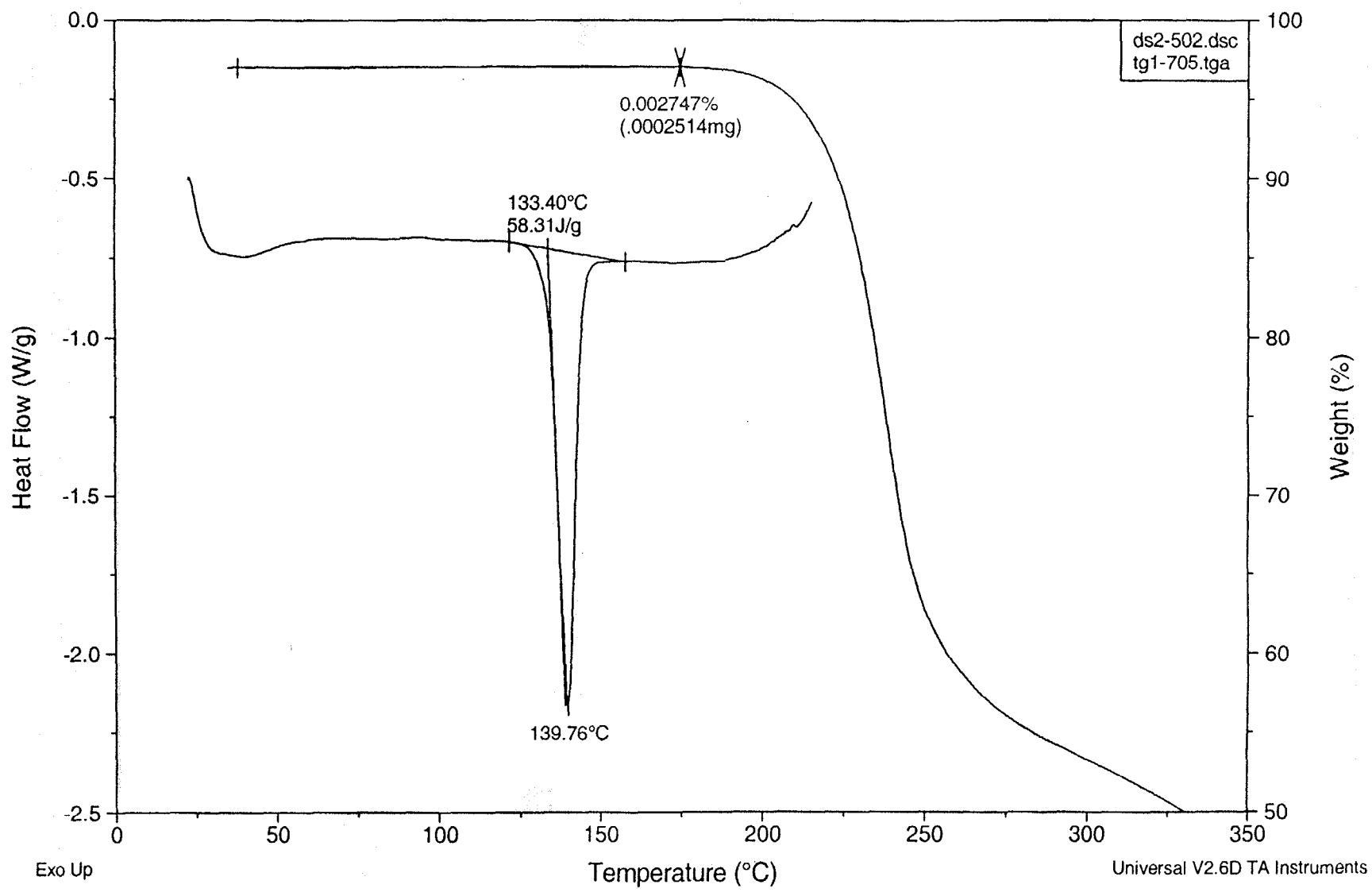
Aperture: 59.00

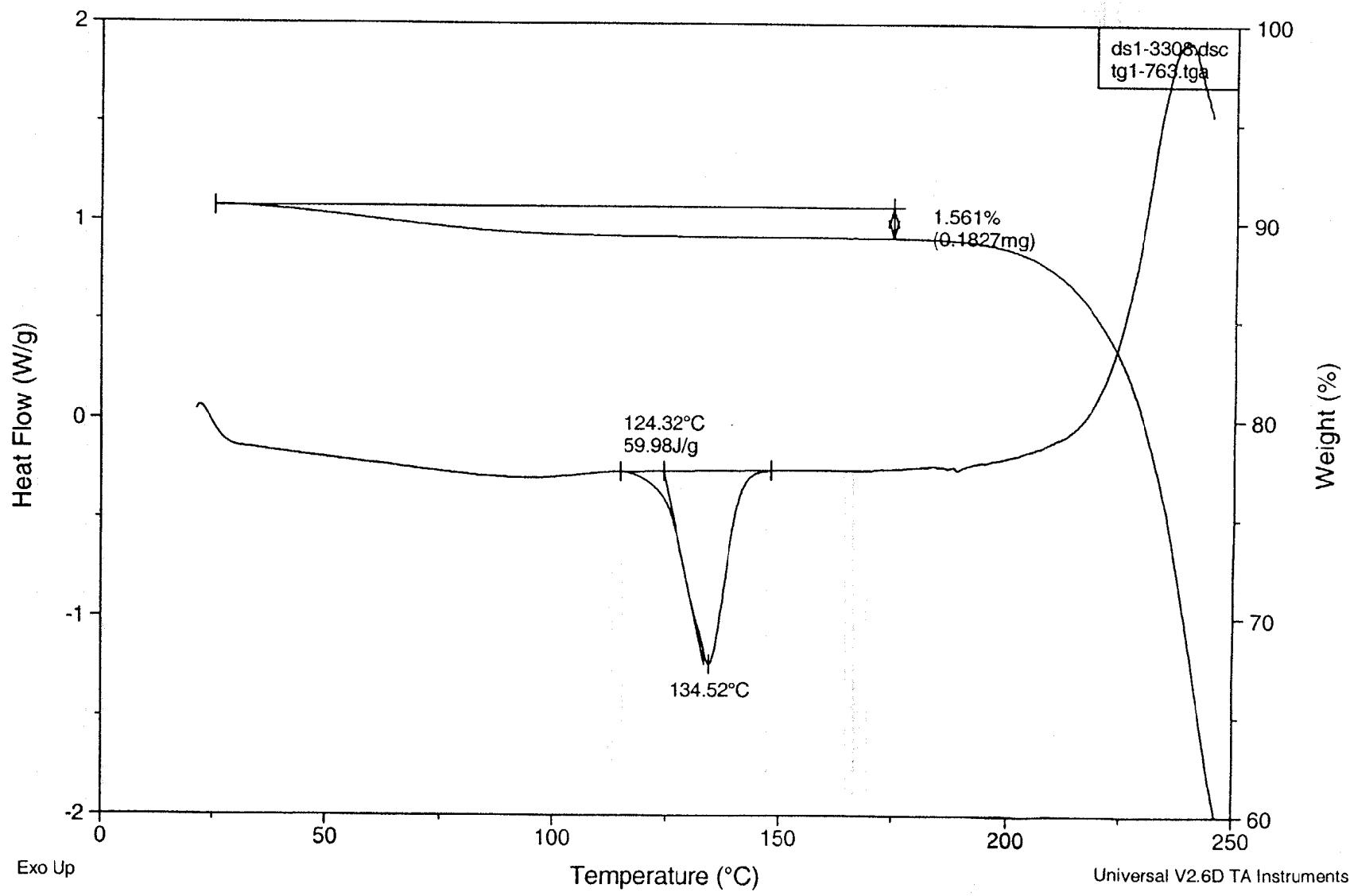












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## Sample Name: cefuroxime

Sample ID: 385-69-01

Lot #:

Notebook Reference: 424-03

Operator: SL

Sample Preparation: microcup

Notes: B(I) in THF/Hexanes crash

## IR Spectrum, Nicolet model 860 FT-IR

## Acquisition Parameters

Collection time: Wed Aug 30 17:51:05 2000

Number of sample scans: 128

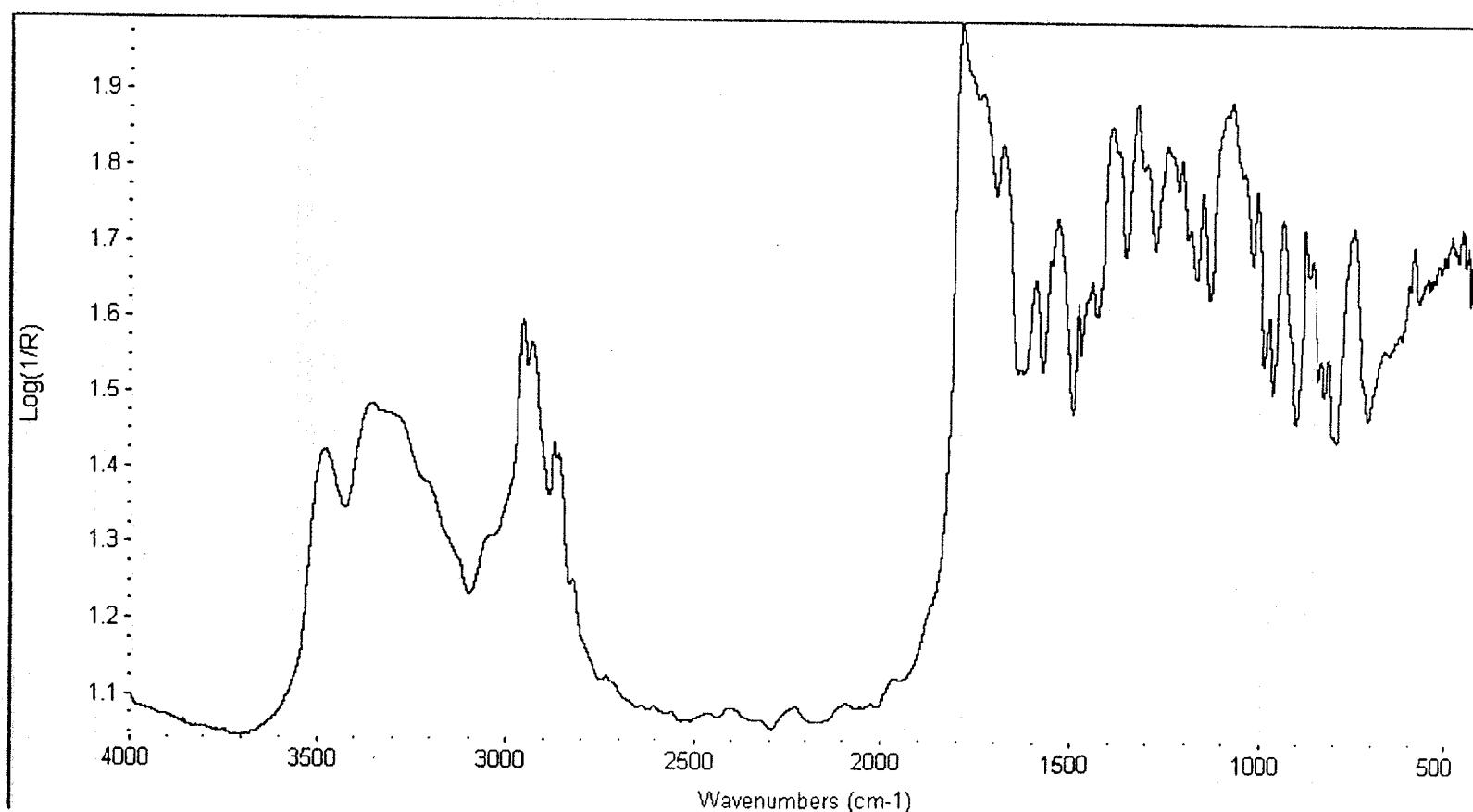
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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## Sample Name: cefuroxime

Sample ID: 9547

Lot #: MRH-0196-120A

Notebook Reference: 424-03

Operator: SL

Sample Preparation: micro cup

Notes: as received

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\rramni1\1D\Data\Spectra\Cefuroxime\9547ir.SPA

## Acquisition Parameters

Collection time: Wed Aug 30 17:25:50 2000

Number of sample scans: 128

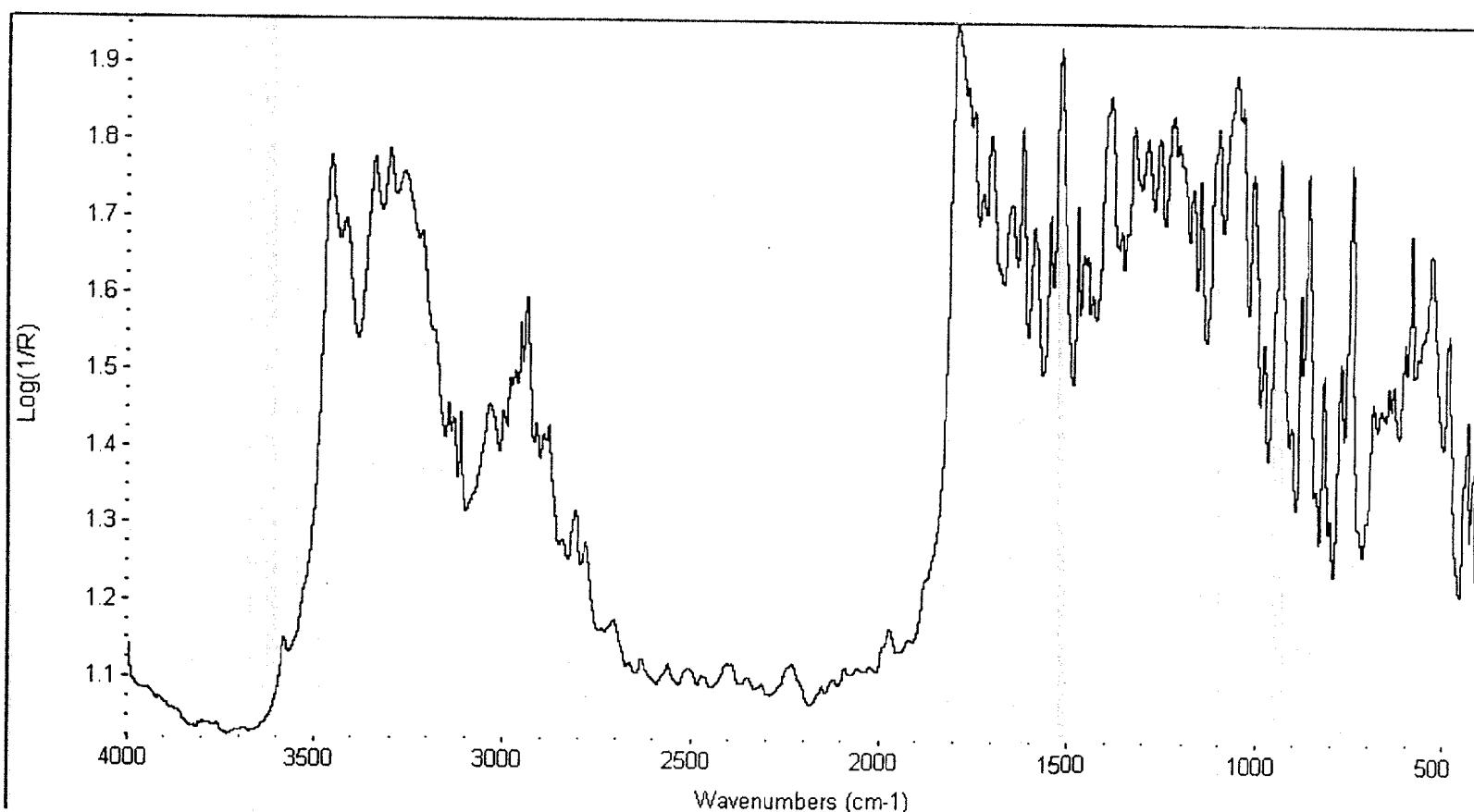
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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## Sample Name: cefuroxime

Sample ID: 385-60-01

Lot #:

Notebook Reference: 395-76

Operator: SL

Sample Preparation: micro cup

Notes: 95% B H<sub>2</sub>O slurry

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\rramni1\DI\DATA\Spectra\Cefuroxime\3856001ir.SPA

## Acquisition Parameters

Collection time: Fri Aug 18 16:36:38 2000

Number of sample scans: 128

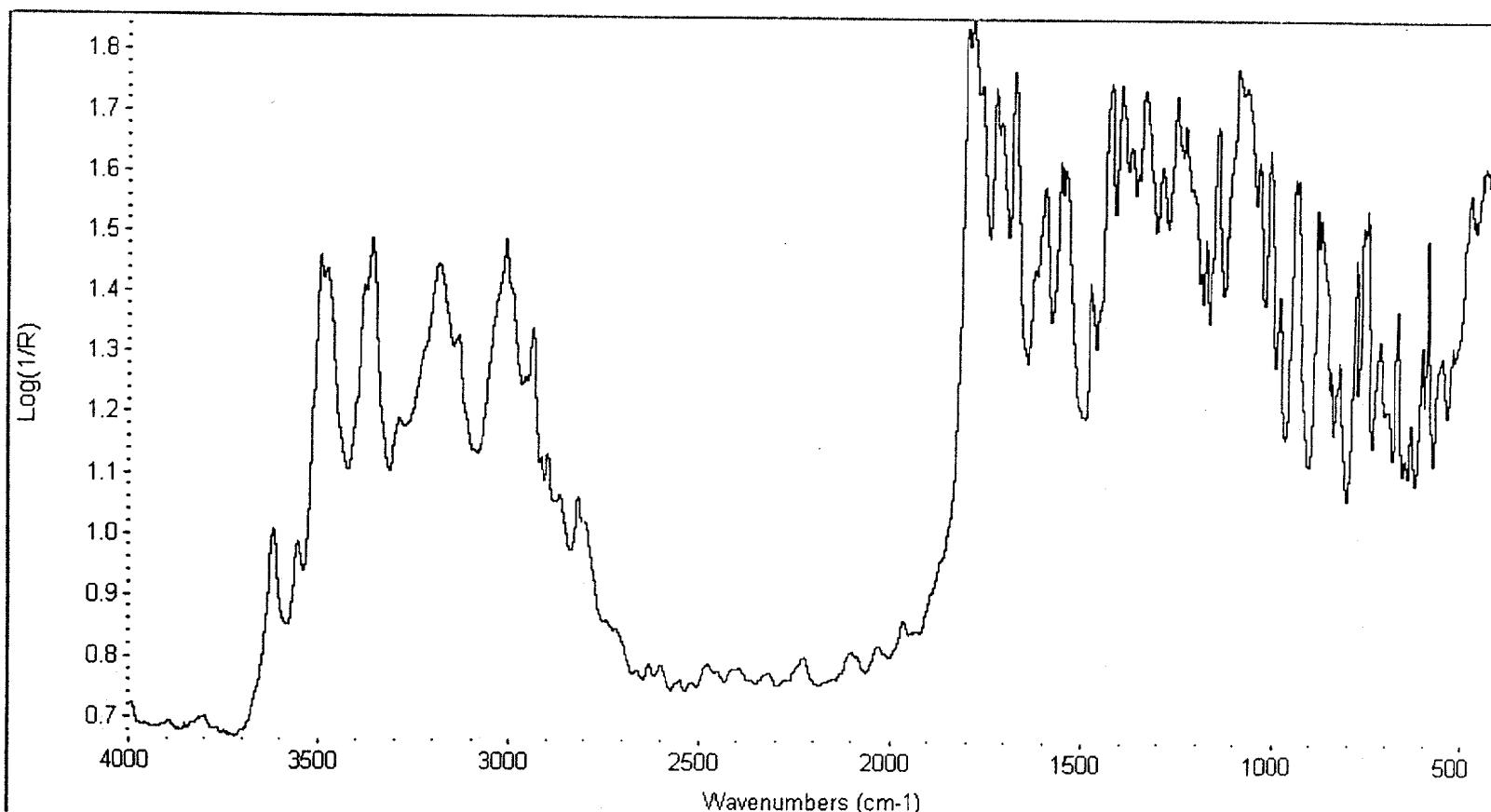
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

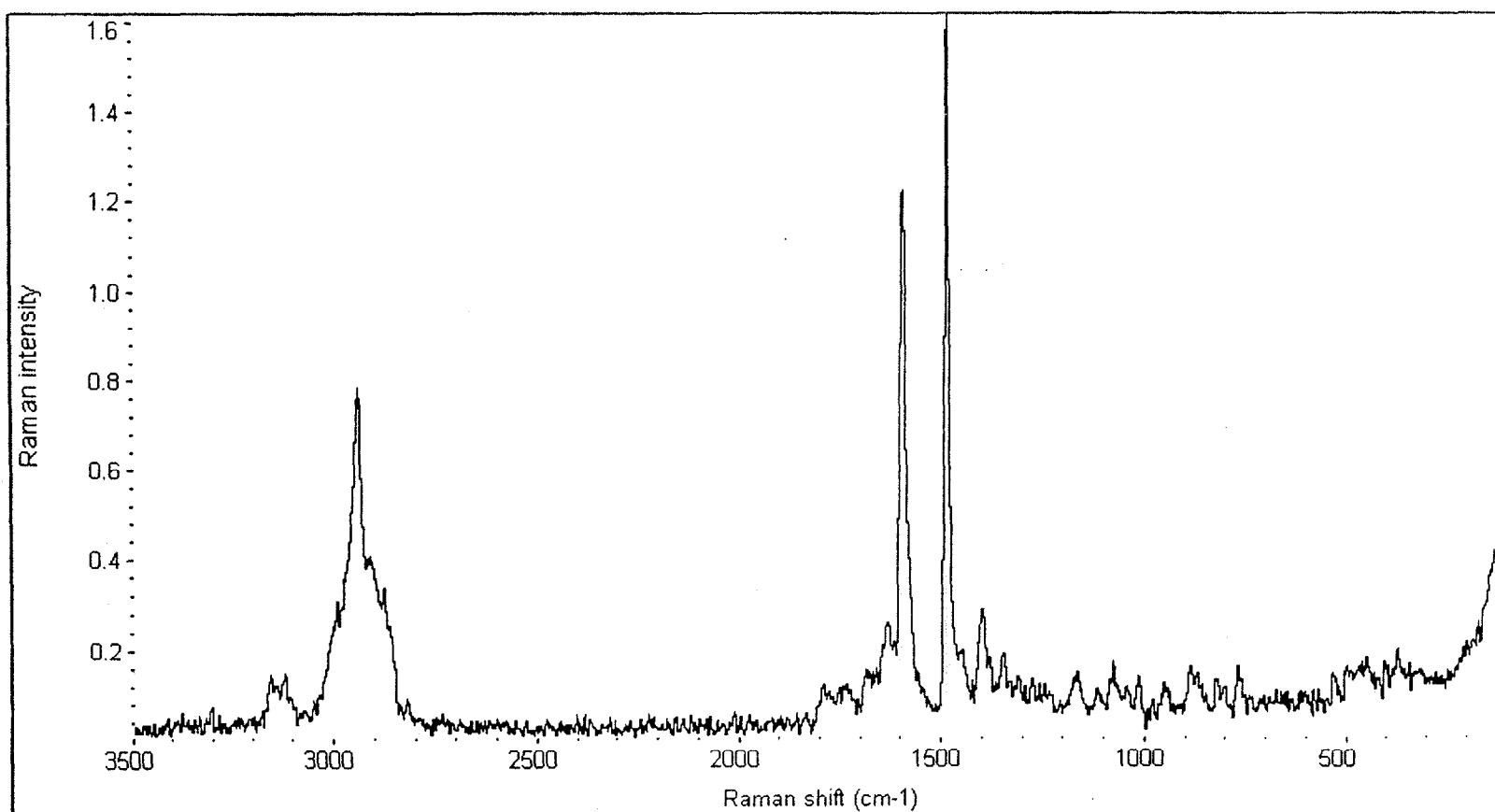
385-69-01; B in THF/Hexanes crash

## Raman Spectrum, Nicolet model 860 FT-Raman

Filename: W:\raman\11D\Data\Spectral\Cefuroxime\3856901rm.SPA

### Acquisition Parameters

Collection time: Tue Aug 22 15:36:24 2000  
Number of sample scans: 128  
Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3165  
Aperture: 59.00



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#9547 as received B(I)

## Raman Spectrum, Nicolet model 860 FT-Raman

Filename: \\rramni1\D\Data\Spectra\Cefuroxime\9547rm.SPA

### Acquisition Parameters

Collection time: Wed Aug 30 16:48:04 2000

Number of sample scans: 128

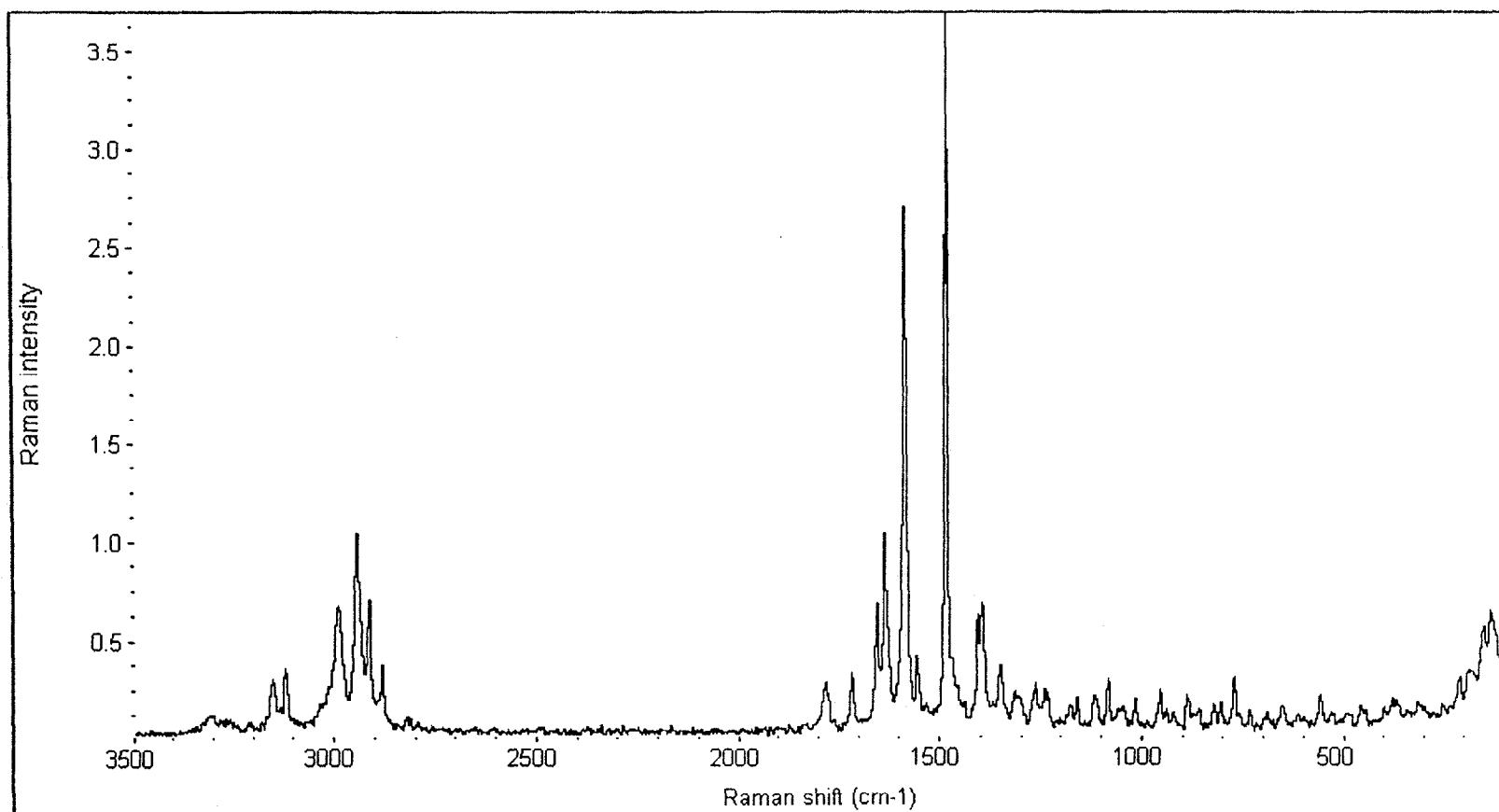
Number of background scans: 0

Resolution: 4.000

Sample gain: 64.0

Mirror velocity: 0.3165

Aperture: 59.00



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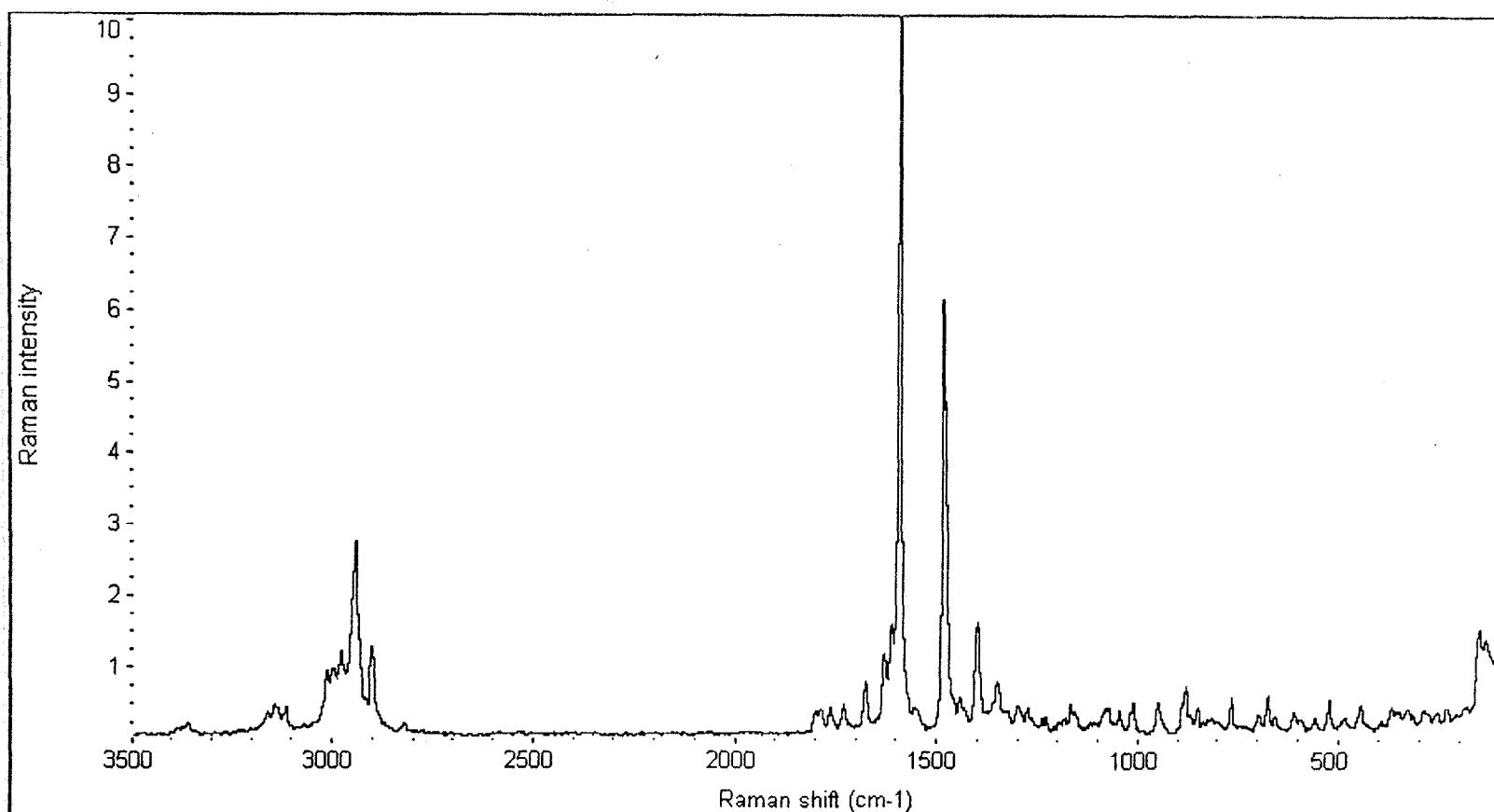
385-60-01; 75% B H<sub>2</sub>O slurry

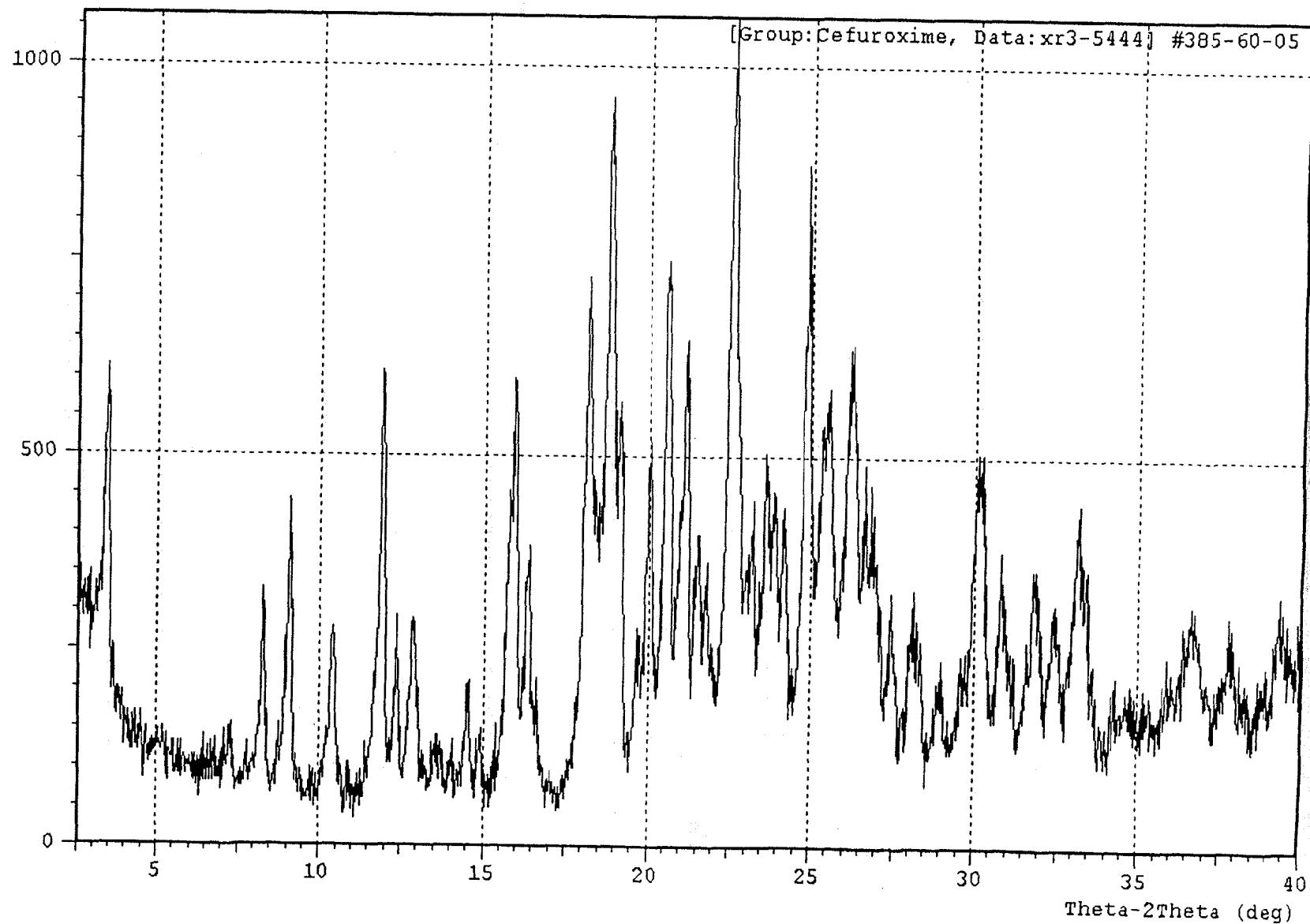
## Raman Spectrum, Nicolet model 860 FT-Raman

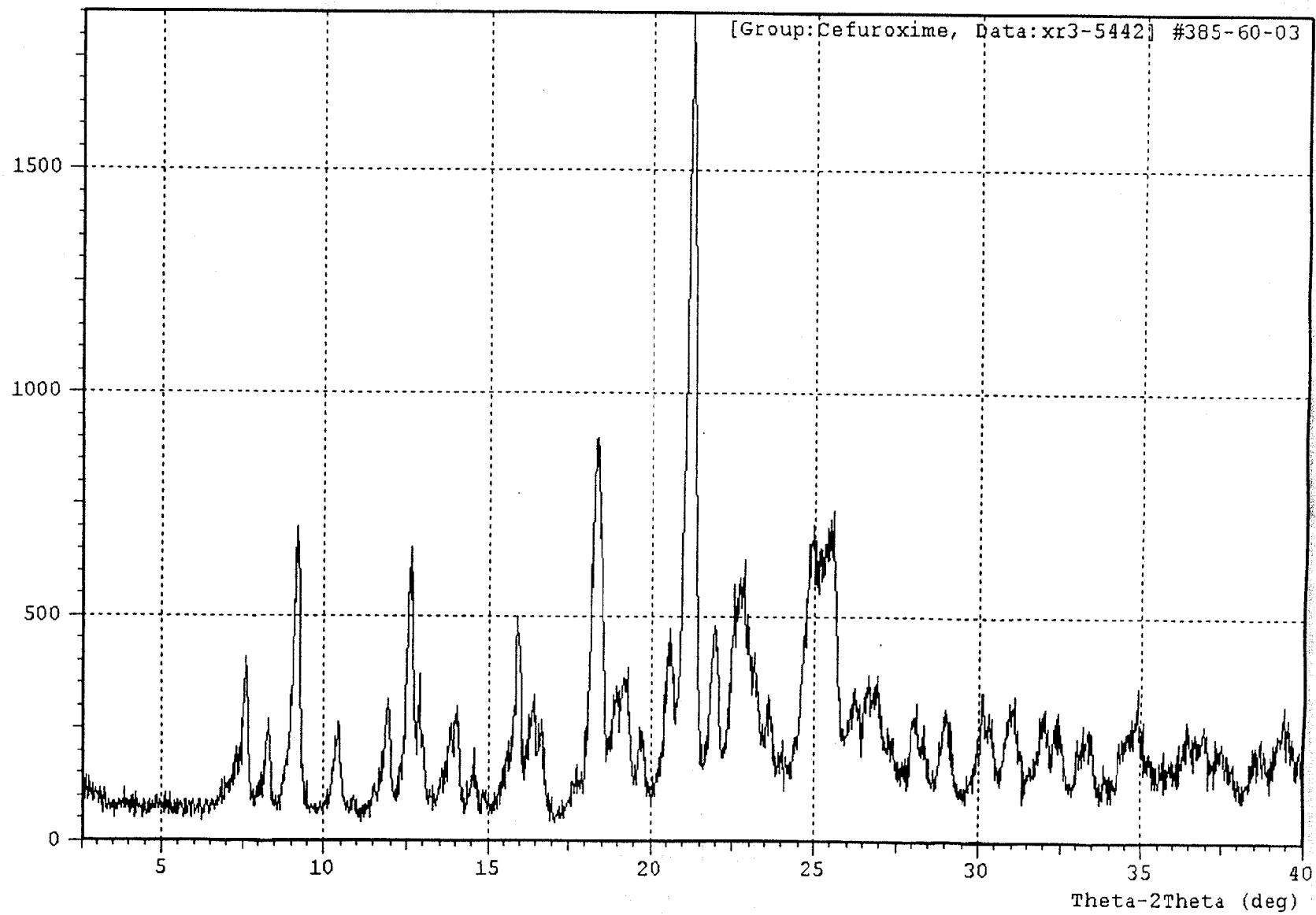
Filename: \\rramni1\D\Data\Spectra\Cefuroxime\3856001rm.spa

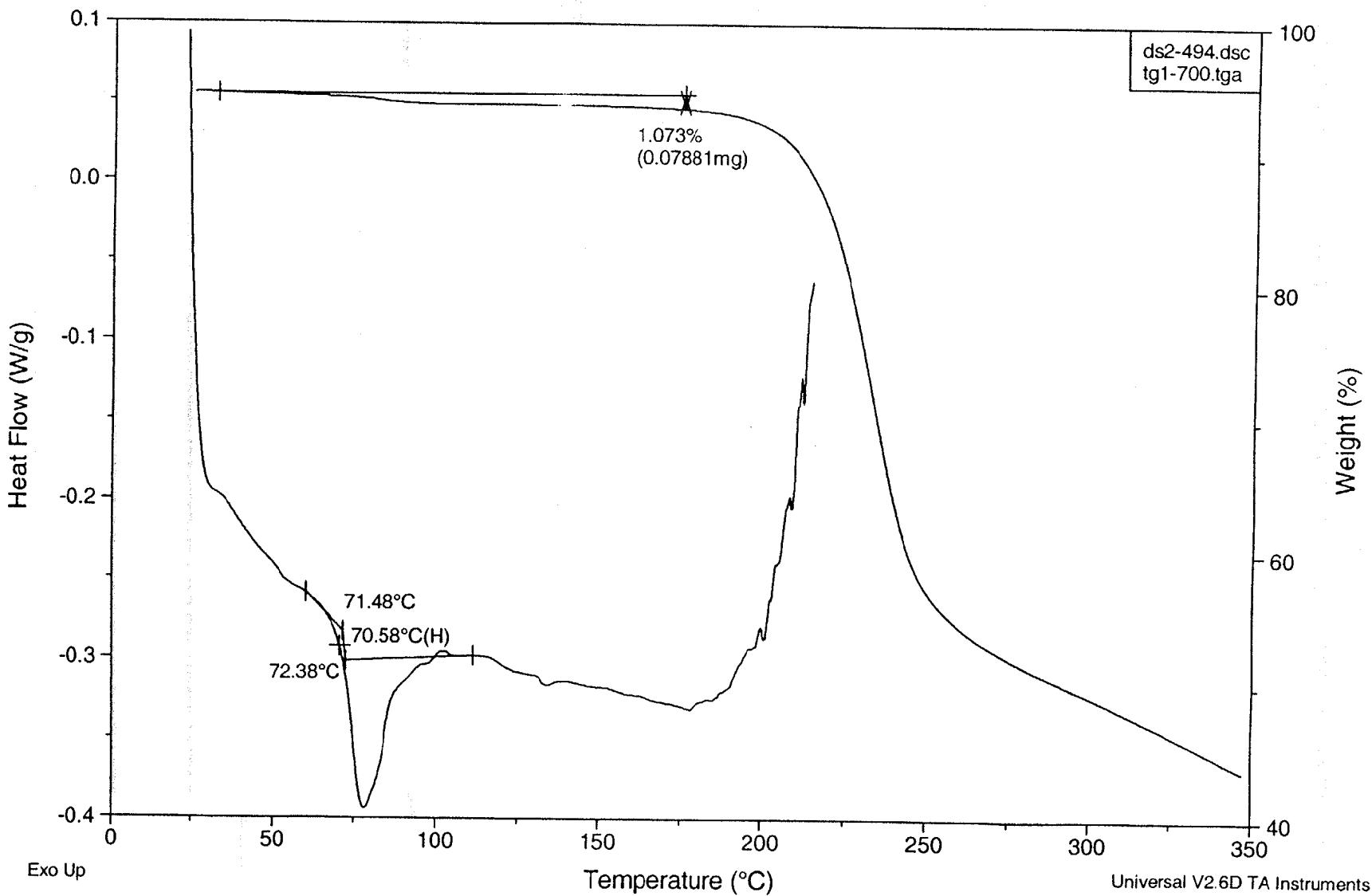
## Acquisition Parameters

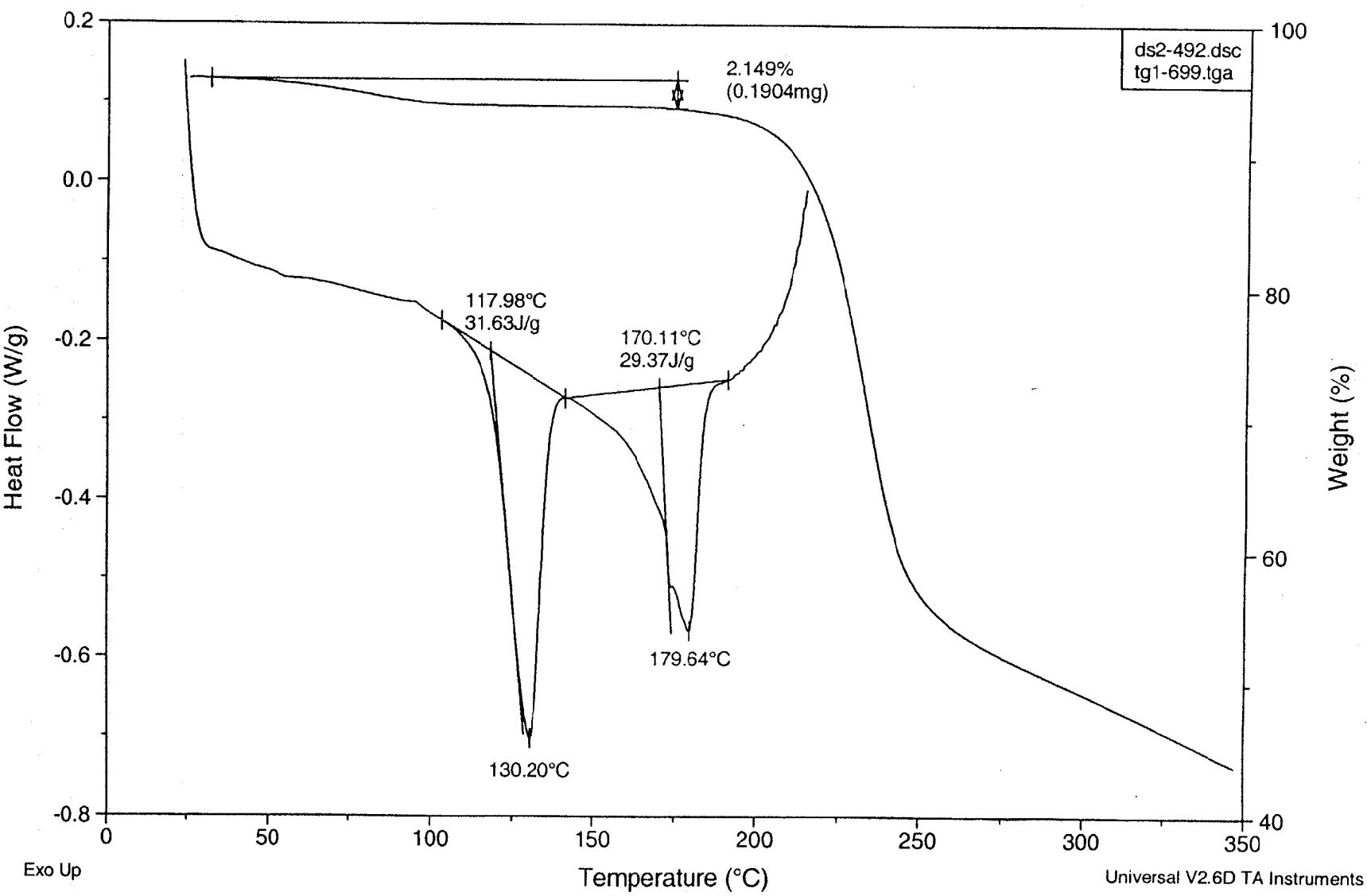
Collection time: Fri Aug 18 11:22:31 2000  
Number of sample scans: 128  
Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3165  
Aperture: 59.00

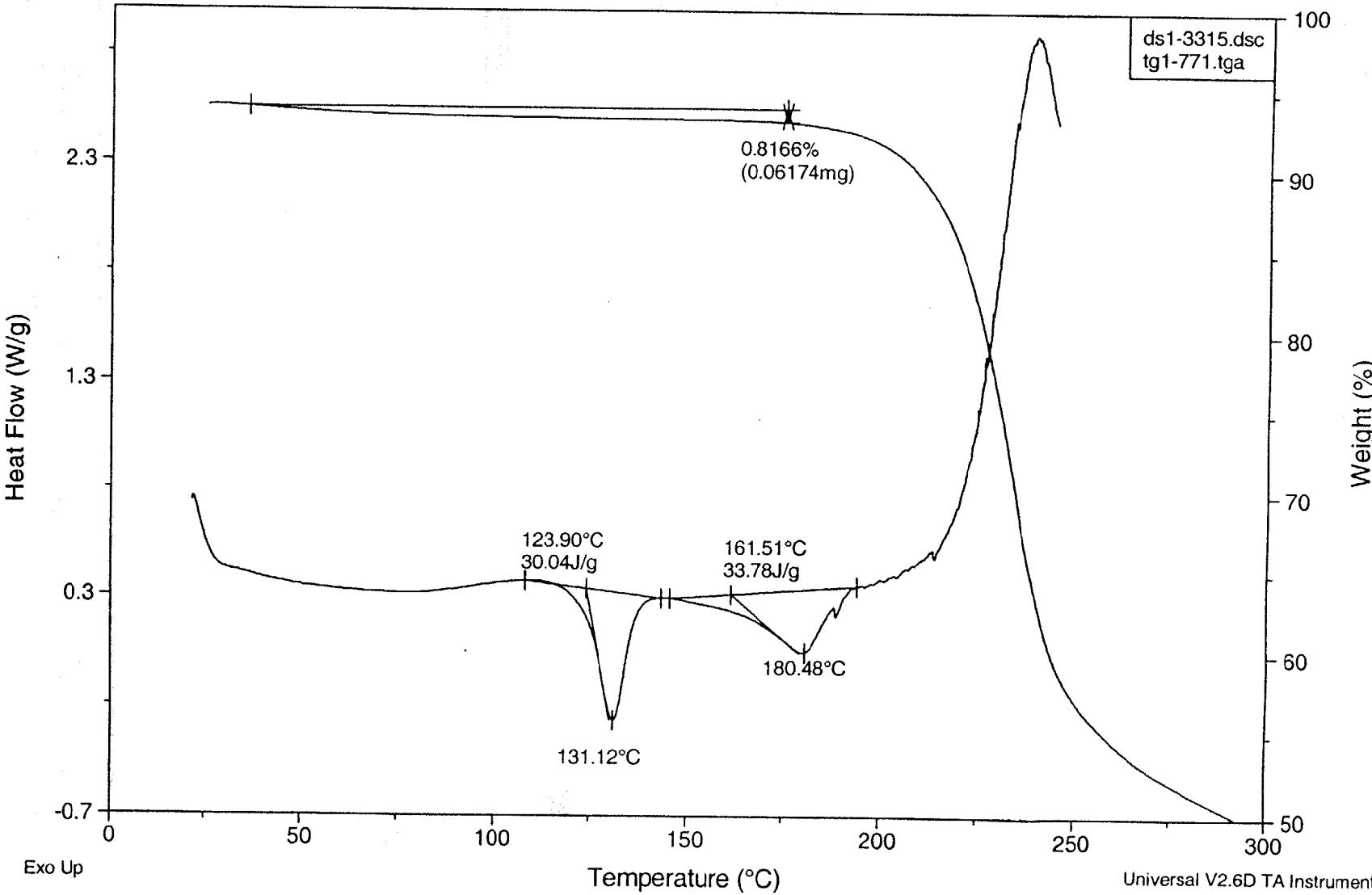


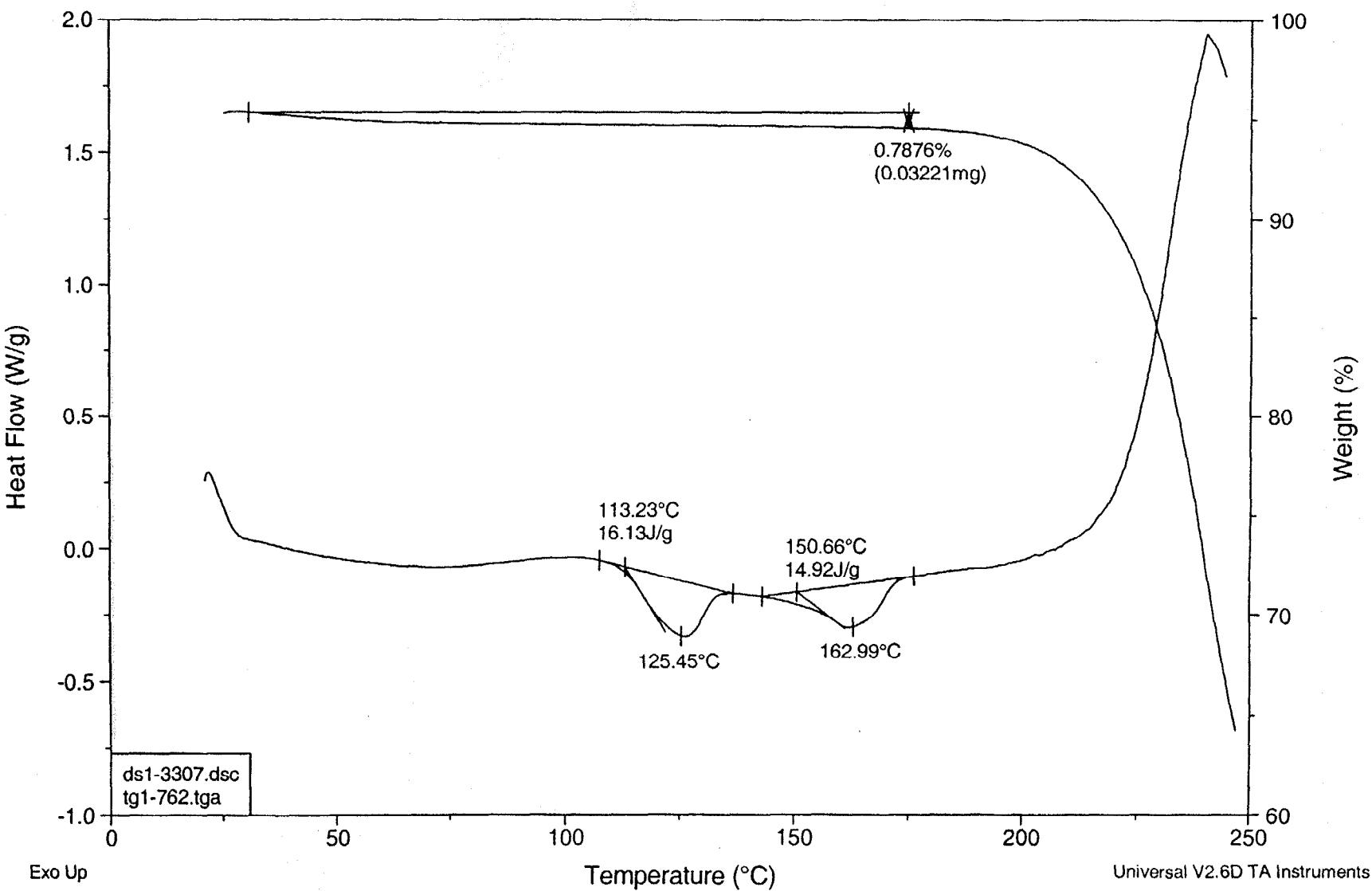












**SSCI, Inc.**

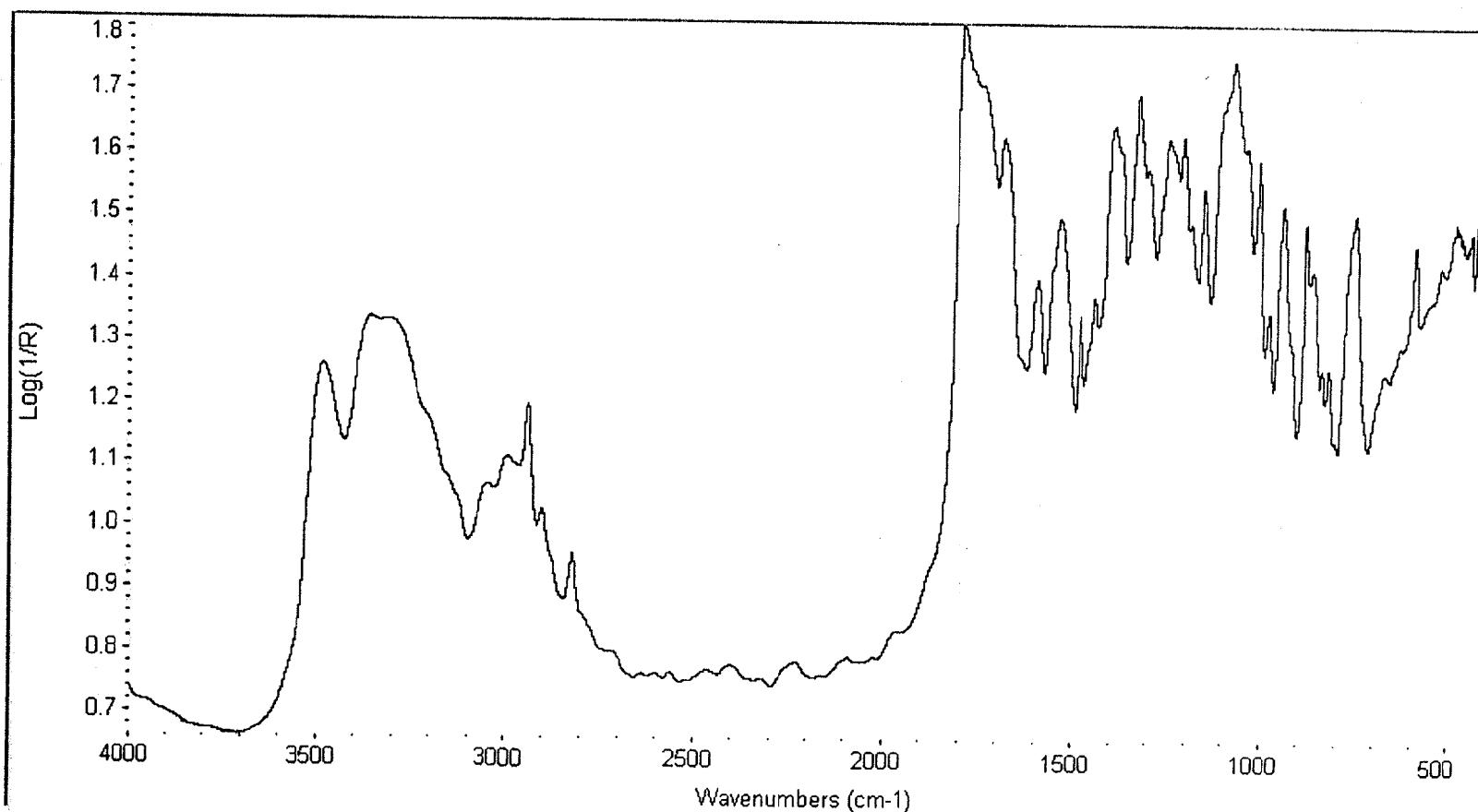
1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

**IR Spectrum, Nicolet model 860 FT-IR**  
**Cefuroxime Axetil Spray Dried; SSCI-9498**

Filename: \lrramni1\lData\Spectra\Cefuroxime\9498ir.SPA

**Acquisition Parameters**

Collection time: Fri Jun 30 15:41:16 2000  
Number of sample scans: 256  
Number of background scans: 256  
Resolution: 4.000  
Sample gain: 8.0  
Mirror velocity: 0.6329  
Aperture: 100.00



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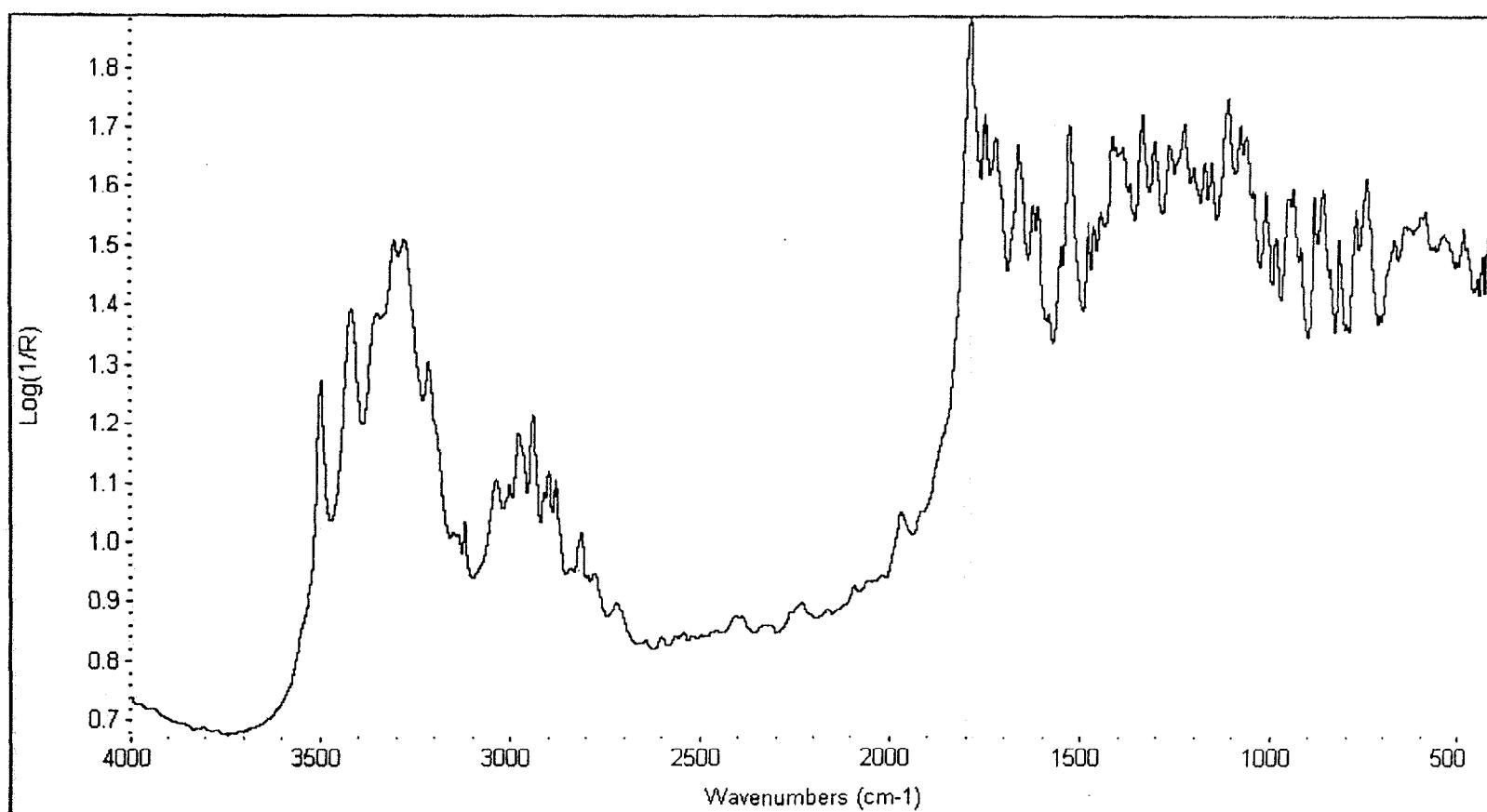
**IR Spectrum, Nicolet model 860 FT-IR**

Crystalline Cefuroxime Axetil; SSCI-9499

Filename: \\rramni1\DLData\Spectra\Cefuroxime\9499ir.SPA

**Acquisition Parameters**

Collection time: Fri Jun 30 15:24:55 2000  
Number of sample scans: 256  
Number of background scans: 256  
Resolution: 4.000  
Sample gain: 8.0  
Mirror velocity: 0.6329  
Aperture: 100.00



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## Sample Name: cefuroxime

Sample ID: 385-60-05

Lot #:

Notebook Reference: 395-85

Operator: SL

Sample Preparation: micro cup

Notes: xtal A/B in H<sub>2</sub>O slurry

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\lrramni1\DLData\Spectra\Cefuroxime\3856005ir.SPA

## Acquisition Parameters

Collection time: Wed Aug 23 16:42:17 2000

Number of sample scans: 128

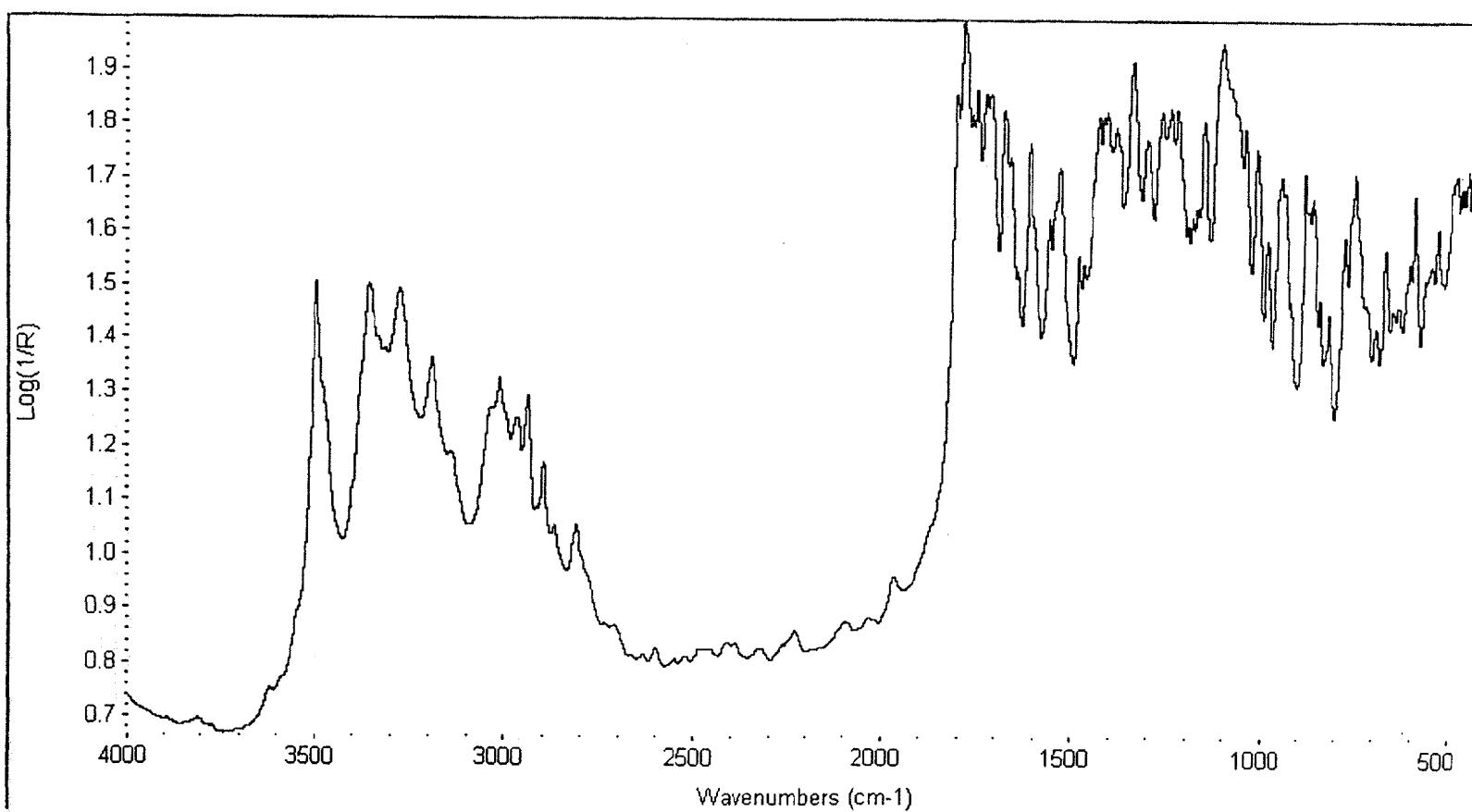
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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## Sample Name: cefuroxime

Sample ID: 385-60-03

Lot #:

Notebook Reference: 395-76

Operator: SL

Sample Preparation: micro cup

Notes: amorphous A/B H<sub>2</sub>O slurry

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\rramni1\DLData\Spectra\Cefuroxime\3856003ir.SPA

## Acquisition Parameters

Collection time: Fri Aug 18 16:27:15 2000

Number of sample scans: 128

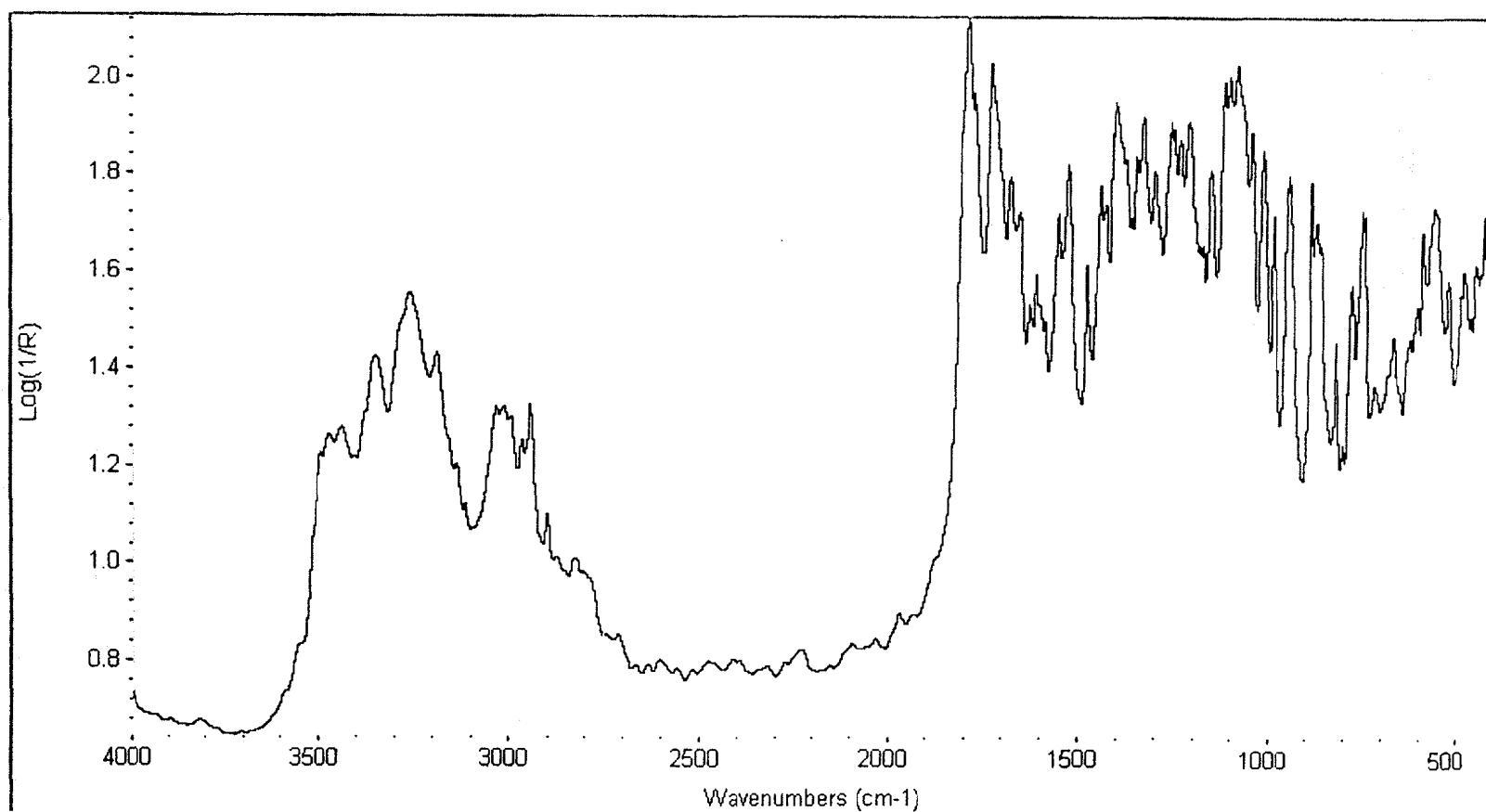
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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Cefuroxime Axetil Spray Dried 9498

**Raman Spectrum, Nicolet model 860 FT-Raman**

Filename: W:\rramni1\1D\Data\Spectral\Cefuroxime9498rm.SPA

**Acquisition Parameters**

Collection time: Thu Jun 29 14:01:53 2000

Number of sample scans: 256

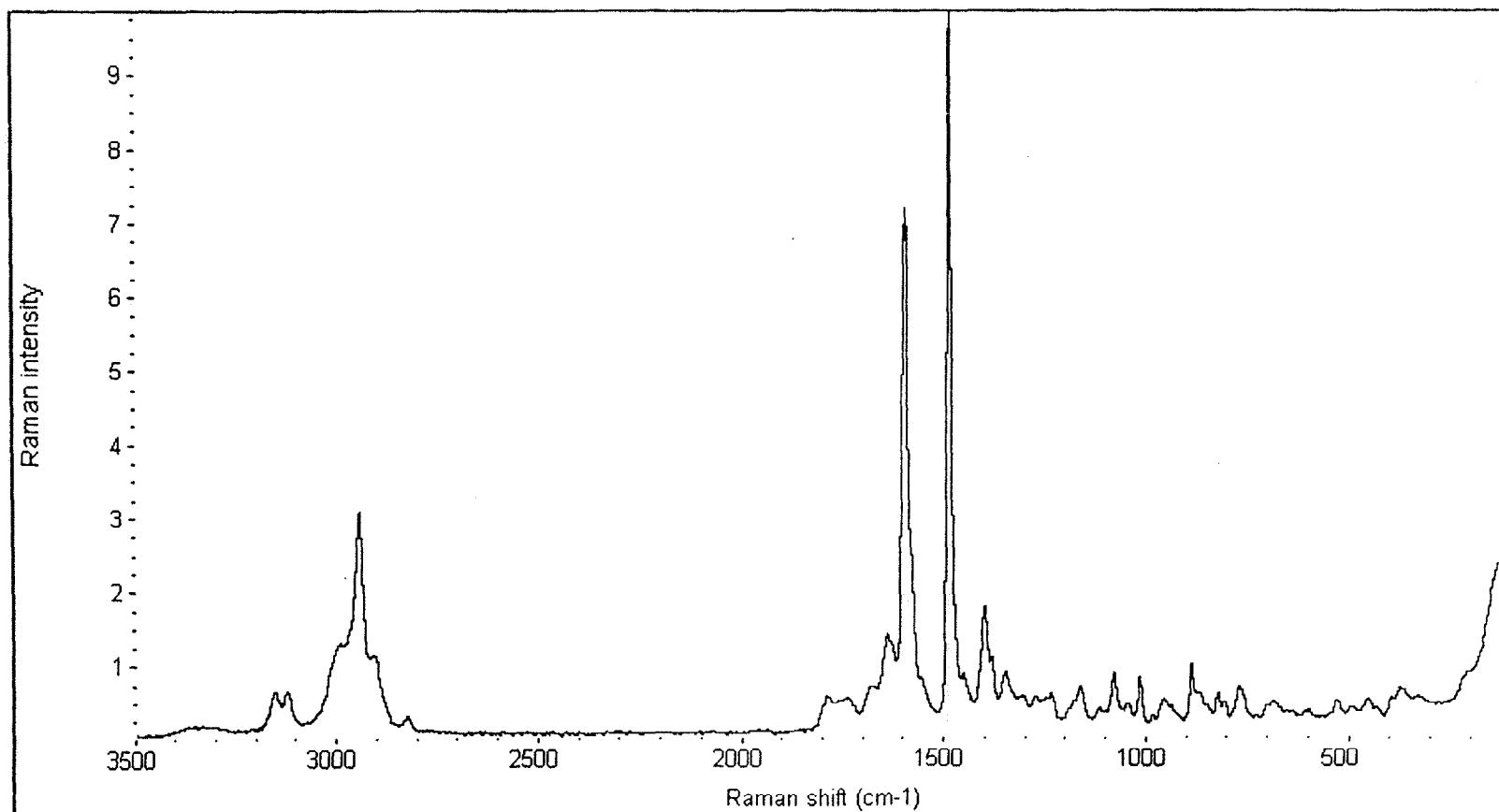
Number of background scans: 0

Resolution: 4.000

Sample gain: 64.0

Mirror velocity: 0.3165

Aperture: 59.00



**SSCI, Inc.**

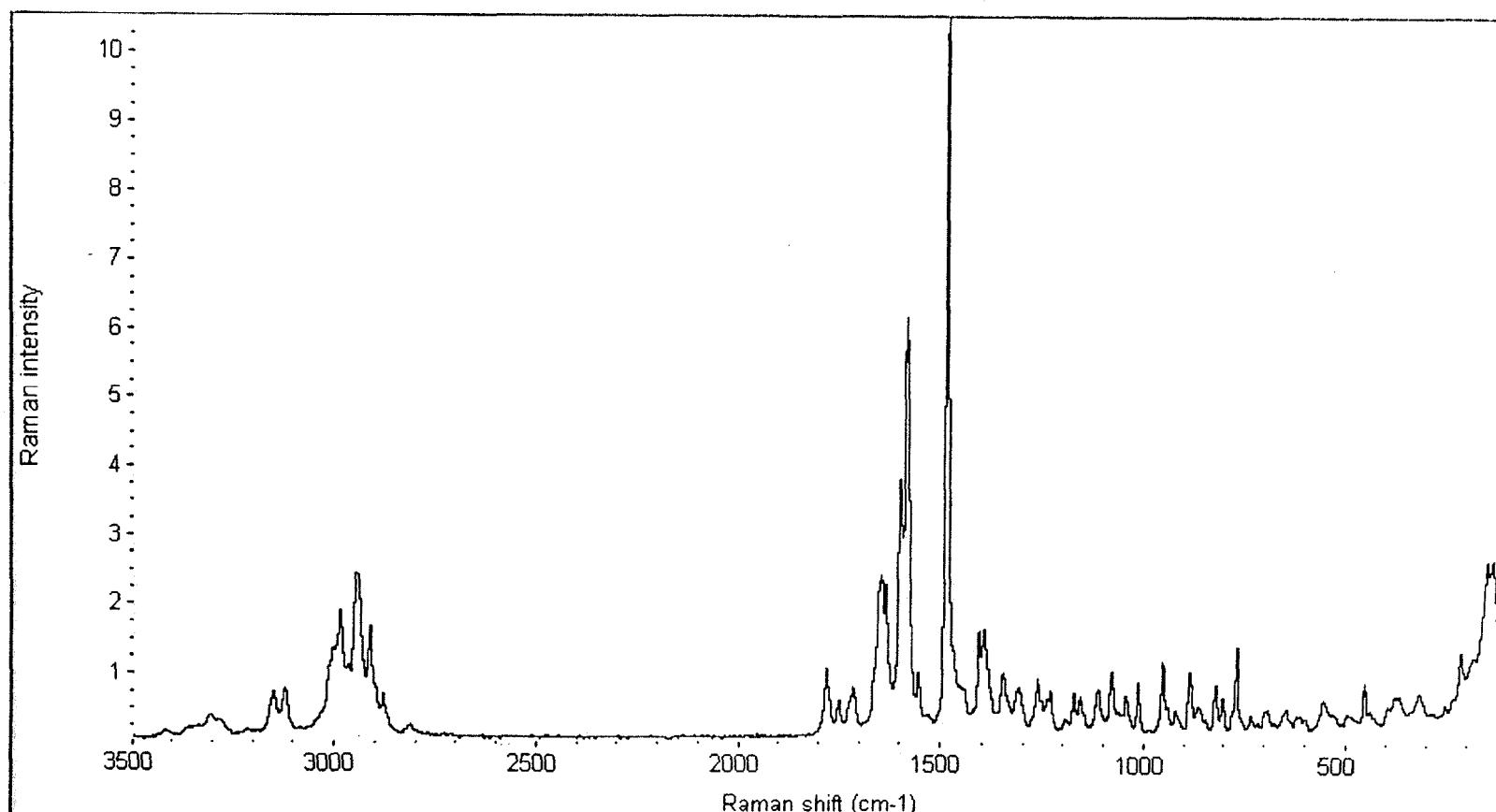
1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

**Raman Spectrum, Nicolet model 860 FT-Raman**  
**Cefuroxime Axetil, Crystalline SSCI S<sub>455</sub>**

Filename: \\rramni1\D\Data\Spectra\Cefuroxime\9499rm.SPA

**Acquisition Parameters**

Collection time: Thu Jun 29 14:42:06 2000  
Number of sample scans: 256  
Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3165  
Aperture: 59.00



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385-60-05; xtal A/B H<sub>2</sub>O slurry

**Raman Spectrum, Nicolet model 860 FT-Raman**

Filename: \lrramni1\1D\Data\Spectra\Cefuroxime\3856005rm.SPA

**Acquisition Parameters**

Collection time: Tue Aug 22 15:21:48 2000

Number of sample scans: 128

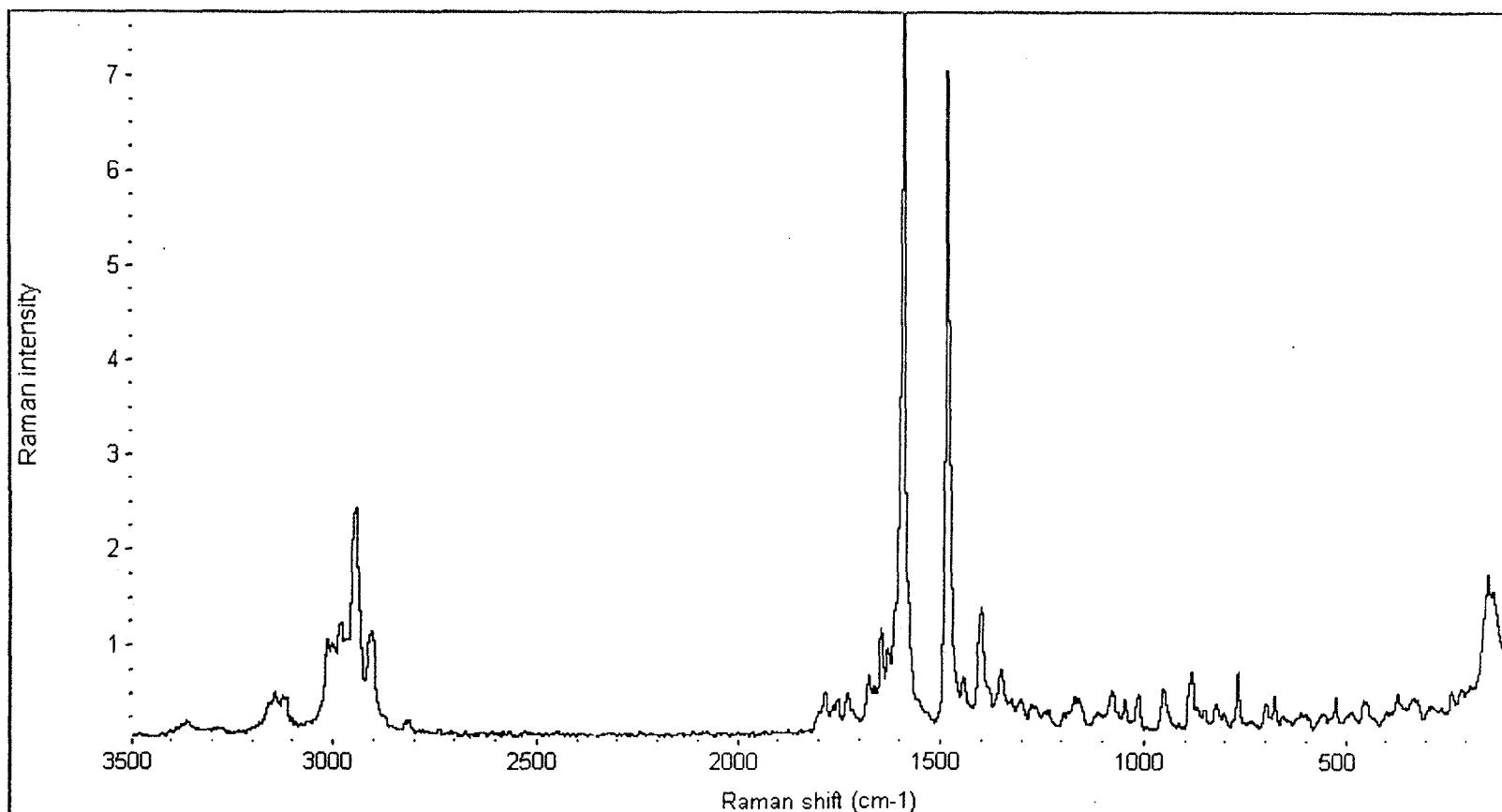
Number of background scans: 0

Resolution: 4.000

Sample gain: 64.0

Mirror velocity: 0.3165

Aperture: 59.00



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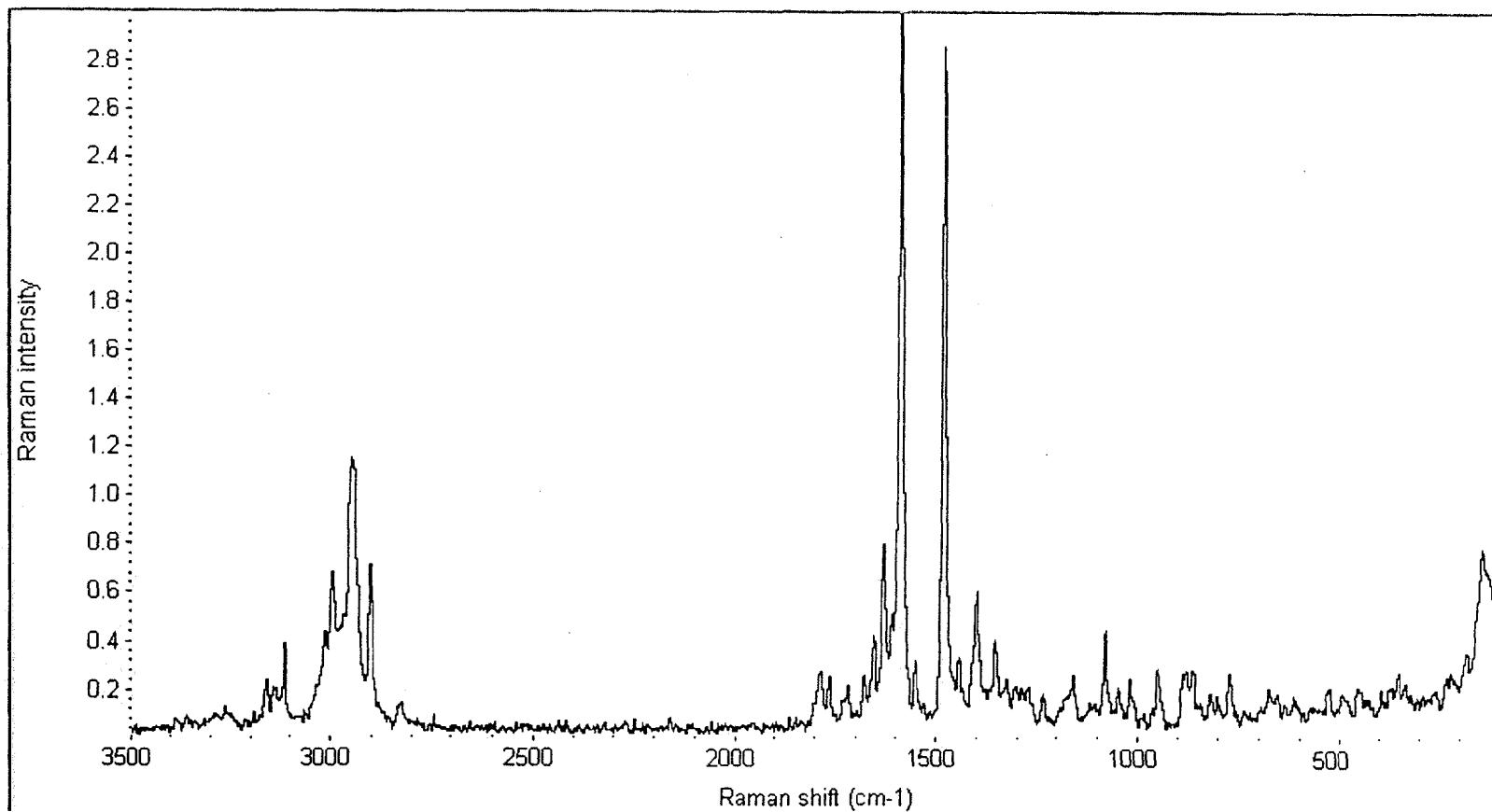
385-60-03; amorph A/B H<sub>2</sub>O slurry

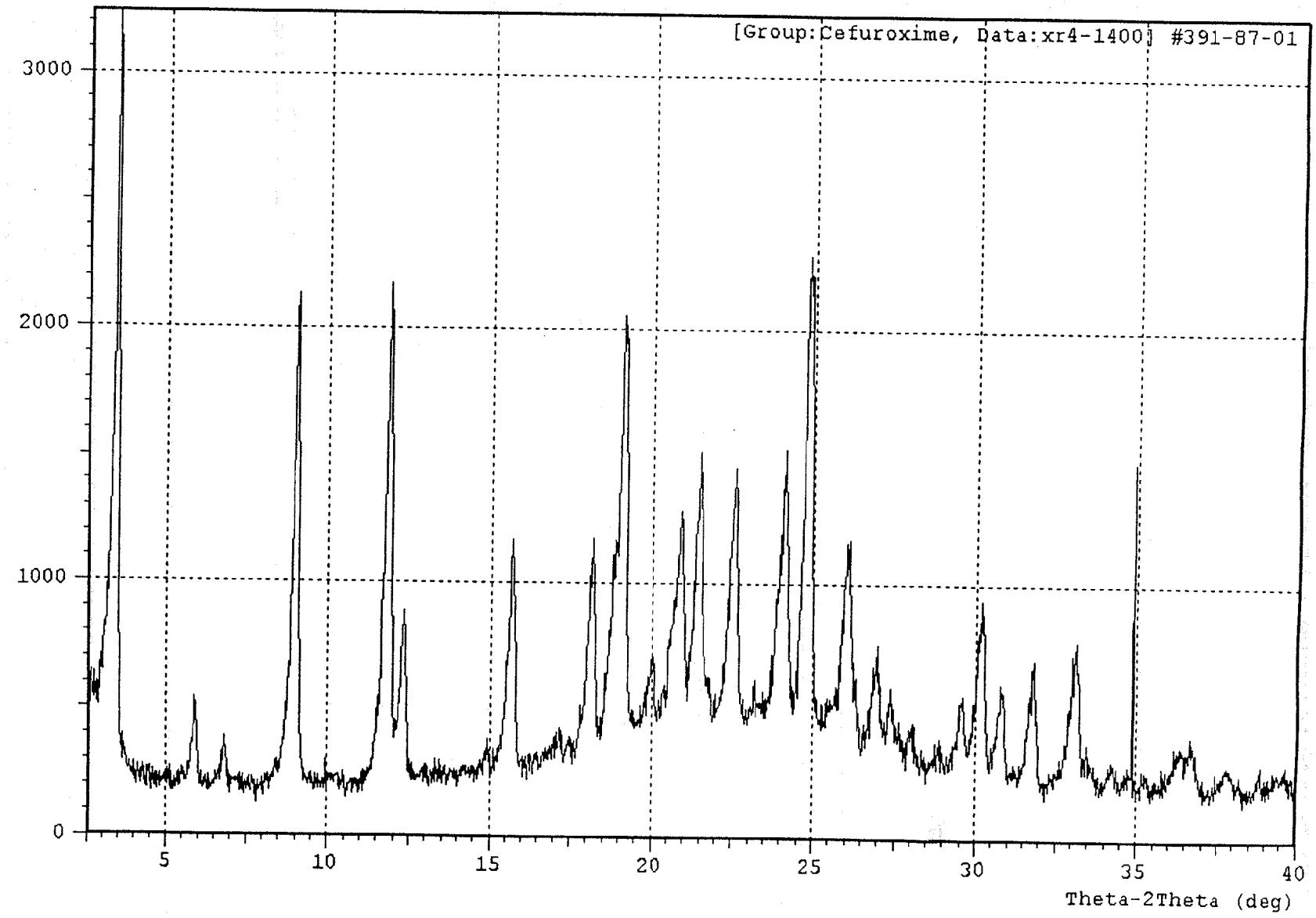
## Raman Spectrum, Nicolet model 860 FT-Raman

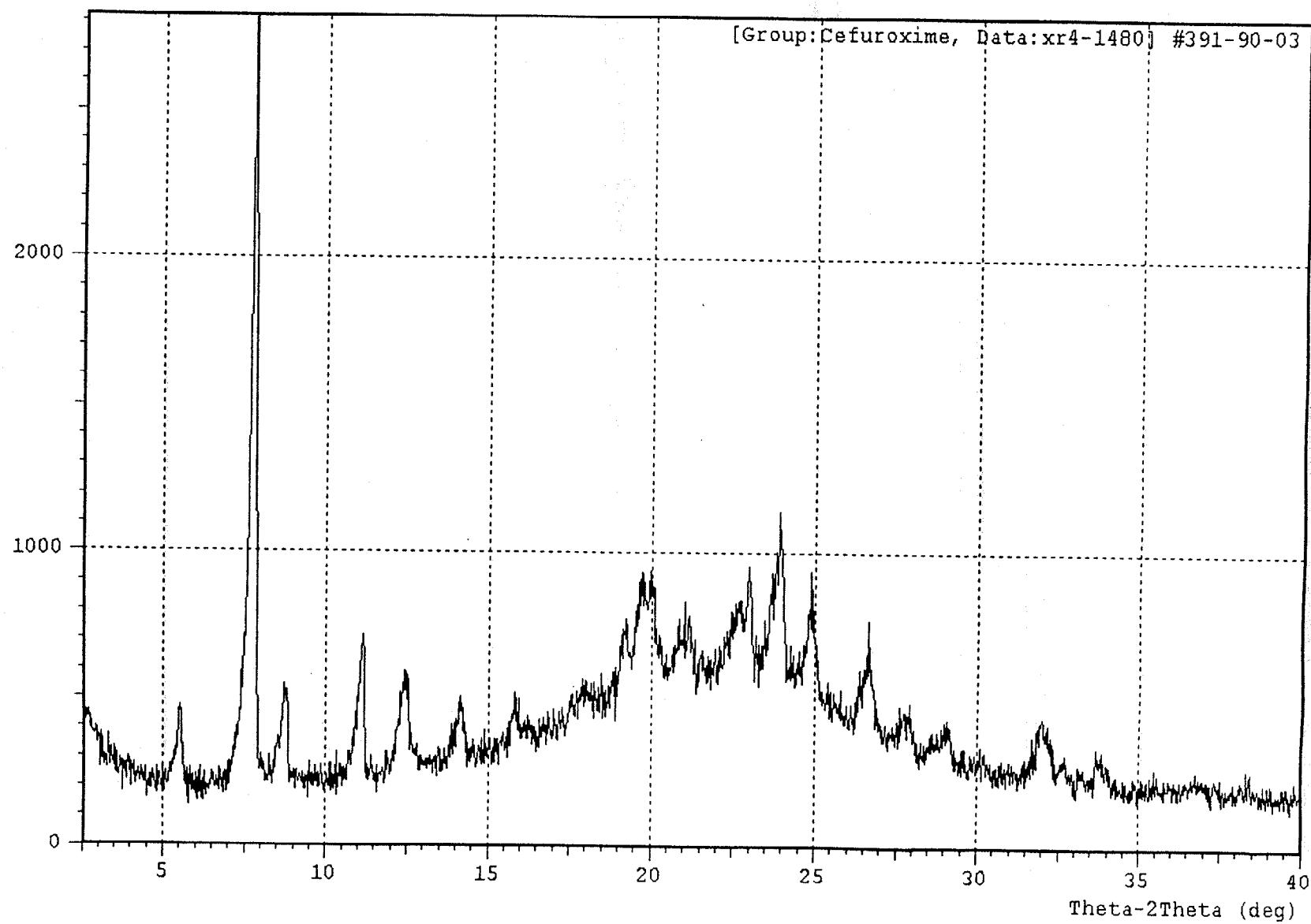
Filename: \\rramni1\DLData\Spectra\Cefuroxime\3856003rm.spa

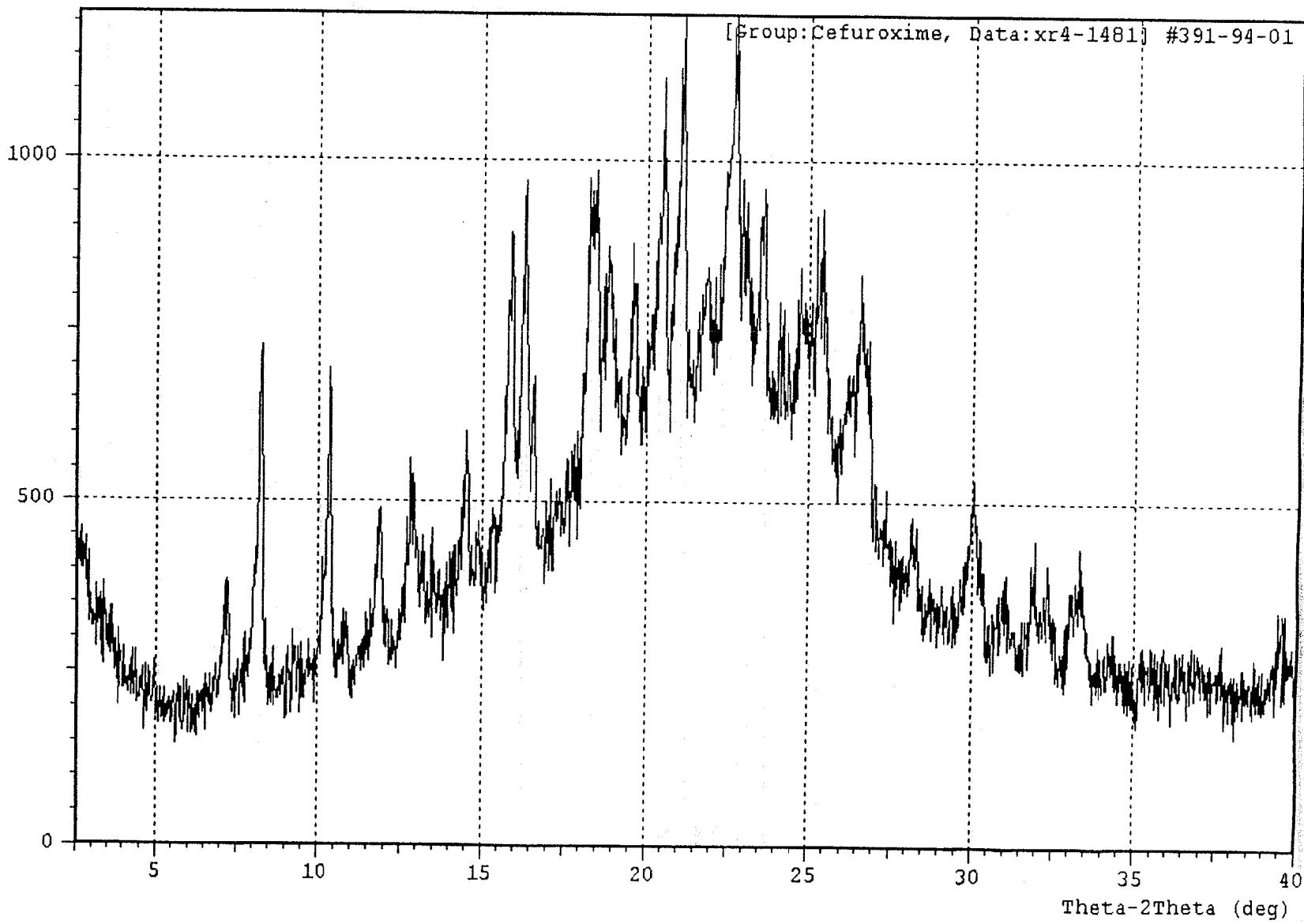
## Acquisition Parameters

Collection time: Fri Aug 18 11:01:46 2000  
Number of sample scans: 128  
Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3165  
Aperture: 59.00

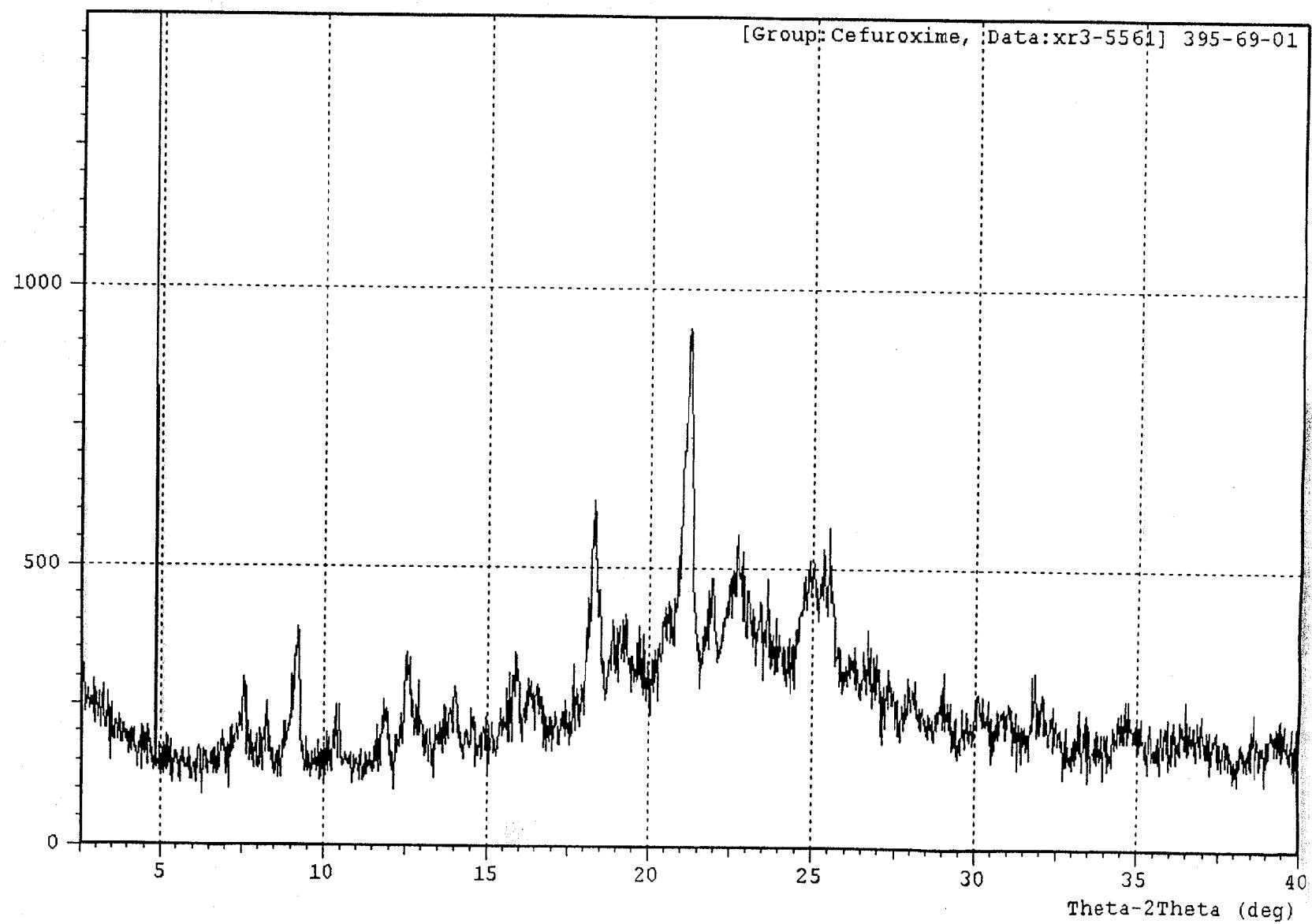


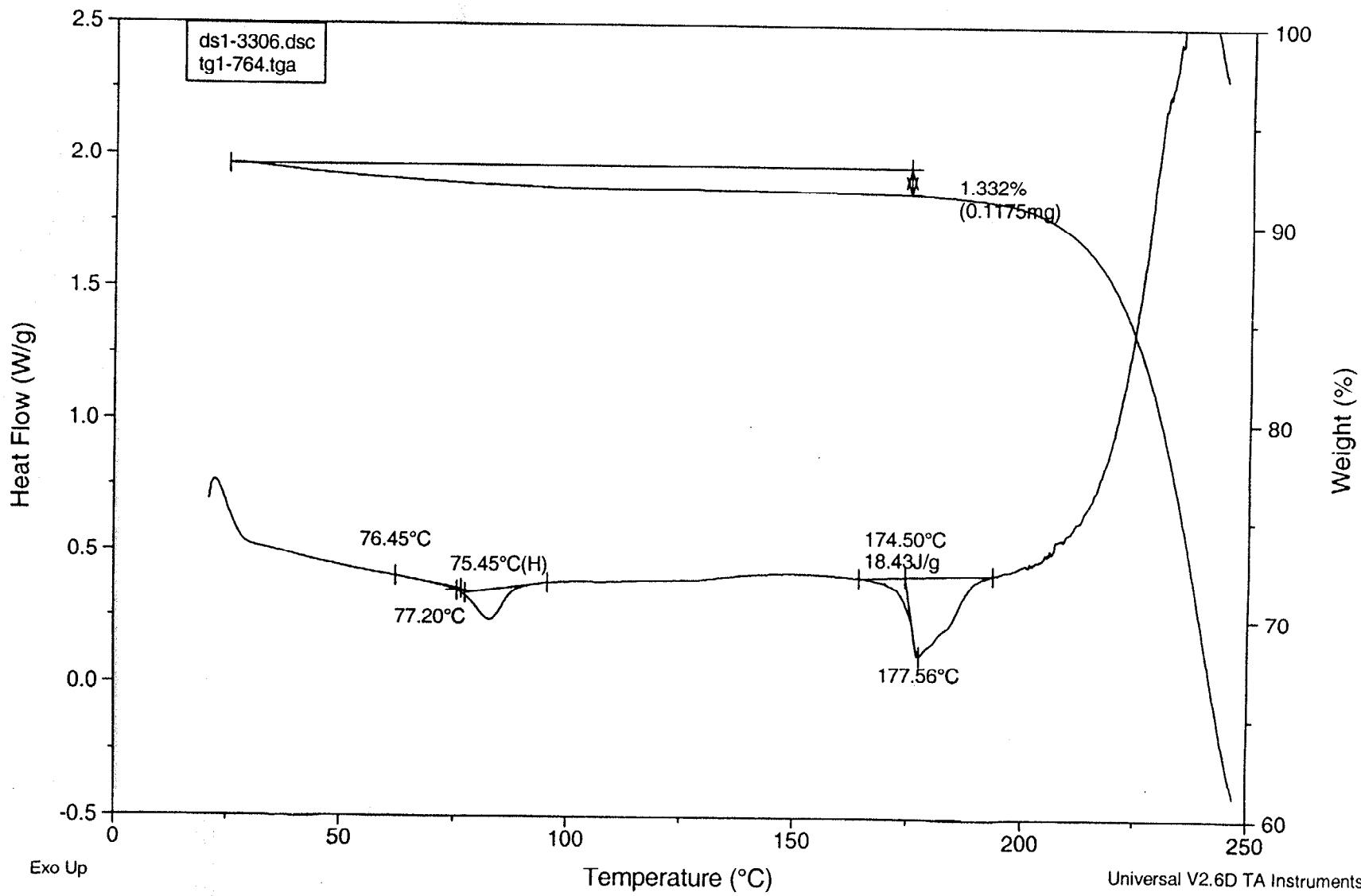


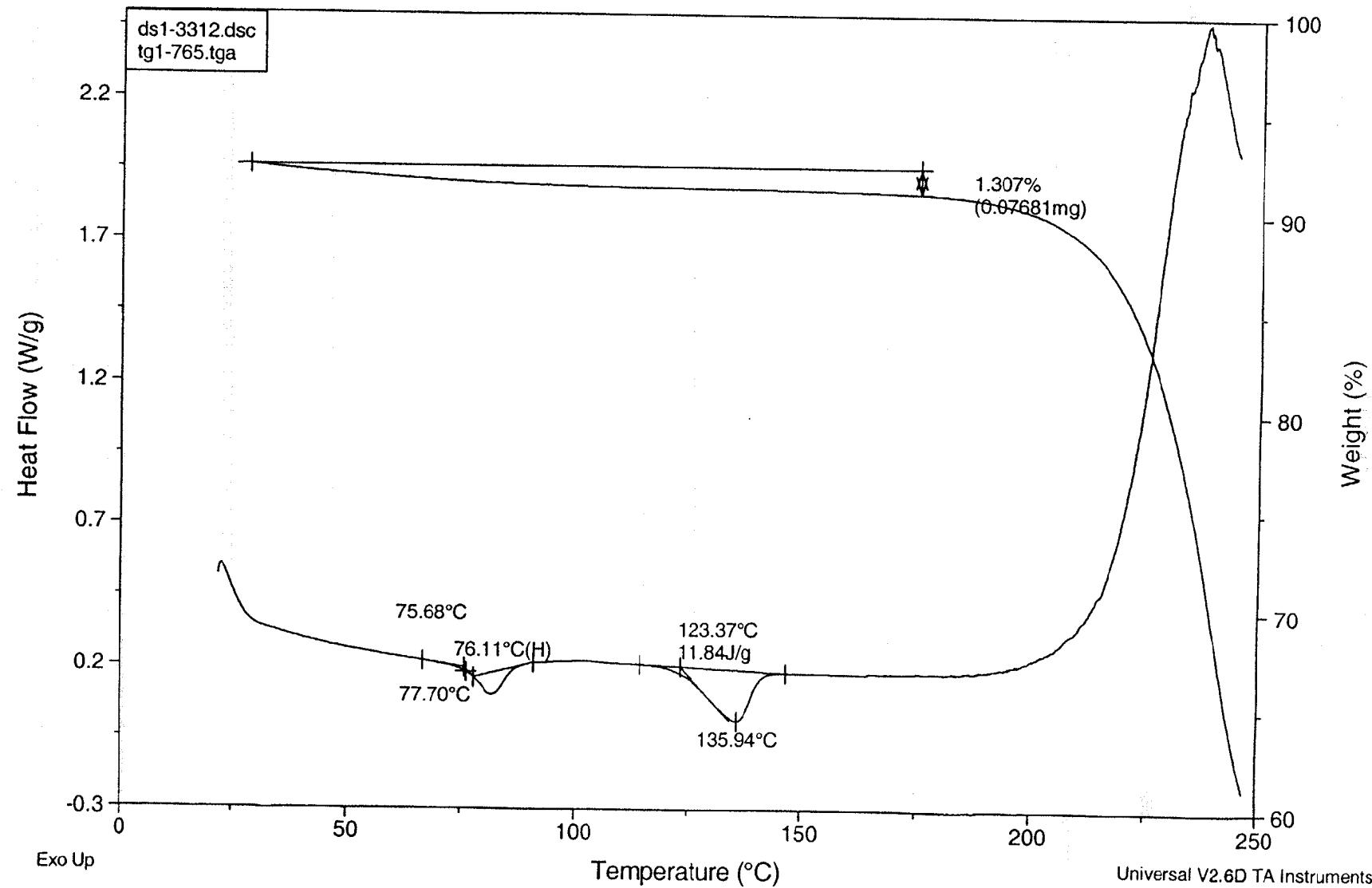


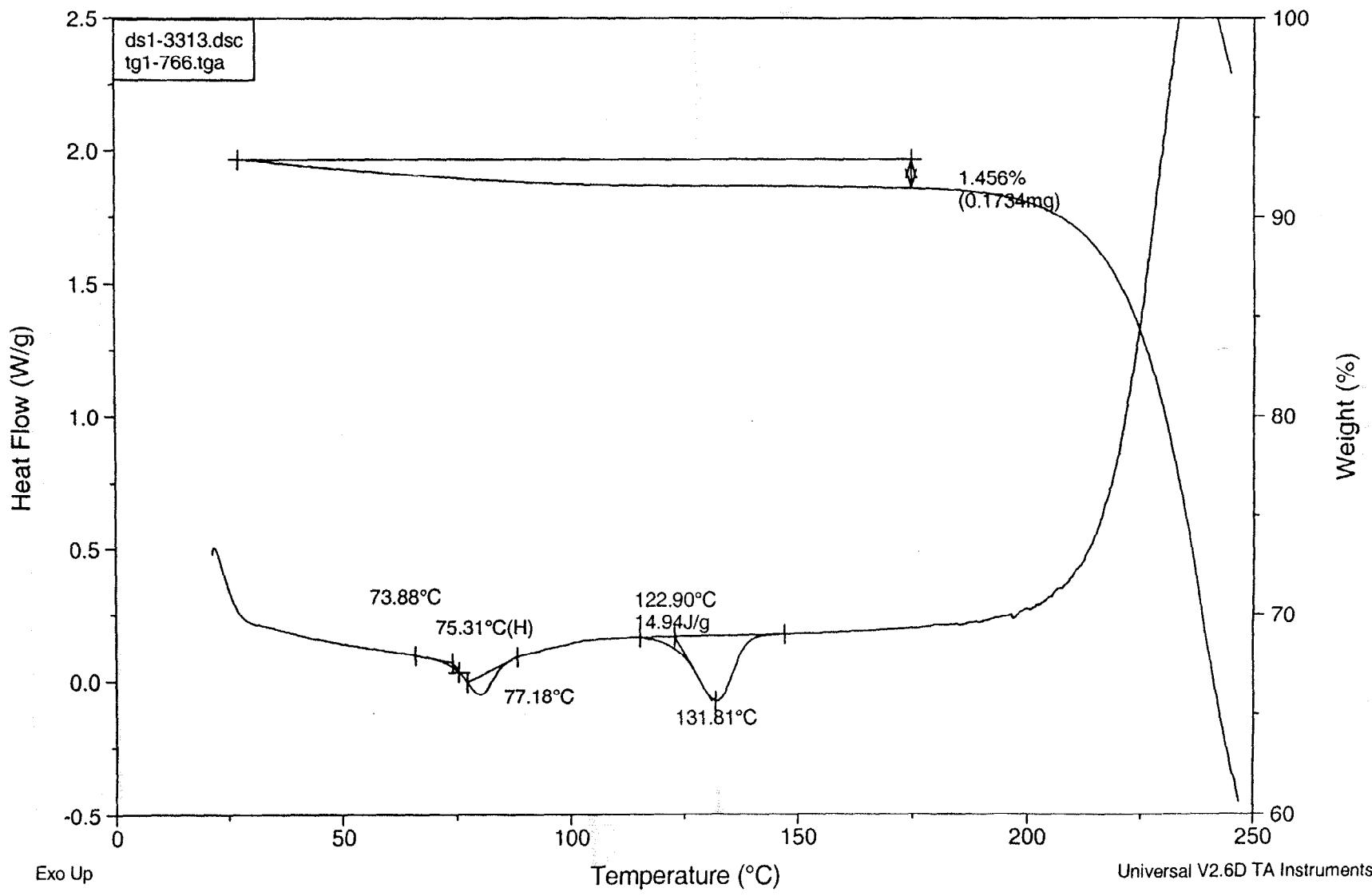


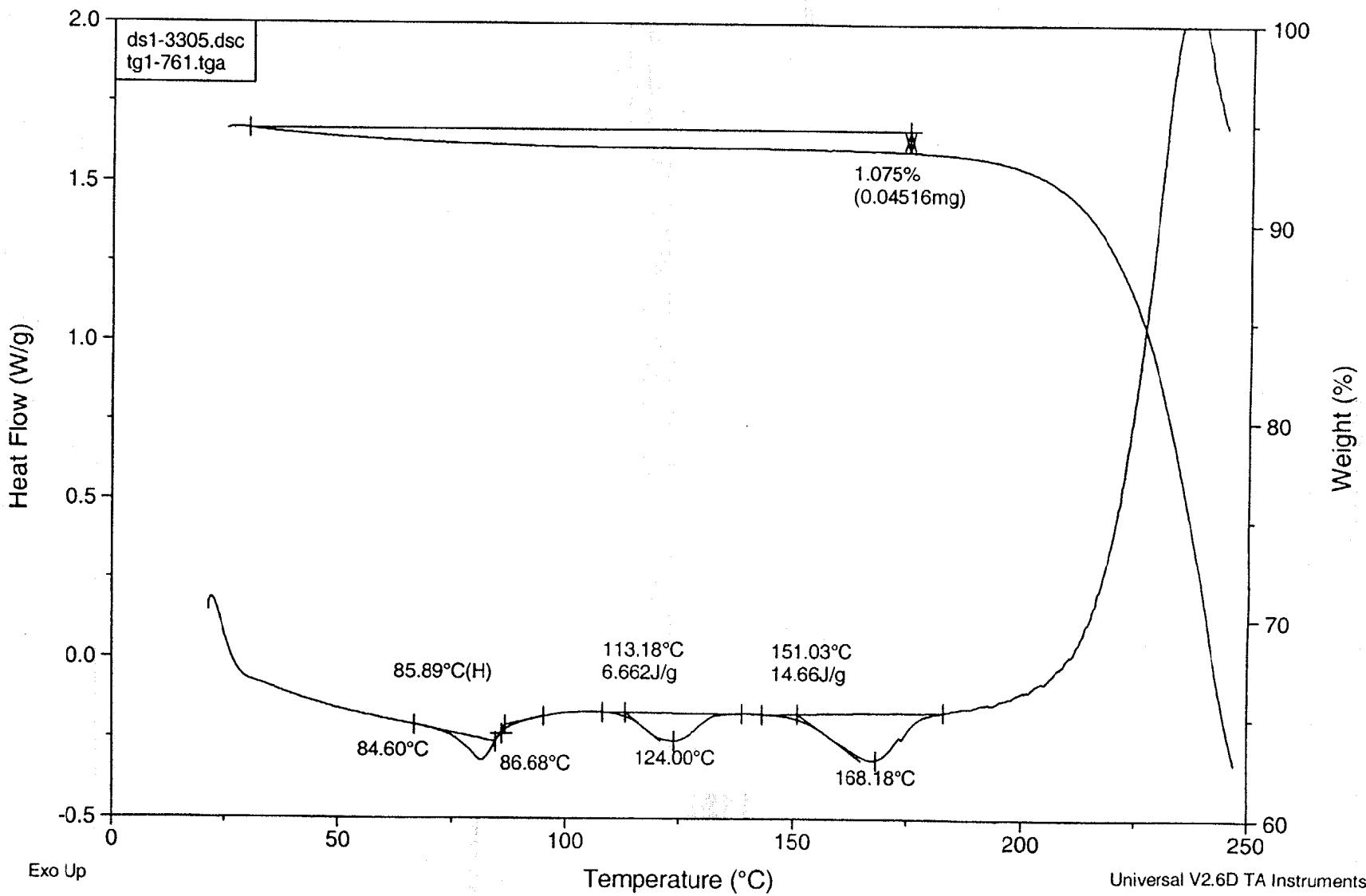
[Group:Cefuroxime, Data:xr3-5561] 395-69-01











# SSCI, Inc.

1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssciinc.com](http://www.ssciinc.com)

## Sample Name: cefuroxime

Sample ID: 391-87-01

Lot #:

Notebook Reference: 395-76

Operator: SL

Sample Preparation: micro cup

Notes: 20% A(l) in amorphous A/B

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\rramni1\DI\Data\Spectral\Cefuroxime\3918701ir.SPA

## Acquisition Parameters

Collection time: Fri Aug 18 16:51:39 2000

Number of sample scans: 128

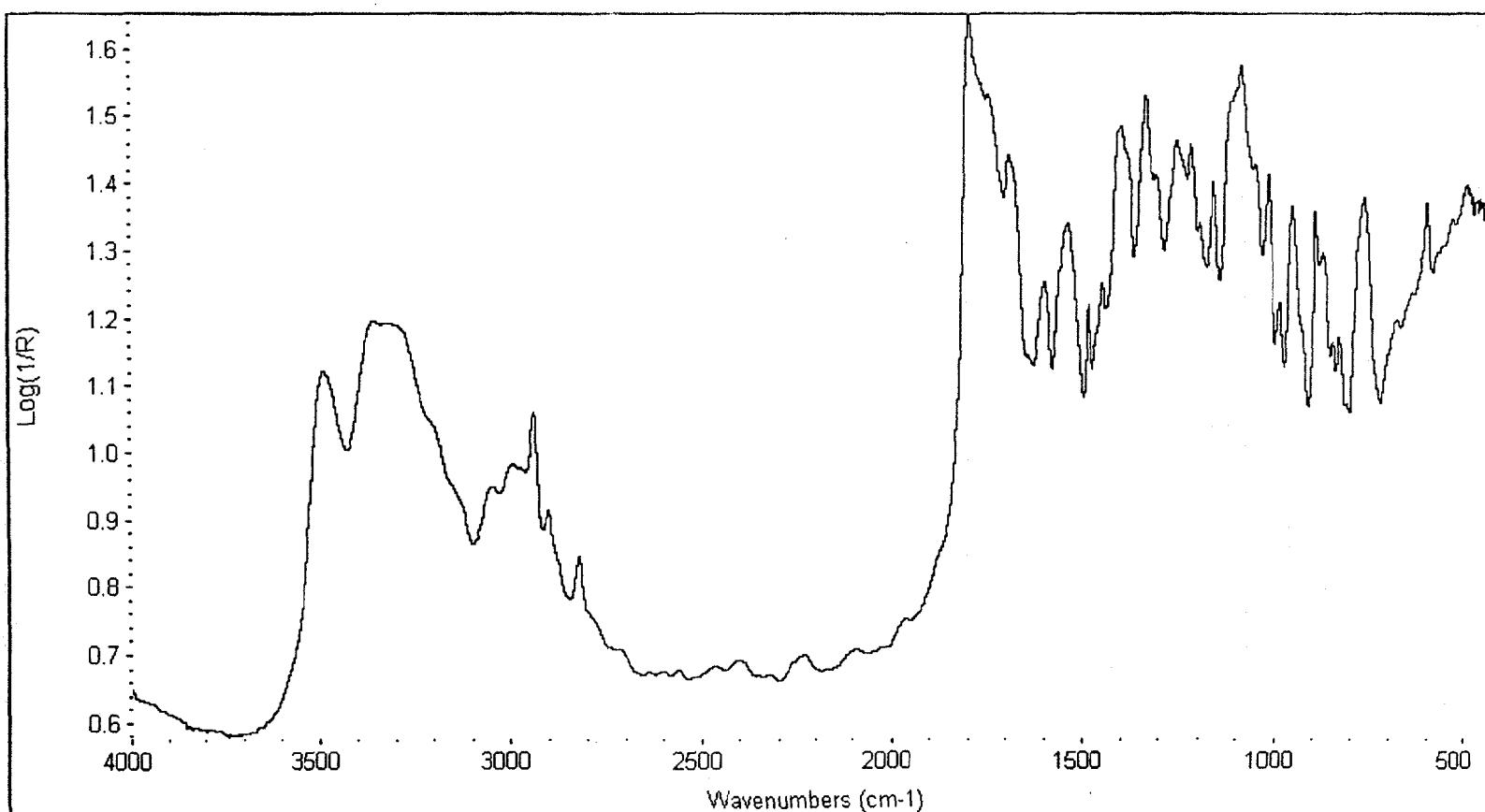
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: www.ssci-inc.com

## Sample Name: cefuroxime

Sample ID: 391-90-03

Lot #:

Notebook Reference: 395-85

Operator: SL

Sample Preparation: micro cup

Notes: 20% B(I) in amorphous A/B

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\rramni1\DATA\Spectral\Cefuroxime\3919003ir.SPA

## Acquisition Parameters

Collection time: Wed Aug 23 16:50:14 2000

Number of sample scans: 128

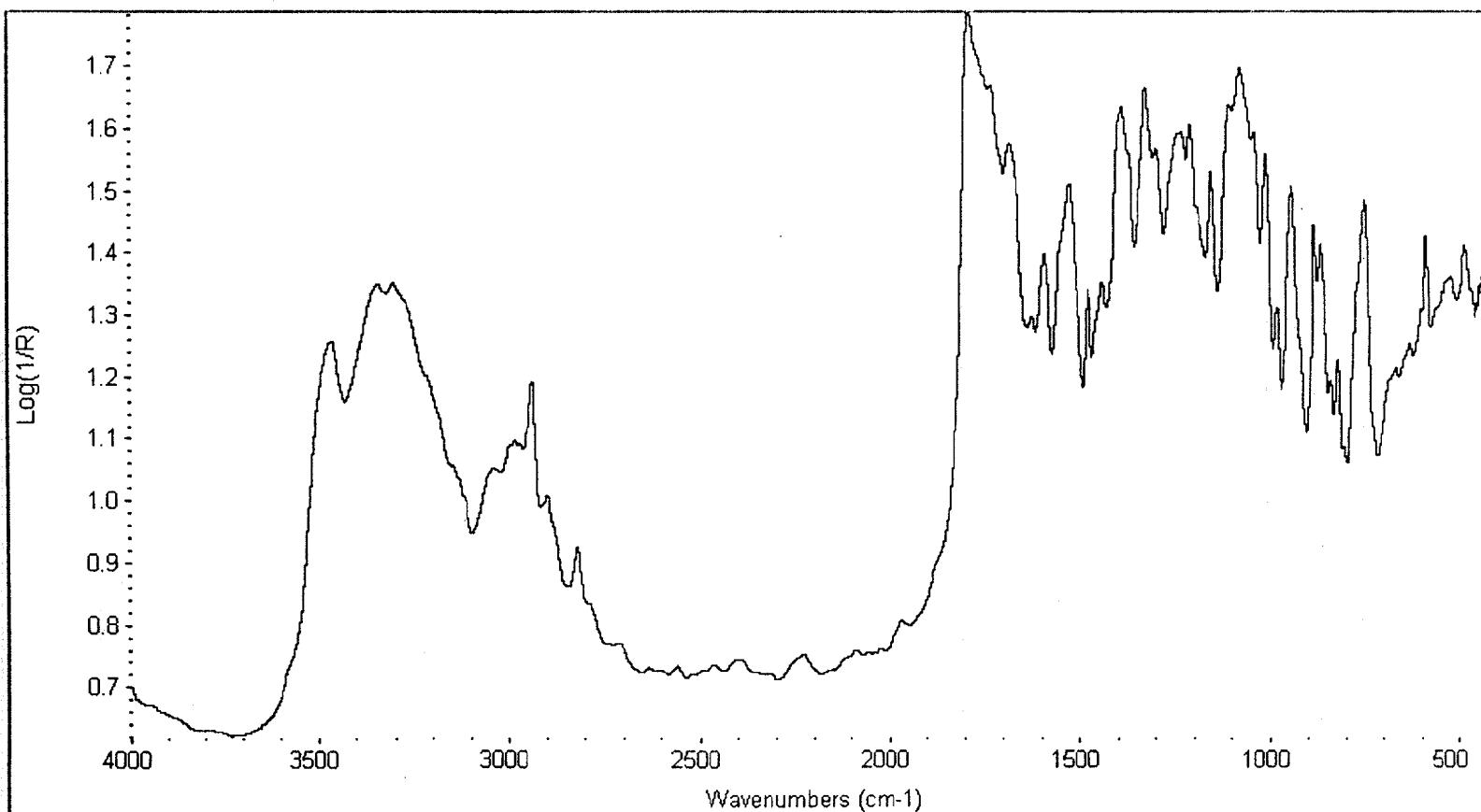
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

## Sample Name: cefuroxime

Sample ID: 391-94-01

Lot #:

Notebook Reference: 395-85

Operator: SL

Sample Preparation: micro cup

Notes: 20% B(II) in amorphous A/B

## IR Spectrum, Nicolet model 860 FT-IR

### Acquisition Parameters

Collection time: Wed Aug 23 16:58:48 2000

Number of sample scans: 128

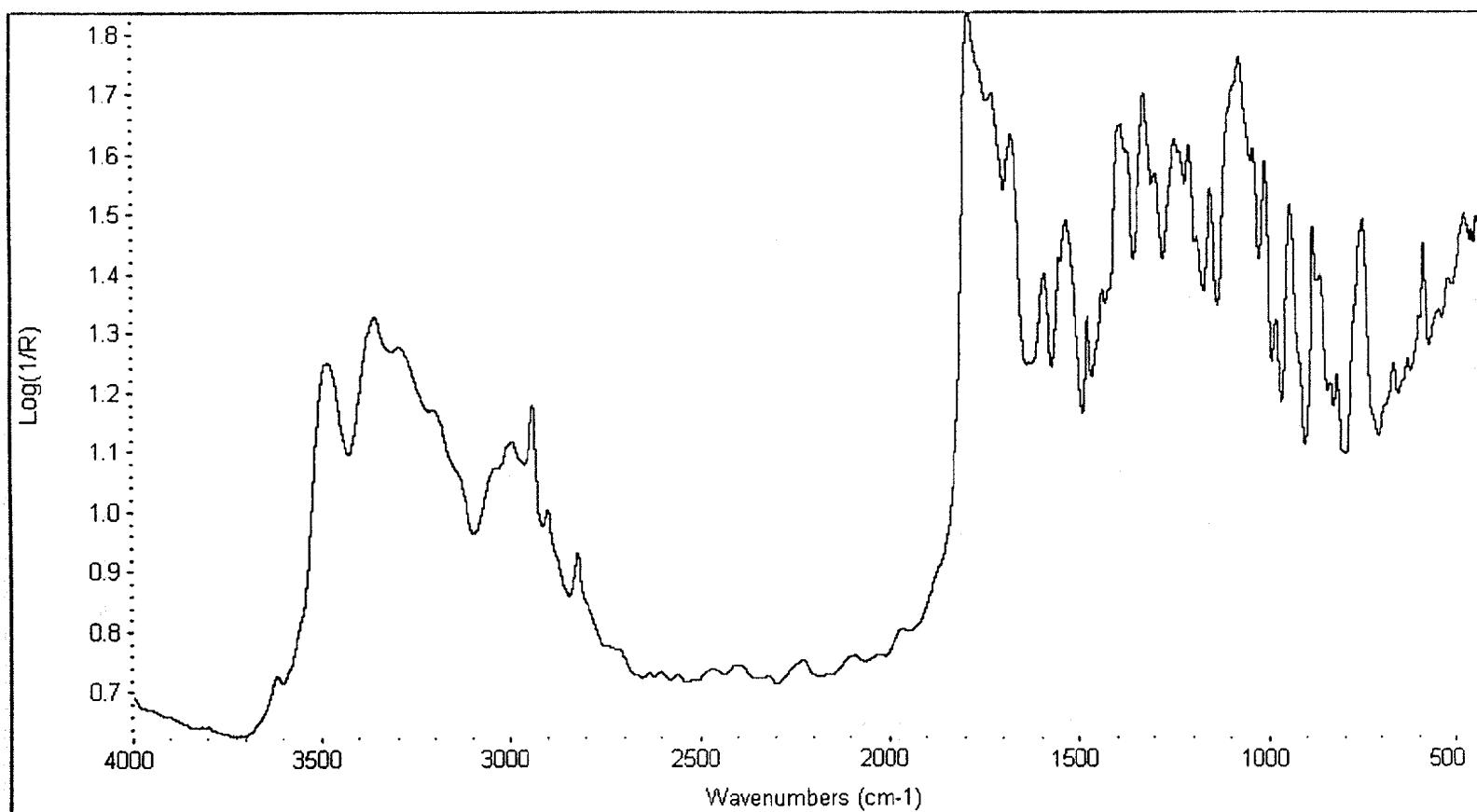
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

## Sample Name: cefuroxime

Sample ID: 395-69-01

Lot #:

Notebook Reference: 395-76

Operator: SL

Sample Preparation: micro cup

Notes: 25% A(II)/B(II) 395-69-01

## IR Spectrum, Nicolet model 860 FT-IR

Filename: \\rramni1\DATA\Spectra\Cefuroxime\3956901ir.SPA

## Acquisition Parameters

Collection time: Fri Aug 18 16:15:46 2000

Number of sample scans: 128

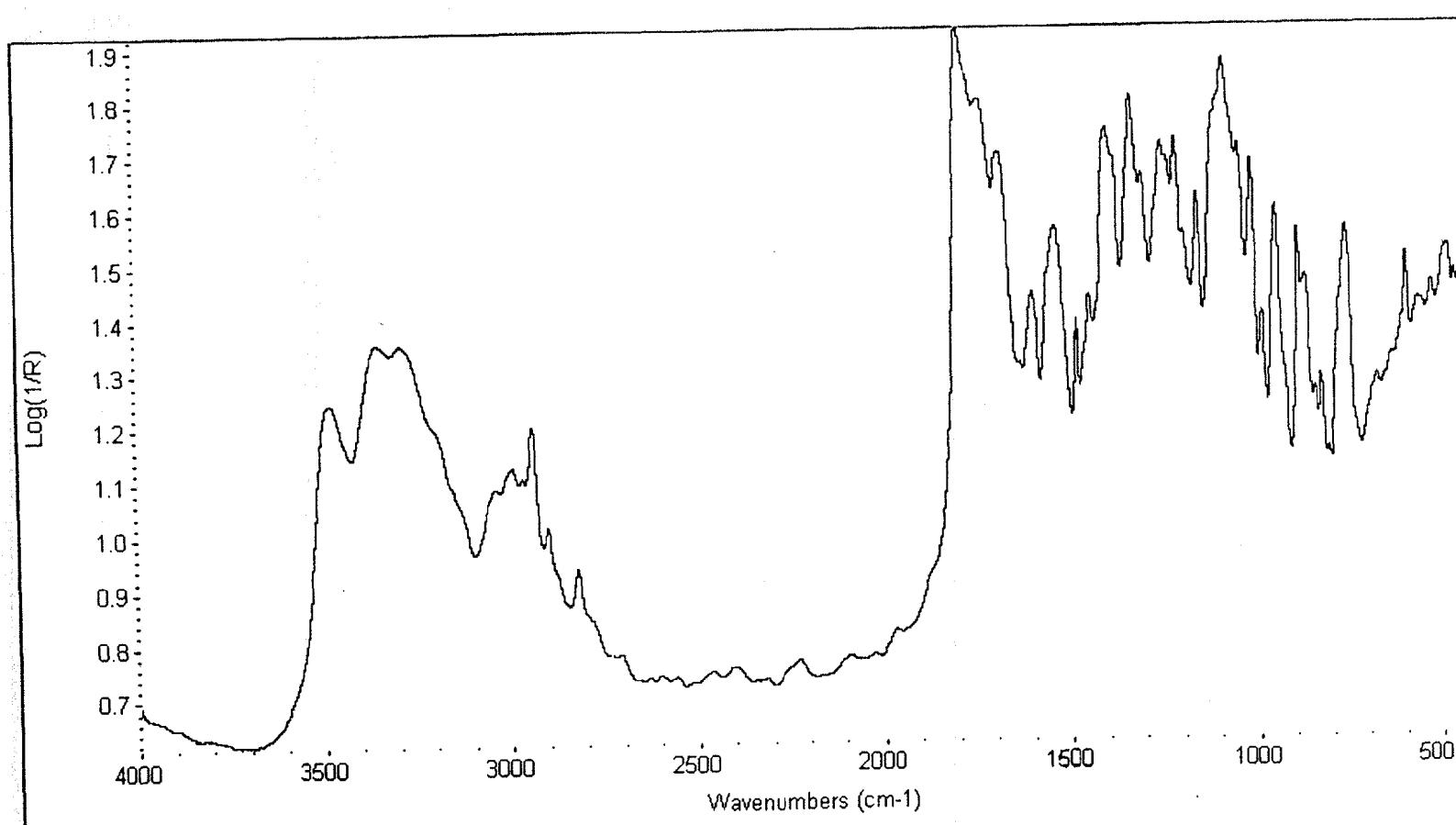
Number of background scans: 128

Resolution: 4.000

Sample gain: 8.0

Mirror velocity: 0.6329

Aperture: 100.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

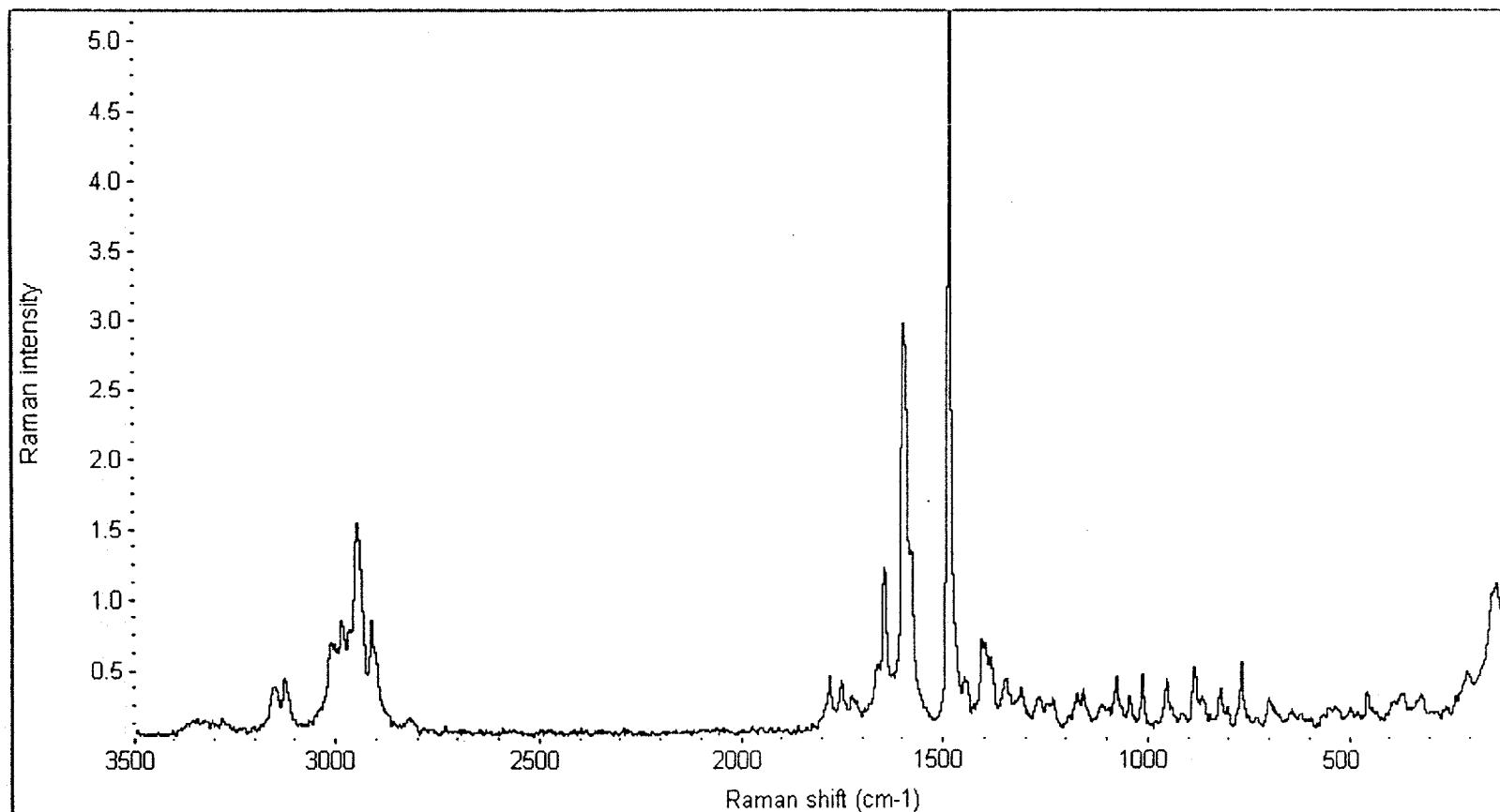
39187-01; 20% A(l) in amorph A/B

## Raman Spectrum, Nicolet model 860 FT-Raman

Filename: \\rramni1\D\Data\Spectra\Cefuroxime\3918701rm.spa

### Acquisition Parameters

Collection time: Fri Aug 18 11:39:06 2000  
Number of sample scans: 128  
Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3165  
Aperture: 59.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

39190-03; 20% B(I) in amorph A/B

## Raman Spectrum, Nicolet model 860 FT-Raman

Filename: \\rramni1\D\Data\Spectra\Cefuroxime\3919003rm.SPA

### Acquisition Parameters

Collection time: Tue Aug 22 16:09:15 2000

Number of sample scans: 128

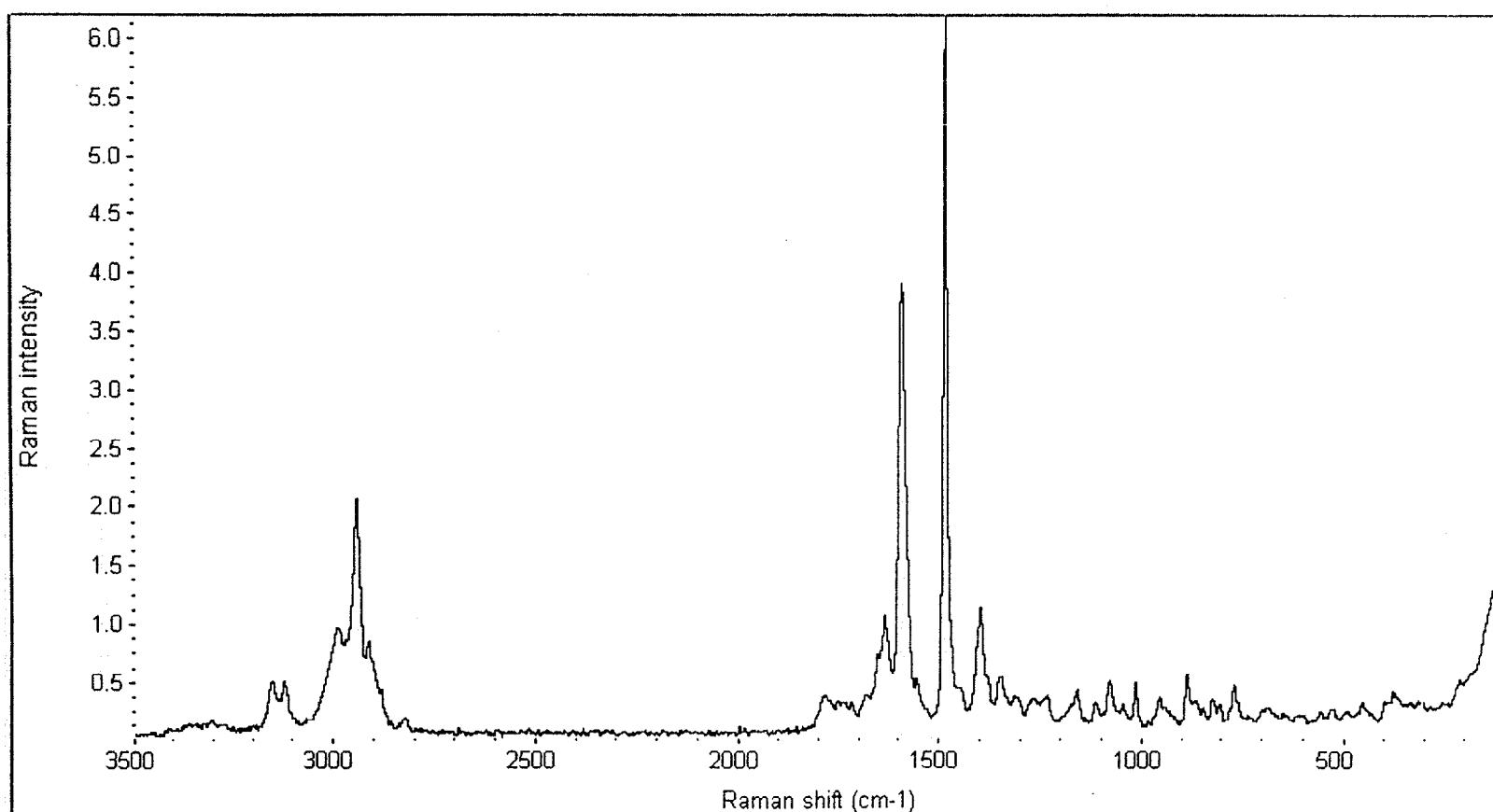
Number of background scans: 0

Resolution: 4.000

Sample gain: 64.0

Mirror velocity: 0.3165

Aperture: 59.00



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1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssciinc.com](http://www.ssciinc.com)

391.94.01 20% B(II) in amorph A/B

**Raman Spectrum, Nicolet model 860 FT-Raman**

Filename: \\rramni1\1D\Data\Spectral\Cefuroxime\3919401rm.SPA

**Acquisition Parameters**

Collection time: Tue Aug 22 15:47:06 2000

Number of sample scans: 128

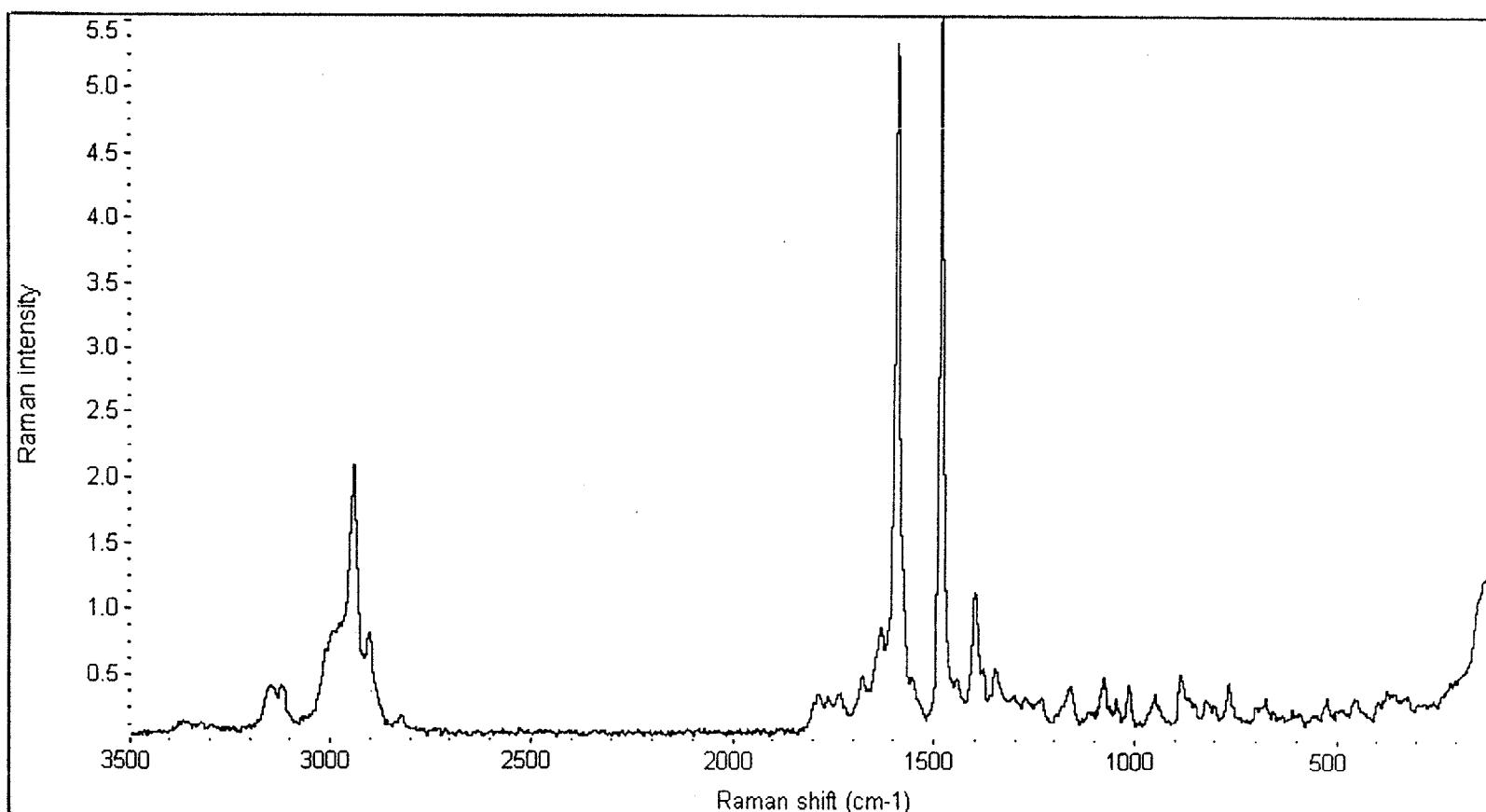
Number of background scans: 0

Resolution: 4.000

Sample gain: 64.0

Mirror velocity: 0.3165

Aperture: 59.00



**SSCI, Inc.**

395-69-01; 25% A(II)/B(II)

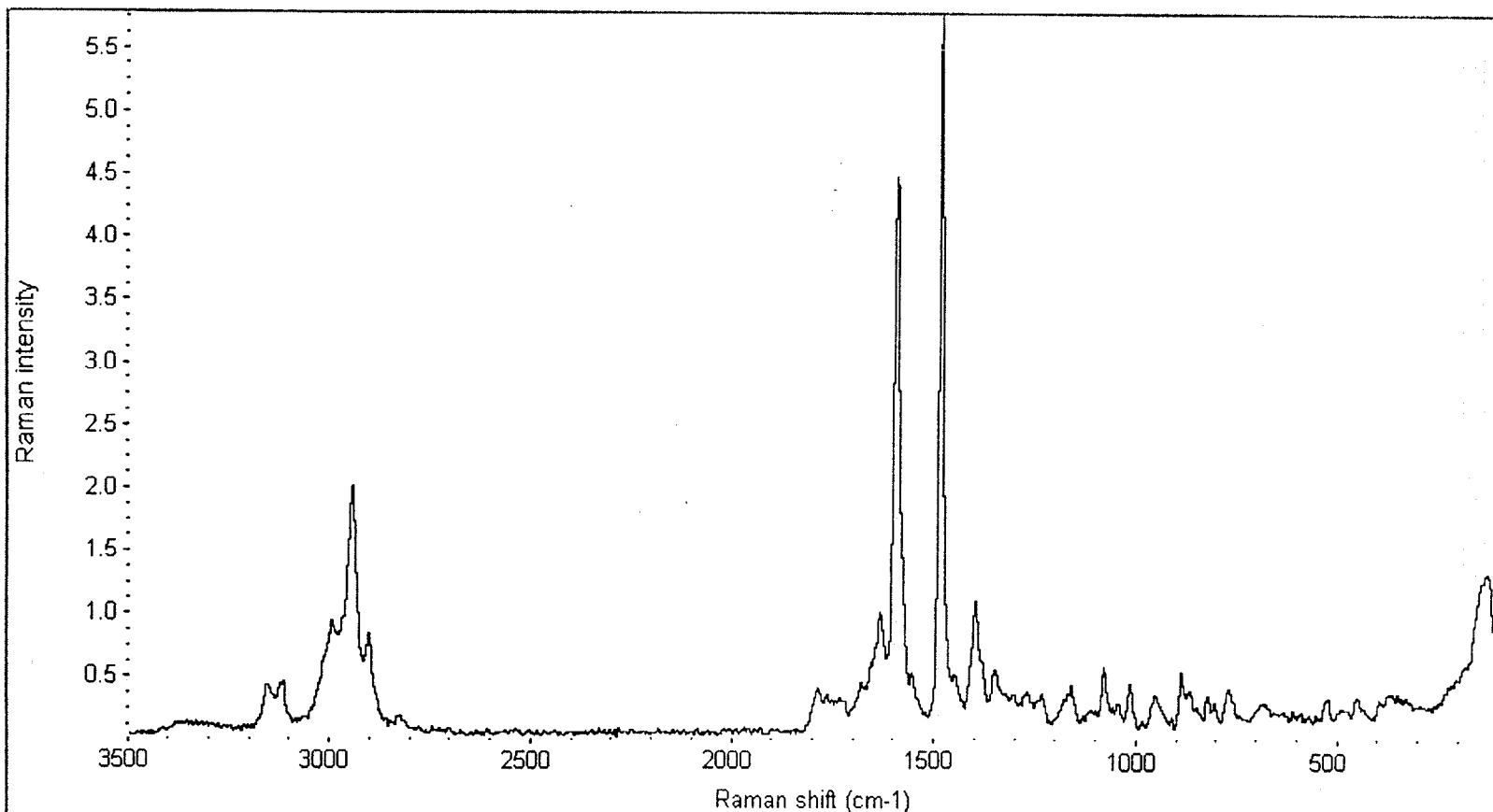
1291 Cumberland Ave., Suite E West Lafayette, IN 47906-1385 Phone: 765.463-0112 Fax: 765.497-2649 URL: [www.ssci-inc.com](http://www.ssci-inc.com)

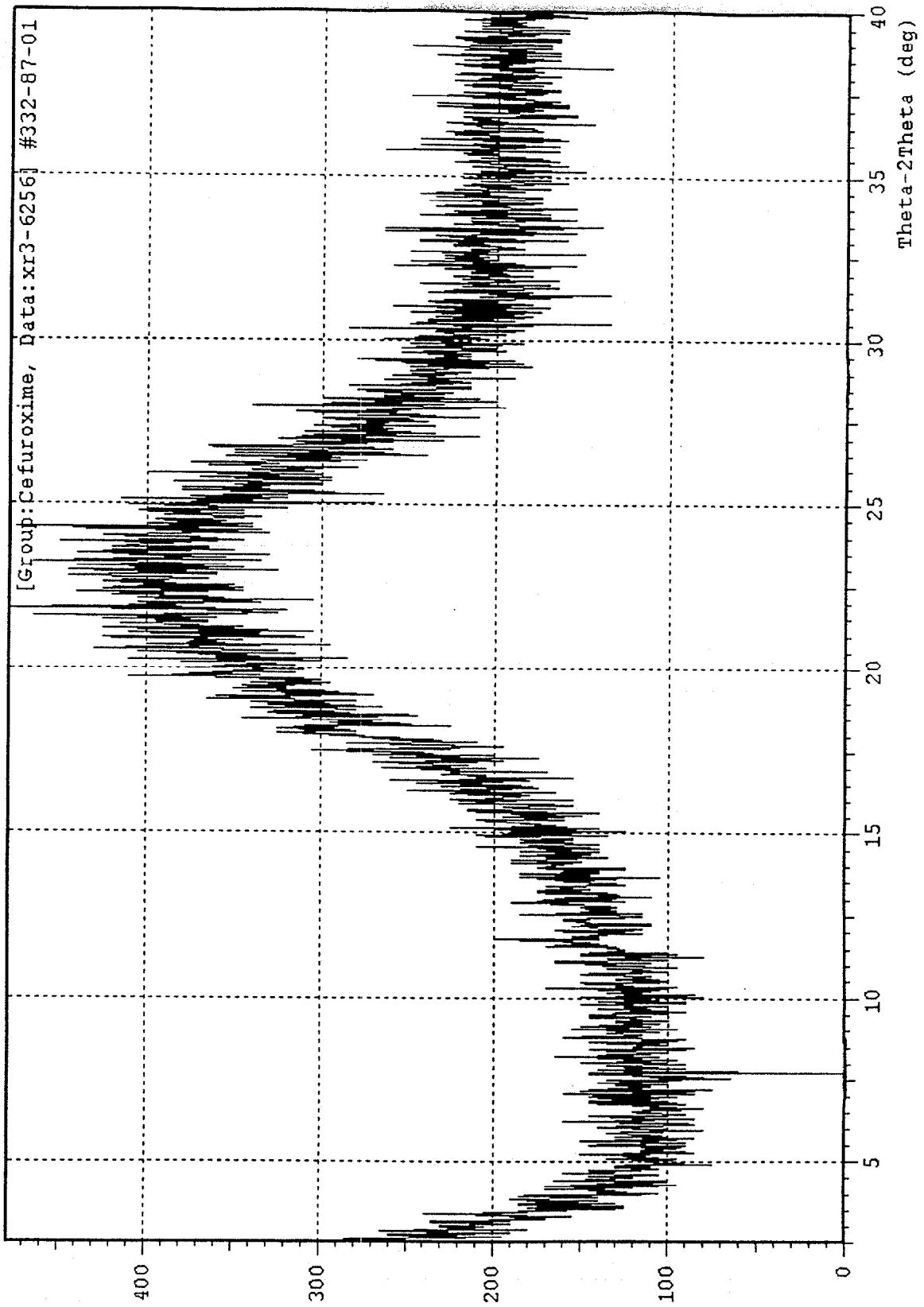
**Raman Spectrum, Nicolet model 860 FT-Raman**

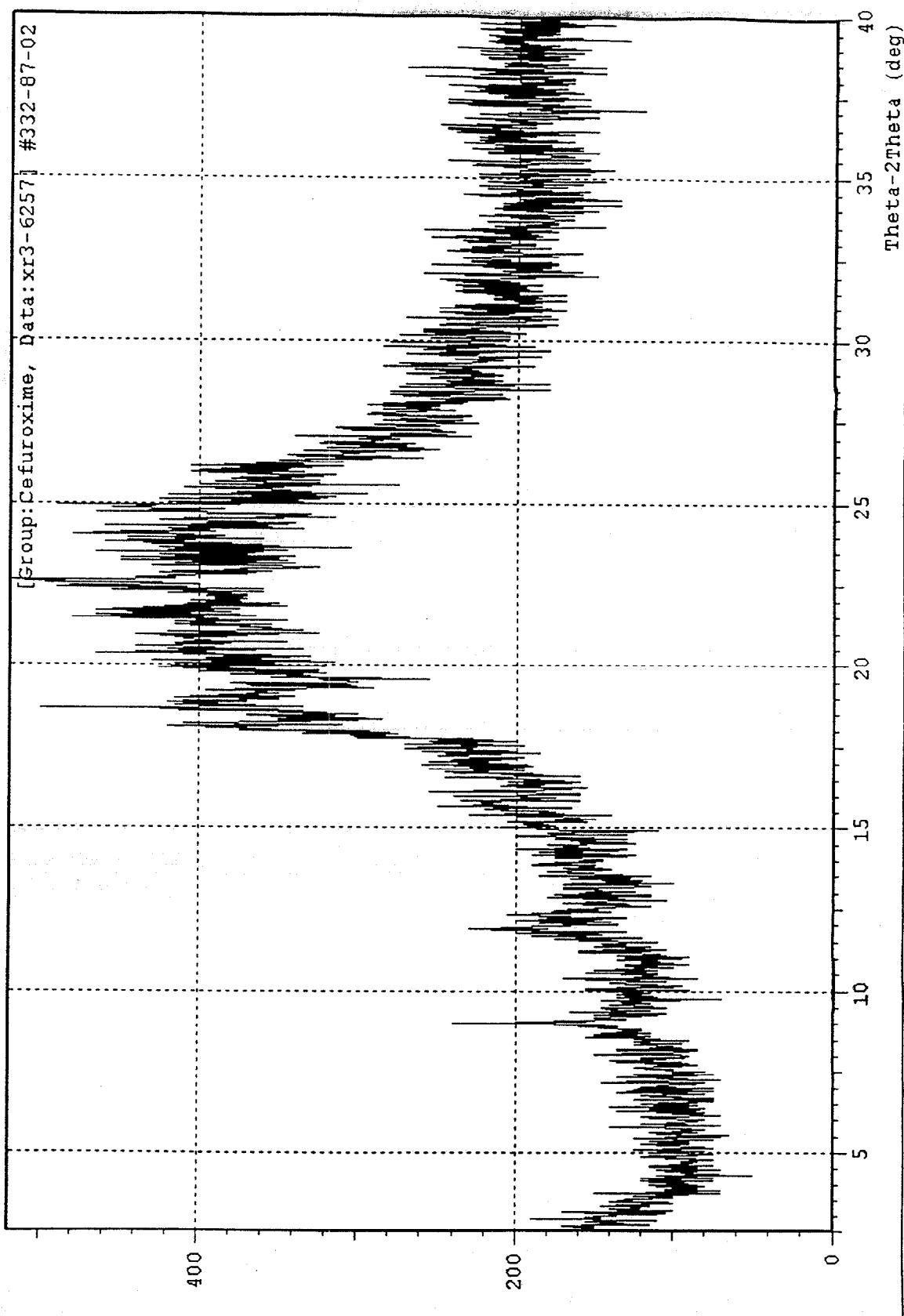
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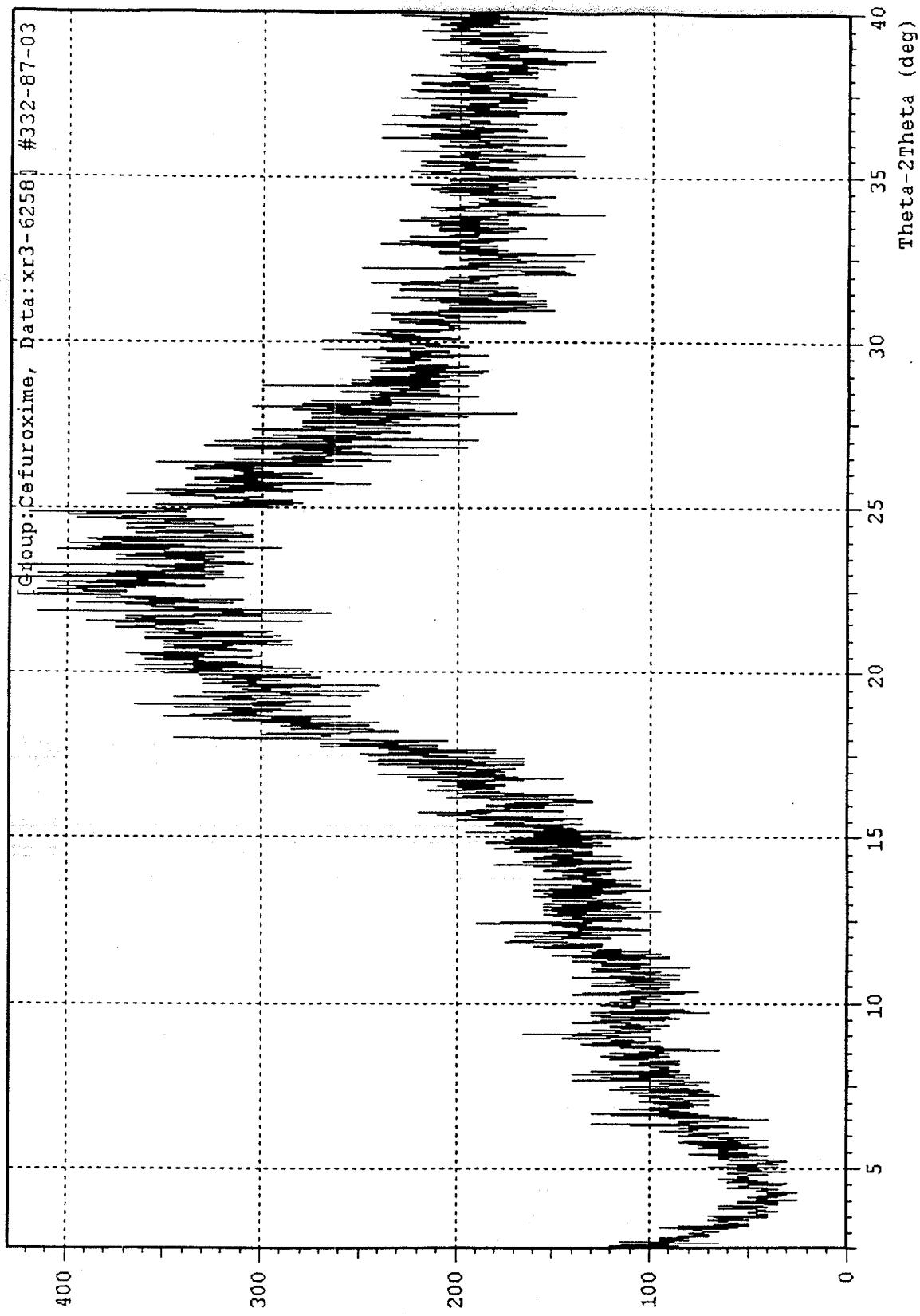
**Acquisition Parameters**

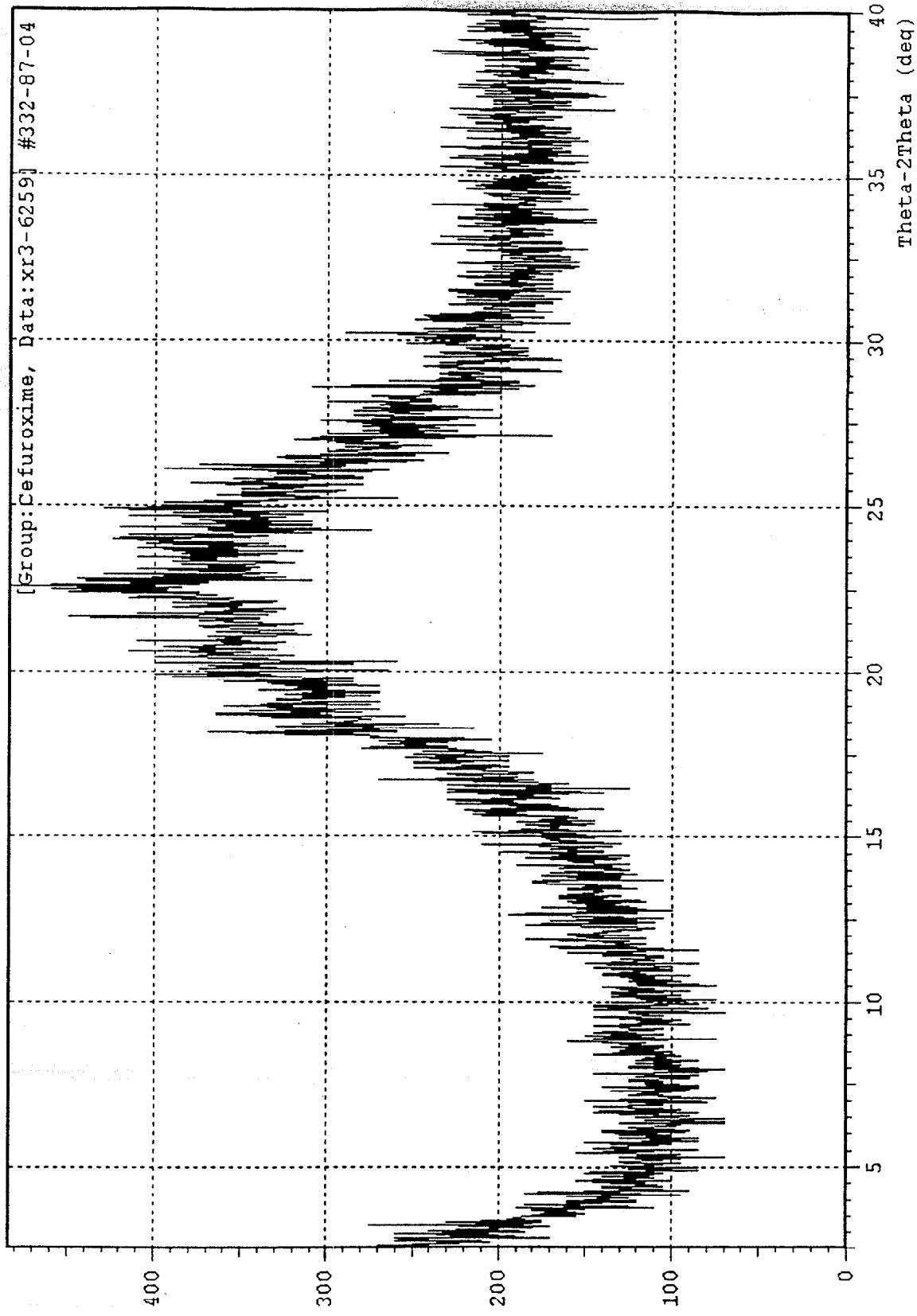
Collection time: Fri Aug 18 10:46:59 2000  
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Number of background scans: 0  
Resolution: 4.000  
Sample gain: 64.0  
Mirror velocity: 0.3165  
Aperture: 59.00

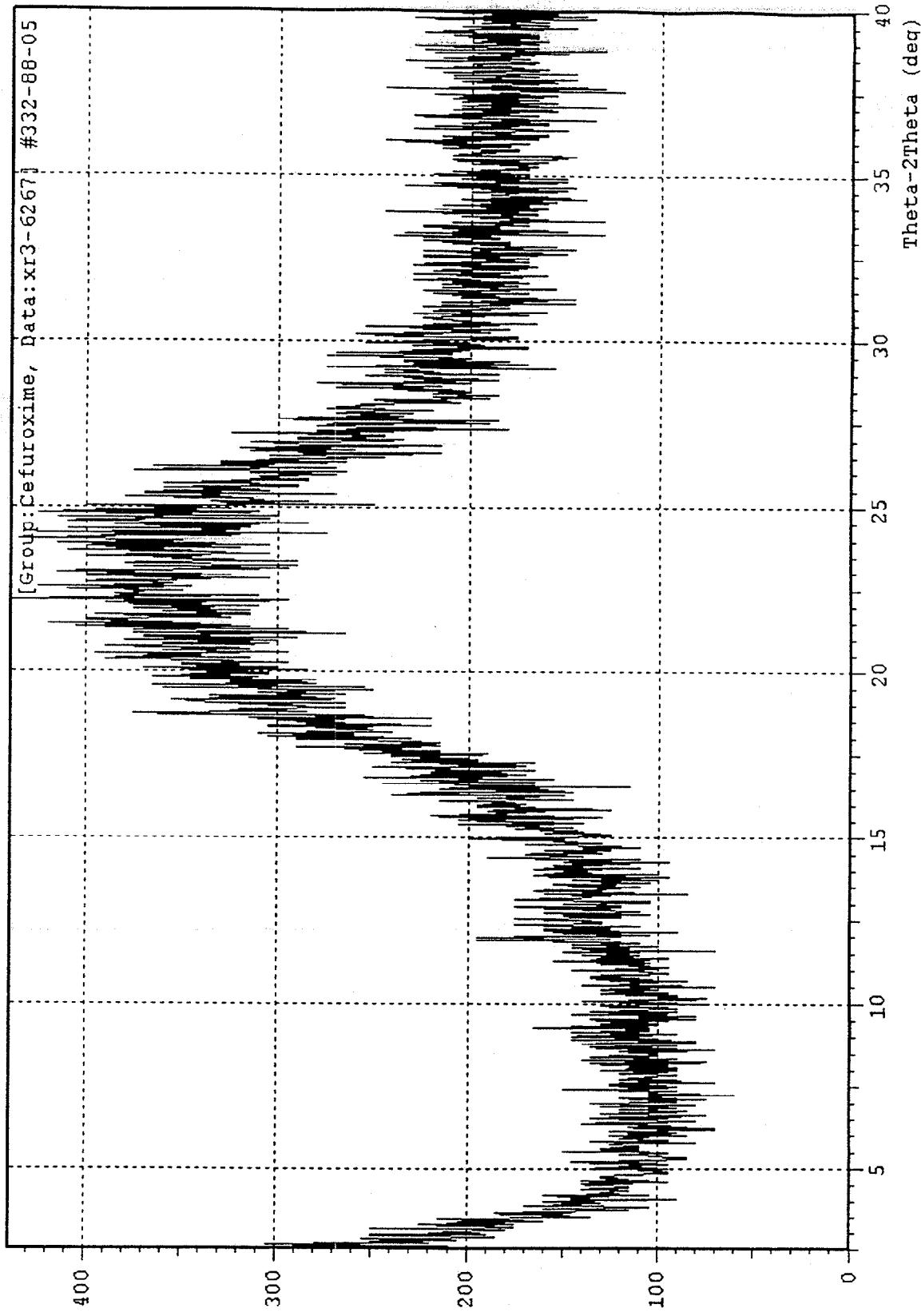


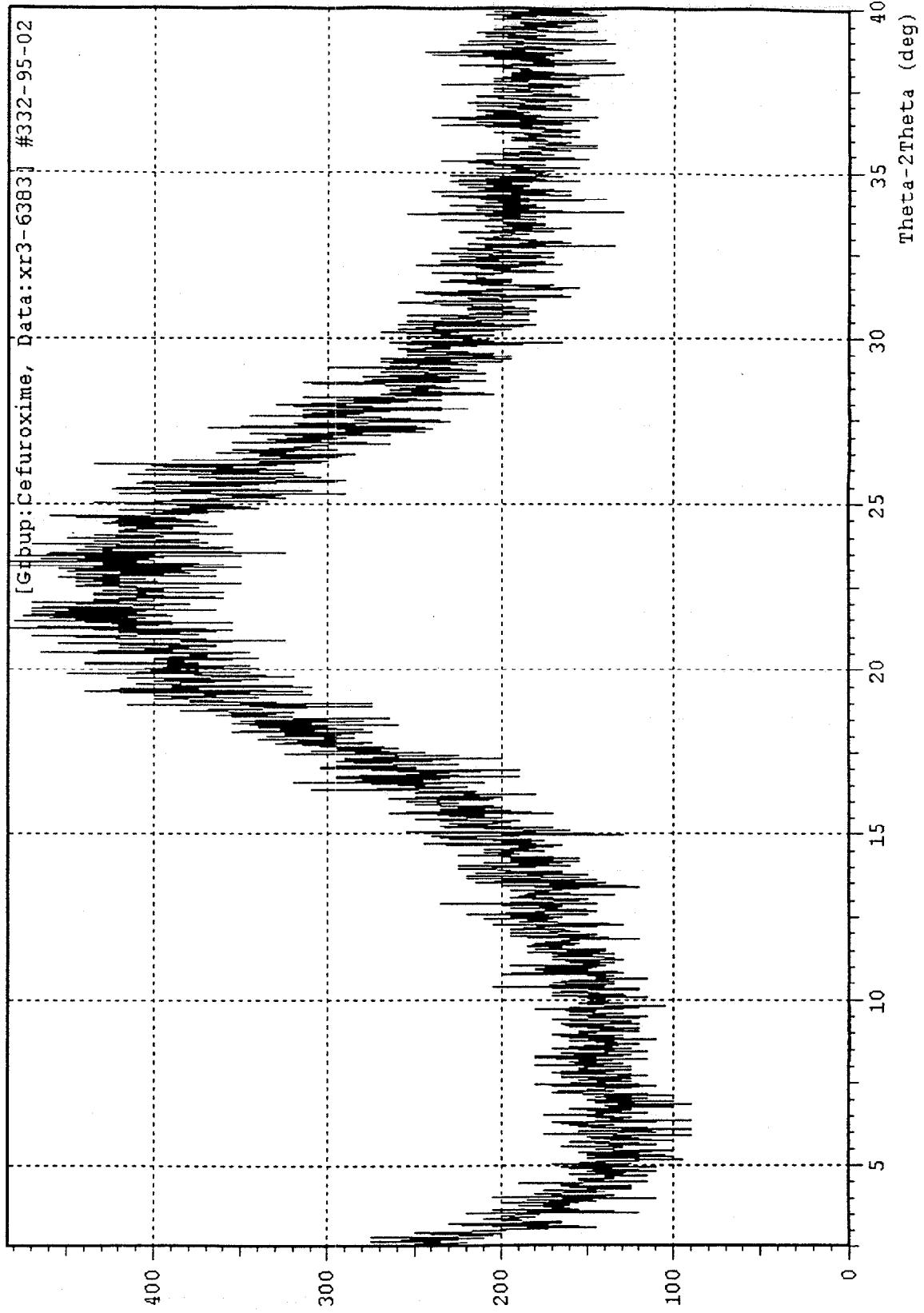


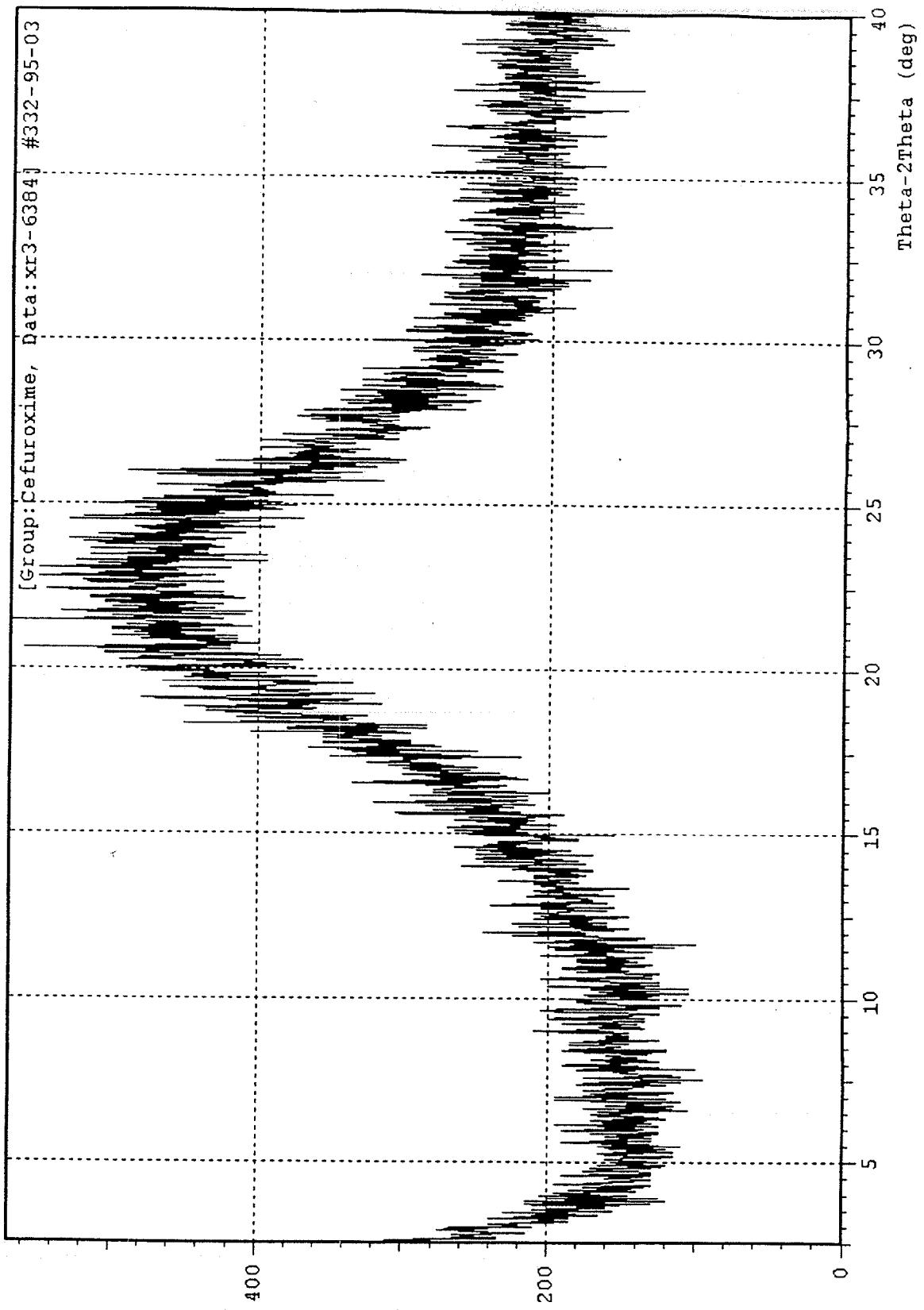


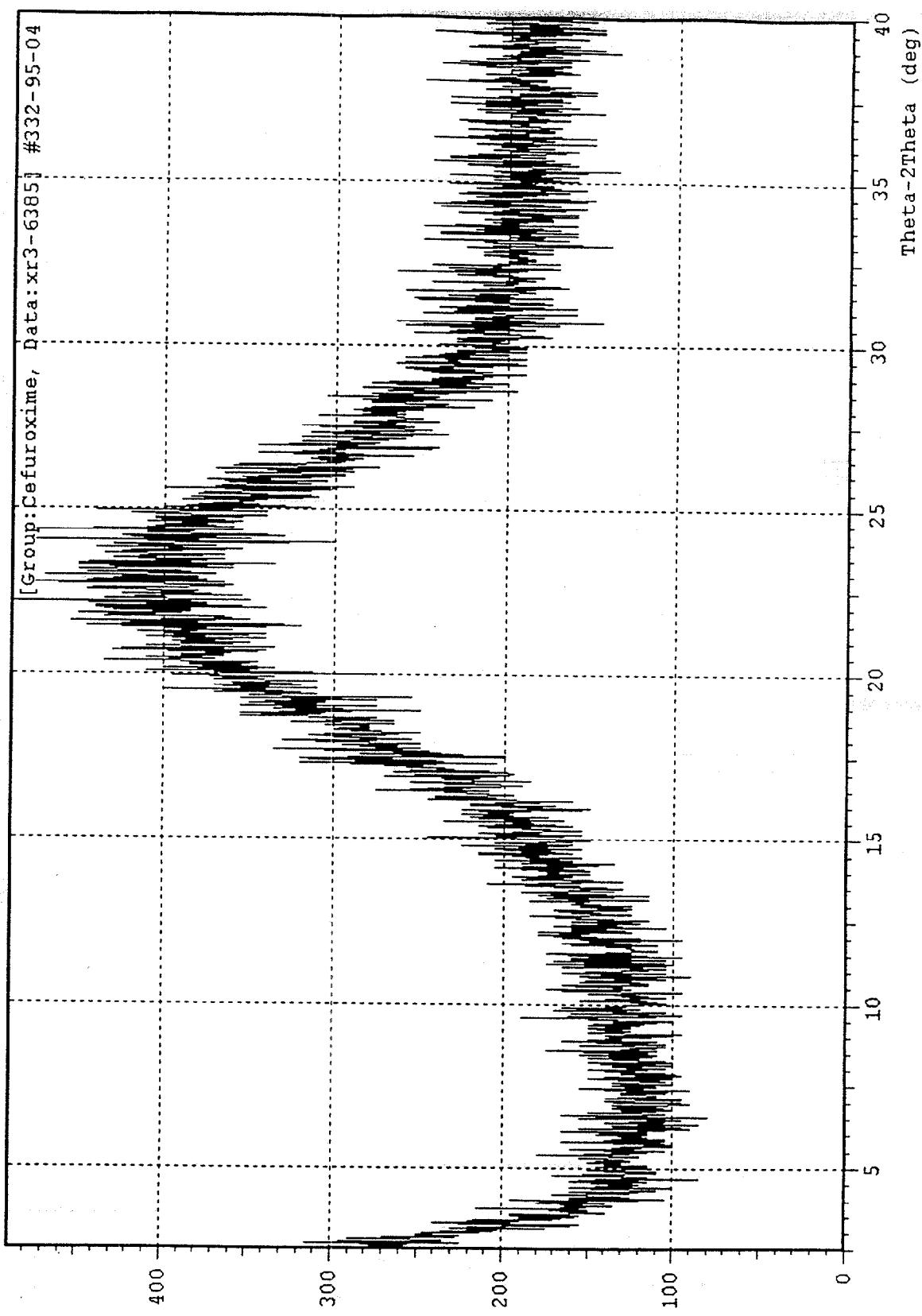


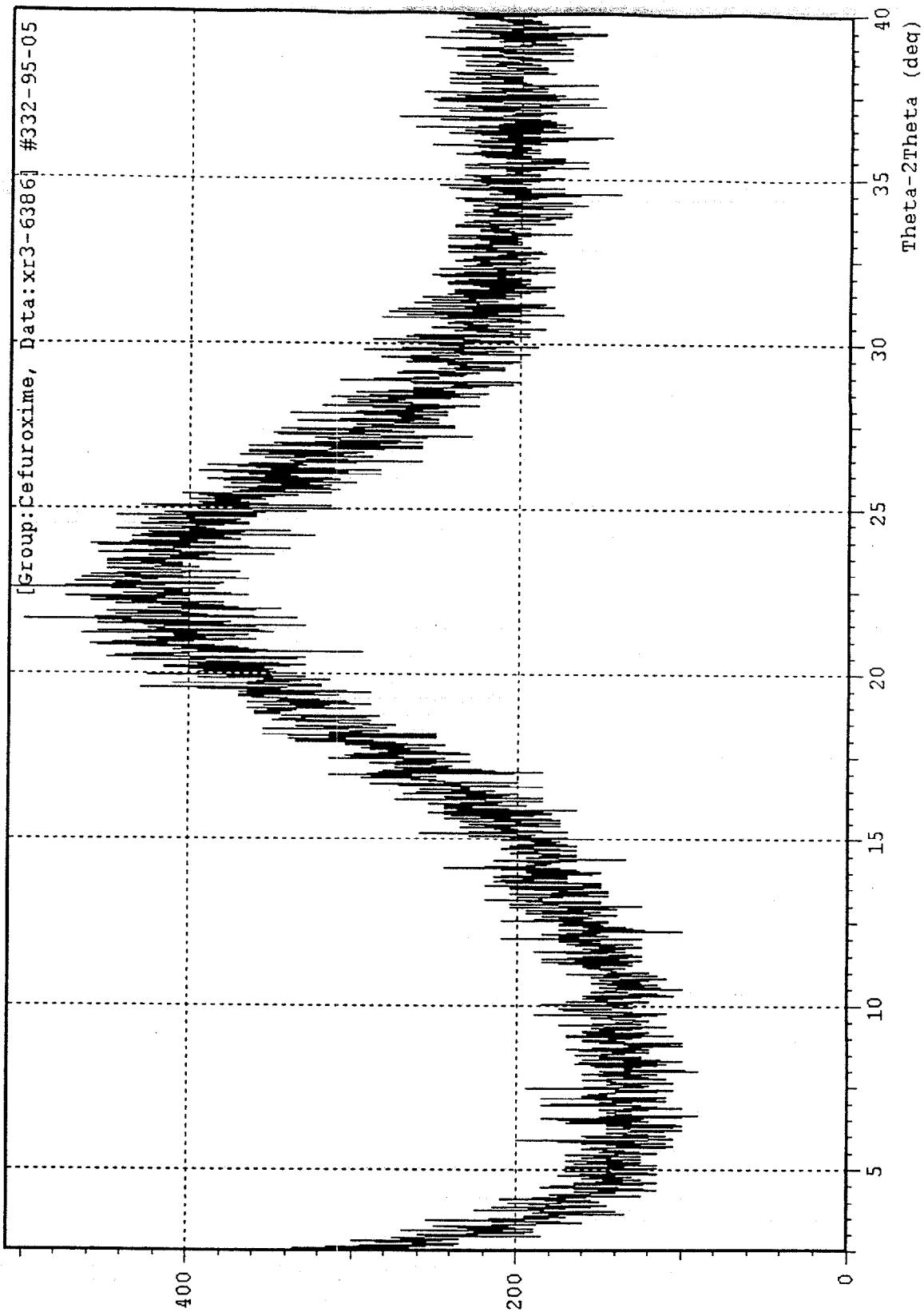


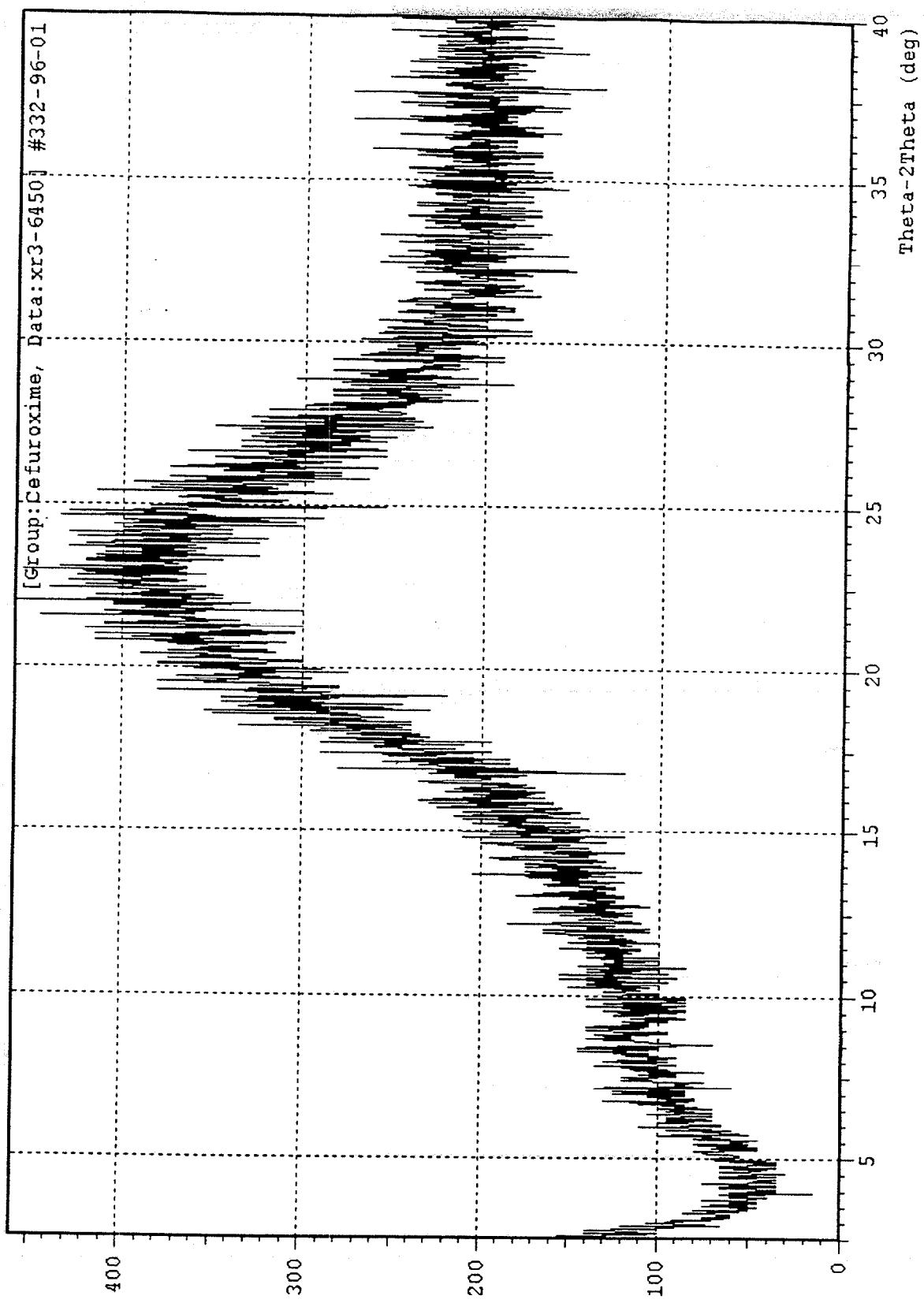


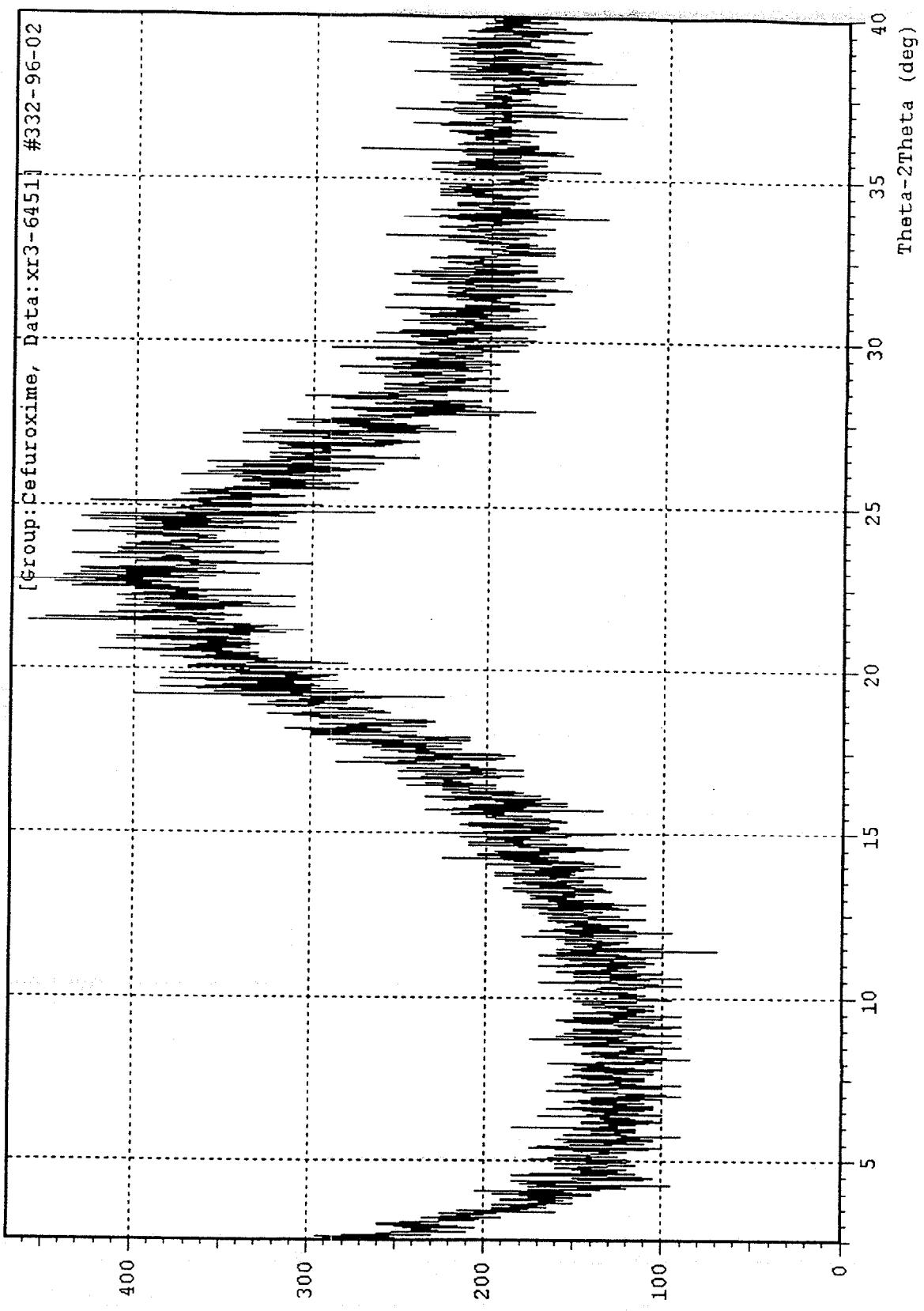


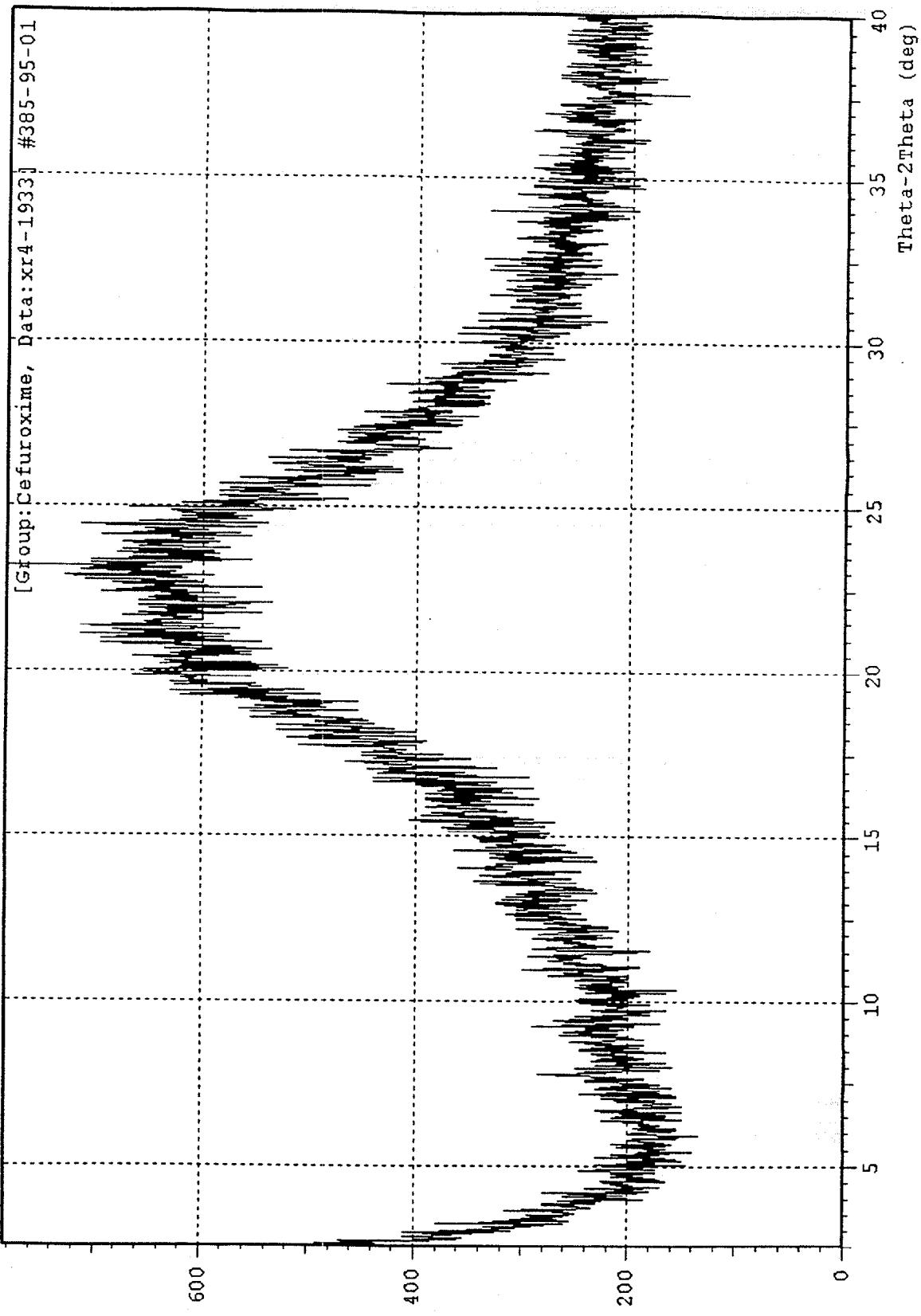


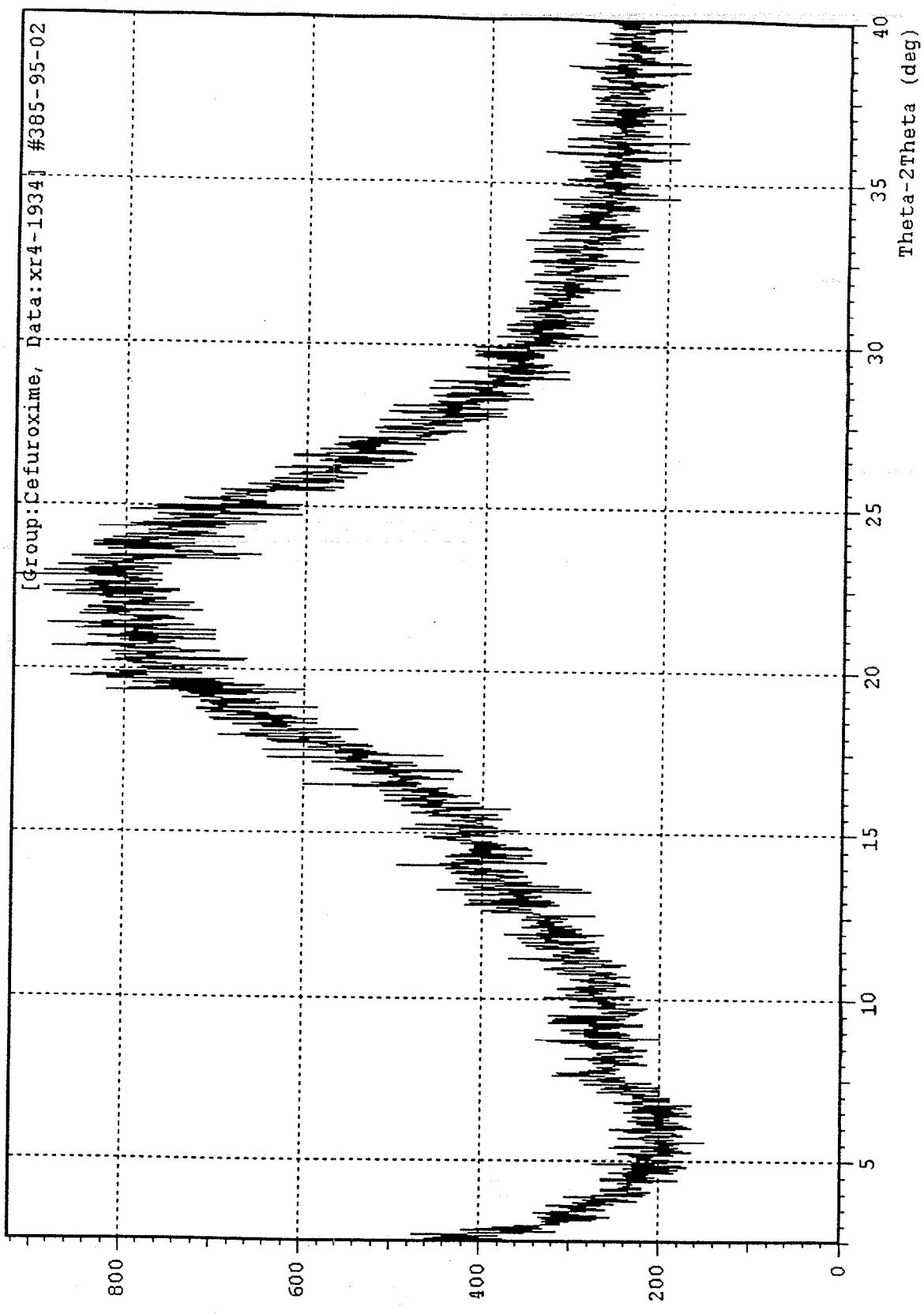


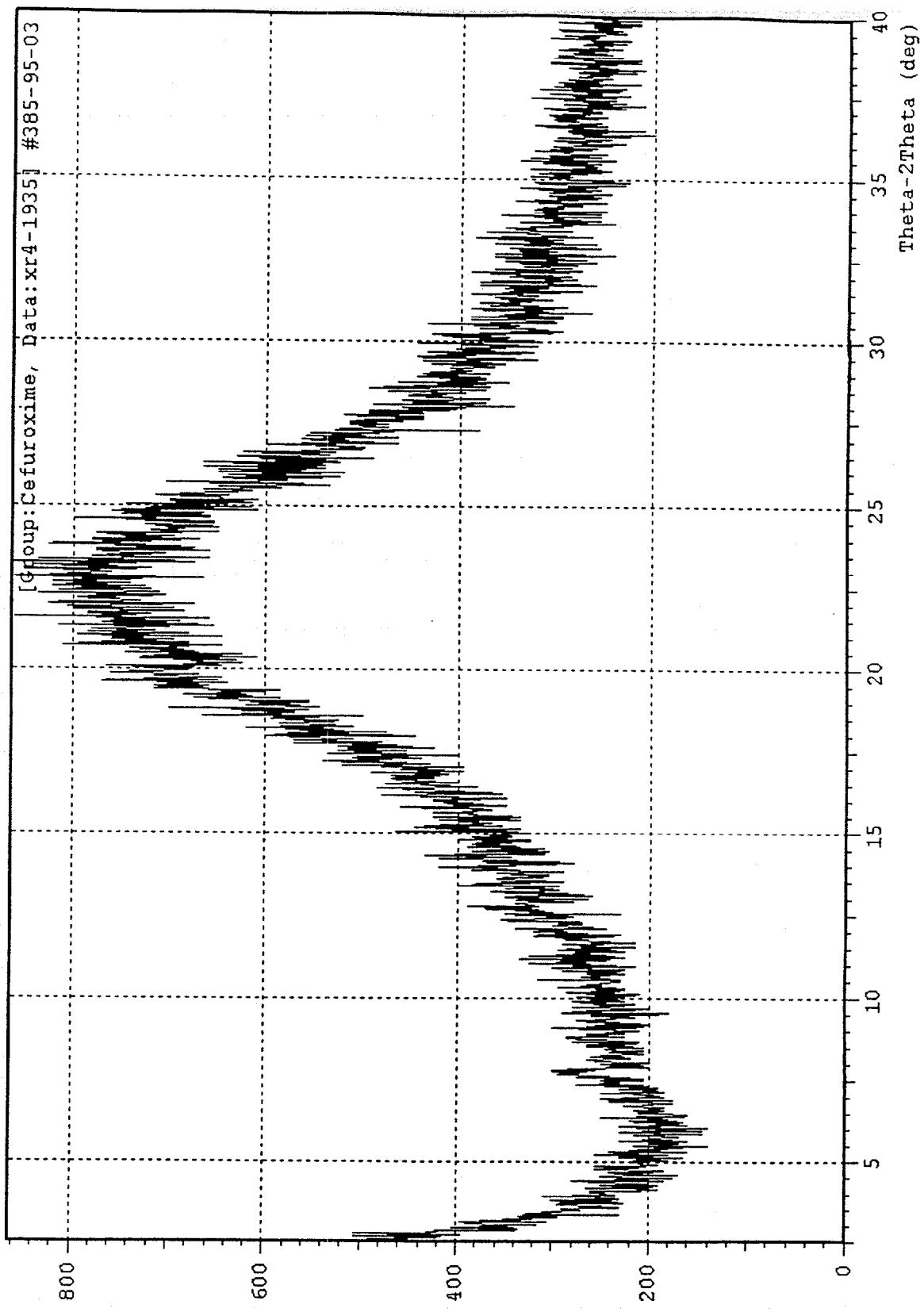


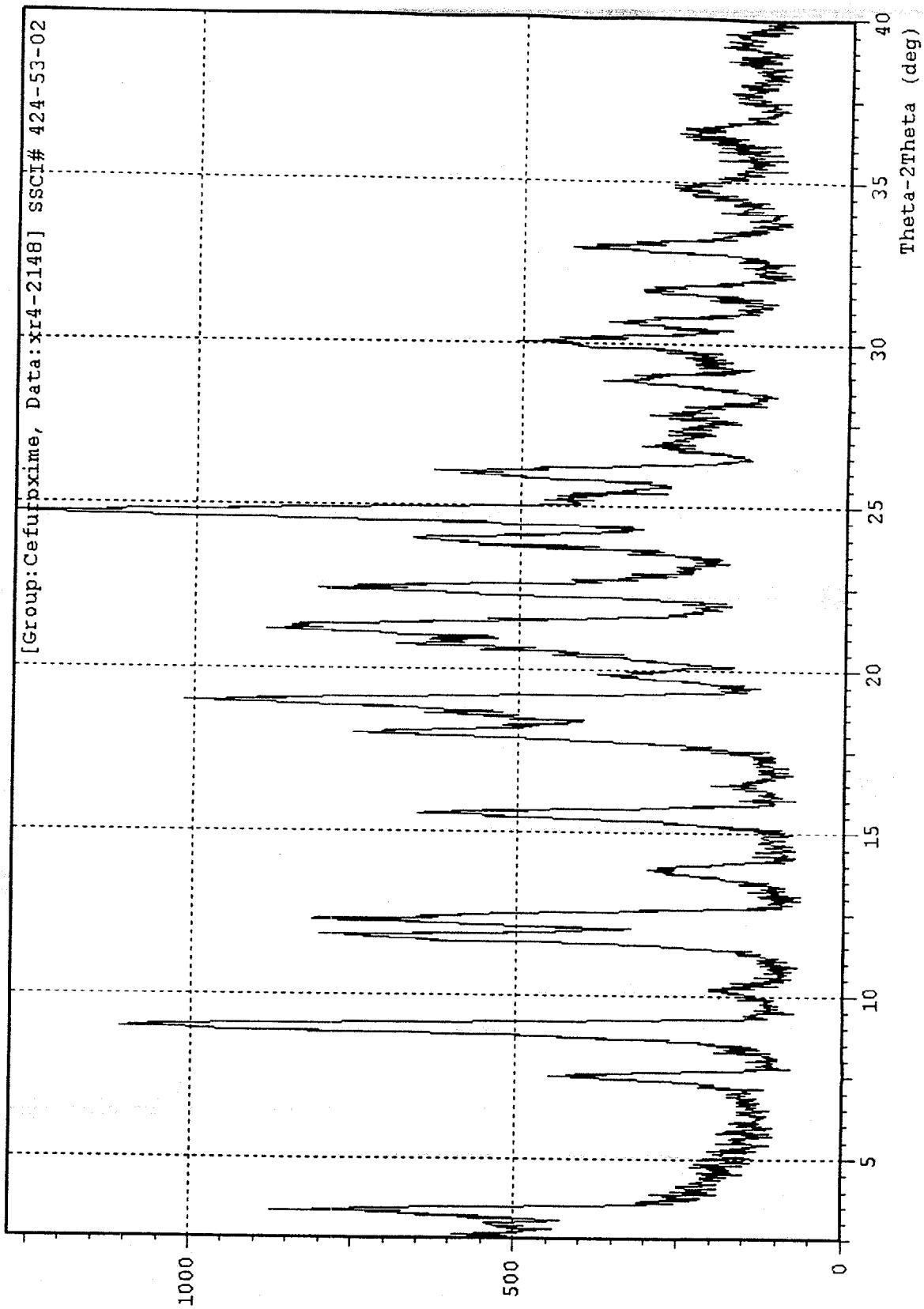


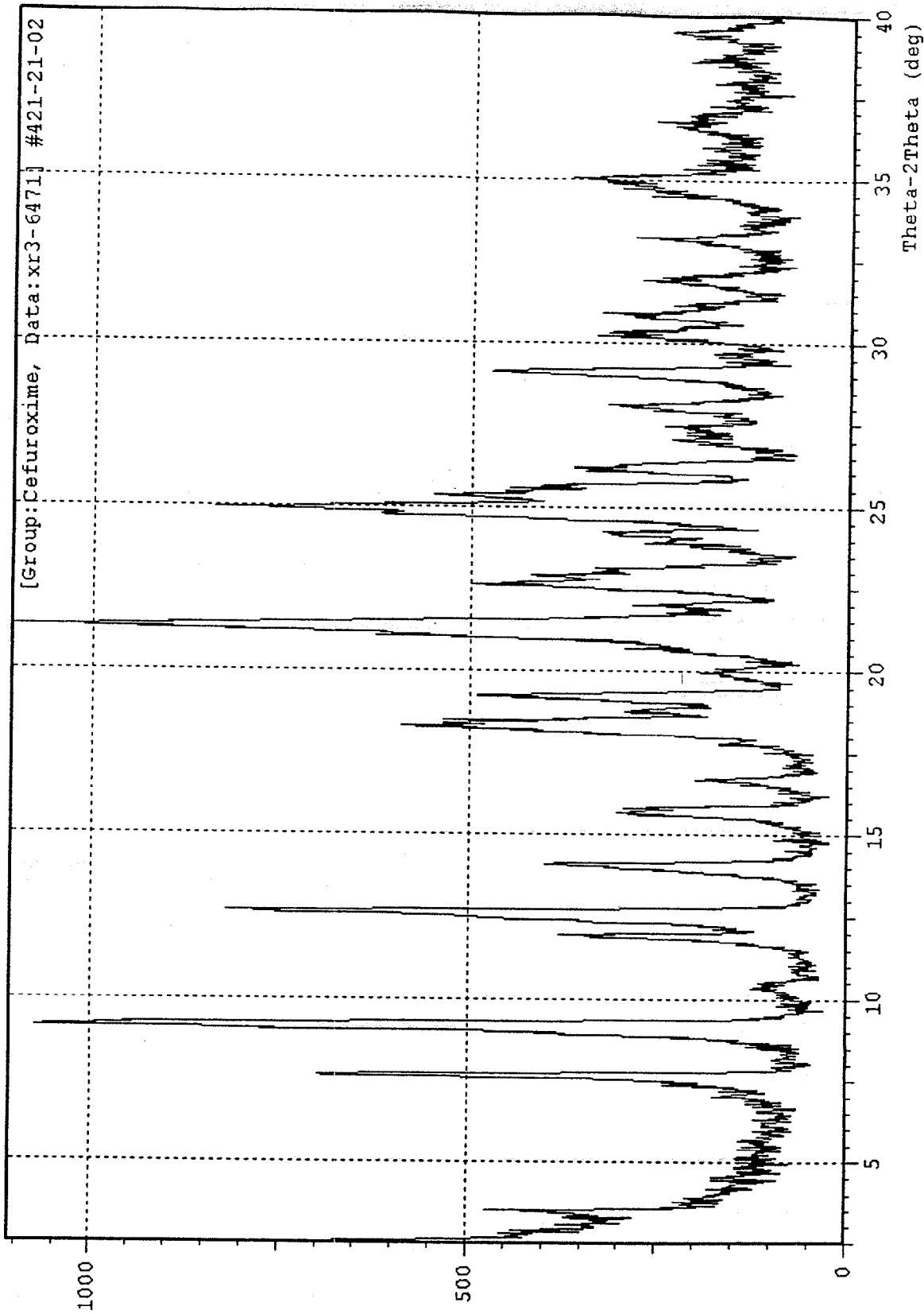


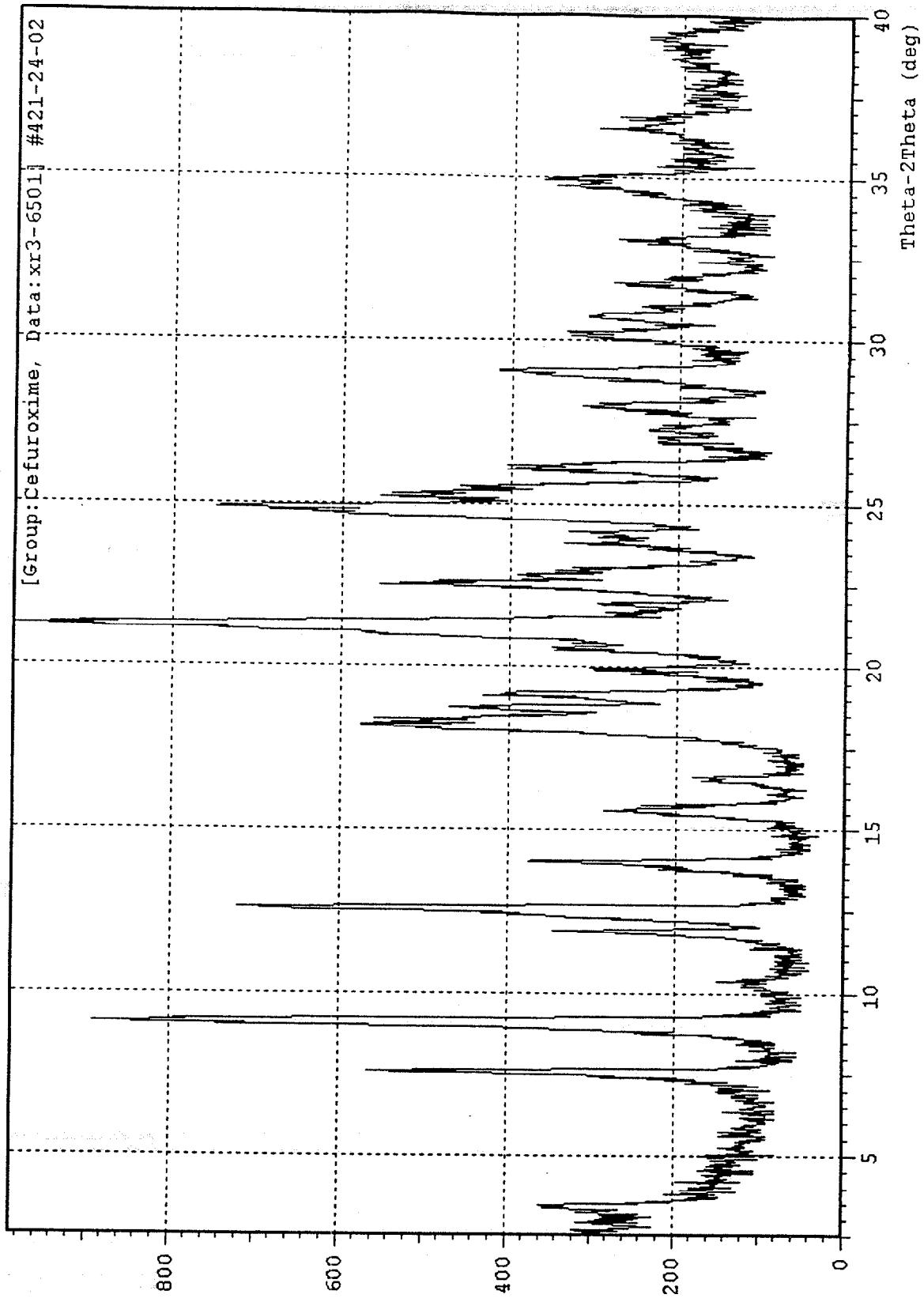


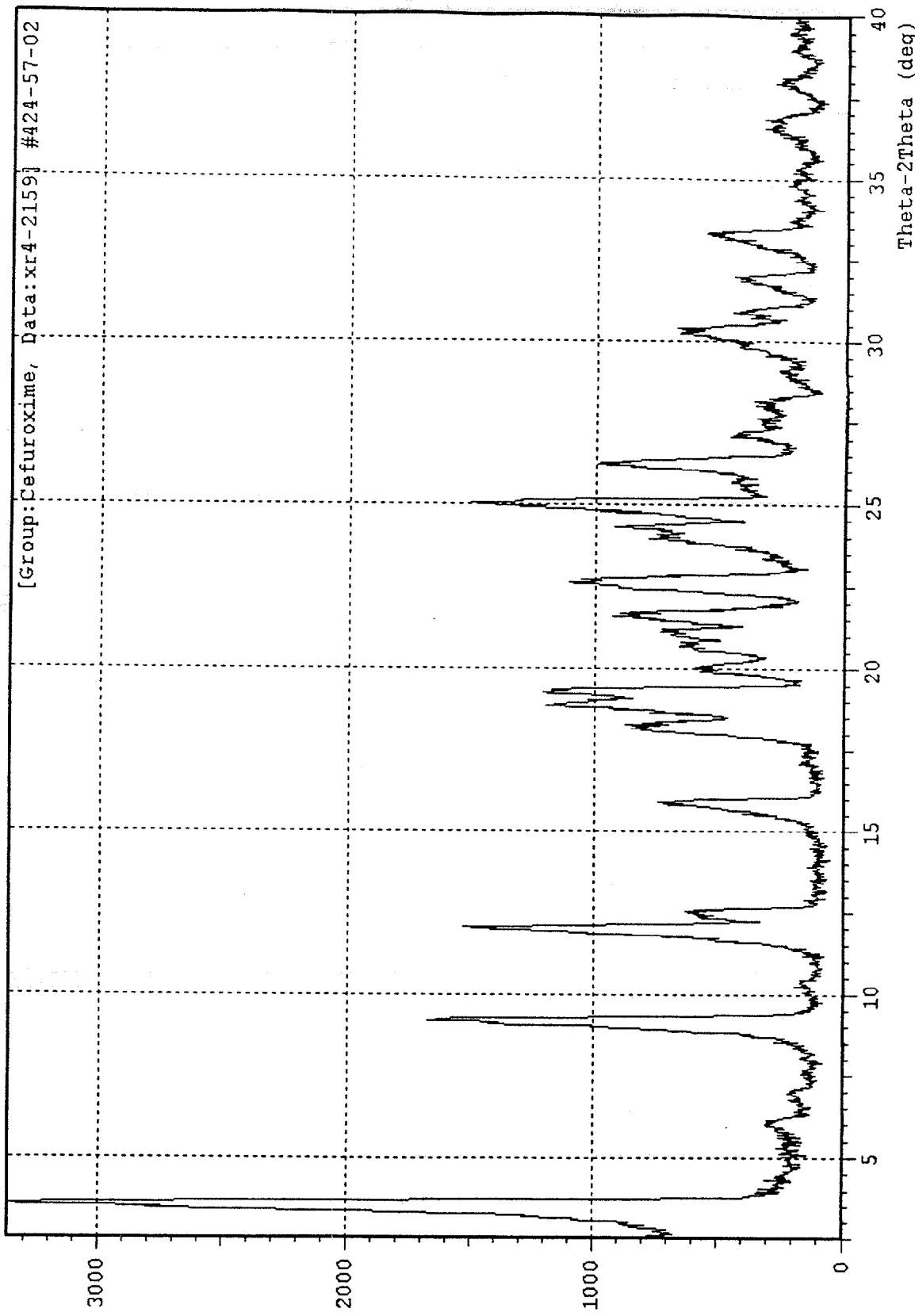


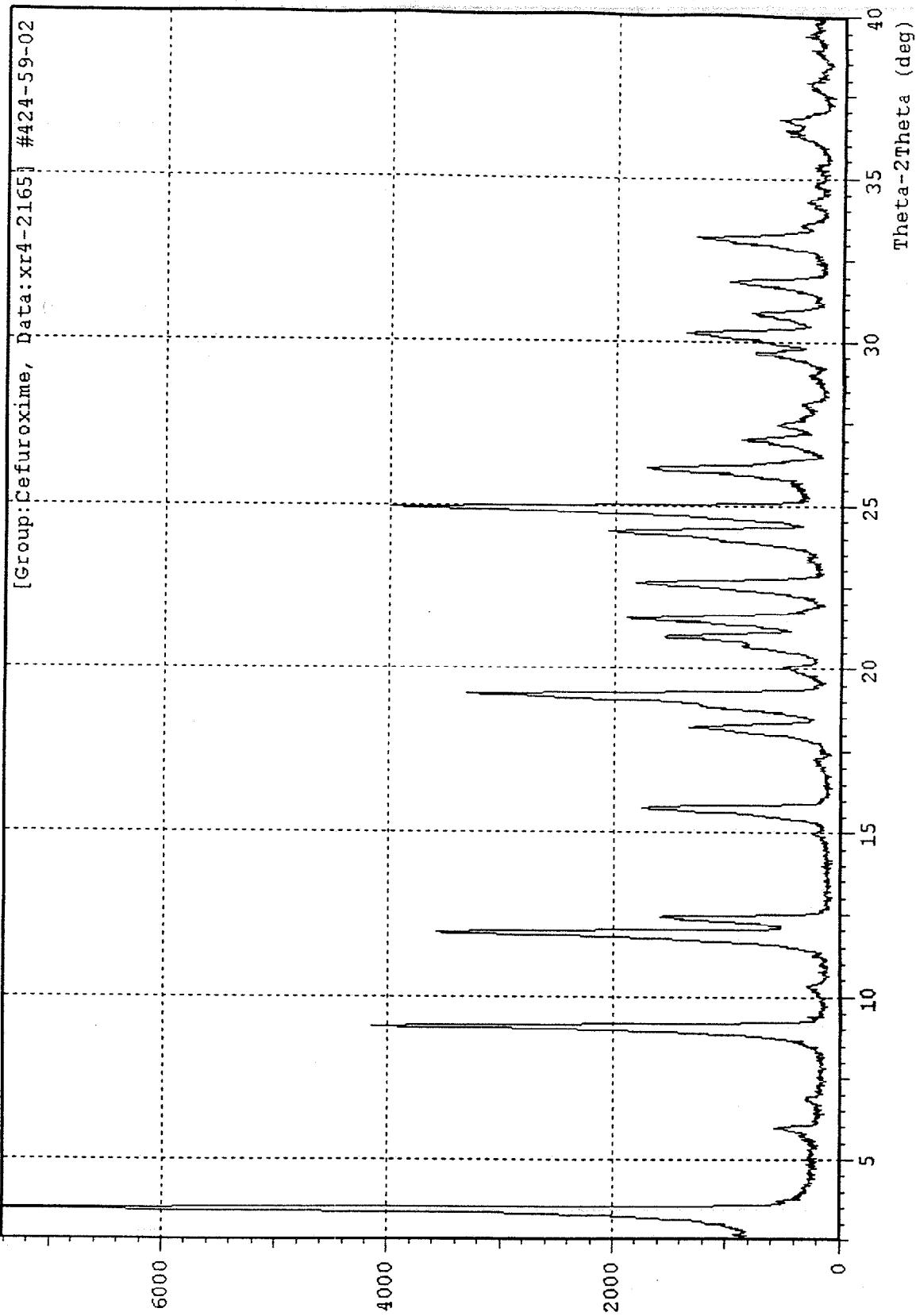


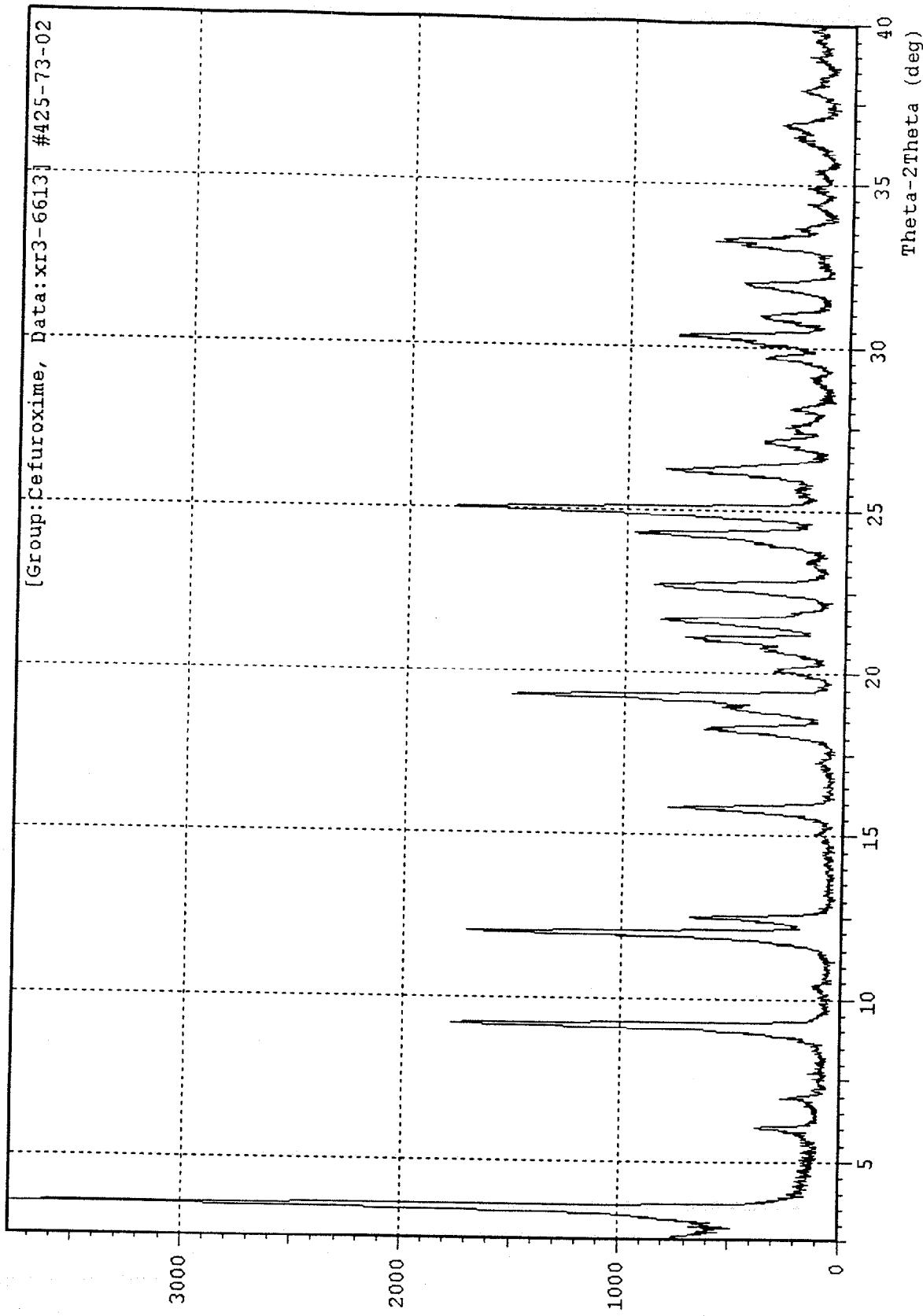


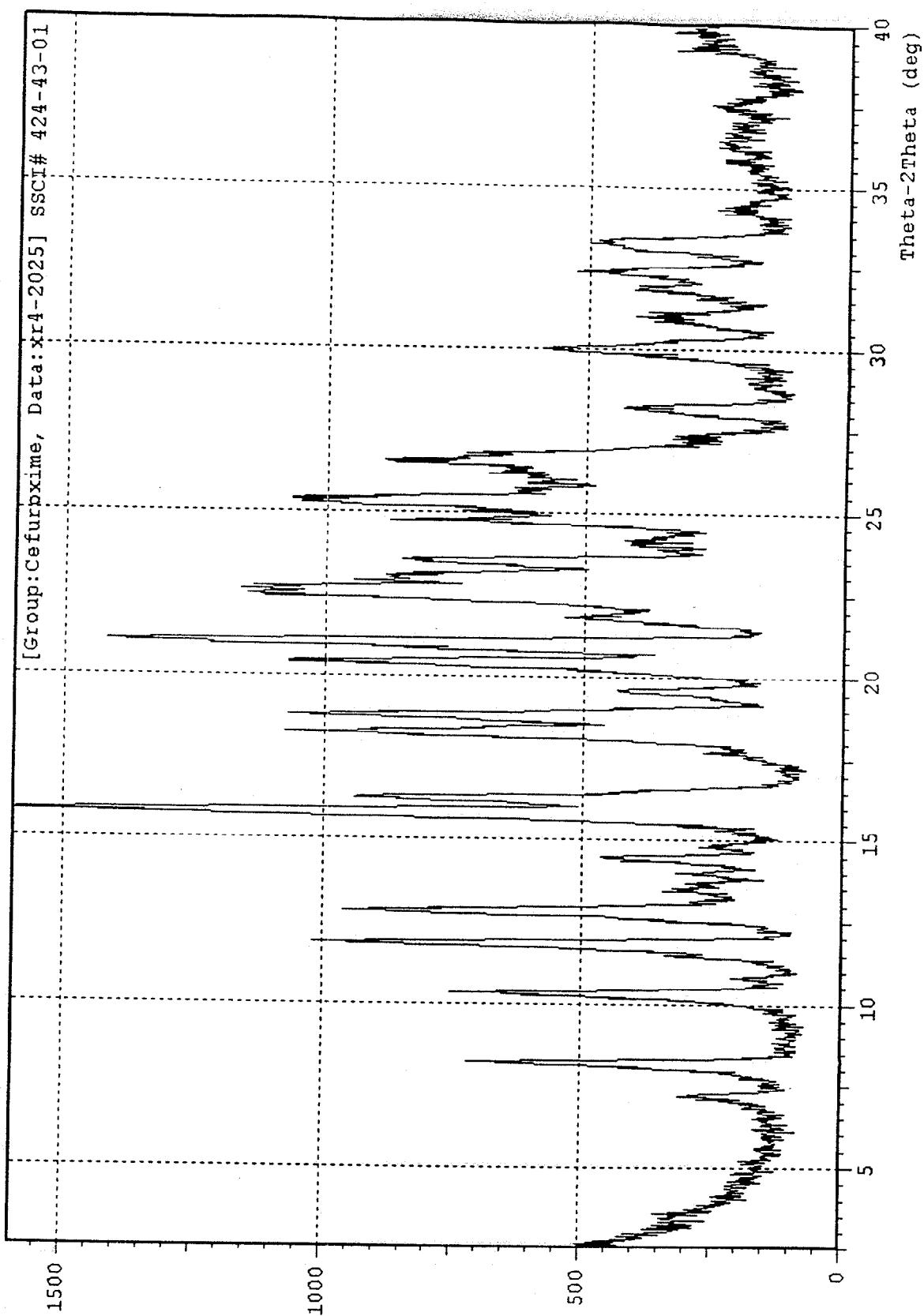


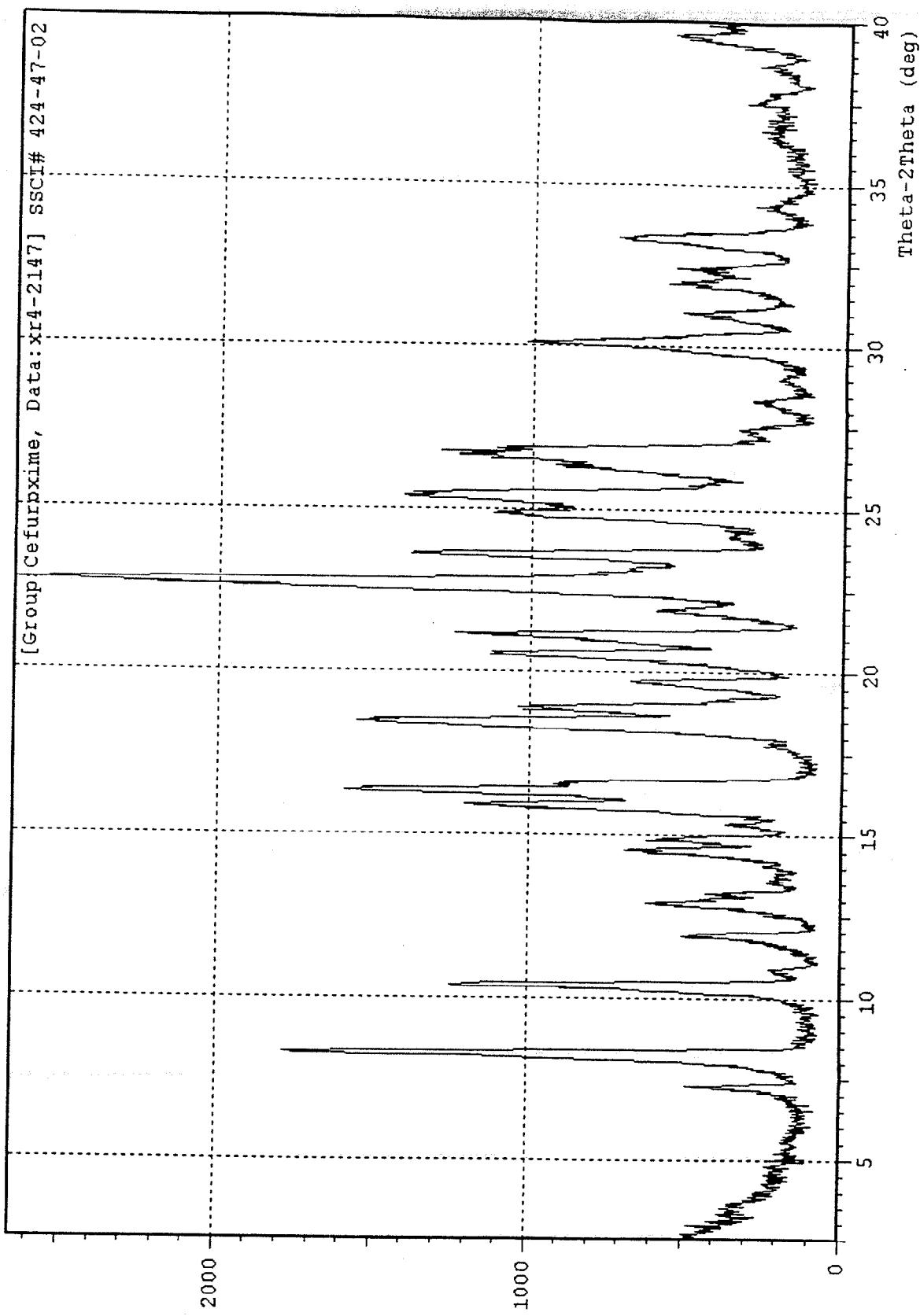


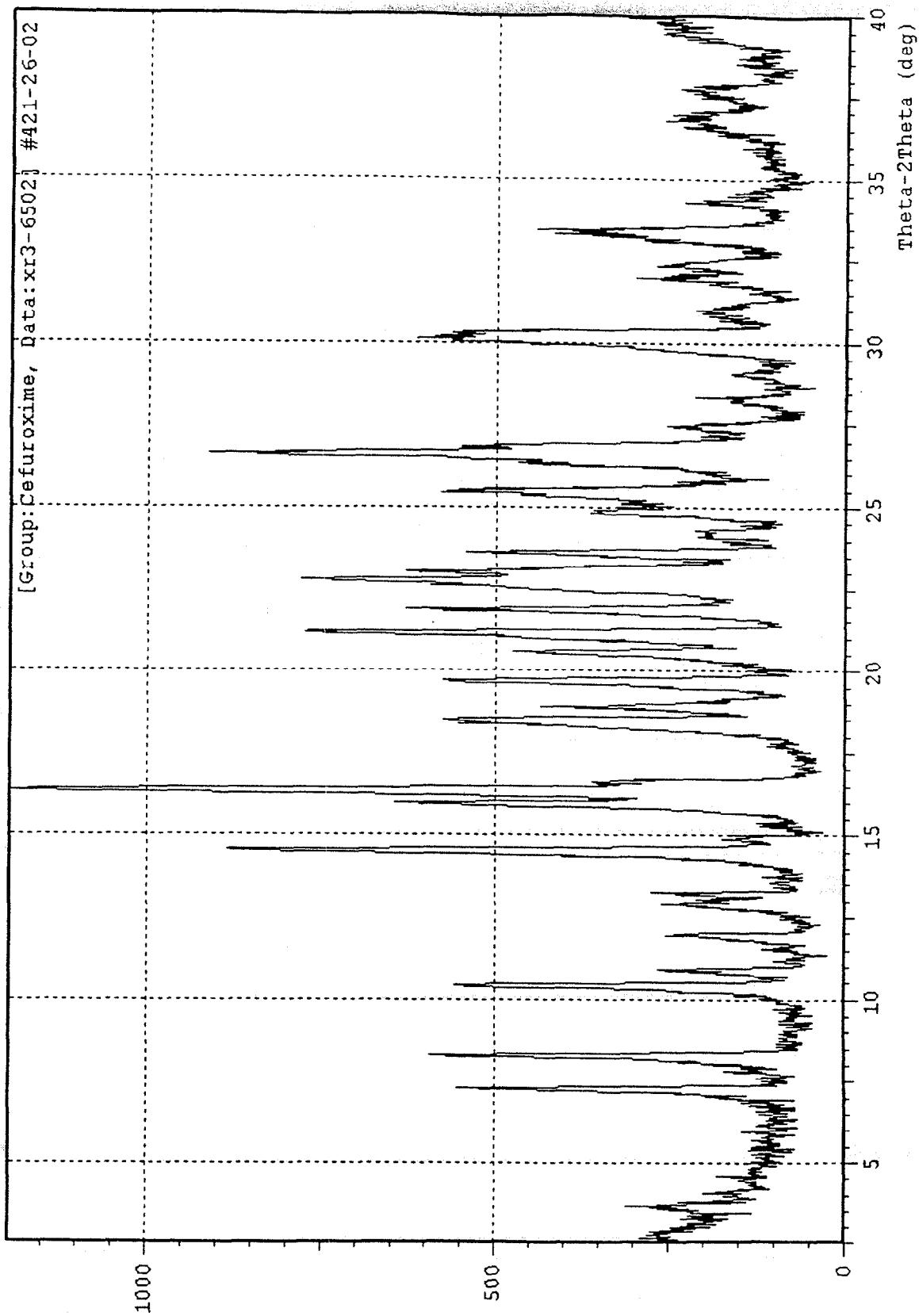


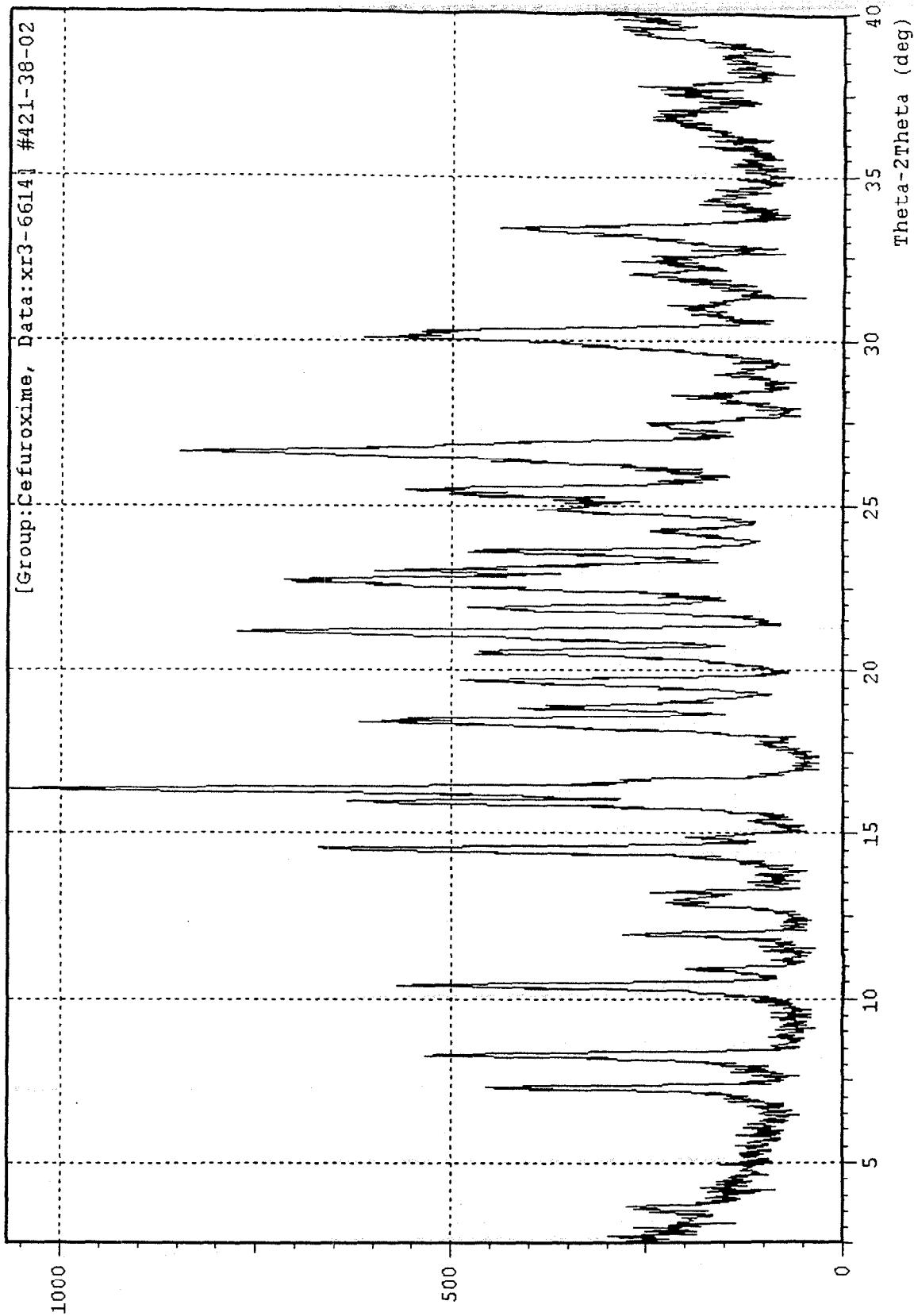


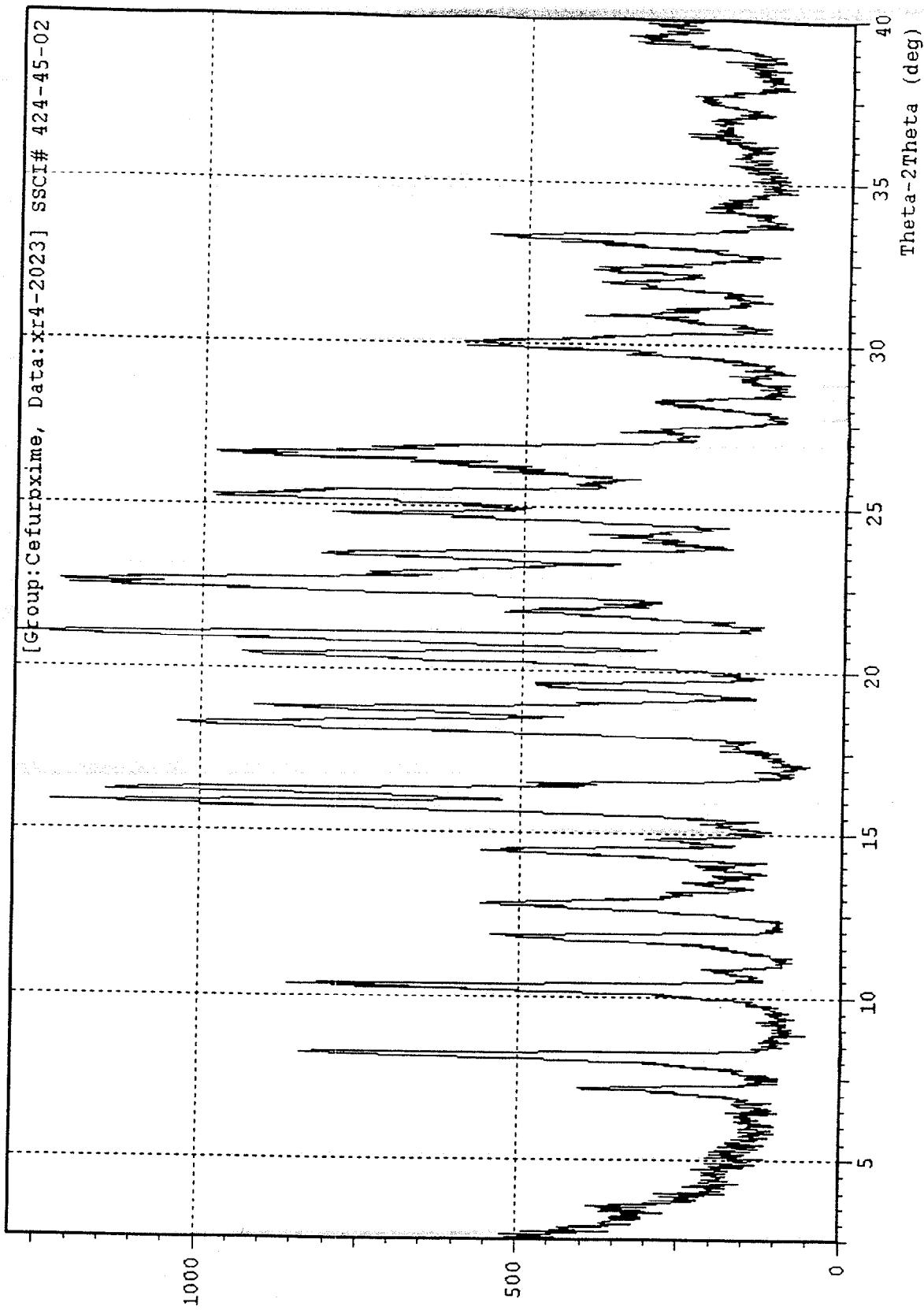


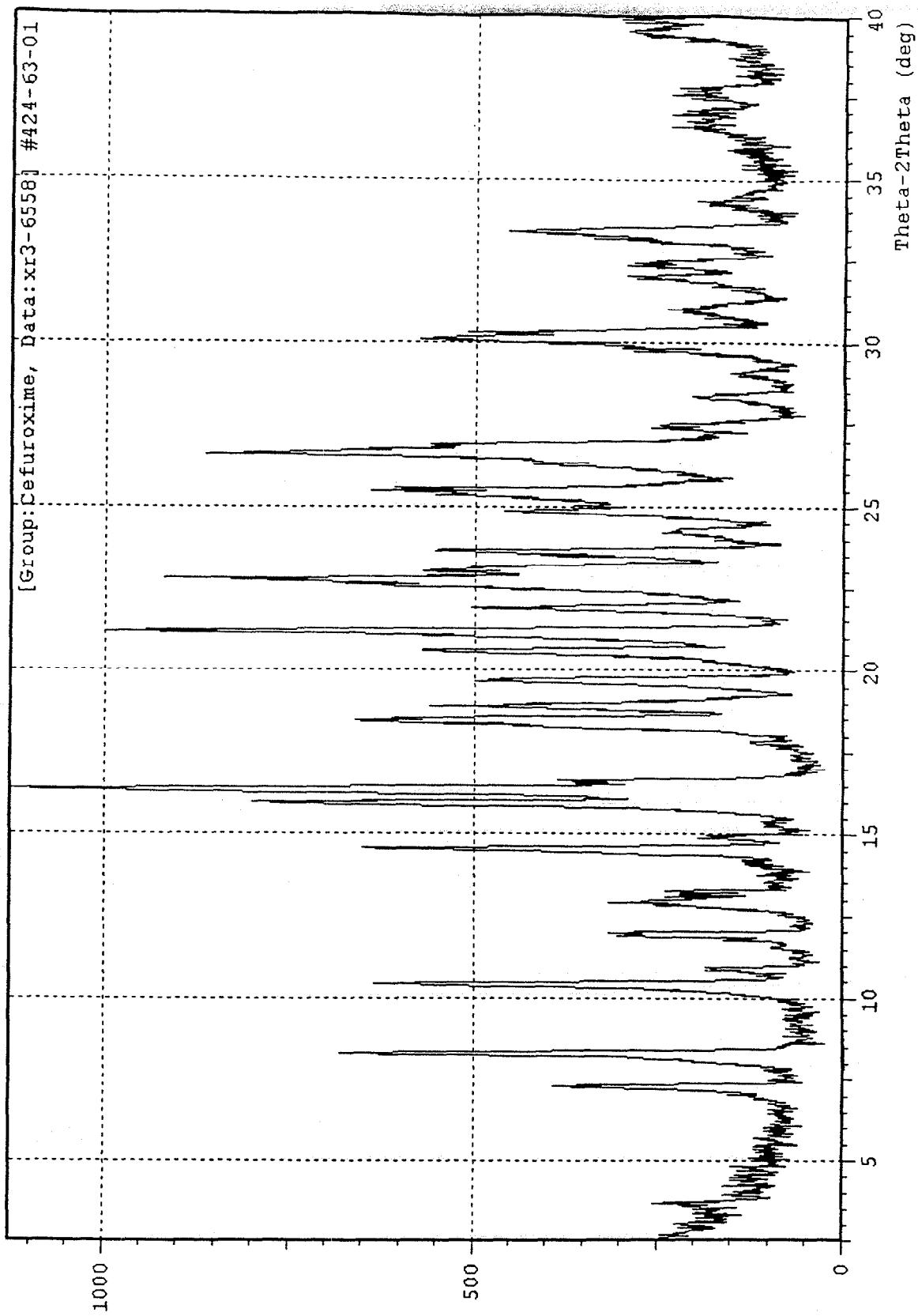




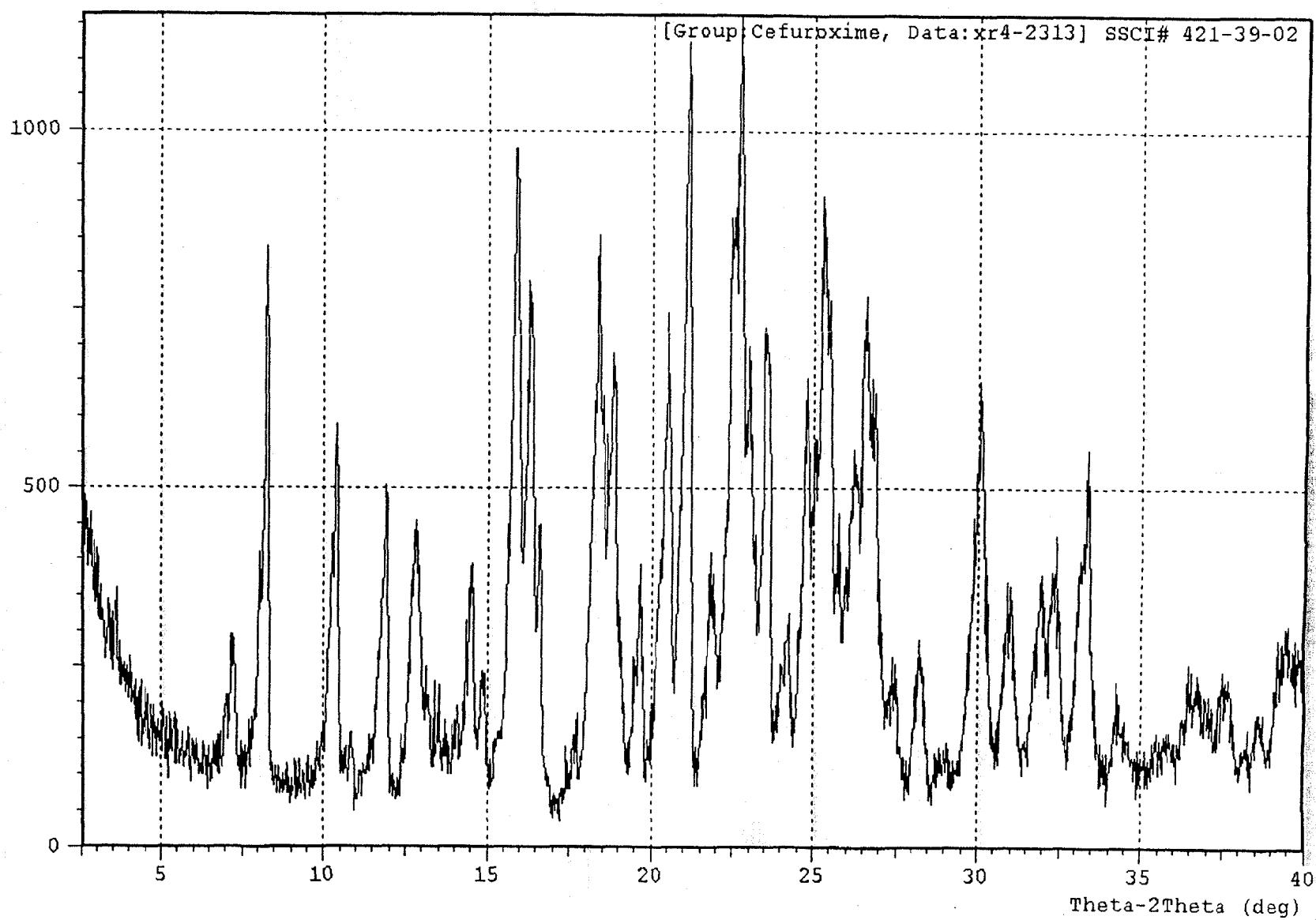


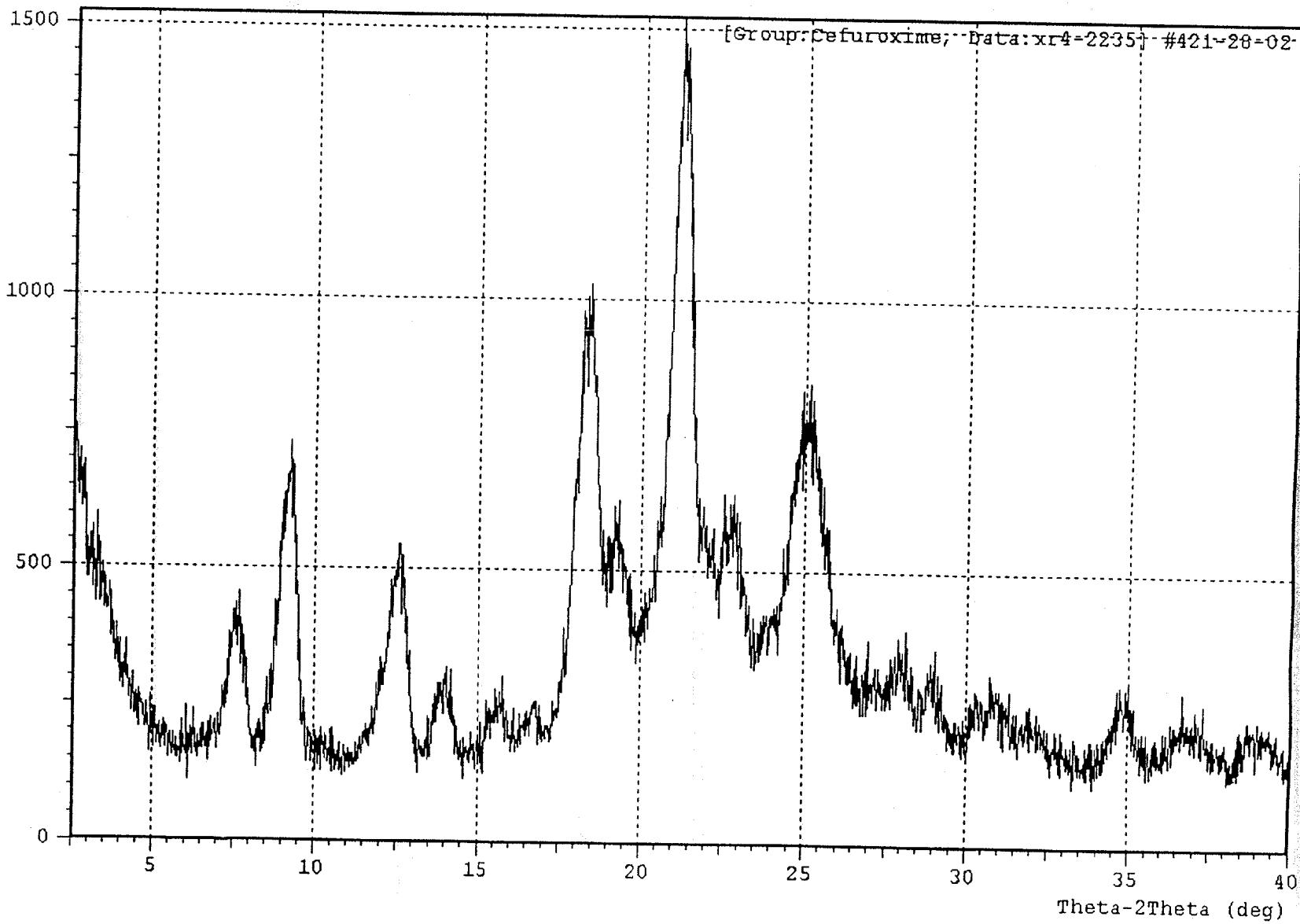




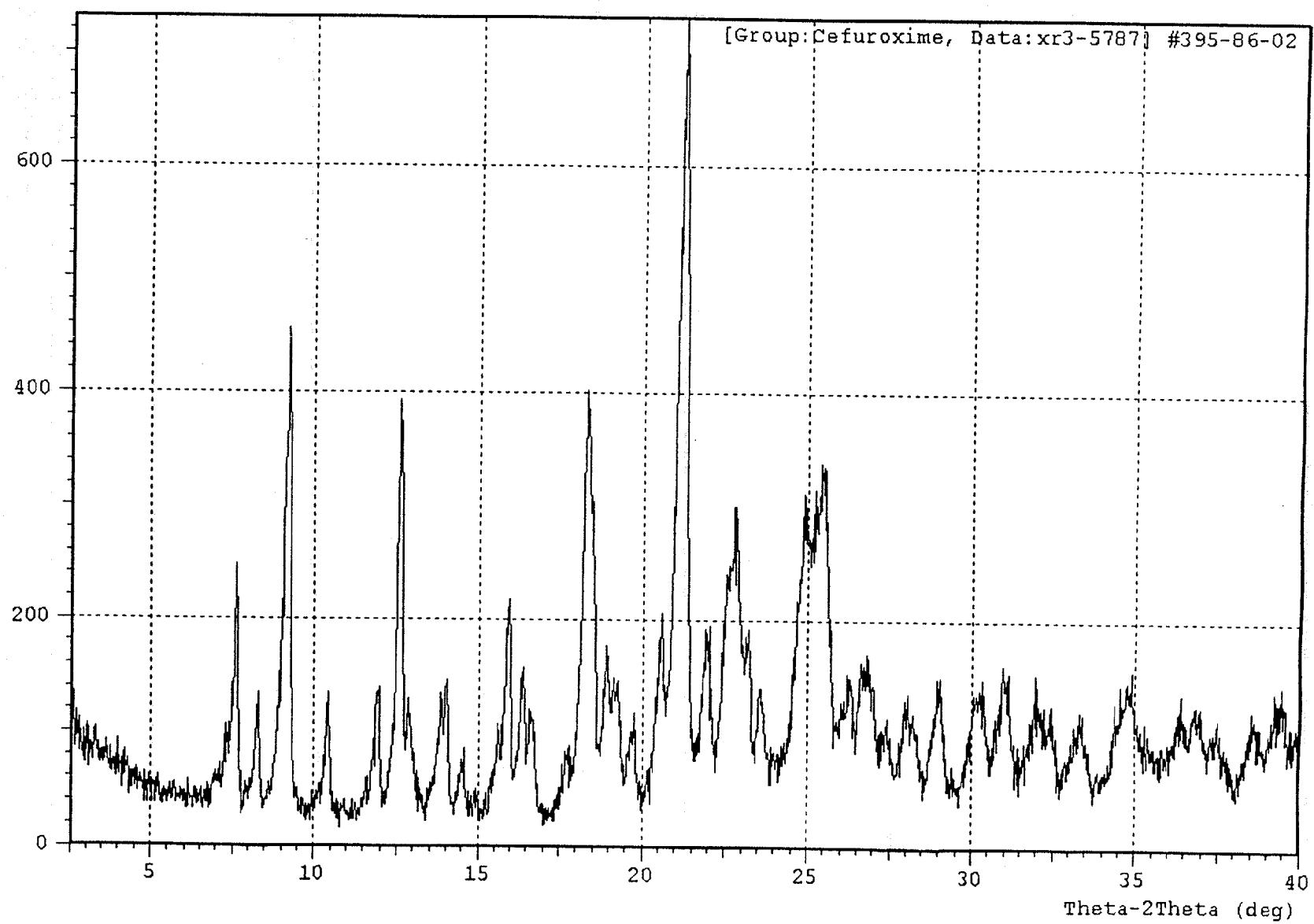


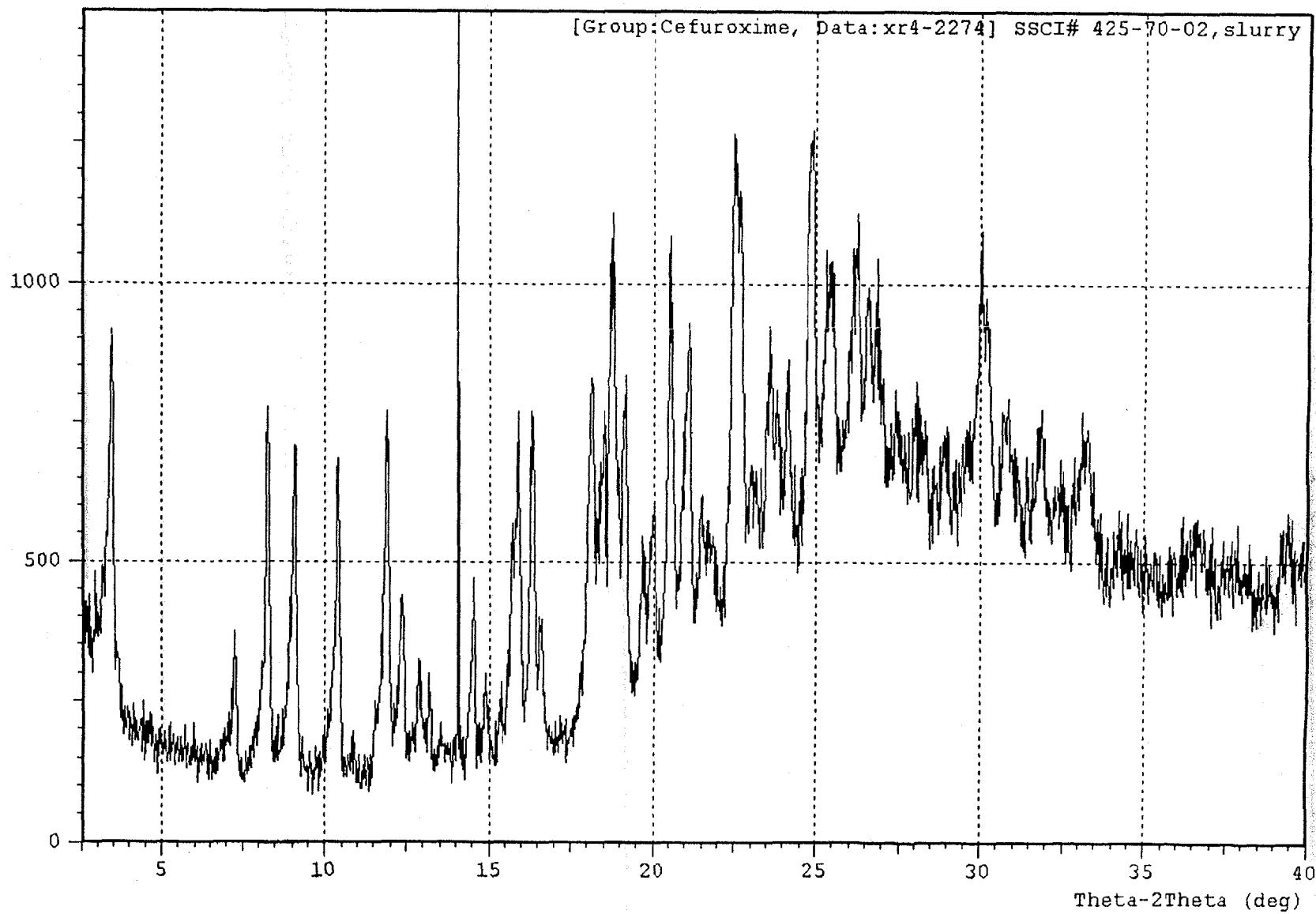
[Group:Cefuroxime, Data:xr4-2313] SSCI# 421-39-02



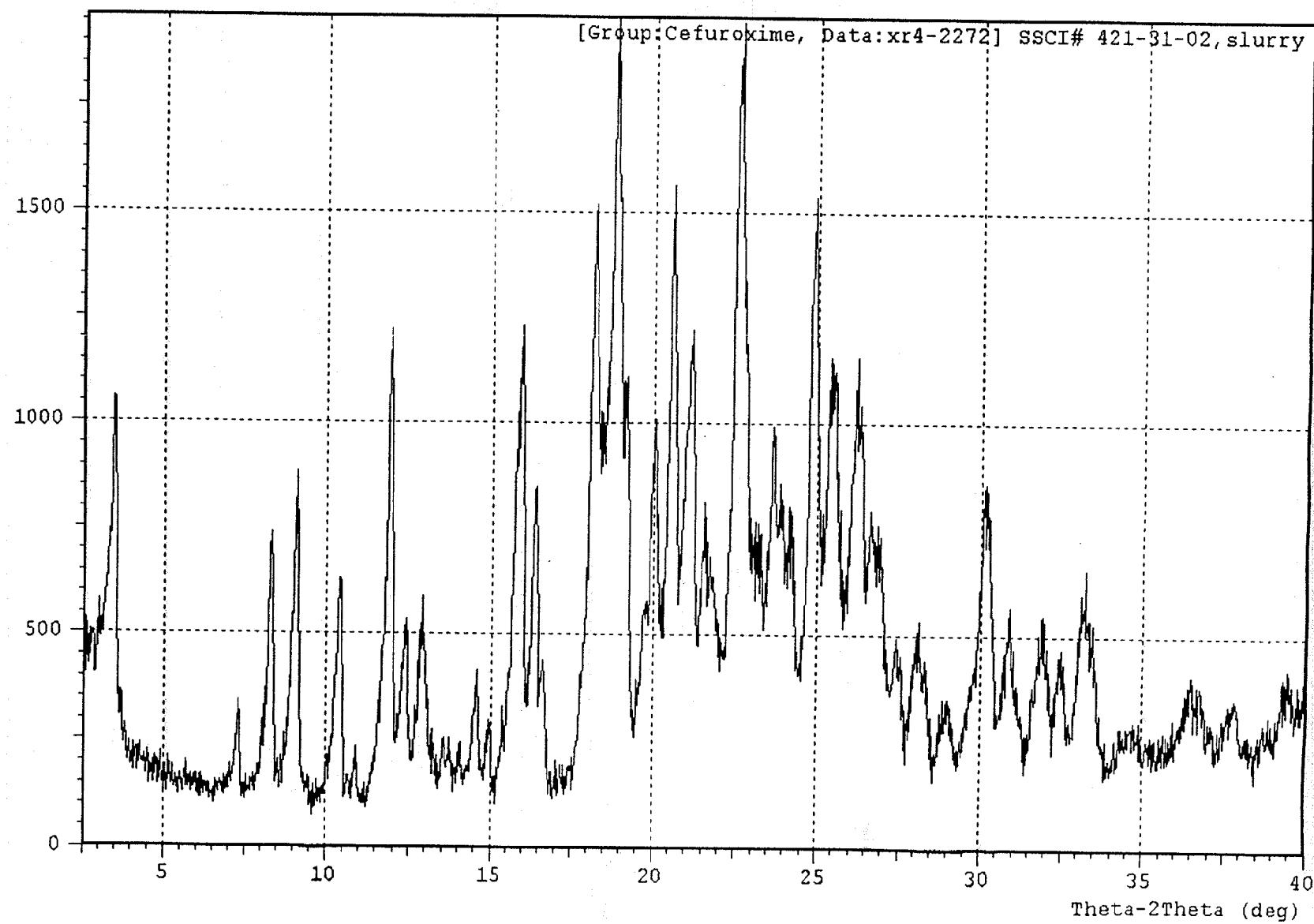


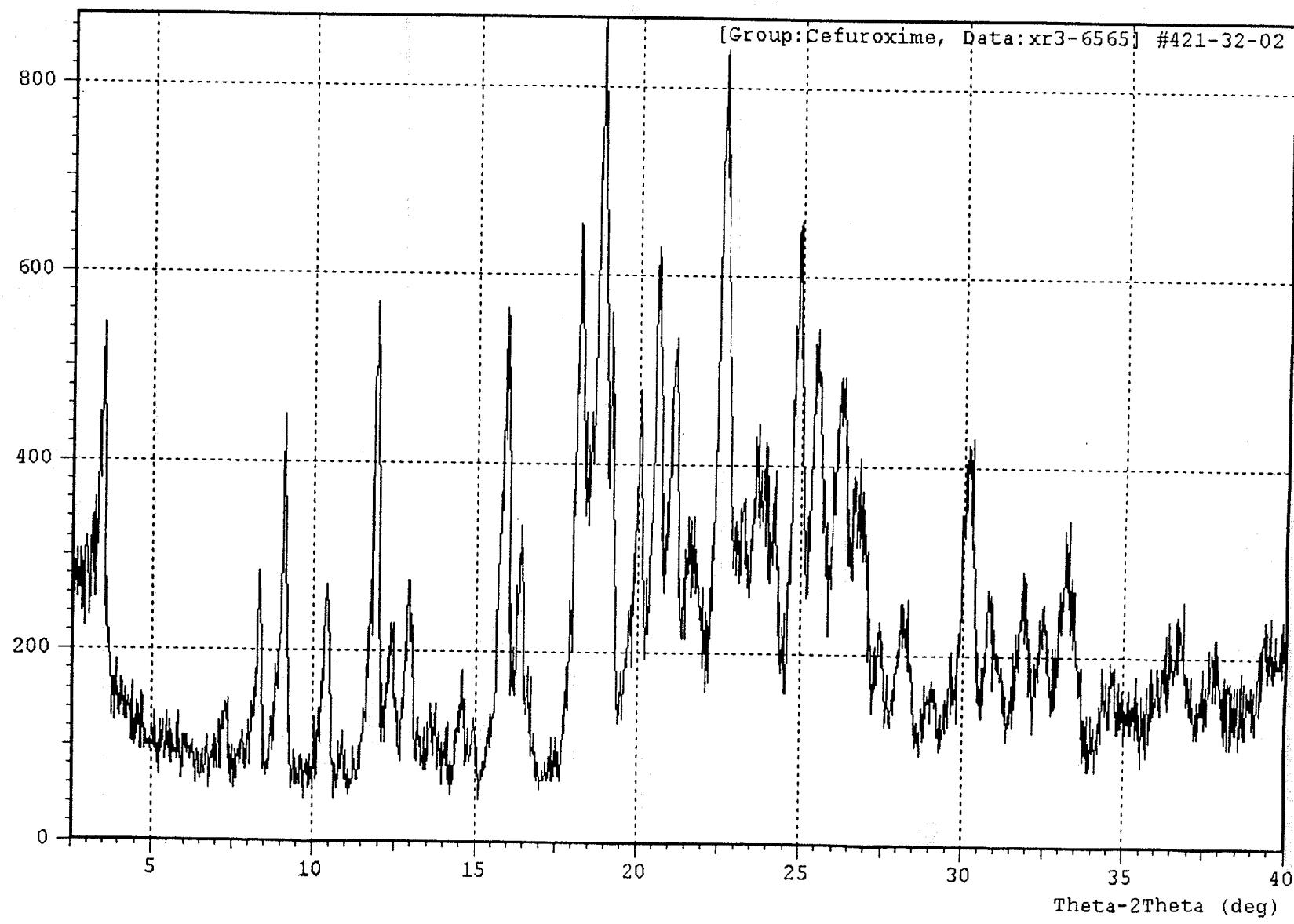
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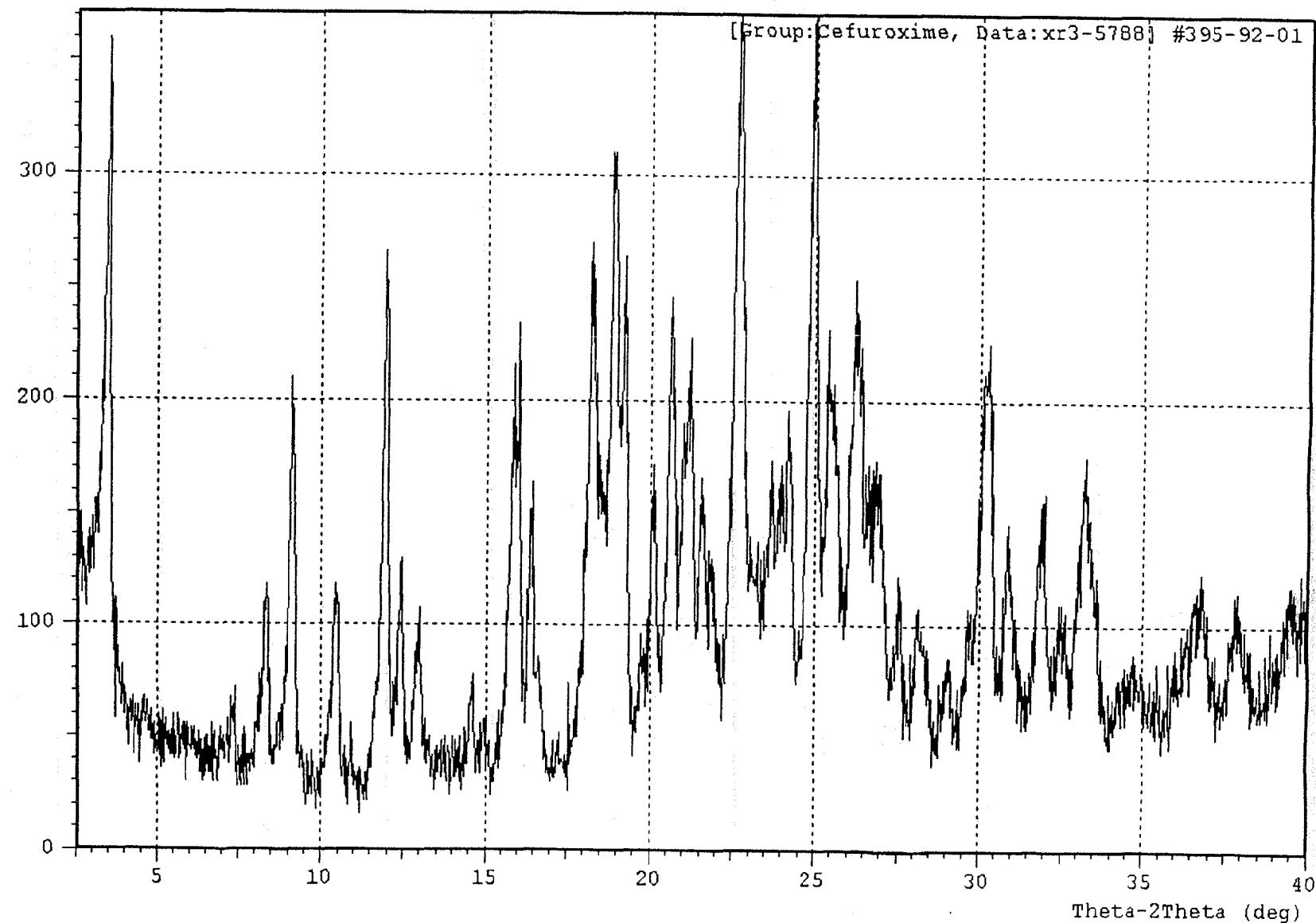


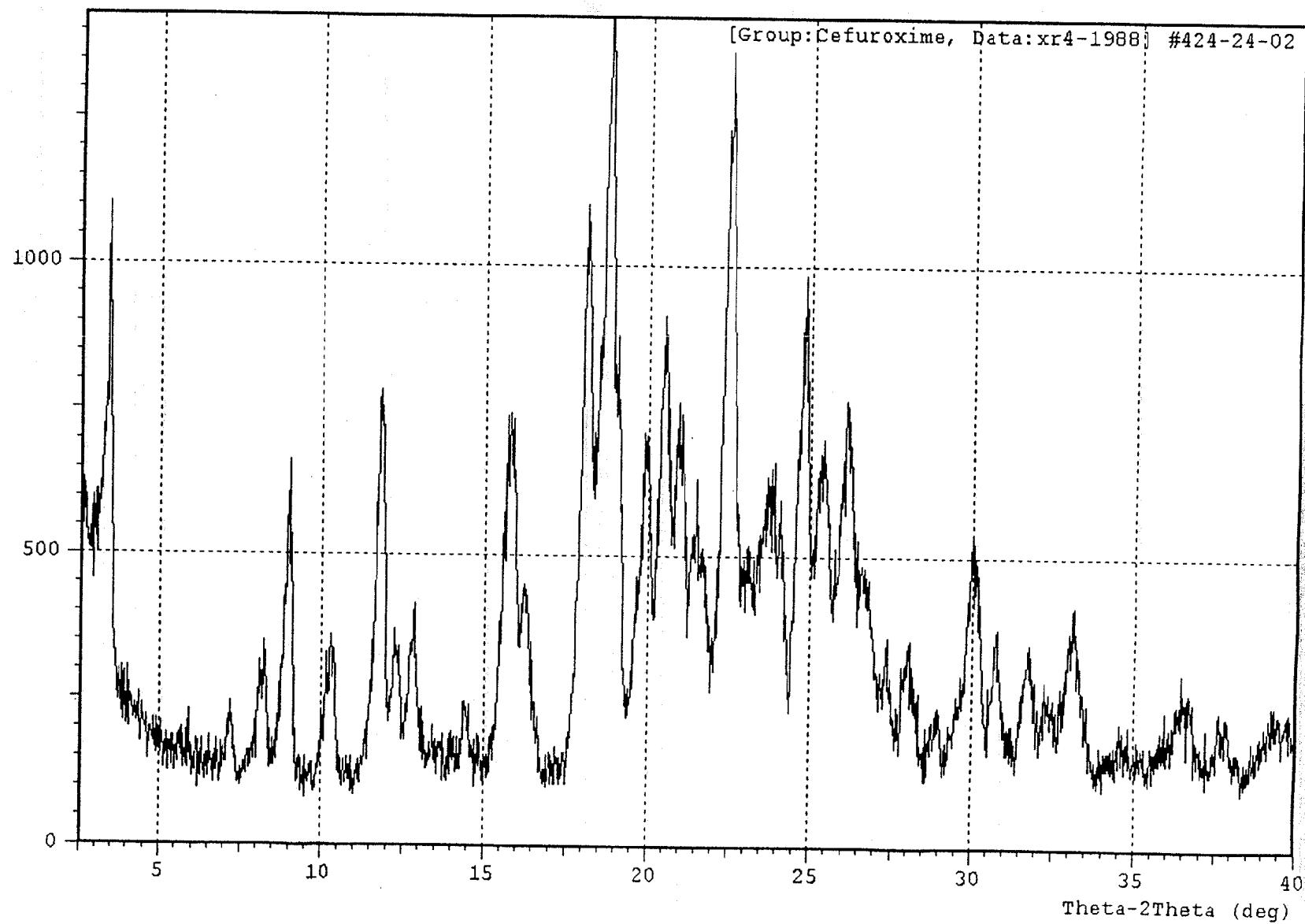


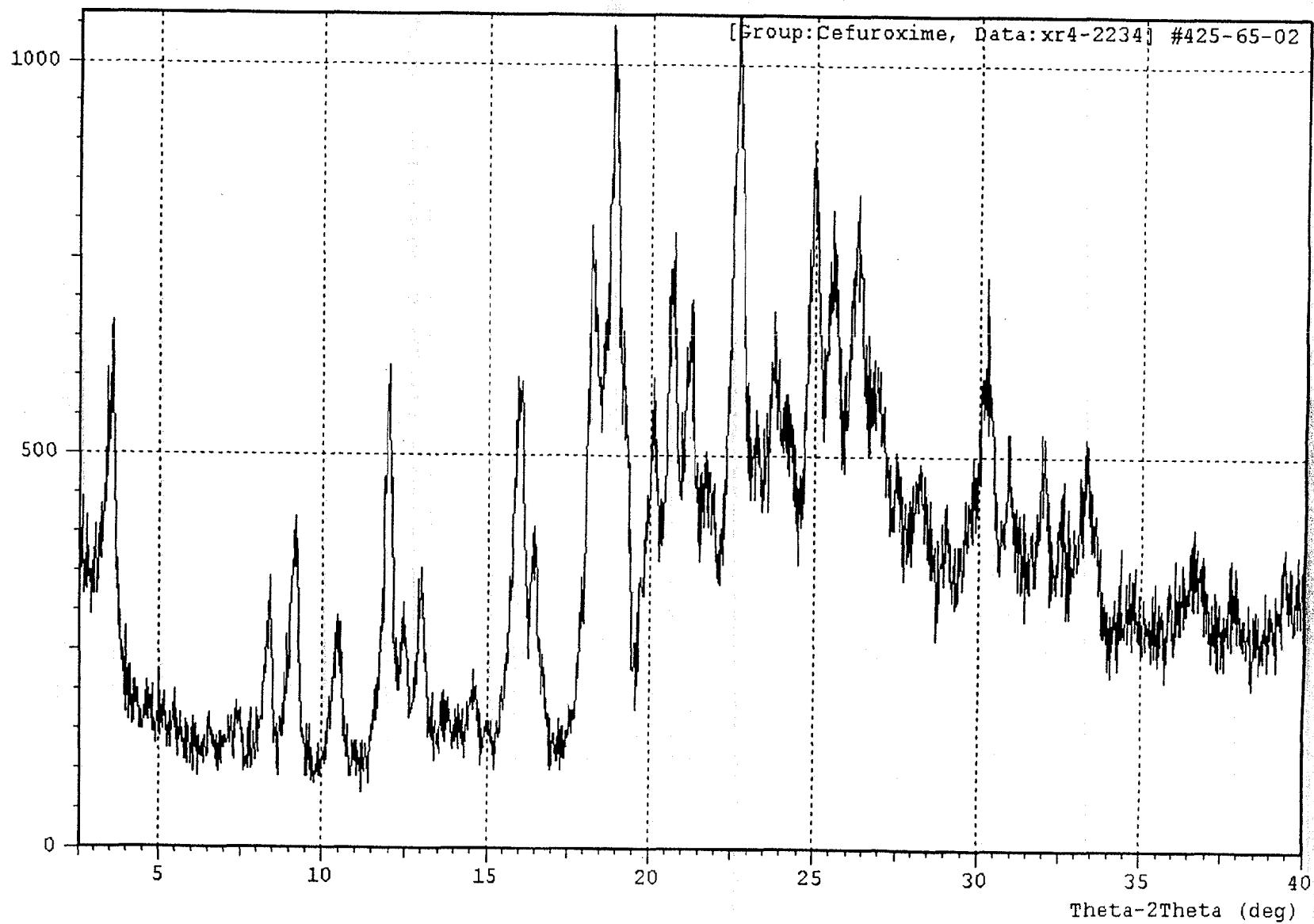
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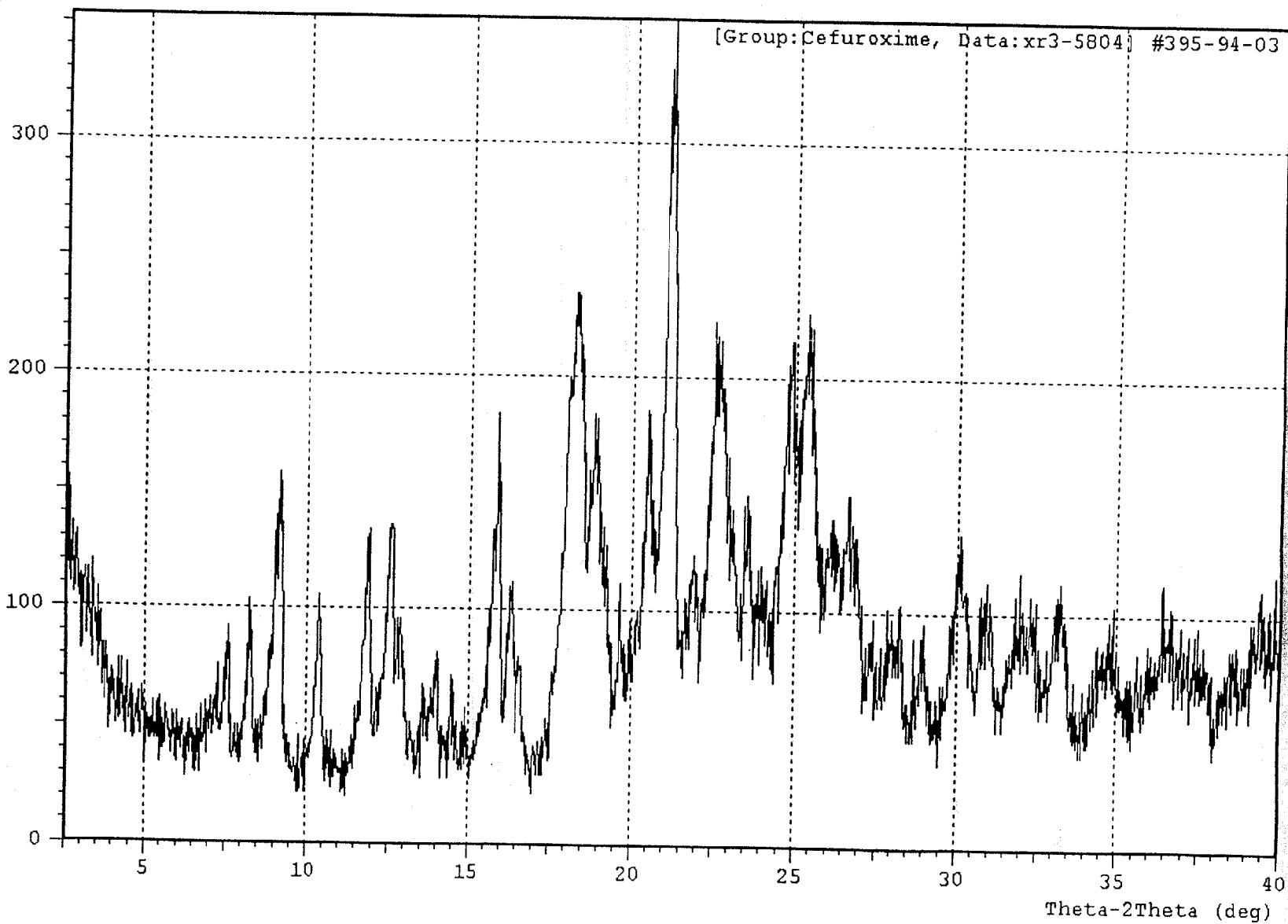


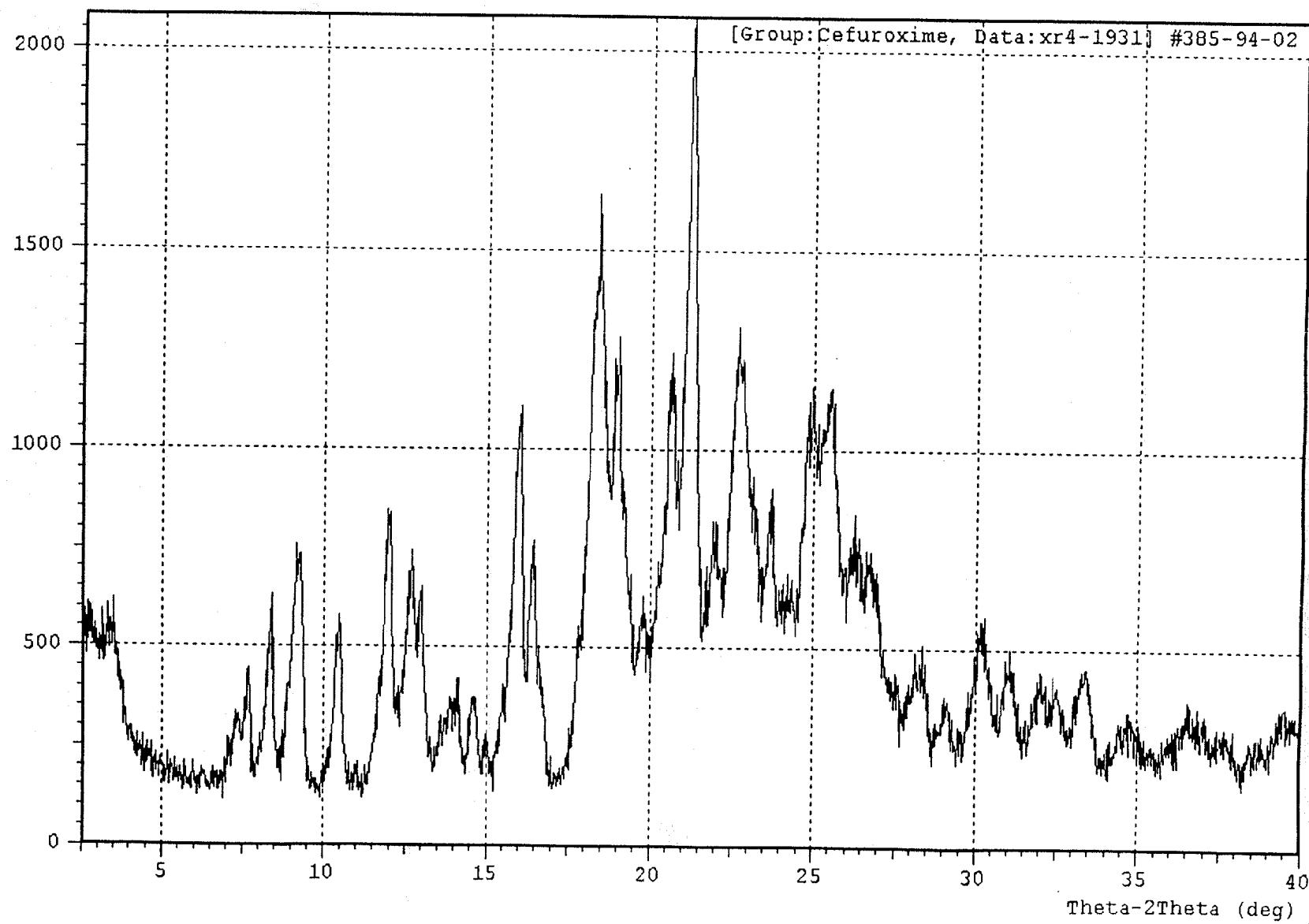


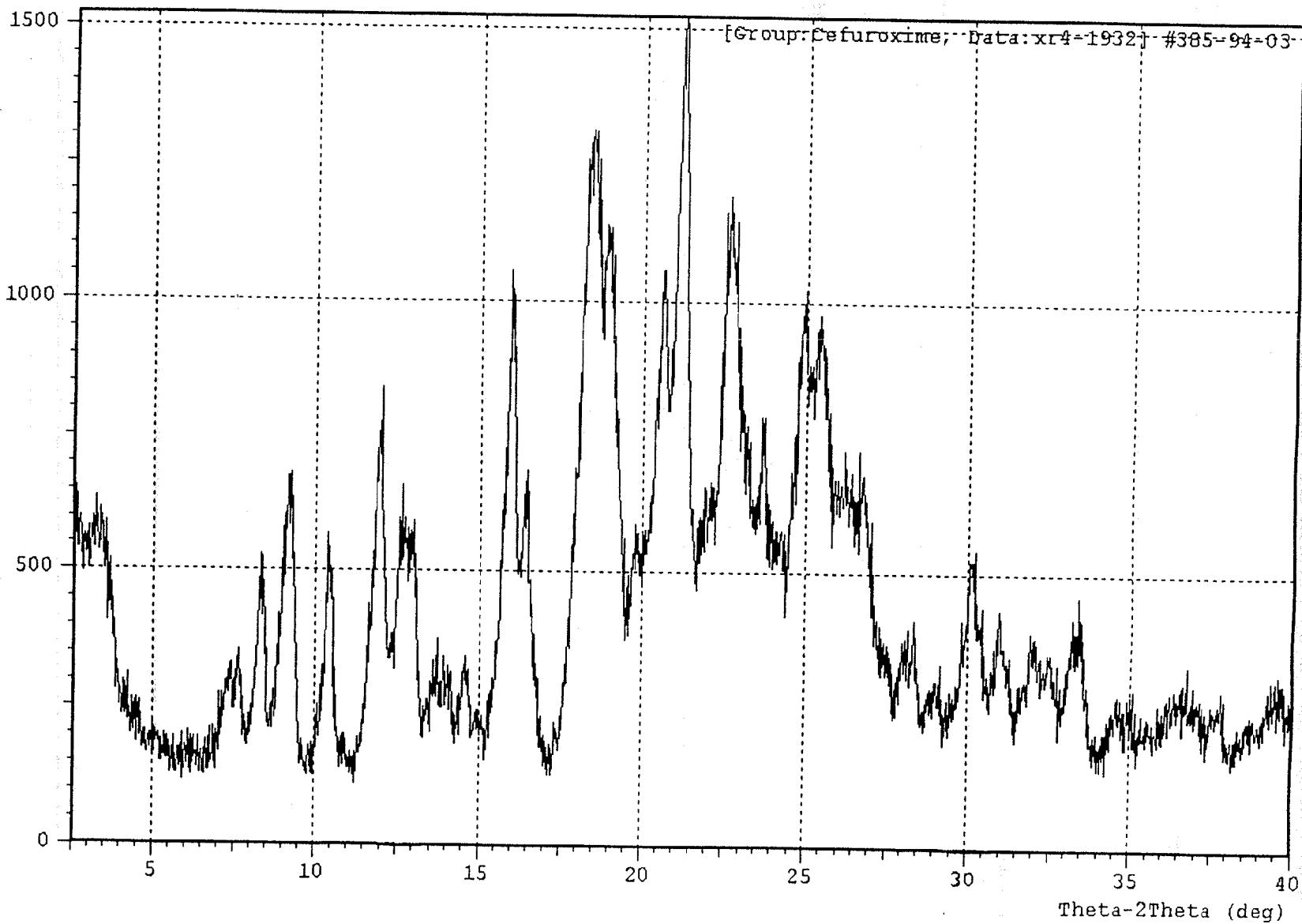




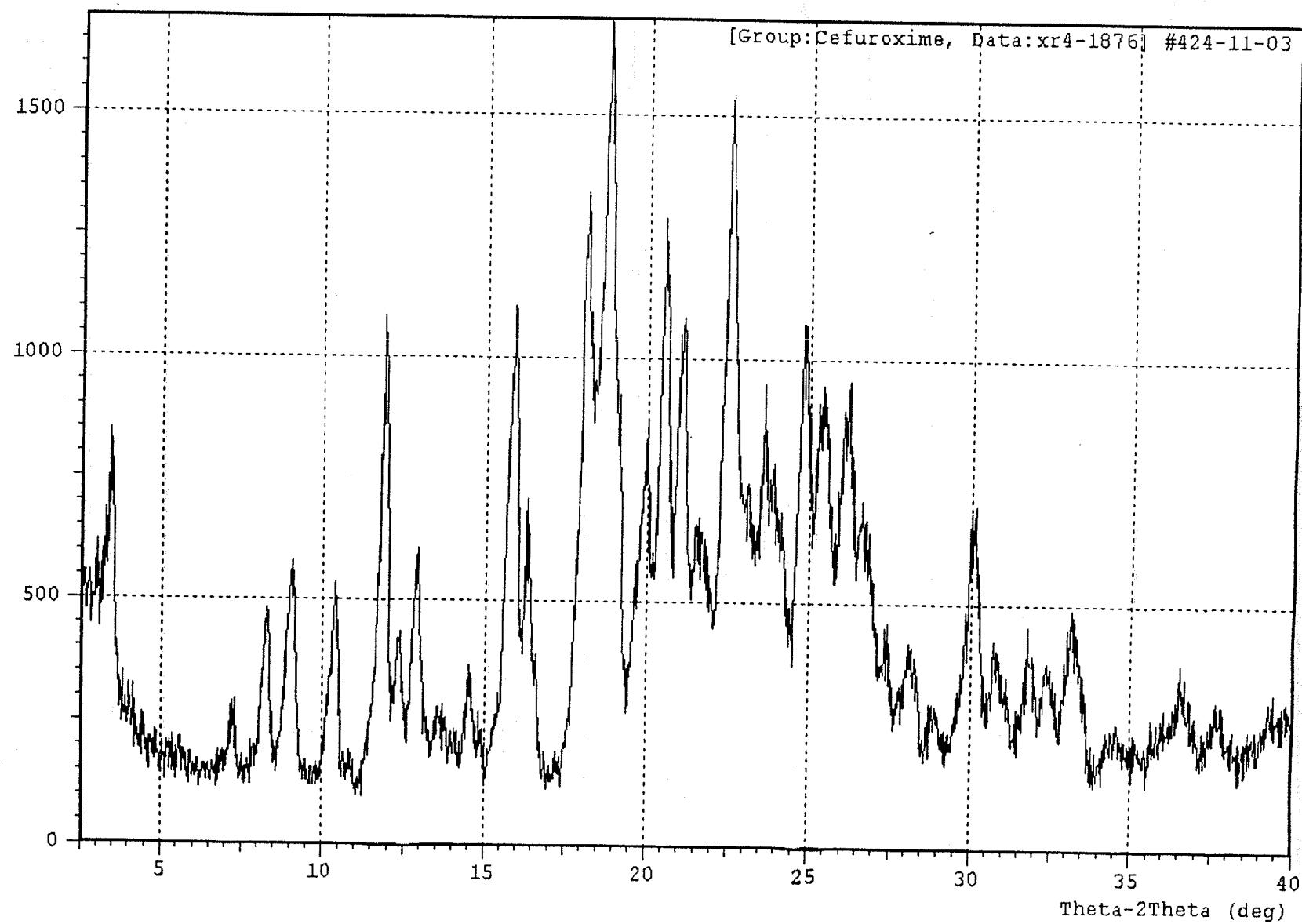




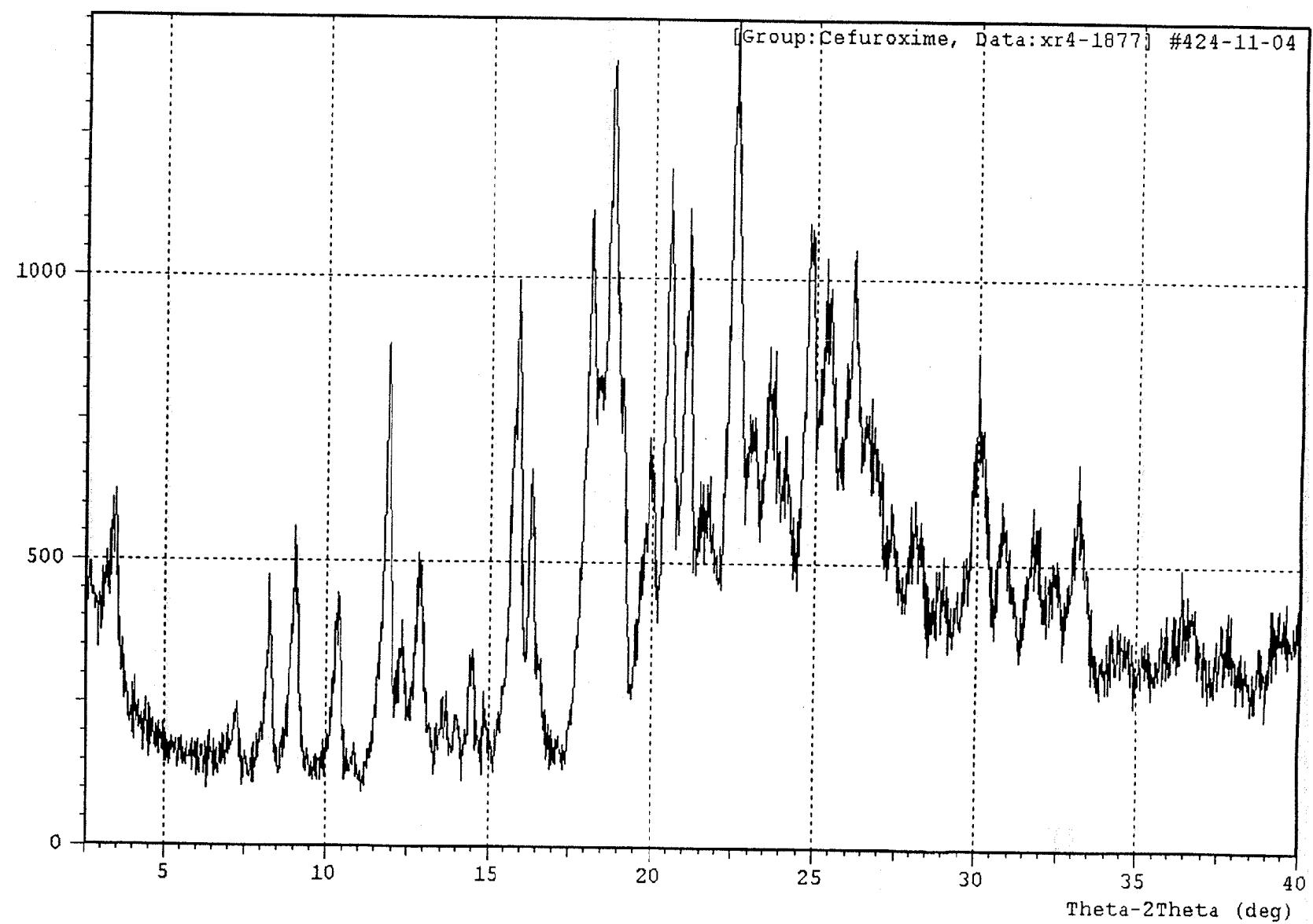




[Group:Cefuroxime, Data:xr4-1876] #424-11-03



[Group:Cefuroxime, Data:xr4-1877] #424-11-04



[Group:Cefuroxime, Data:xr4-2312] SSCI# 421-34-02

