Technical Report No. LWL-CR-04C72

DRUG CORRELATION SPECTROSCOPY

Final Report
Contract No. DAAH01-73-C-0142
Modification No. P00002
MIPR No. 3.00004

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R. P. Kenan, K. C. Brog, G. T. Ruck, and
W. H. Jones, Jr.
Battelle
Columbus Laboratories
Tactical Technology Center
505 King Avenue
Columbus, Ohio 43201

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FOREWORD

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ABSTRACT

The paramters pertinent to the development of a compact instrument to detect and reliably identify drugs and related compounds in bulk and in urine were investigated. The program was conducted with emphasis on using correlation interferometry. Studies indicated that the interferometric approach should be complemented with additional enhancement techniques to better assure the success of the proposed instrument.

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INTRODUCTION

The objective of this program was to develop an inexpensive compact spectroscopic instrument that could be used by nontechnical personnel in the field to detect rapidly and reliably evidence of drug usage through urine analysis. Ideally, the instrument should require little or no sample preparation and should give unambiguous results that would be admissible as evidence in a court of law. It would also be desirable that this same instrument be capable of identifying drugs in bulk form. An instrument concept that could lead to a mass-produced field device costing less than $10,000 would find wide-scale use for drug control.

This program was devoted to the development of a spectroscopic instrument to meet the objectives of the program with emphasis on a correlation interferometry spectrometer. The program was divided into three parts. The first part, which is described in the next section of this report, was a laboratory study of drug spectroscopy and separation techniques to determine useful spectral regions, resolution requirements, sample processing procedures, and to establish detection limits. The second part, covered in the third section of this report, was devoted to studying simple interferogram correlation for use in automated drug detection. During the third part of the program; recommendations were developed for the future development of instrumentation. These recommendations are discussed on pages 13 through 17.

DRUG SPECTROSCOPY AND SEPARATION TECHNIQUES

The preliminary research consisted of determining general sampling conditions and instrumental parameters for the Digilab Fourier Transform Spectrometer (FTS).

It was determined that the optimum cell thickness is 50 microns. A spectrum of water at this thickness is shown in Figure 1.* Most of the drug identification in H_2O solution utilizes the H_2O window between 1500 and 900 cm^{-1}. (This infrared transmitting window is determined not only by H_2O, but also by the absorption characteristics of the Irtran-2 crystals used for the cell windows.) A thicker cell might not give enough transmission in the 1500 to 900 cm^{-1} range to overcome the digital noise. In a thinner cell, the absorption bands of the drug would not be strong enough for reliable identification.

The original cells used for the solution studies had Irtran-2 windows and a polyethylene gasket. In these cells, interference fringes often were superimposed on the spectra which would obscure the absorption bands of the drug. At the Sponsor's suggestion that the apparent fringes might be caused by stress-induced compression of the gasket, the polyethylene gaskets were replaced with metal gaskets. This eliminated the fringes and all subsequent work was done in cells using these metal gaskets. Since Irtran-2 cuts off part of the H_2O window, polyethylene cells were tried. Although these cells extended the water window, polyethylene has many weak absorption bands in the 1500 to 900 cm^{-1} range which hamper the observation of the drugs.

While it is easier to ratio spectra against air, ratioing against pure H_2O extends the window area, allowing observation of more absorption bands of the drug.

Using the cell conditions and instrumental parameters described above, Figure 2 was obtained, which shows the infrared spectrum of a 2 parts per 10^3 (by weight) solution of sulfonate soap in H_2O. It should be noted that with signal averaging and scale expansion, the absorption bands of the sulfonate soap (1050 and 1120 cm^{-1}) are practically full scale, yet still exhibit a low noise level. This indicates that the instrumental settings were good and much lower concentrations of sulfonate soap in water can be detected.

Since the extinction coefficients of the absorption bands of a drug and of a sulfonate might be drastically different in the 1500 to 900 cm^{-1} range, spectra of cocaine in H_2O were then observed. Figure 3 shows the infrared spectra of a 22 parts per 10^3 solution of cocaine in H_2O. This high concentration solution is shown only to indicate the frequencies of the absorption band of

*Figures 1 through 23 are given in the Appendix.

cocaine. Figure 4 shows the infrared spectrum of 1 part per 10^3 solution of cocaine in H_2O. In this spectrum the signal-to-noise ratio was lower. (due to the lower signal) so the infrared plot was electronically smoothed. Thus, while the spectral resolution is not so good as in Figure 3, the identifying absorption bands of cocaine are readily apparent and of sufficient intensity to indicate that lower concentration solutions could be observed. Note in Figure 4 that the absorption band at 1050 cm^{-1} is stronger than the band at 1120 cm^{-1}, while in Figure 3 the reverse is true. As we go to lower concentrations, impurity bands can become a problem, and this is the probable cause of the 1050 cm^{-1} band in Figure 4. Yet even with impurities present, the drug can still be identified.

Before trying to extend the limit of detectability of cocaine in H_2O by special instrumental techniques or by solvent extraction, it was felt advisable to look at the spectra of other drugs in H_2O. Some examples of these spectra are shown in Figures 5 through 10. While the results were encouraging (detectability of 1 part in 10^4), some of these results are not as satisfactory. Figure 5 shows the infrared spectrum of a nearly saturated solution of amphetamine sulfate in H_2O. Exact concentrations were not measured since the major use of this solution was for obtaining the frequencies of the infrared absorption bands of amphetamine sulfate. From Figure 5 it can be seen that the absorption bands due to the amphetamine grouping are weak in intensity by comparison to the strong S-O vibration near 1100 cm^{-1}. A 1 part amphetamine sulfate per 10^3 parts H_2O spectrum is shown in Figure 6. Even at this fairly high concentration only the strong S-O absorption band is clearly identifiable. Moreover, observation of this one band would not be sufficient to positively identify the amphetamine sulfate since other drugs are also used as the sulfate. Bands due to amphetamine vibrations (all the frequencies in Figure 5 except the 1100 cm^{-1} band) must be observed in order to clearly identify the drug as an amphetamine. Similar results were obtained for morphine sulfate (only the S-O absorption band could be detected in 1 part per 10^3 solutions).

Figure 7 shows the frequencies of the infrared absorption bands (indicated by arrows) of a nearly saturated solution of sodium phenobarbital. In Figure 8 (a 5 part per 10^3 solution) all of these absorption bands are clearly observable. The spectrum of a 1 part per 10^3 solution of sodium

phenobarbital is shown in Figure 9. Here the 1570 cm^{-1} band is still very strong compared to the noise background, the 1270 and 1295 cm^{-1} frequencies are clearly observable, and the bands near 1350 and 1400 cm^{-1} can be faintly detected. These results are more encouraging; it should be possible to detect the sodium phenobarbitol in concentrations less than 1 part in 10^4 even without solvent extractions. Thus, the results for sodium phenobarbital are like those for cocaine, and it is interesting to note that neither of these drugs contains a sulfate group. Possibly the sulfate group affects the intensity of the infrared bands of the organic portion of the drug.

It is known that heroin changes to and is detected (in body fluids) as morphine. A spectrum of a nearly saturated solution of heroin in H_2O is shown in Figure 10. This spectrum bears no resemblance to the spectrum of morphine sulfate, so it is obvious that heroin does not change form rapidly in water solutions. In light of the results obtained from the drug sulfates, it was deemed necessary to try solvent extractions in order to improve detection sensitivities. In one experiment, 1 ml of a 1 part in 10^3 solution of cocaine in H_2O was mixed with 1 ml of chloroform and the chloroform layer was removed using a separatory funnel. The chloroform fraction was then evaporated to dryness over low heat ($\sim$50 C) and the residue weighed. Assuming pure cocaine, almost 100 percent of the cocaine was recovered. This residue was dissolved in the minimum amount of chloroform and the solution placed in a NaCl cavity-type cell for infrared analysis. The infrared spectrum obtained from this solution is shown in Figure 12 (the infrared spectrum of pure chloroform in a cavity cell is shown in Figure 11). Comparison of the spectra of Figures 11 and 12 shows that the infrared absorptions due to cocaine are clearly visible (these bands are marked with arrows in Figure 12). Because chloroform is the solvent instead of water, NaCl cells can be used in place of Irtran-2 cells. The combined use of chloroform and NaCl opens many additional infrared windows for observation of the cocaine absorption bands. Thus we can see cocaine absorptions over the entire frequency range of 3800 to 600 cm^{-1}. (It must also be mentioned that the use of NaCl cavity cells greatly decreases the costs involved in sampling compared to the use of Irtran-2 cells.) It is especially important that the cocaine carbonyl absorptions (1720 to 1770 cm^{-1}) can be observed since these are the strongest absorption bands of the cocaine molecule. Thus, a 1 part per 10^3 solution of cocaine in H_2O can be easily extracted with $CHCl_3$ and this extracted cocaine can be easily identified

directly in chloroform. Comparison of the spectra of equivalent concentrations of cocaine in $CHCl_3$ (Figure 12) to those of cocaine in H_2O (Figure 4) clearly shows that cocaine can be more readily detected via the $CHCl_3$ extraction than directly in H_2O. Figure 13 shows the result when the computer is used to ratio the spectra of Figures 11 and 12. While the cell thicknesses are not exactly the same (all of the chloroform bands are not eliminated), the cocaine absorption bands are even easier to observe (marked by arrows in Figure 13). Thus, the $CHCl_3$ extraction procedure appears very promising.

One hundred ml of a 1 part in 10^5 solution of cocaine in water was mixed with 5 ml of $CHCl_3$. The chloroform layer was separated as described before, but here during the evaporation process, the temperature became too high ($\sim$200 C). Thus, it is possible that some of the cocaine decomposed or was lost. In spite of this, the spectrum of this extract (Figure 14) still shows absorption bands identifiable as being due to cocaine.

This detection limit for cocaine in H_2O can be extended to 1 part in 10^6 by exercising greater care in the extraction procedure. It has been possible to detect amphetamine, morphine, and phenobarbital in the concentration ranges of one part in 10^5 or 10^6 by performing a solvent extraction followed by concentration (or solvent removal step). Even the sulfates (morphine and amphetamine) can be detected in these ranges by increasing the volume of solution being extracted. However, in order for a technician in the field to perform this analysis and to obtain legally admissible results, the extraction procedure needs to be simplified. Therefore, efforts were directed to simplification of the extraction procedure and consideration of a low-cost, easy-to-use infrared cell. In addition, actual urine (instead of H_2O) solutions need to be studied since the impurities extracted from urine (via the $CHCl_3$ solvent) can affect the detection limit. In fact, these urine impurities now seem to be the limiting factor for the detection of drugs in solution rather than the sensitivity of the interferometer.

With the above goals in mind, attention was given to $CHCl_3$ extractions from urine. During the extractions it was observed that the $CHCl_3$-urine mixture separated into three layers (when the urine pH was not changed). The top layer was a clear yellow liquid, probably urine. The middle layer was a cloudy viscous white emulsion, and the bottom layer was a clear colorless liquid, probably $CHCl_3$. The infrared spectrum of the bottom layer is shown in Figure 15 and indeed appears to be only $CHCl_3$ with no urine impurities.

If the clear $CHCl_3$ layer would extract enough of the drug for detection, this would be a simple means of performing the necessary extraction and it would be easy to design a cell for any nonskilled person to use. Therefore, solution of 1 part of cocaine per 10 parts of urine was made and extracted with $CHCl_3$. The $CHCl_3$ layer was removed and infrared spectra of this layer were obtained without any solvent evaporation. This spectrum is shown in Figure 16. Figure 17 shows this spectrum ratioed against the infrared spectrum of $CHCl_3$ (instead of air as in Figures 15 and 16.) Due to an instrumental quirk the urine extraction spectrum was put in the reference beam so the cocaine absorption peaks (of Figure 17) are in the opposite direction from those of Figure 16. From either Figure 16 or 17 the absorption bands due to cocaine are clearly visible indicating that some cocaine can be extracted from urine by this simplified procedure which avoids most of the urine impurities. However, the intensity of the cocaine absorption bands in Figure 16 would indicate a solution of about 1 part per 10^3 (See Figure 12). Since we started with a 1 part in 10 solution this indicates that only about 1 percent of the cocaine is in the clear bottom layer and the other 99 percent must be in the middle layer of urine impurities and $CHCl_3$. Thus, in order to achieve the desired sensitivity for cocaine, we will have to contend with the urine impurities.

A large quantity of urine was collected from a single donor (the urine used in this experiment is from a different donor than the urine used in the above-described experiment). This urine was divided into six equal portions of 100 ml each. To three portions of the urine, enough cocaine was added to make a 5 part per 10^3 solution of cocaine in urine. The pH of these cocaine-urine solutions was determined to be approximately 6. The pH of two of these solutions was raised with NH_4OH to about 8 and 10, respectively. The pH of the three remaining pure urine samples was adjusted so that one sample was at 6, one at 8, and one at 10.

All six samples were then extracted with 200 ml of $CHCl_3$. After a short period of shaking, the mixture was allowed to separate, and the $CHCl_3$ layer was removed. After evaporation of the $CHCl_3$, the residues were weighed and the infrared spectra of the residues were obtained. These spectra are shown in Figures 18 through 23. The amount of each residue is listed in Table 1.

TABLE 1. RESIDUES (PART RESIDUE PER TOTAL WEIGHT URINE)$_3$ OBTAINED BY $CHCl_3$ EXTRACTION OF 5 PARTS PER 10^3 COCAINE IN URINE OR PURE URINE

	pH = 6	pH = 8	pH = 10
Cocaine in urine	3.9/1000	4.5/1000	3.3/1000
Urine	∿ 6/100,000	3.2/100,000	2/100,000

The spectra in Figures 18, 19, and 20 are of the residues of the $CHCl_3$ extracts of the cocaine in urine solutions, while the spectra of Figures 21, 22, and 23 are of the residues of the $CHCl_3$ extracts of pure urine. It is easy to observe from Figures 18, 19, and 20 that the spectra clearly show absorption bands due to cocaine. In fact, by comparing these spectra to those seen in Figures 21, 22, and 23, it is apparent that the spectra of Figures 18, 19, and 20 are mainly of cocaine with no obvious absorption bands due to urine impurities. Also, the spectra of Figures 18, 19, and 20 are almost identical, indicating little effect due to varying the pH of the solutions. On the other hand, the spectra of the residues of the extracts of pure urine vary with changing pH. At the present time the spectrum (Figure 23) of the residue at pH 10 appears most satisfactory for detecting cocaine (based on the fact that the absorption bands in the 1400 to 600 cm^{-1} are weaker than at other pH's). Thus, the urine impurities extracted at pH = 10 interfere less with the strong cocaine absorptions at 1280 and 720 cm^{-1}. However, from the standpoint of extraction simplicity, other pH's might be better. Future experiments would help to establish which pH is best.

From Table 1 it can be seen that the amount of cocaine extracted does not bear any direct relationship to the pH, but the amount of urine impurities does bear a direct relationship to pH. At the present time, it is not clear why the extractions of cocaine listed in Table 1 yielded 60 to 90 percent of the total amount of cocaine in the solution, while in the previous experiment only about 1 percent of the cocaine could be extracted. Other urine samples will have to be investigated to clarify this point.

While the limits of detection of cocaine in urine have not yet been established, the amount of extracted urine impurities listed in Table 1 gives some indication of these limits. Near the 1 part cocaine per 10^5 parts urine level, the amounts of extracted cocaine and urine will be nearly equal. From comparison of the spectra in Figures 18 through 23, one can visualize that at the 1:1 (cocaine:urine impurities) level, the urine impurities will begin to interfere with detection of the cocaine. However, specialized techniques (such as rationing backgrounds) should permit the identification of one part of cocaine in 10^6 parts of urine.

A small amount of effort was expended on two other sample preparation procedures. The first, which was suggested by the Sponsor, was the possibility of extracting drugs from urine by means of ion-exchange materials, and obtaining drug spectra directly on the ion-exchange material. This procedure was tried but did not prove feasible, however, since ion-exchange resins show a strong absorption in the 1500 to 900 cm^{-1} region, and four ceramic fiber filter papers supplied by the Sponsor gave zero percent transmission in the 4000 to 600 cm^{-1} range which masked the drug absorption bands.

The filter-paper spectra were obtained on the samples "as received". Even if thinner samples were used it is estimated that any window between 1600 and 800 cm^{-1} would be too small to be useful for drug analysis. The second sample preparation procedure to be investigated was frustrated multiple interal reflection (FMIR).

FMIR spectra of cocaine were obtained, using progressively smaller amounts of cocaine. At the lowest concentration (0.1 mg of cocaine) reasonable spectra were obtained. Using calculations based on a crude estimate of the volume of our liquid cell, shows that this compares to a solution run of about 3 parts in 10^4. Judging from the quality of the FMIR spectra obtained, this could be extended to 1 part in 10^5 and perhaps to 1 part in 10^6. While this is somewhat better than any spectra obtained directly on urine solutions, it would involve an extraction step (to get the drug on the FMIR rod) or an evaporation step (to remove the liquids) and would require about 0.01 mg of the drug. Under these conditions even better spectra could be obtained by doing a $CHCl_3$ extraction and getting the spectra by means of micro KBr pellet techniques.

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* These were Fiberfrax: HiFi 660F, H-880F, 550F, and 970F.

Thus, whether the spectra are obtained in solution, by FMIR techniques, or by extraction techniques, the limiting factor is the amount of urine impurities. This limits the analyses to a sensitivity of about 1 part in 10^6.

INTERFEROGRAM CORRELATION

It was decided that it would be more economical to simulate the drug identification procedure on the Battelle CDC 6400 computer rather than by purchasing, assembling, testing, and modifying the actual hardware of the instrument. Real interferograms of drug solutions were used as data for the computer programs (see Table 2 for a list of these interferograms). These interferograms were obtained with the Digilab equipment used for the first part of this program. All of the interferograms were taken using water solutions in a 25-μm-thick sample cell and an optical filter to limit the energy to 1540 cm^{-1} and less. (The water and cell essentially provide a low frequency limit of 900 cm^{-1}.) They are partial two-sided interferograms that have a mirror displacement or a retardation range from -0.137 to + 1.158 mm. The instrument was not purged with a dry gas so there is also a fairly large absorption of several narrow lines due to atmospheric water vapor in addition to the broader lines of the sample.

TABLE 2. LIST OF INTERFEROGRAMS

Interferogram No.	Number of Scans	Sample
1	10	Concentrated cocaine
2	1	Concentrated concaine
3	1	1/2 concentrated cocaine
4	1	Concentrated morphine
5	1	Mixture of 1/2 concentrated cocaine and concentrated morphine
6	1	Water
7	1	None

The first calculations that were tried were simple auto- and cross-correlations at zero relative displacement between the two interferograms. This calculation can be shown to be proportional to the correlation at zero relative displacement of the respective spectra. The raw correlations were calculated by taking the sum of the point-by-point product of the interferograms. The raw cross-correlations were normalized to unity by dividing them by the square root of the product of the auto-correlations of the component interferograms. This was done for two ranges of retardations: from 0 to 1.139 mm and from 0.032 to 1.139 mm. The first range gave very high cross-correlations for all of the drugs and combinations tried. The second range did not give quite as large cross-correlation, since the large central peaks that are common to all the interferograms were ignored. However, the discrimination between the drugs was not significantly improved. These large correlations are not too surprising, since most of the absorption is due to water and water vapor.

In an attempt to reduce or eliminate the effect of water and water vapor, the water interferogram (No. 6) was scaled and subtracted point by point from the sample interferograms before the correlations were calculated. The scaling factor for the water interferogram was calculated to make the remaining interferogram orthogonal to the water interferogram. Three ranges of mirror displacement were used for the orthogonalization: 1.139 mm, 0.032 to 1.139 mm, and 0 to 0.009 mm. The remaining drug interferograms also had cross-correlations that were about the size of their auto-correlations, also again giving poor discrimination between drugs. The results of these calculations are presented in Table 3. The orthogonal remainder were then plotted, point by point, and from the plots it appears as if the interferograms are dominated by noise for mirror displacements larger than about 0.170 mm. This means that signal-averaged interferograms will probably be required if it is necessary to use an absorbing solvent such as water.

The last computation that was applied to the digital interferograms was a simulation of a correlation interferogram technique reported by Dick and Levy[1]*. The technique is to measure the correlation between the unknown or sample interferogram and the phase of the known or reference interferogram. We calculated this by taking the sum of the point-by-point product of one interferogram with the algebraic sign of the reference interferogram. This process is the analytical equivalent of using the reference interferogram

TABLE 3. AUTO-CORRELATIONS - CROSS-CORRELATIONS[a]

Interferogram Nos.[c]	Mirror Retardation Range					
	0-1.139	0.032-1.139	0-1.139	0.032-1.139	0-1.139	0.032-1.139
	Water Orthogonalization Range					
	None	None	0-1.139	0.032-1.139	0-0.009	0-0.009
1,1	-	--	0.9922	0.5721	0.9945	0.7235
2,2	25.56	0.9023	0.9229	0.6162	0.9243	0.7173
3,3	25.65	0.7579	0.6374	0.4540	0.6392	0.5494
4,4	26.85	0.7312	0.6648	0.4400	0.6687	0.5582
5,5	30.75	0.8682	0.7272	0.5063	0.7302	0.6235
6,6	21.22	0.6173	--	--	--	--
1,2	-- --	-- --	0.7769 (0.8119)	0.4261 (0.7177)	0.7787 (0.8122)	0.5499 (0.7633)
2,3	25.26 (0.9867)	0.5602 (0.6774)	0.4405 (0.5743)	0.2653 (0.5016)	0.4420 (0.5751)	0.3635 (0.5791)
2,4	-- (0.9831)	-- (0.6063)	-- --	-- --	0.3573 --	0.3309 --
2,5	-- (0.9866)	-- (0.6568)	-- --	-- --	0.4654 --	0.3874 --
2,6[b]	22.86 (0.9817)	0.4202 (0.5361)	-0.2642×10^{-12} --	-0.8392×10^{-13} --	-- --	-- --
3,4	25.94 (0.9885)	0.4873 (0.6308)	0.3500 (0.5376)	0.1897 (0.4245)	0.3526 (0.5394)	0.2959 (0.5344)

TABLE 3. AUTO-CORRELATIONS - CROSS-CORRELATIONS[a] (continued)

Interferogram Nos.[c]	Mirror Retardation Range 0-1.139	0.032-1.139	0-1.139	0.032-1.139	0-1.139	0.032-1.139
	Water Orthogonalization Range None	None	0-1.139	0.032-1.139	0-0.009	0-0.009
3,5	27.81	0.5620	0.4122	0.2303	0.4145	0.3361
	(0.9904)	(0.6928)	(0.6054)	(0.4804)	--	--
3,6	23.04	0.4332	--	--	--	--
	(0.9875)	(0.6333)	--	--	--	--
4,5	28.47	0.5578	0.4321	0.2272	0.4355	0.3449
	(0.9908)	(0.6926)	(0.6214)	(0.4813)	--	--
4,6	23.57	0.4240	--	--	--	--
	(0.9875)	(0.6311)	--	--	--	--
5,6	25.24	0.4727	--	--	--	--
	(0.9881)	(0.6165)	--	--	--	--
1,3	--	--	0.5169	0.3101	--	--
	--	--	(0.6500)	(0.6085)	--	--
1,4	--	--	0.4103	0.2578	--	--
	--	--	(0.5051)	(0.5139)	--	--
1,5	--	--	0.5219	0.3087	--	--
	--	--	(0.6144)	(0.5735)	--	--
1,6[b]	--	--	-0.2540×10^{-12}	-0.2805×10^{-13}	--	--
	--	--	--	--	--	--

(a) Values not in parentheses are multiplied by 10^{-8}, while the numbers in parentheses are cross correlations normalized to unity.

(b) Water subtracted only from concentrated cocaine interferogram.

(c) The interferogram numbers are identified in Table 2.

recorded on a magnetic disc (after Dick and Levy) as the reference input to a phase-sensitive detector. These results again did not give obvious discrimination between the drugs; however, the interpretation of the results is not perfectly clear. The interpretation problems arise from the fact that the digital interferograms as presented by the Digilab instrument do not reflect the total energy incident upon the detectors. Also, any phase changes between interferograms can have a pronounced effect on the calculated correlation. These problems lead to problems in scaling the correlation.

The above results show that a simple correlation of the raw interferogram will not be sufficient to yield the desired results. More sophisticated signal-processing techniques will have to be used. These techniques, surveyed in the third part of the program, are discussed below.

RECOMMENDATIONS FOR FUTURE DEVELOPMENT OF INSTRUMENTATION

In the previous section of this report it was concluded that correlation interferometry based on simple mathematical correlation techniques would not provide an adequate basis for a practical inexpensive instrument capable of detecting trace levels of drugs and their metabolites in human urine, which by itself can have a wide variety of spectral characteristics. For this reason, consideration was given to the use of other techniques which have proven valuable in handling similar spectroscopic problems. The principal objective of this part of the program was to recommend a prototype instrument which could be used both in the laboratory for developmental purposes and then in the field to assess its operational reliability. The information from these studies would then be used for the design and engineering of devices which could be mass produced. The prototype instrumentation recommended offers a wide variety of capabilities for investigating a number of different combinations of spectroscopic and data-processing techniques which are designed to enhance the detection and discrimination capabilities of the data correlation techniques. The data correlation techniques would ultimately be used to make a final decision on whether or not a particular drug is present and to ascertain

* References are given on page 18.

the reliability of this decision. This instrumentation could be used to determine the optimum combination of these techniques for this application and to assess their ultimate detection limits. The final field device to which this effort would lead would be considerably less complex than the more versatile instrumentation proposed for the initial developmental studies. The suggested approach is completely general in that the device can, in principle, be preprogrammed to detect any drug. Its ultimate capabilities, however, will depend on the interferences present.

General Approach

It is well established that drugs can be detected in liquids such as human urine through analysis of absorption spectra obtained in the infrared region of the spectrum between 2.5 and 20 microns. Nearly all drugs, though, do have characteristic spectral features in both the ultraviolet and the visible regions. Therefore, some consideration should also be given to these regions to see if they offer any potential advantages which might merit further exploitation.

The practical detection capabilities of the spectroscopic techniques are limited primarily by the presence of both known and unknown impurities which add to the spectral complexity. However, by fully exploiting the information content of multicomponent spectra, it is often possible to extend the detection limits and increase measurement reliability. Recent developments in transform and correlation spectroscopy coupled with procedures commonly used for information analysis such as data correlation, signal-enhancement, filtering, and pattern-recognition techniques can be used to great advantage in extracting the maximum information from complex spectral data. The operations involved in these procedures can be performed rather conveniently with a spectrometer system interfaced with a dedicated minicomputer. Computer requirements can be reduced by means of the spectroscopic correlation techniques which can be performed entirely by the spectrometer system prior to any computer processing of data.

Details of the proposed system are shown schematically in the block diagram presented in Figure 24. This instrument can be used for evaluating correlation, modulation, and double-beam techniques along with computer data processing techniques. Data output would be available in both

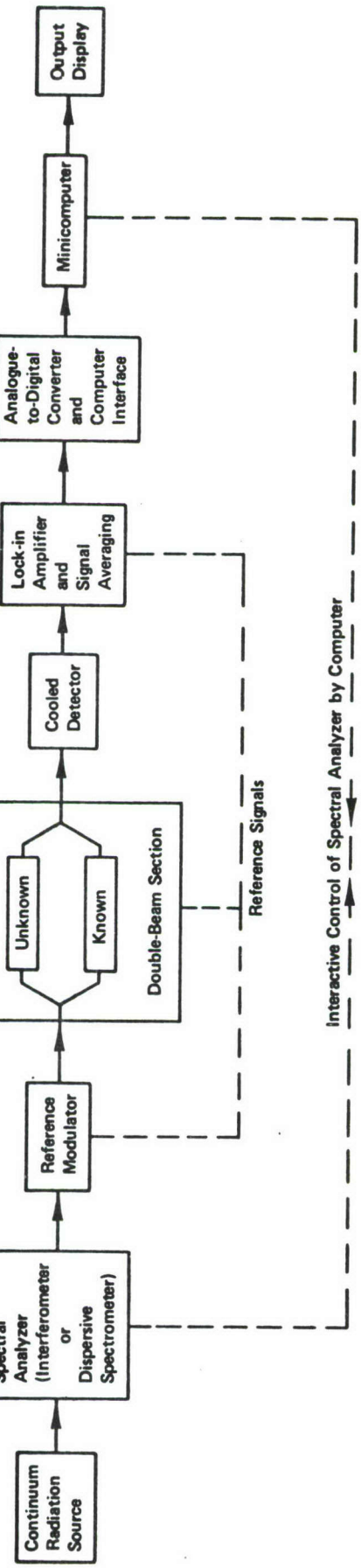


FIGURE 24. BLOCK DIAGRAM OF SPECTROSCOPIC INSTRUMENTATION FOR DRUG DETECTION

analogue and digital forms to facilitate exploration of alternative methods of data analysis.

The radiation source shown in Figure 24 would be either an infrared or other appropriate source capable of supplying continuum radiation for the absorption measurements. The double-beam section would contain a mirror-type chopper to alternate the spectrometer beam between an unknown sample and a reference sample. Either an interferometer or dispersive spectrometer can be employed as the spectrum analyzer. For this particular application, the interferometer was selected in view of final device considerations. For some cases, however, the dispersive spectrometer may prove advantageous. The dispersive system is more amenable to the mask techniques which can be used for performing correlation and transform processes optically thus reducing computer requirements. Appropriate photomultipliers and infrared detectors would be used in the different regions of the spectrum. Analogue signal processing would include state-of-the-art lock-in and signal-averaging techniques. An analogue-to-digital converter and computer interface would be used to provide input to a minicomputer. The minicomputer would perform the signal-enhancement, pattern-recognition, and final data-correlation processes leading to a decision as to whether or not a particular drug or its metabolites are present in a urine sample. The operation of the interferometer would also be controlled by the computer.

The double-beam or difference provision in the proposed system is used to cancel or minimize major component interferences. Generally two-beam instrumentation is employed with the unknown sample in one beam and a reference sample in the other. By balancing the absorption in the two beams the contributions of major interfering absorbers can be removed, enhancing the detection sensitivity for the low-concentration constituents of interest. In the proposed apparatus, a chopper will be used to alternate the spectrometer beam between the sample and reference cells with the difference spectrum observed by means of a single detector. Consideration must be given to the choice of optimum reference samples. Known components of spectra can also be removed to enhance trace-level contributions using digital processing techniques; however, the recommended instrumental approach should be more economical and simpler to implement in terms of a field instrument.

The reference modulator would perform an optical cross-correlation[4] by modulating the absorption in a reference cell containing only the species of

interest. Through this means it is possible to recover the spectrum for the reference species in a complex mixture using appropriate electronic processing procedures. This can be accomplished by placing the modulated reference cell in the spectrometer beam in series with the unknown sample. In the case of the application at hand, a set of reference cells containing the individual drugs of interest can be compared with the unknown sample to detect the presence of one or more specific drugs. Experiments will be required to determine optimum modulation frequencies and amplitudes, and appropriate reference-cell concentrations.

Both conventional short-path absorption cells and internal reflection probes[5] could be considered for passing the optical absorption beam through the sample. The internal reflection probe consists of a high-index plate with the absorption beam entering and exiting through the same end of the plate, leaving the other end completely free for being brought in contact with the sample which can be either a solid, liquid, or powder. Field penetration by the internally reflected beam detects the absorption in the surrounding sample. The number of reflectances can be adjusted to control the total absorption path through the sample. These probes are generally more rugged and easier to clean than the conventional cells.

SUMMARY

In H_2O solutions, the limit of detectability of cocaine is 1 part in 10^4. For drugs with a sulfate group the detection limit is less than 1 part in 10^4, and about the same (1 part in 10^4) for drugs without a sulfate group. By use of a simple $CHCl_3$ extraction the detection limit for cocaine in H_2O can easily be extended to 1 part in 10^6. By increasing the volume of solution being extracted, a 1 part in 10^6 detection limit can be reached for all drugs (even those with a sulfate group, such as morphine and amphetamine). In fact, for pure H_2O solutions the detection limit could be extended past 1 part in 10^6 (since H_2O impurities are less than these). However, in urine solutions the detection limit is governed by the impurity level, and this would definitely place the detection limit near 1 part in 10^6. Thus, to get beyond 1 part in 10^6 will involve the use of such techniques as ion-exchange resins or FMIR spectroscopy.

Preliminary interferogram correlation studies indicated that this technique by itself would not provide an adequate basis for a practical instrument capable of detecting trace levels of drugs and their metabolites in human urine because of the natural spectral variations in urine from different individuals. For this reason, consideration was given to complementing the interferometric approach with additional enhancement techniques to better assure the success of the desired instrument. Recommendations are presented for the design of a prototype instrument based on the use of correlation interferometry aided by correlation-spectroscopic and data processing techniques.

REFERENCES

(1) Dick, R., and Levy, G., "Correlation Interferometry", Aspen International Conference on Fourier Spectroscopy, 1970, AFCRL-71-0019, Special Report No. 114 (January 5, 1971).

(2) Willis, H. A., and Miller, R. G. J., "Difference Spectroscopy in the Near Infrared", Proceedings of the Conference on Molecular Spectroscopy, E. Thornton and H. W. Thompson, Editors, Pergamon Press (1959).

(3) Stewart, J. E., Infrared Spectroscopy, Marcel Dekker, Inc. (1970).

(4) Goody, R., "Cross-Correlating Spectrometer", J. Opt. Soc. Am., 58, p 900 (1968).

(5) Harrick, N. J., "The Internal Reflection Probe", Anal. Chem., 43, p 1533 (1971).

FIGURE 1. SPECTRUM OF H_2O (50-MICRON CELL)

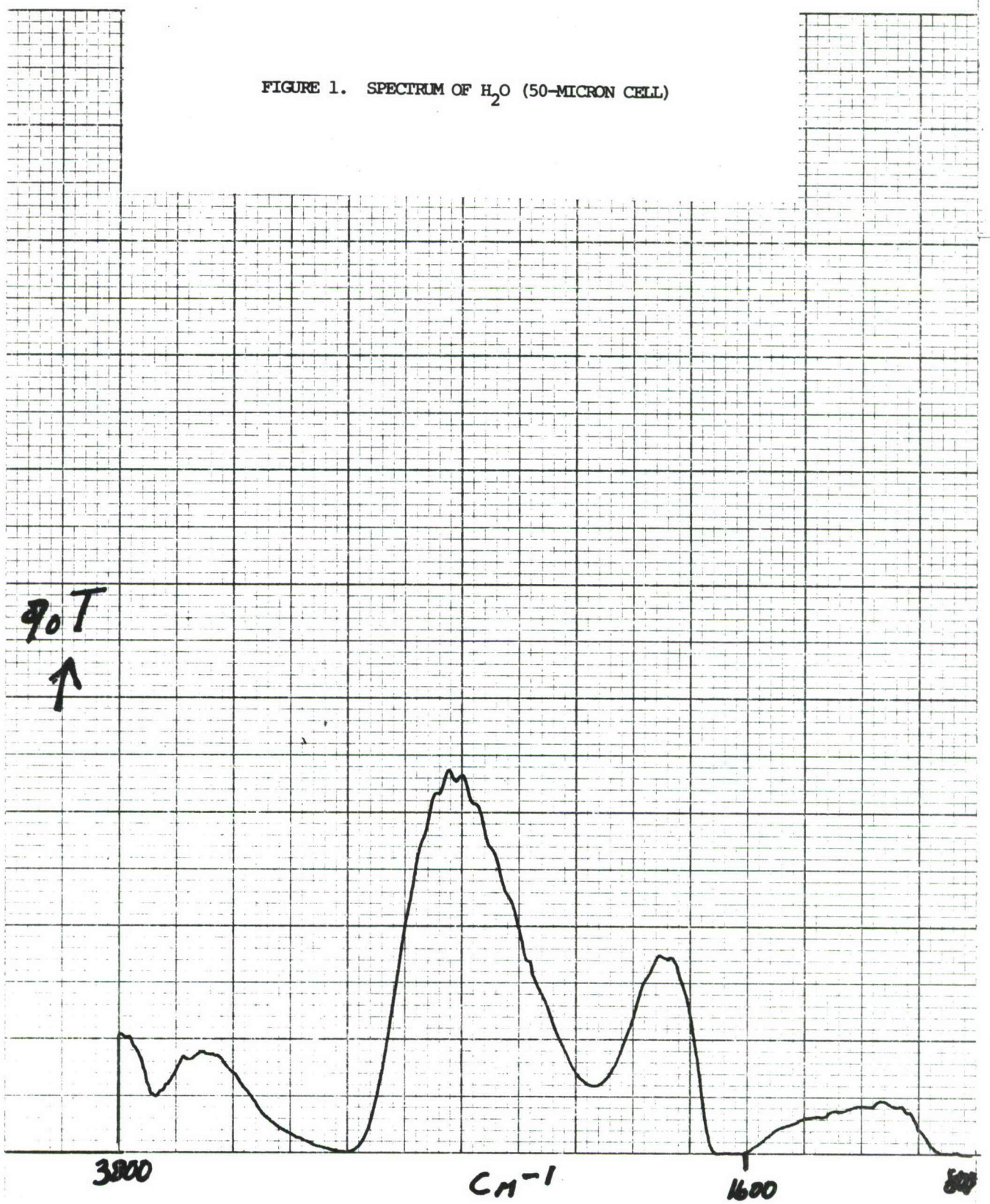
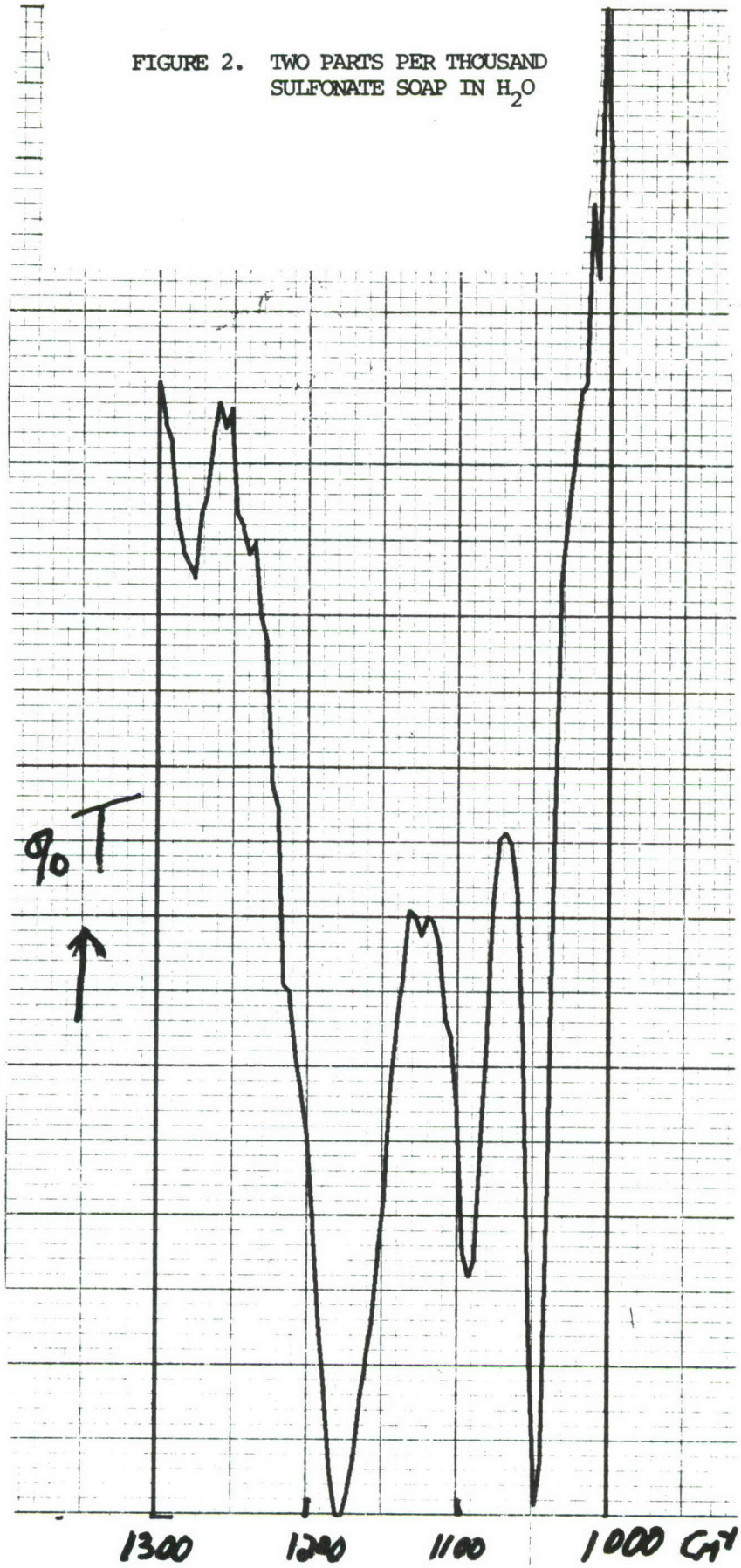


FIGURE 2. TWO PARTS PER THOUSAND SULFONATE SOAP IN H_2O



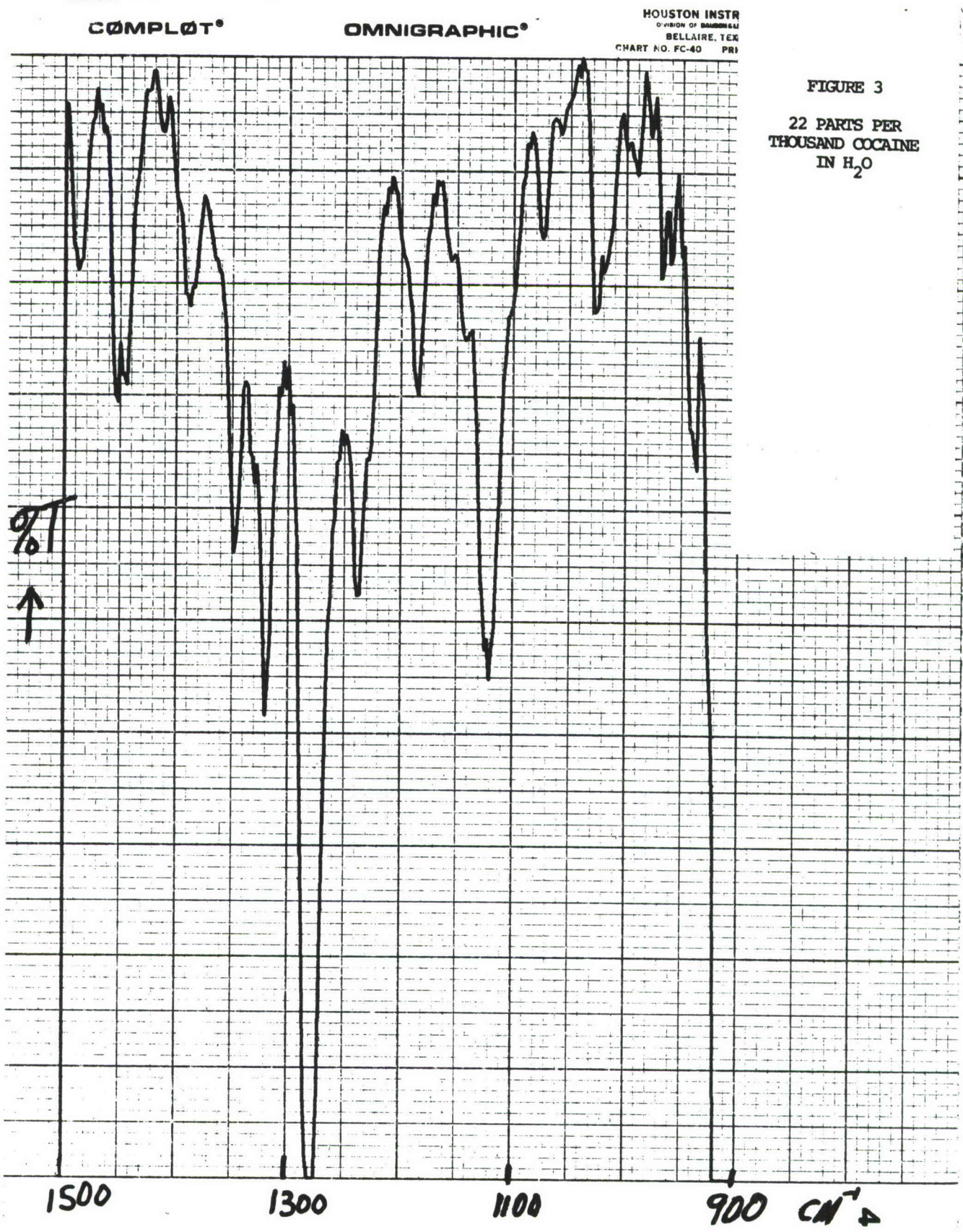


FIGURE 3

22 PARTS PER THOUSAND COCAINE IN H_2O

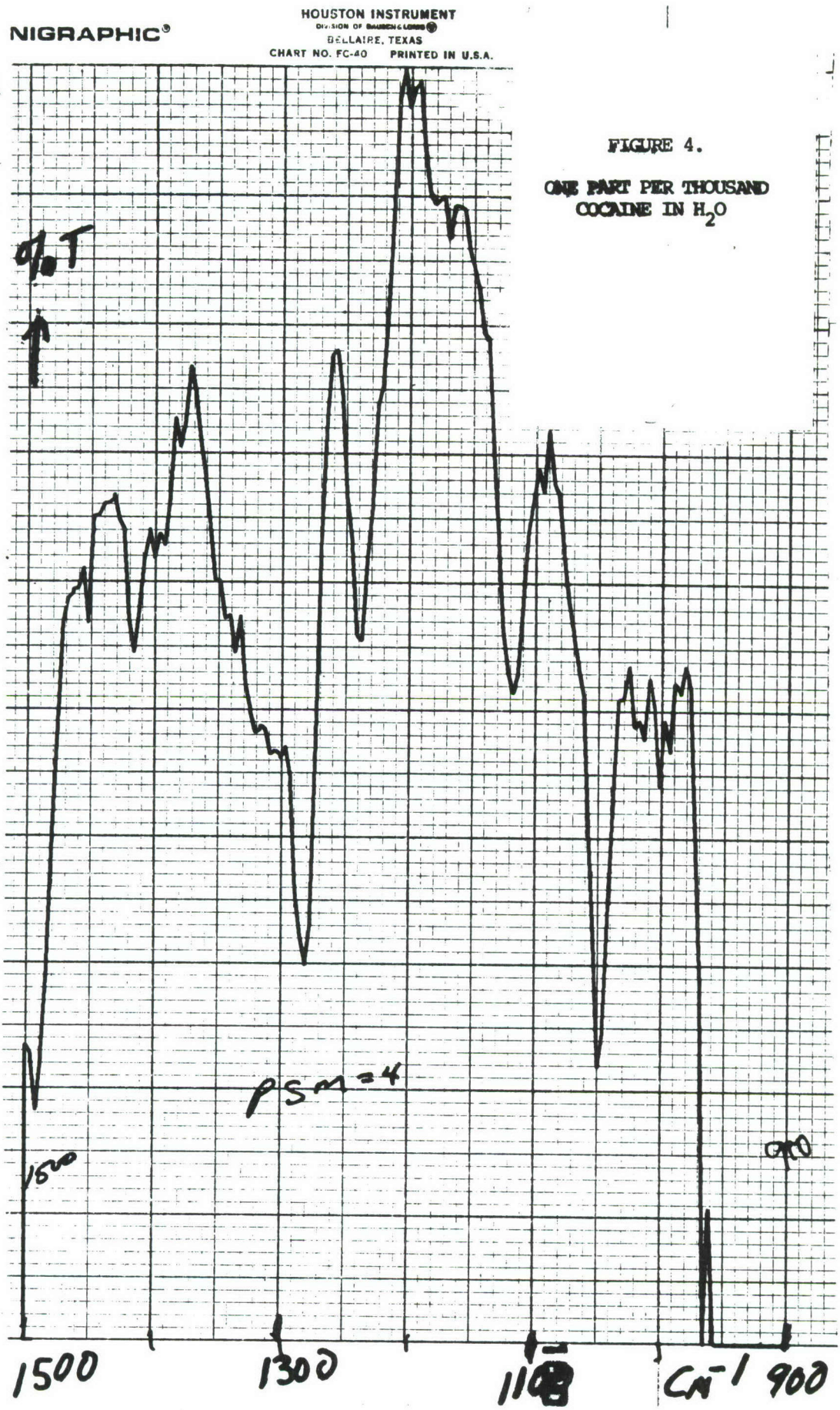


FIGURE 4.

ONE PART PER THOUSAND COCAINE IN H_2O

FIGURE 5. NEARLY SATURATED SOLUTION OF AMPHETAMINE SULFATE IN H_2O

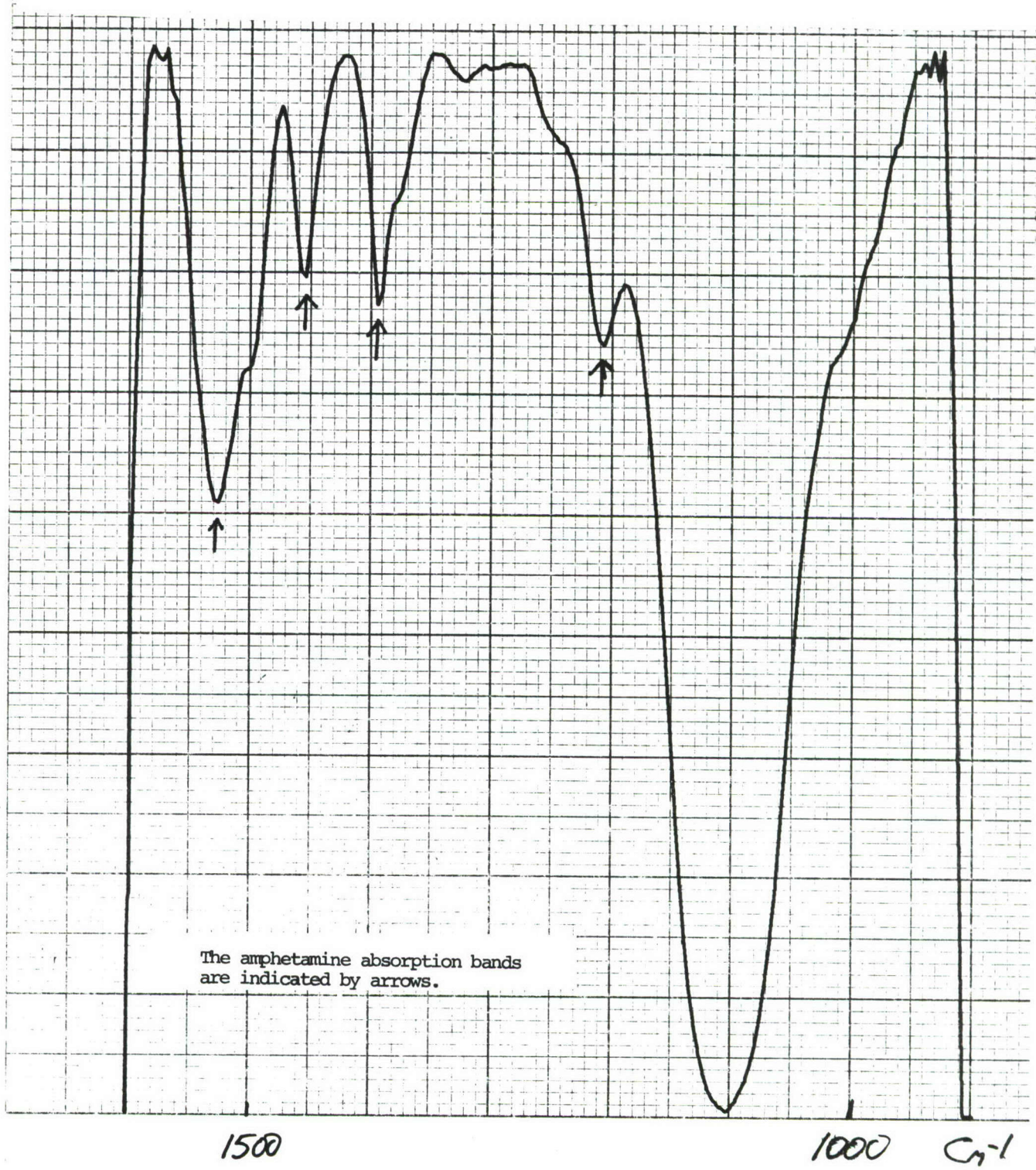


FIGURE 6. AMPHETAMINE SULFATE - ONE PART PER THOUSAND SOLUTION IN H_2O

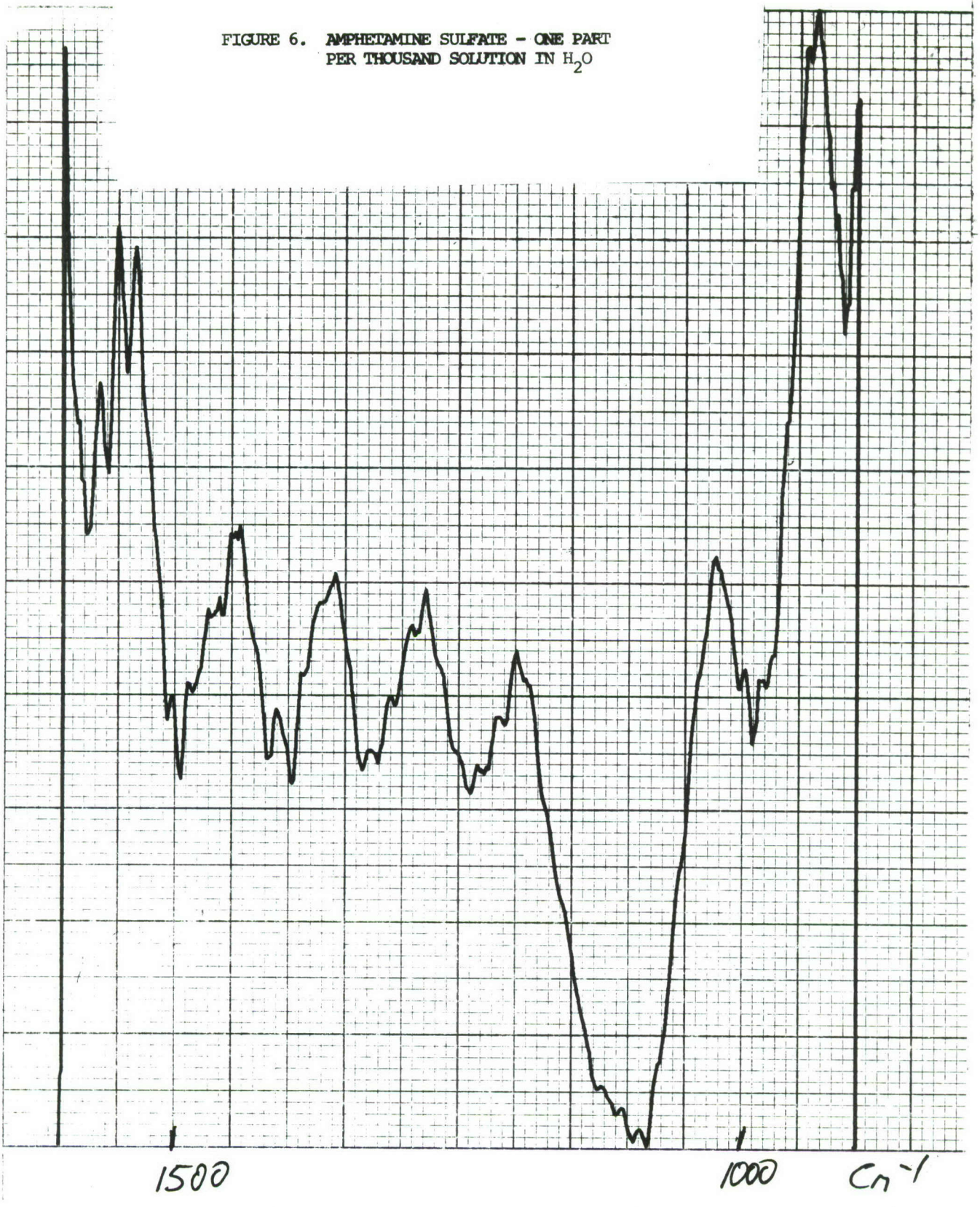


FIGURE 7. NEARLY SATURATED SOLUTION OF SODIUM PHENOBARBITAL IN H_2O

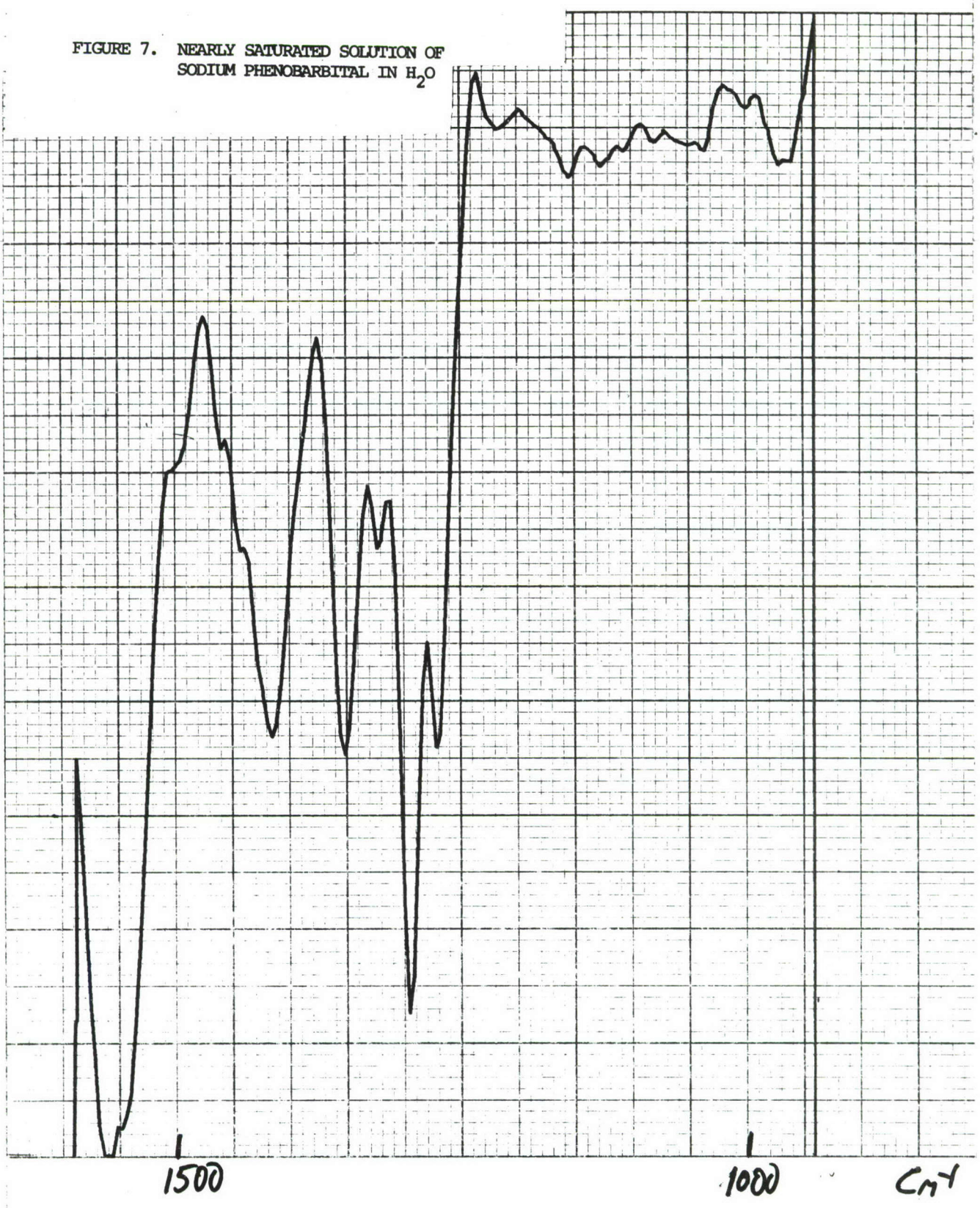


FIGURE 8. SODIUM PHENOBARBITAL - FIVE PARTS PER THOUSAND SOLUTION IN H_2O

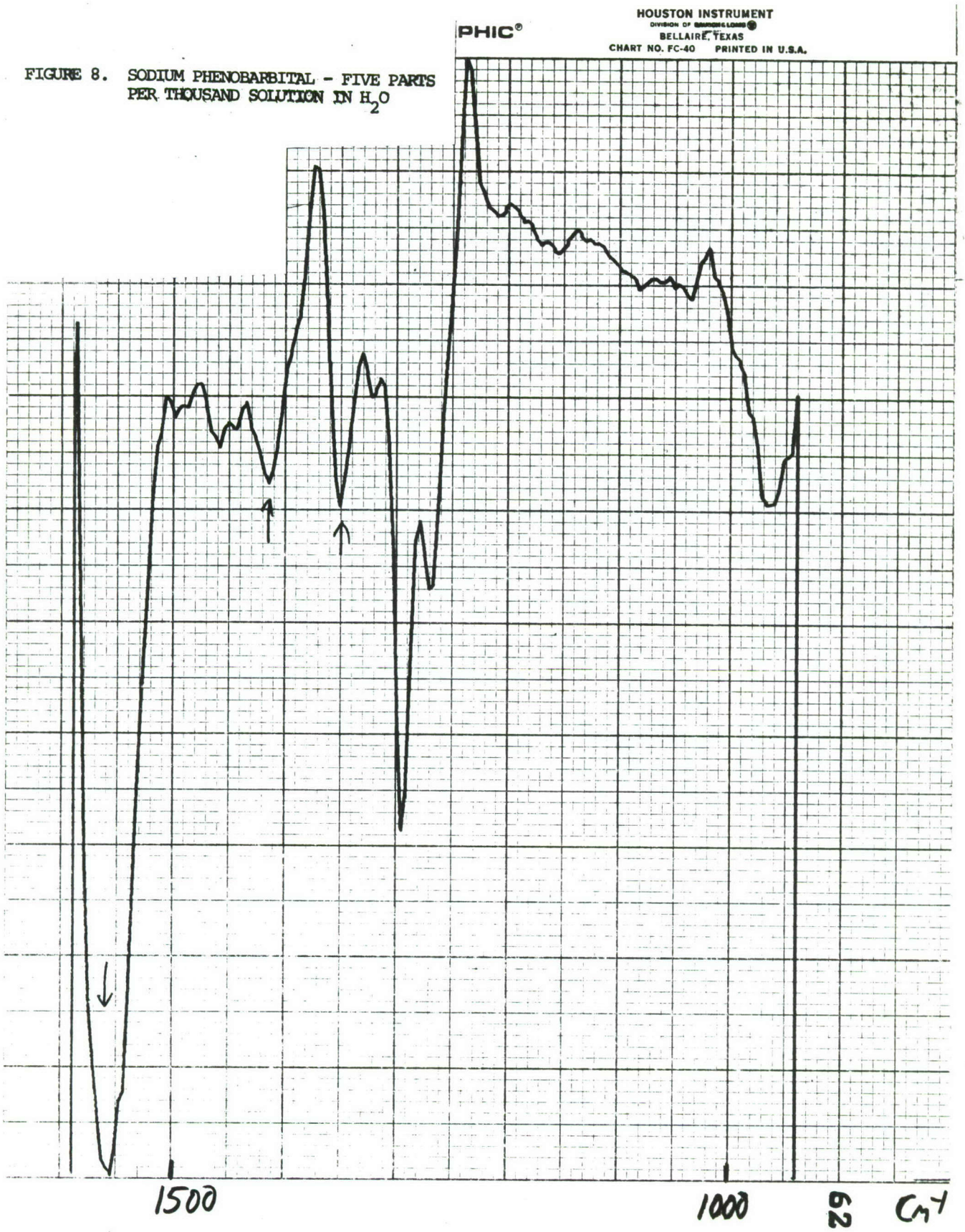


FIGURE 9. SODIUM PHENOBARBITAL - ONE PART PER THOUSAND SOLUTION IN H_2O

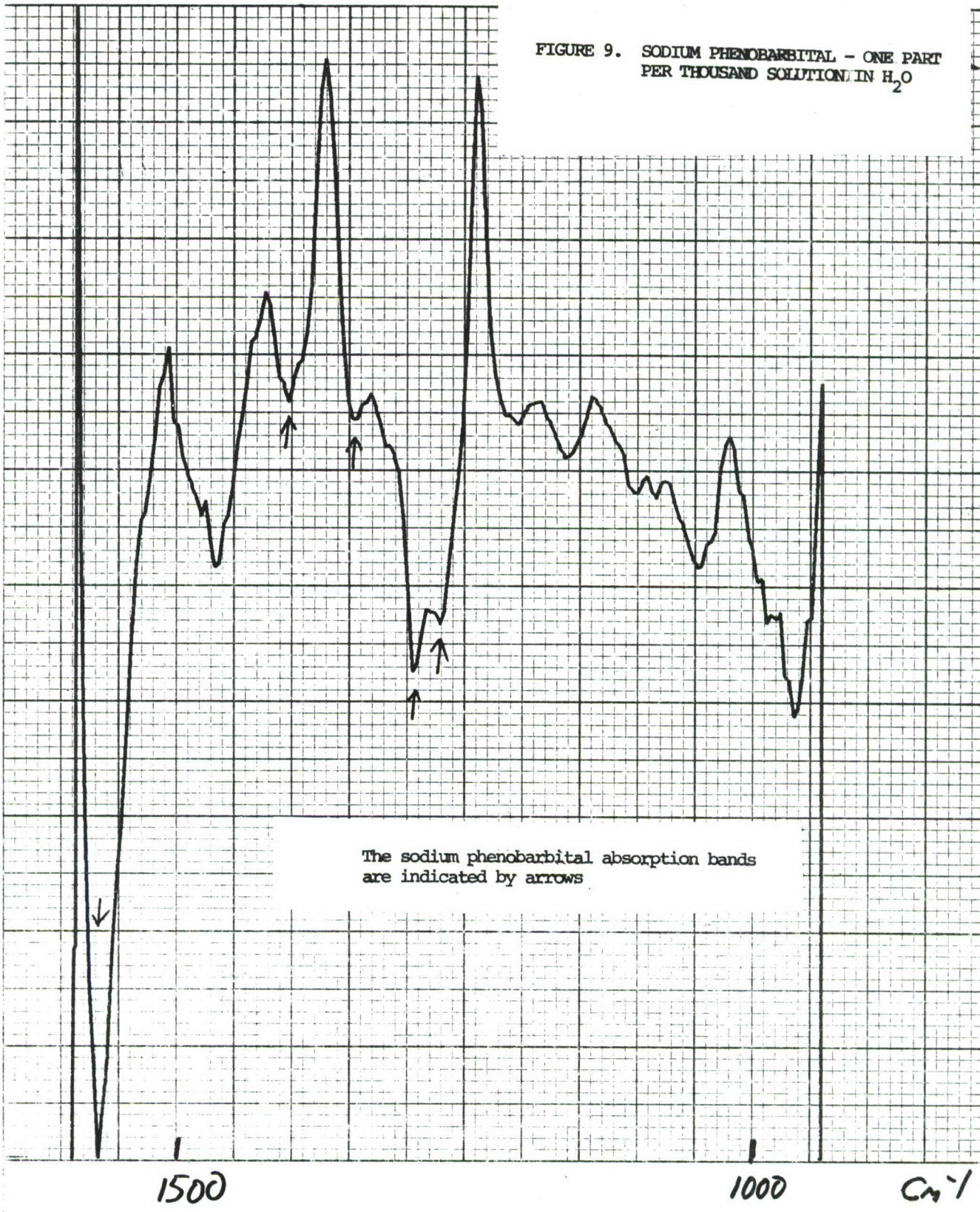
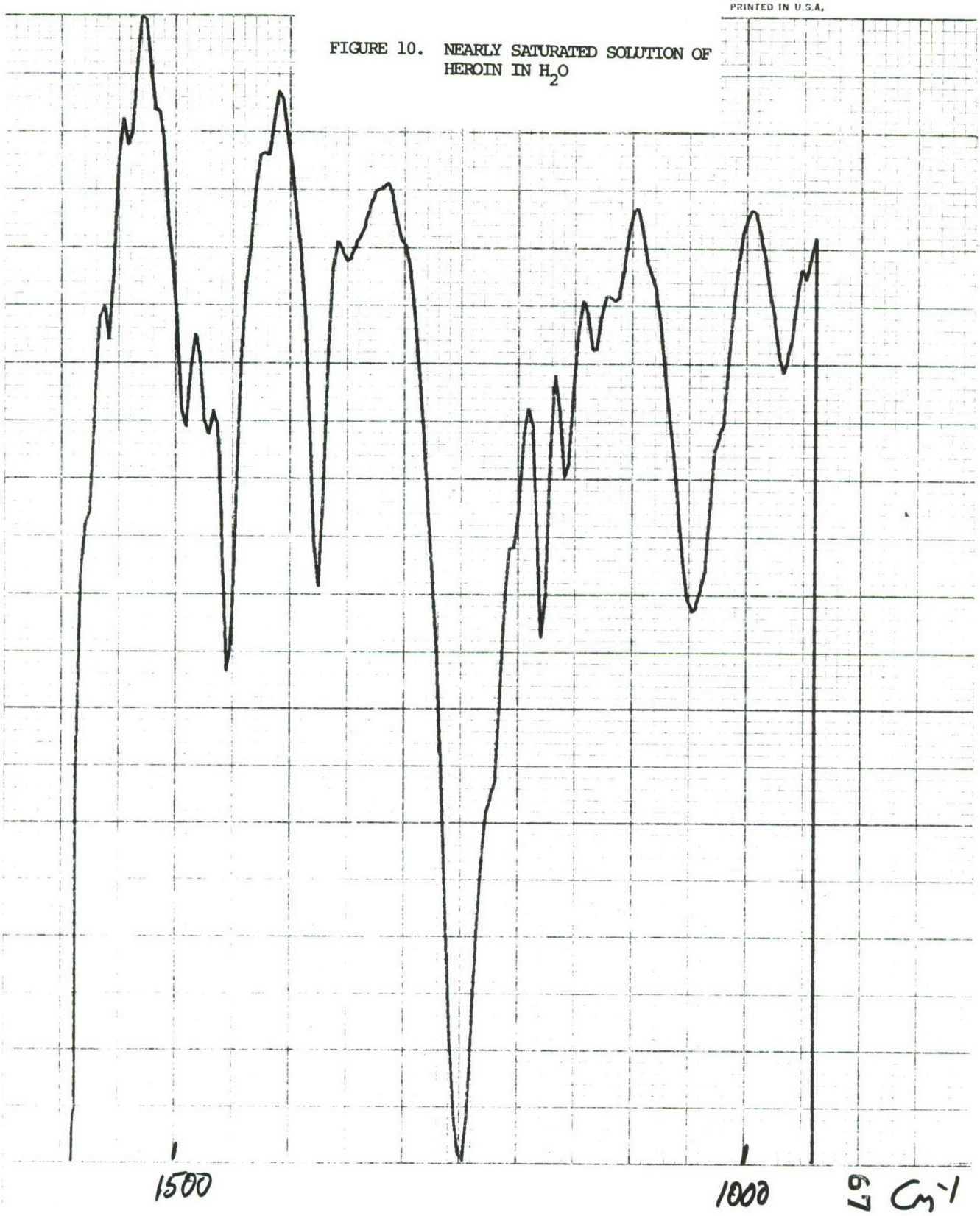


FIGURE 10. NEARLY SATURATED SOLUTION OF HEROIN IN H_2O



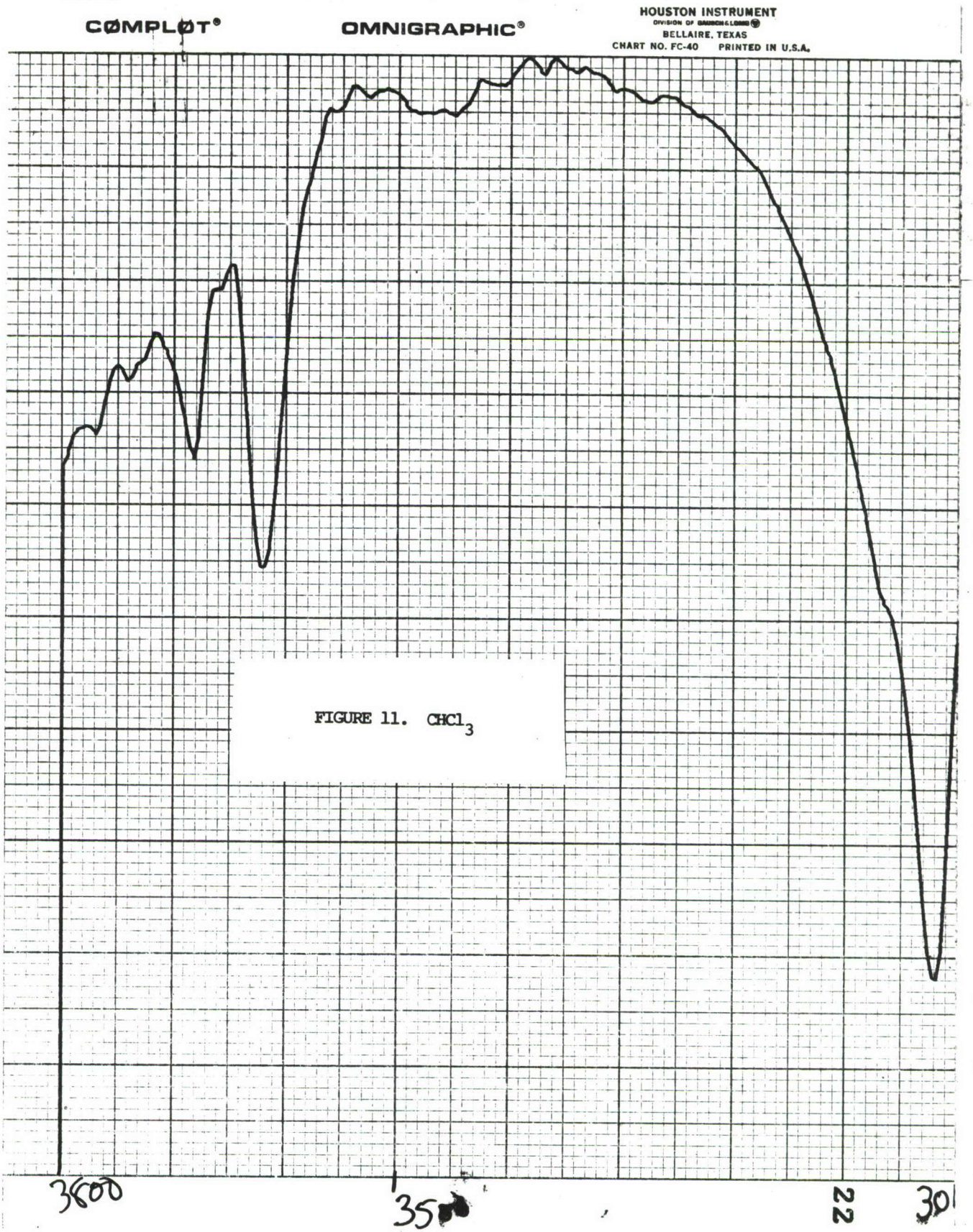


FIGURE 11. $CHCl_3$

FIGURE 11. (continued - 2)

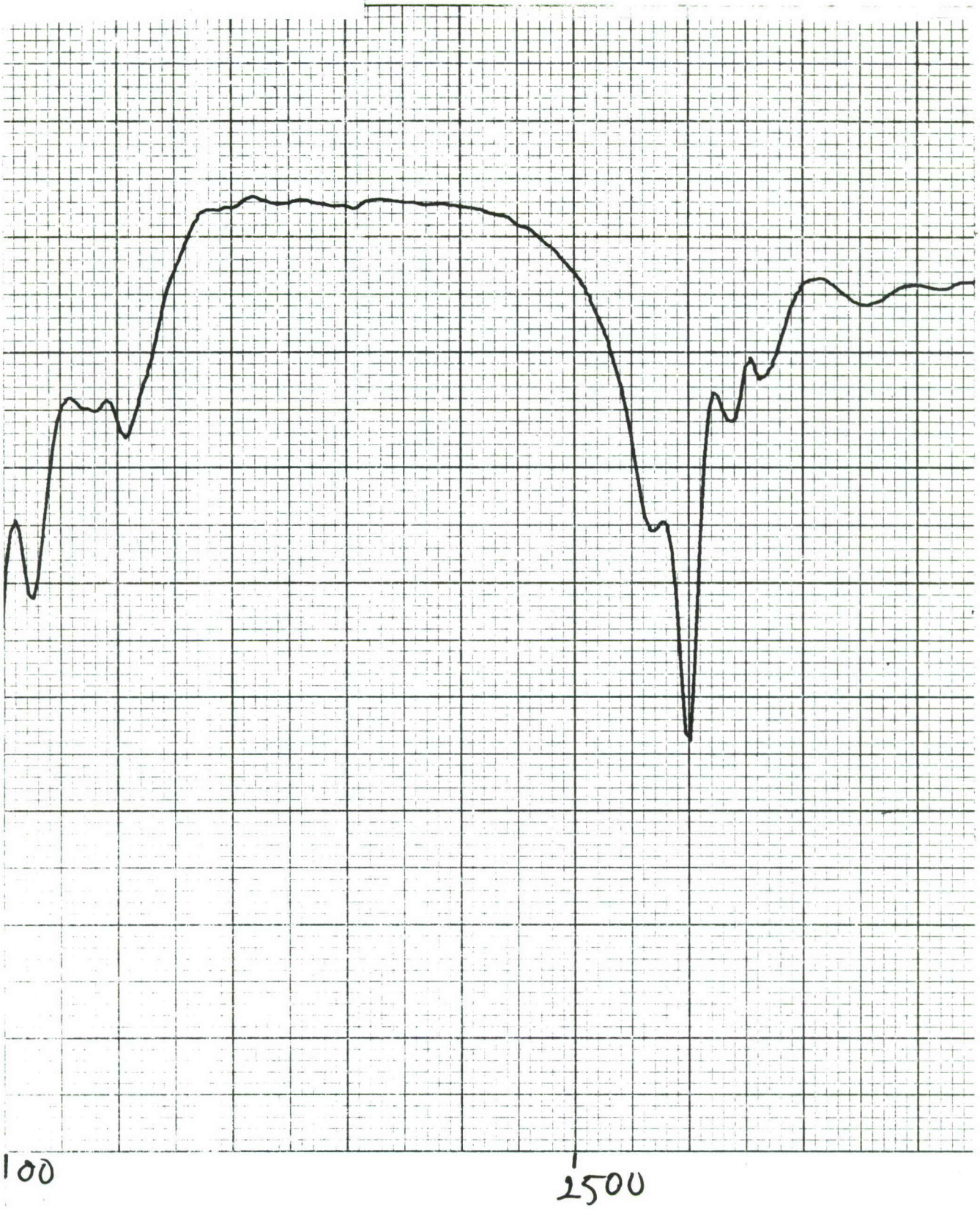
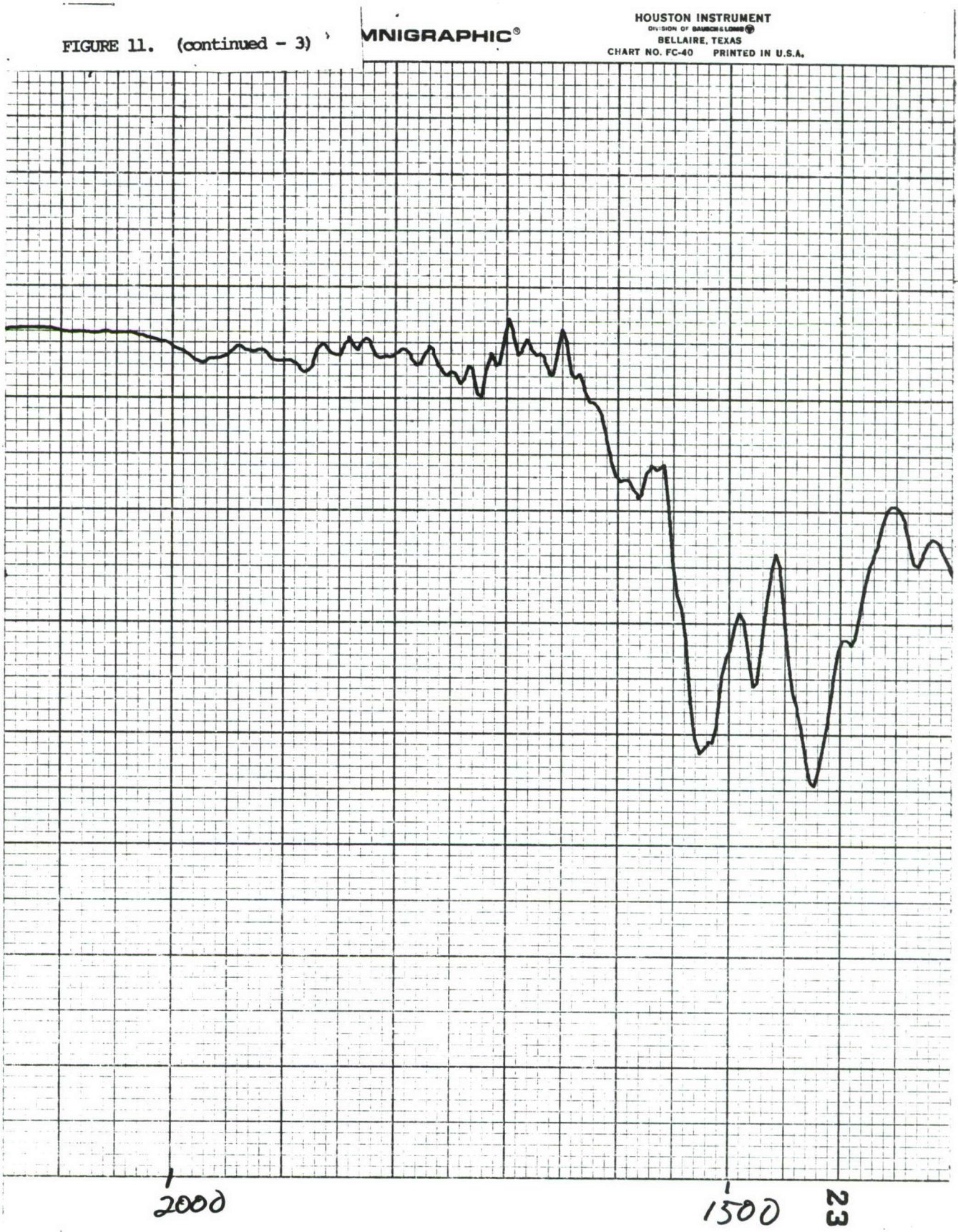


FIGURE 11. (continued - 3)



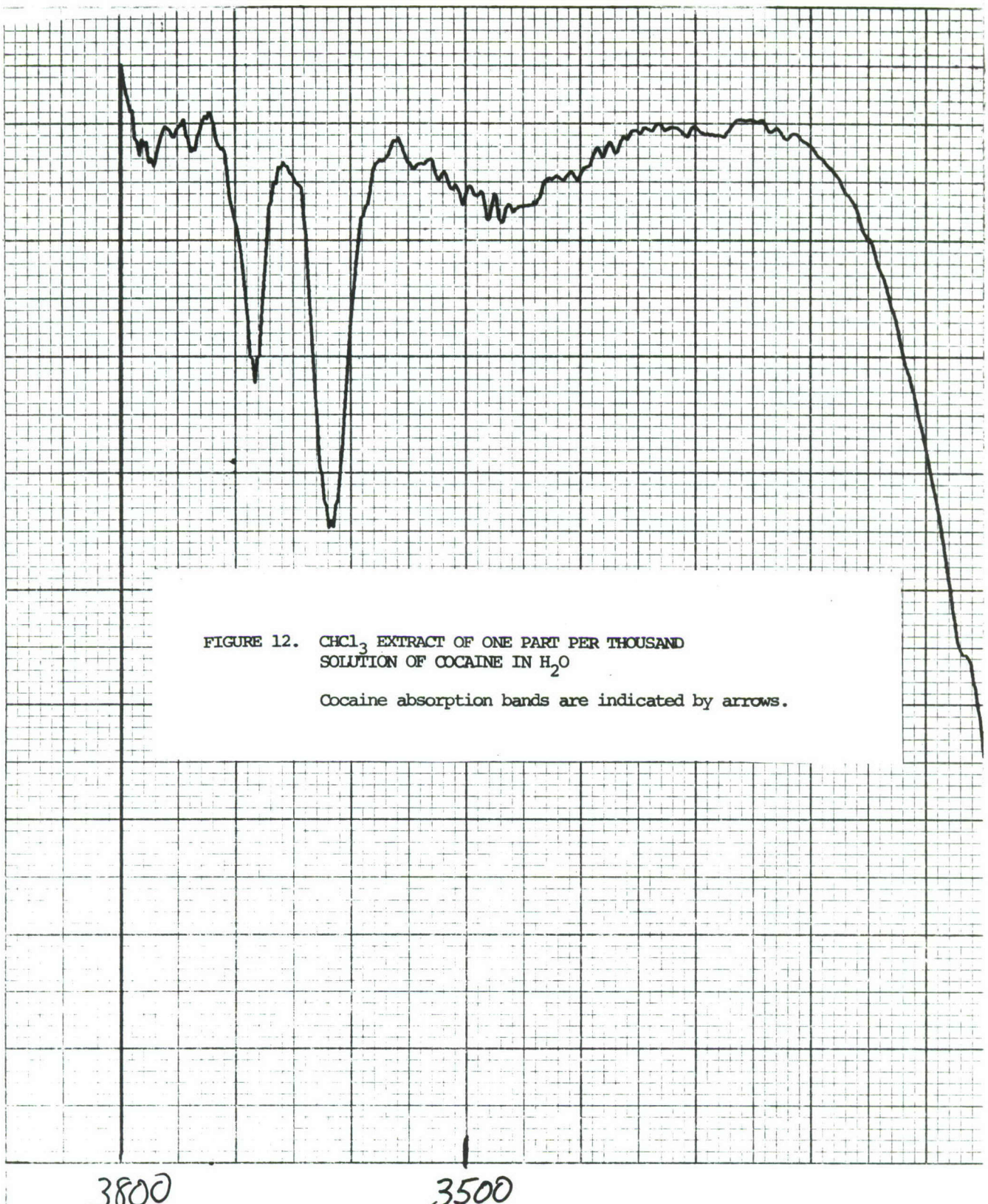
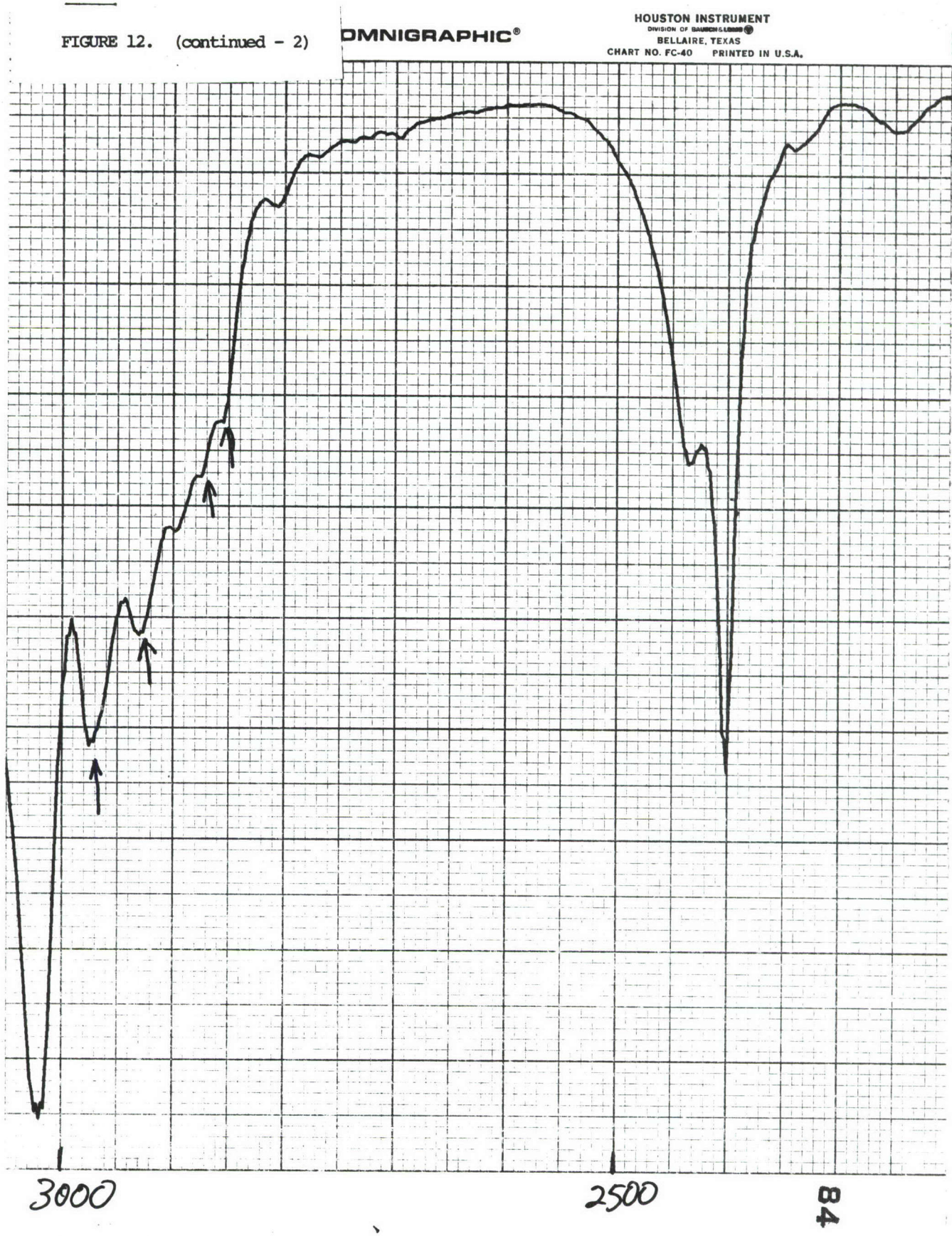


FIGURE 12. $CHCl_3$ EXTRACT OF ONE PART PER THOUSAND SOLUTION OF COCAINE IN H_2O

Cocaine absorption bands are indicated by arrows.

FIGURE 12. (continued - 2)



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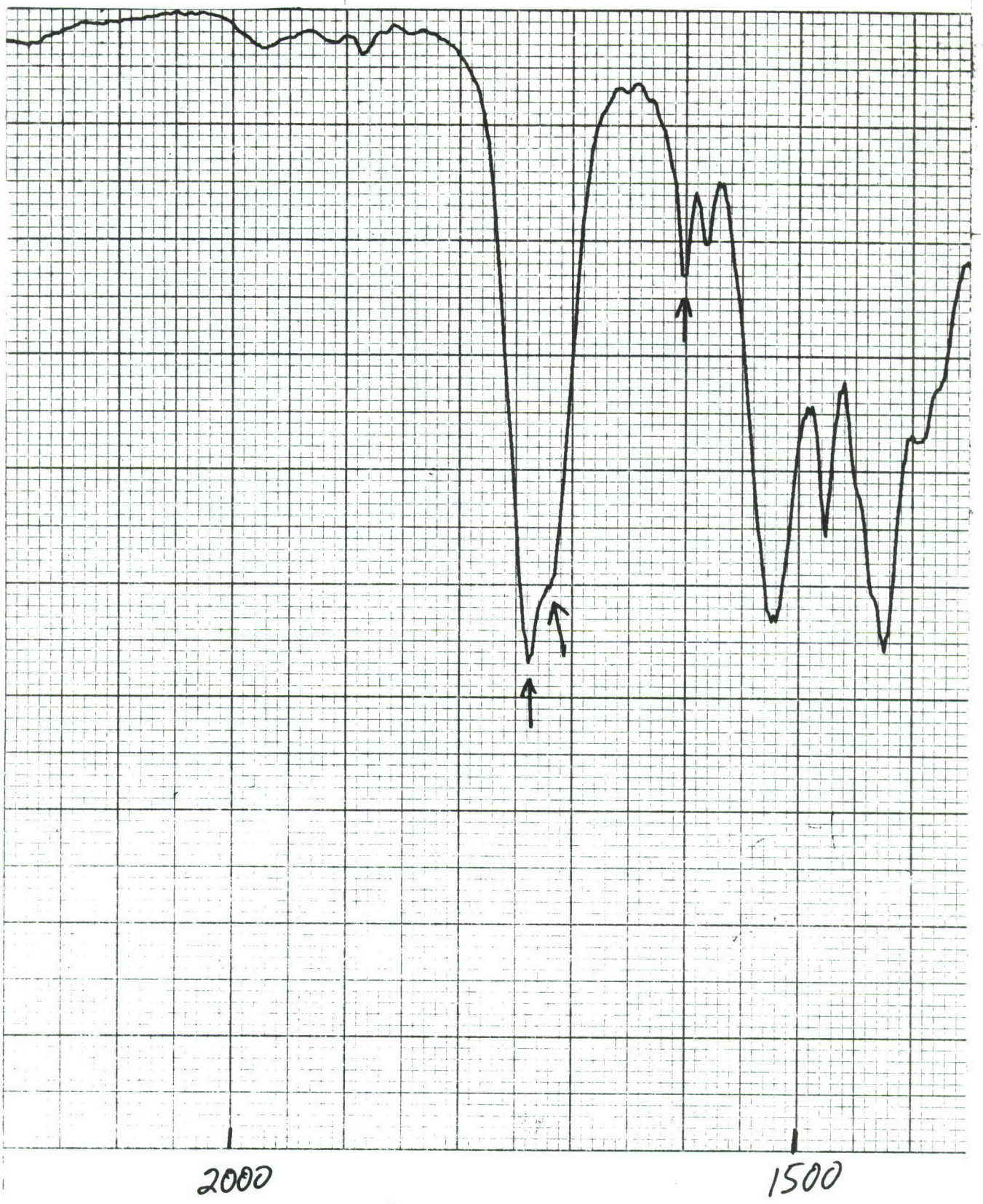
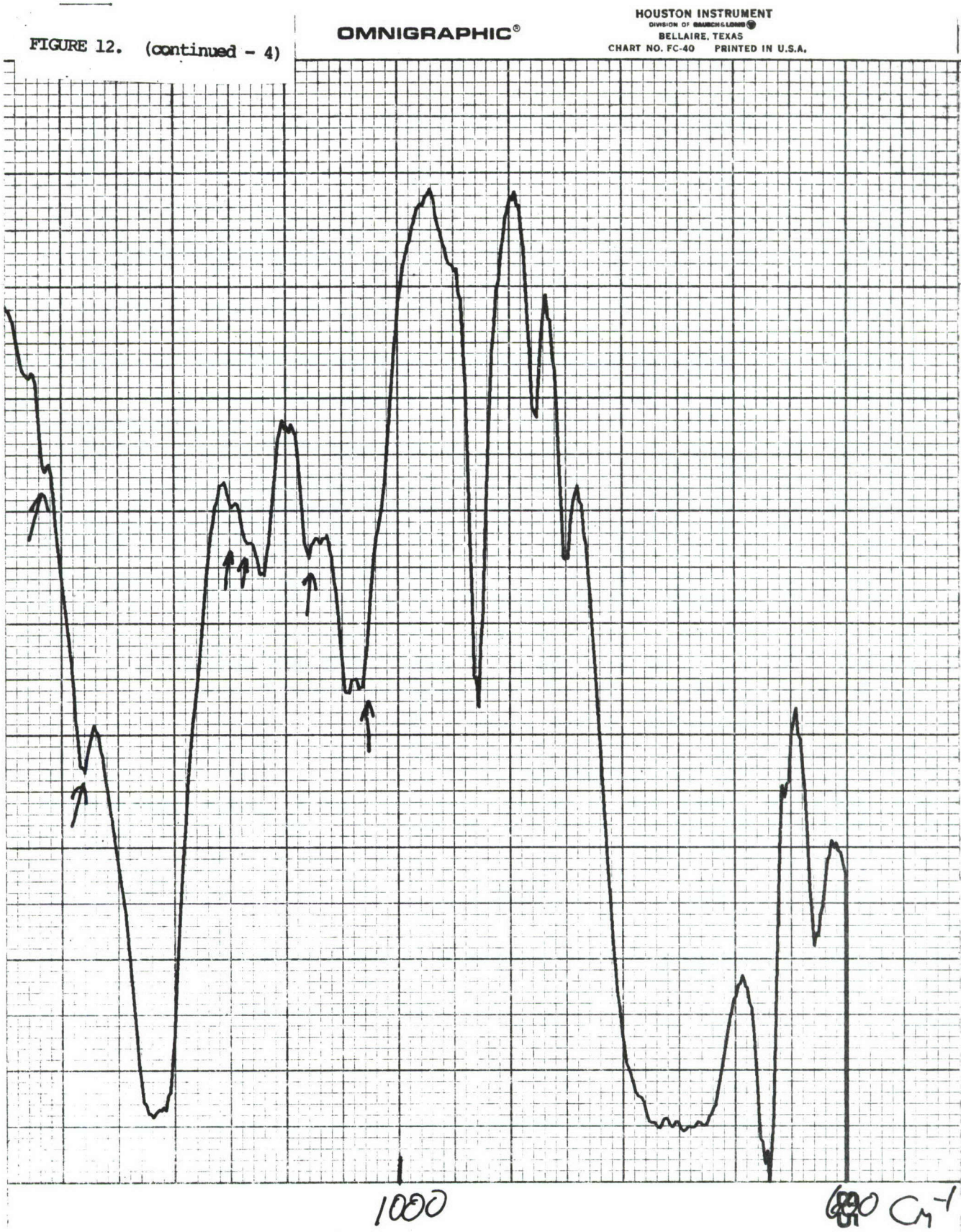


FIGURE 12. (continued - 4)



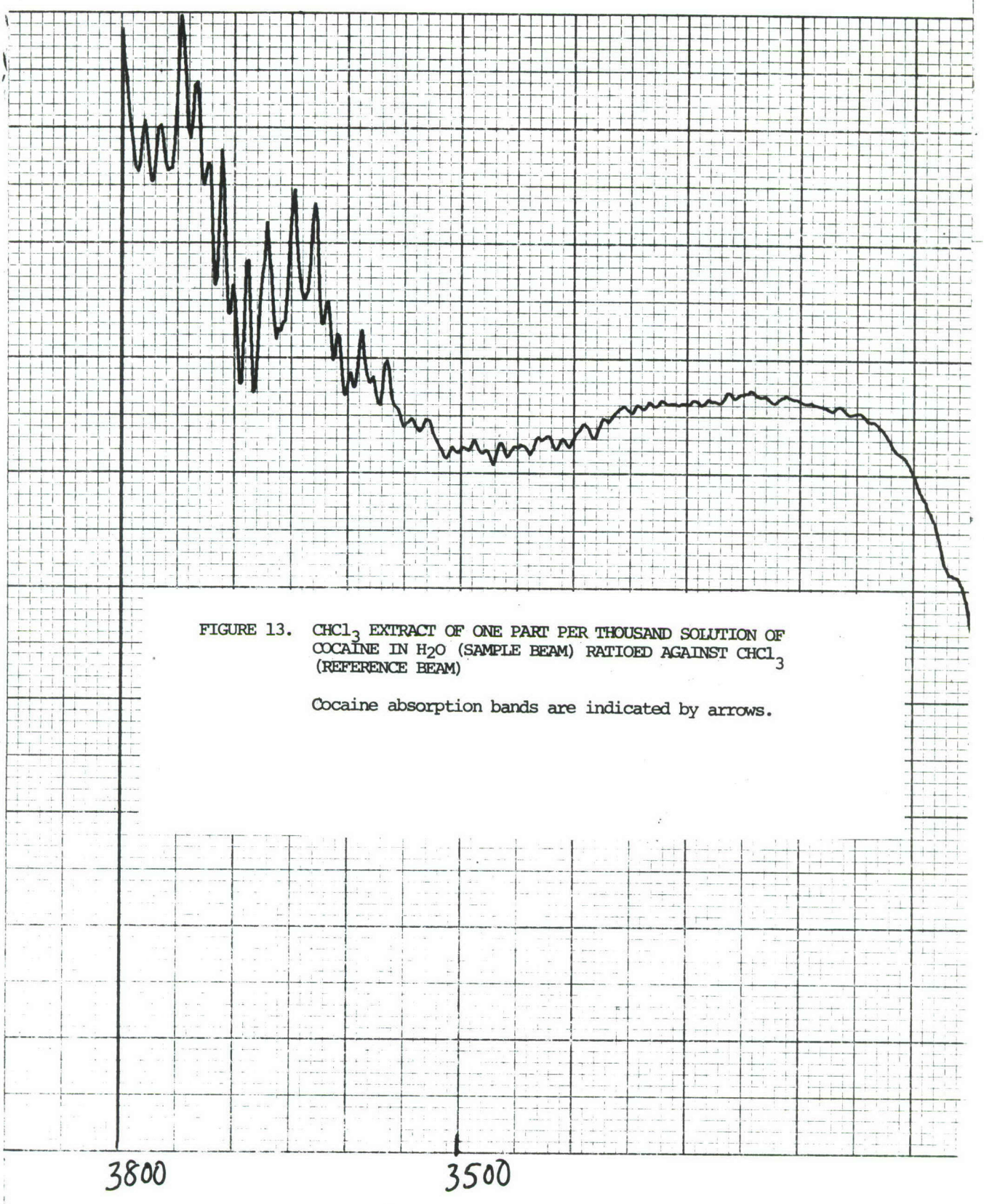


FIGURE 13. $CHCl_3$ EXTRACT OF ONE PART PER THOUSAND SOLUTION OF COCAINE IN H_2O (SAMPLE BEAM) RATIOED AGAINST $CHCl_3$ (REFERENCE BEAM)

Cocaine absorption bands are indicated by arrows.

FIGURE 13 (continued - 2)

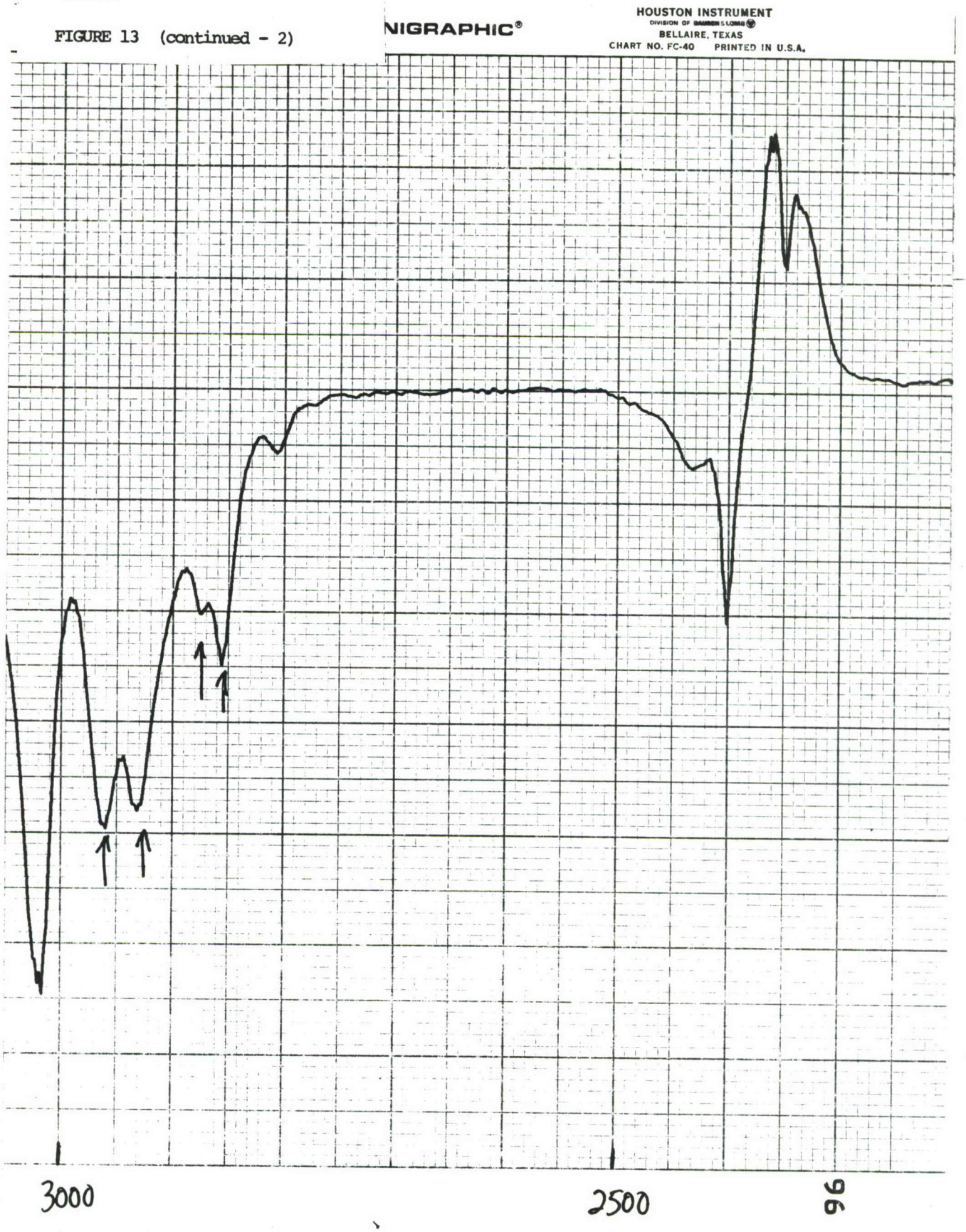
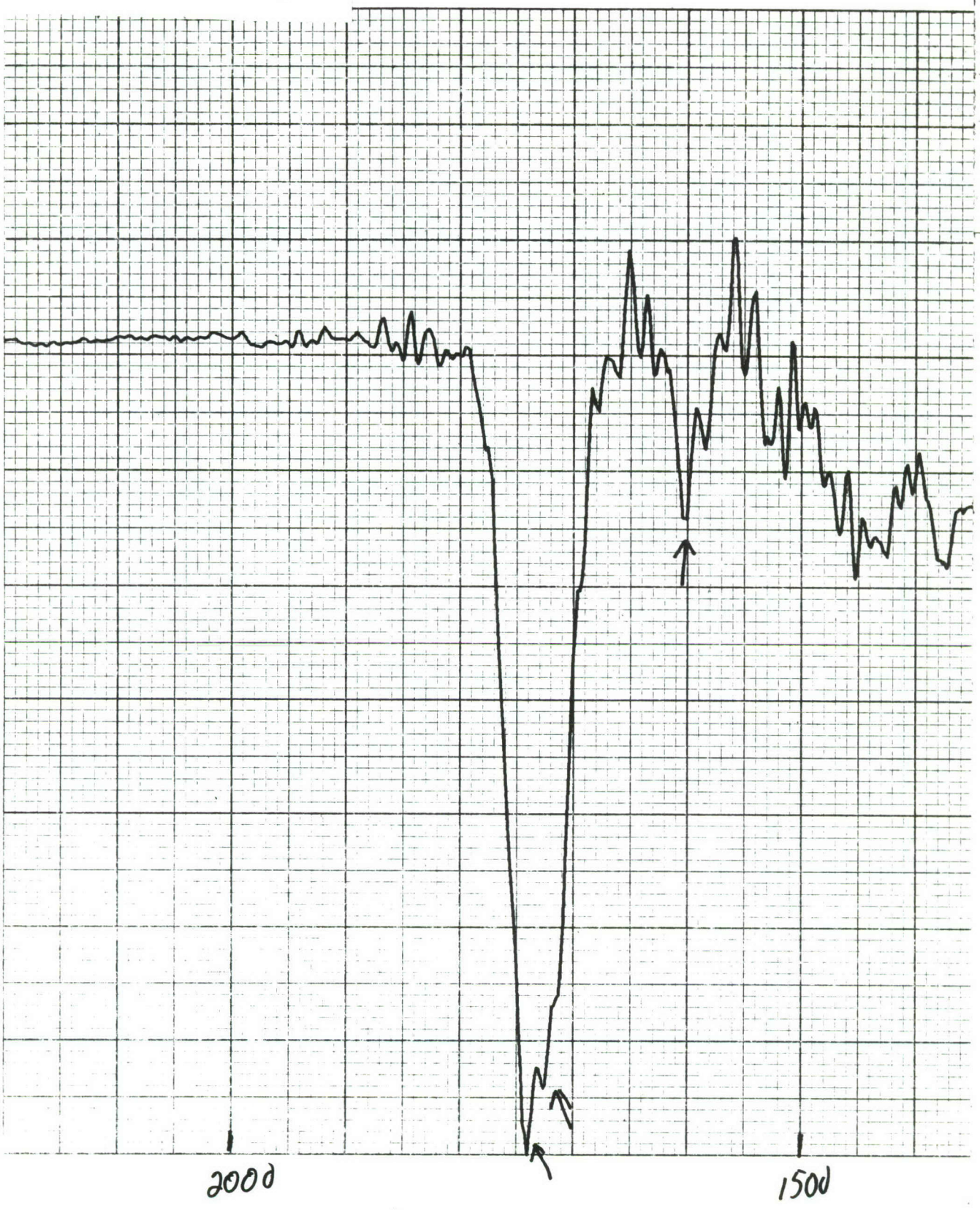


FIGURE 13 (continued - 3)



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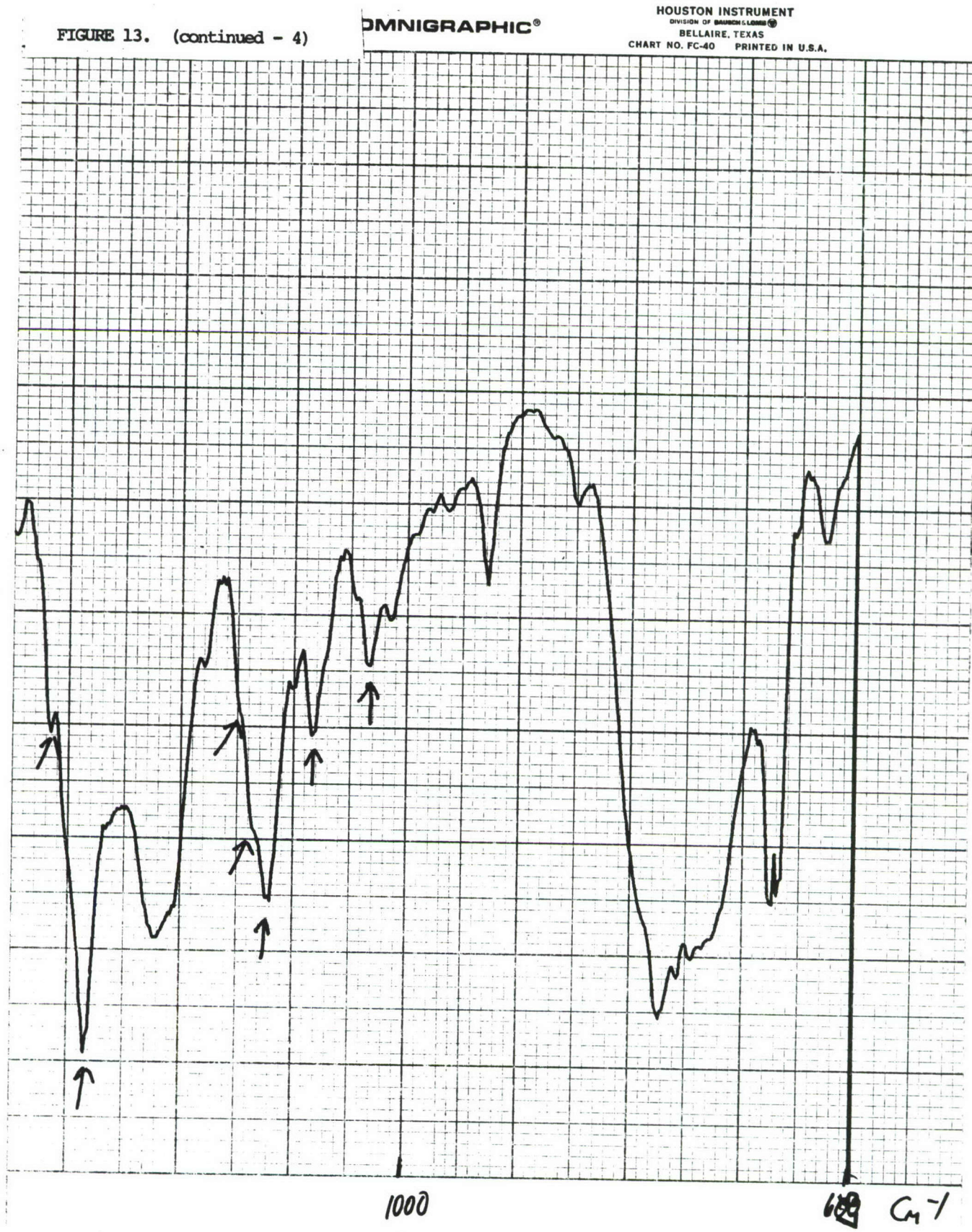


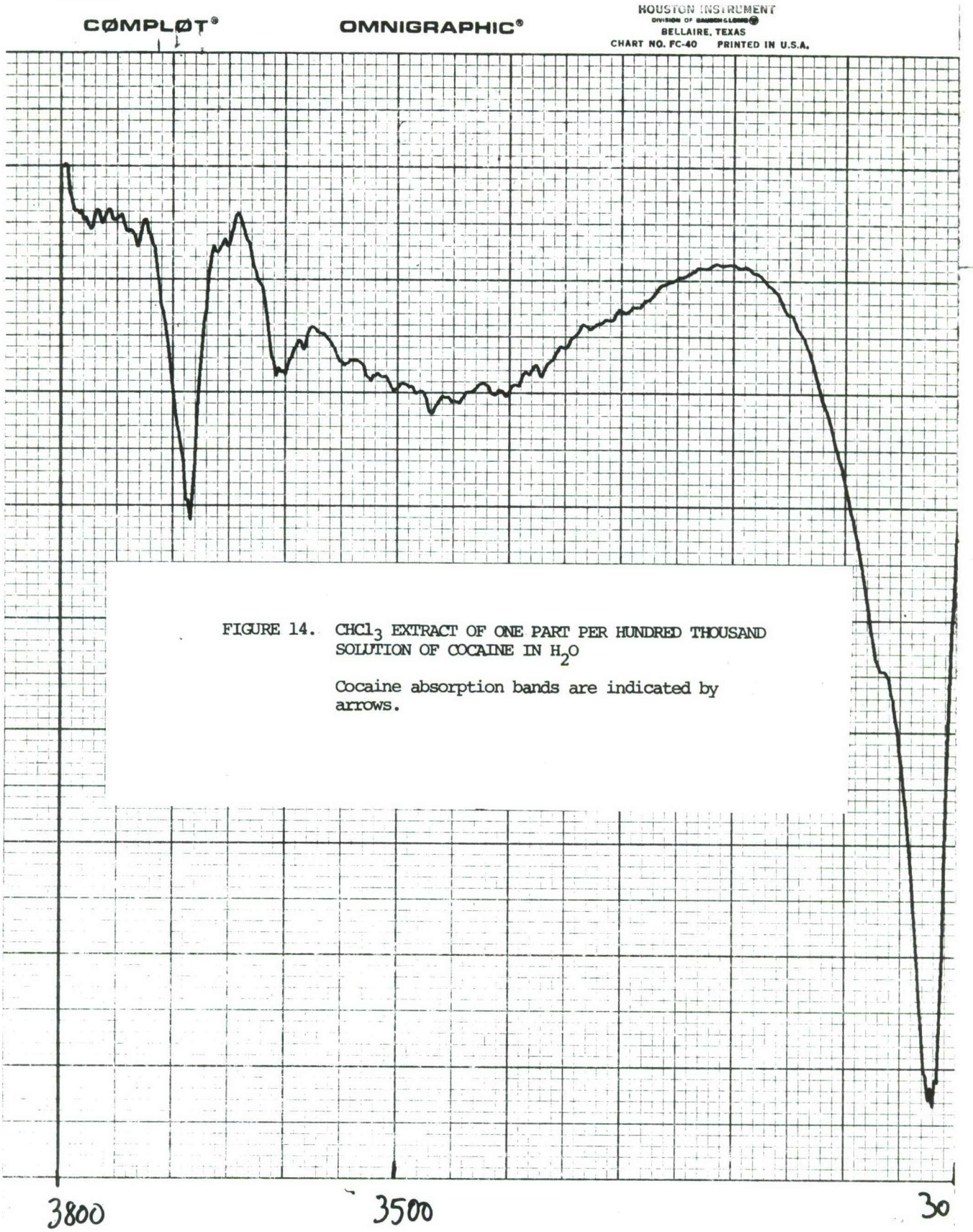


FIGURE 14. $CHCl_3$ EXTRACT OF ONE PART PER HUNDRED THOUSAND SOLUTION OF COCAINE IN H_2O

Cocaine absorption bands are indicated by arrows.

FIGURE 14. (continued - 2)

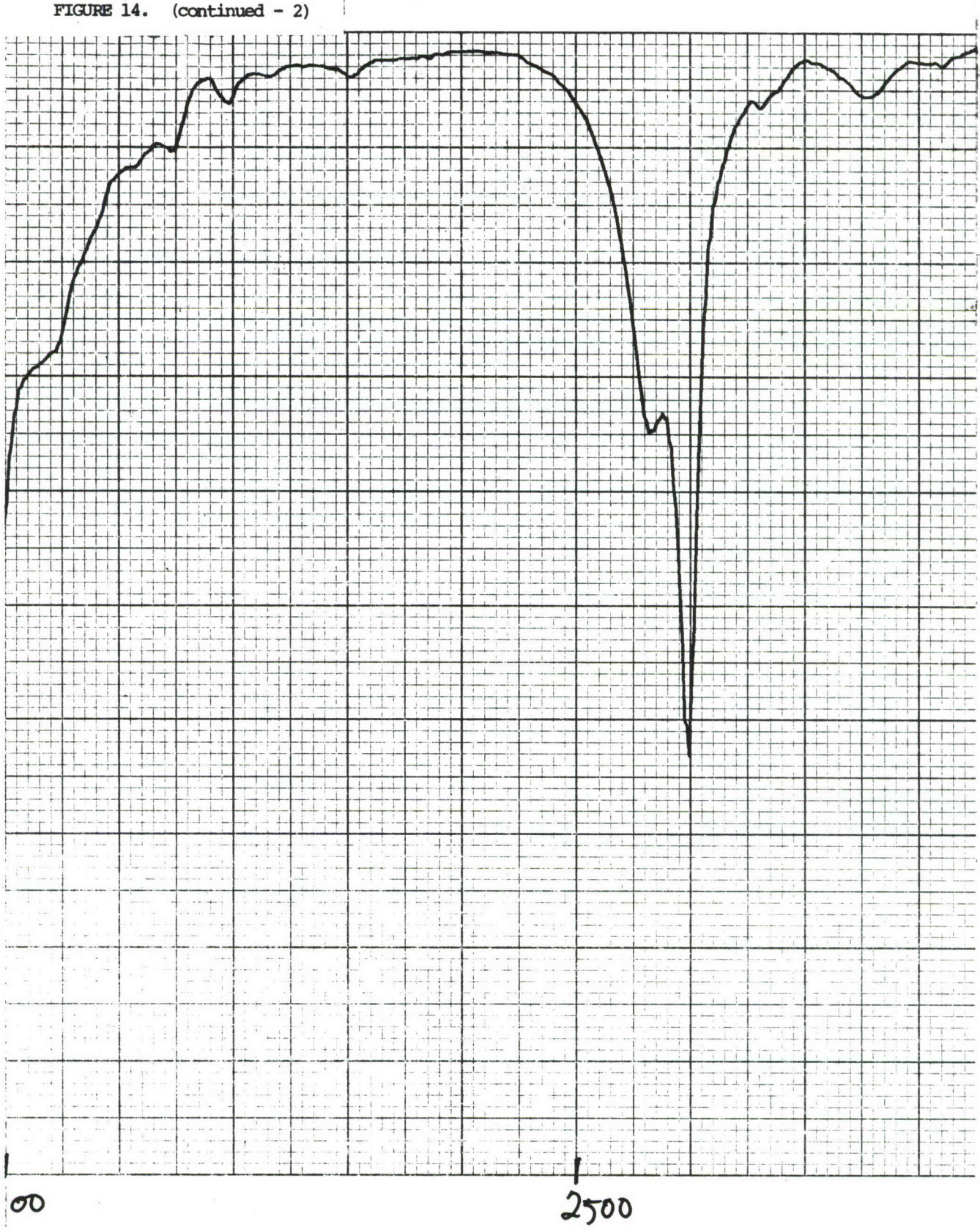


FIGURE 14. (continued - 3)

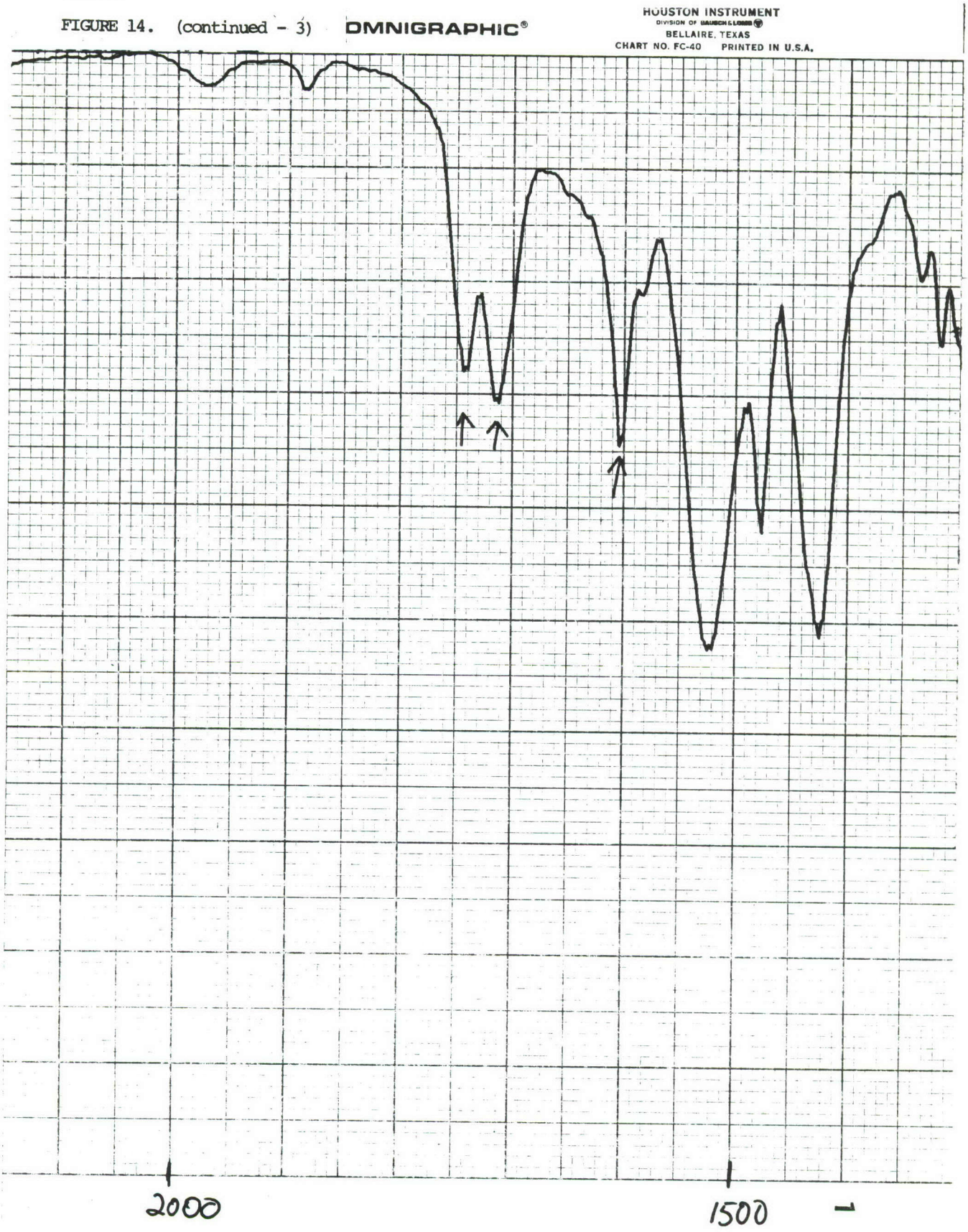
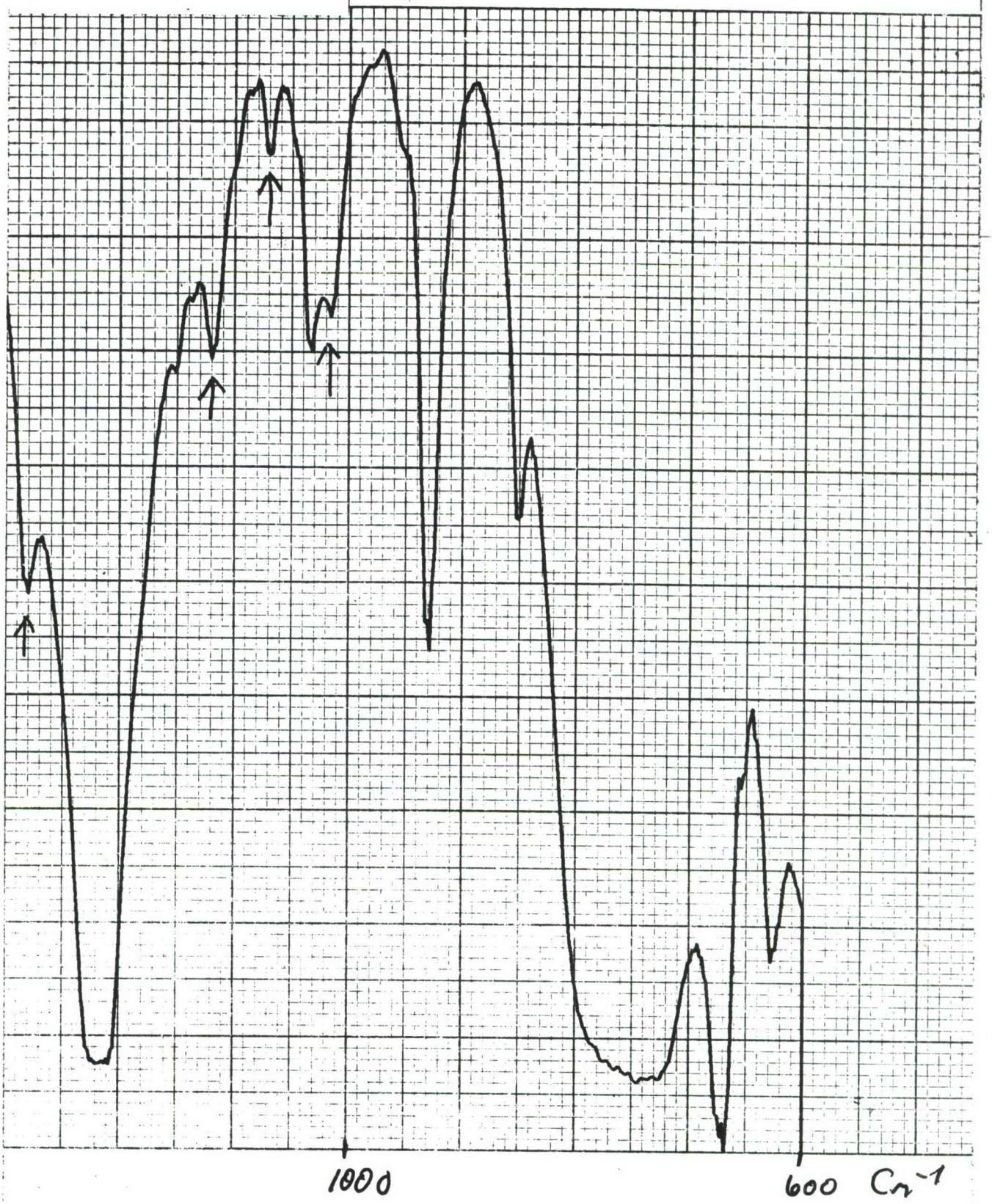


FIGURE 14. (continued - 4)



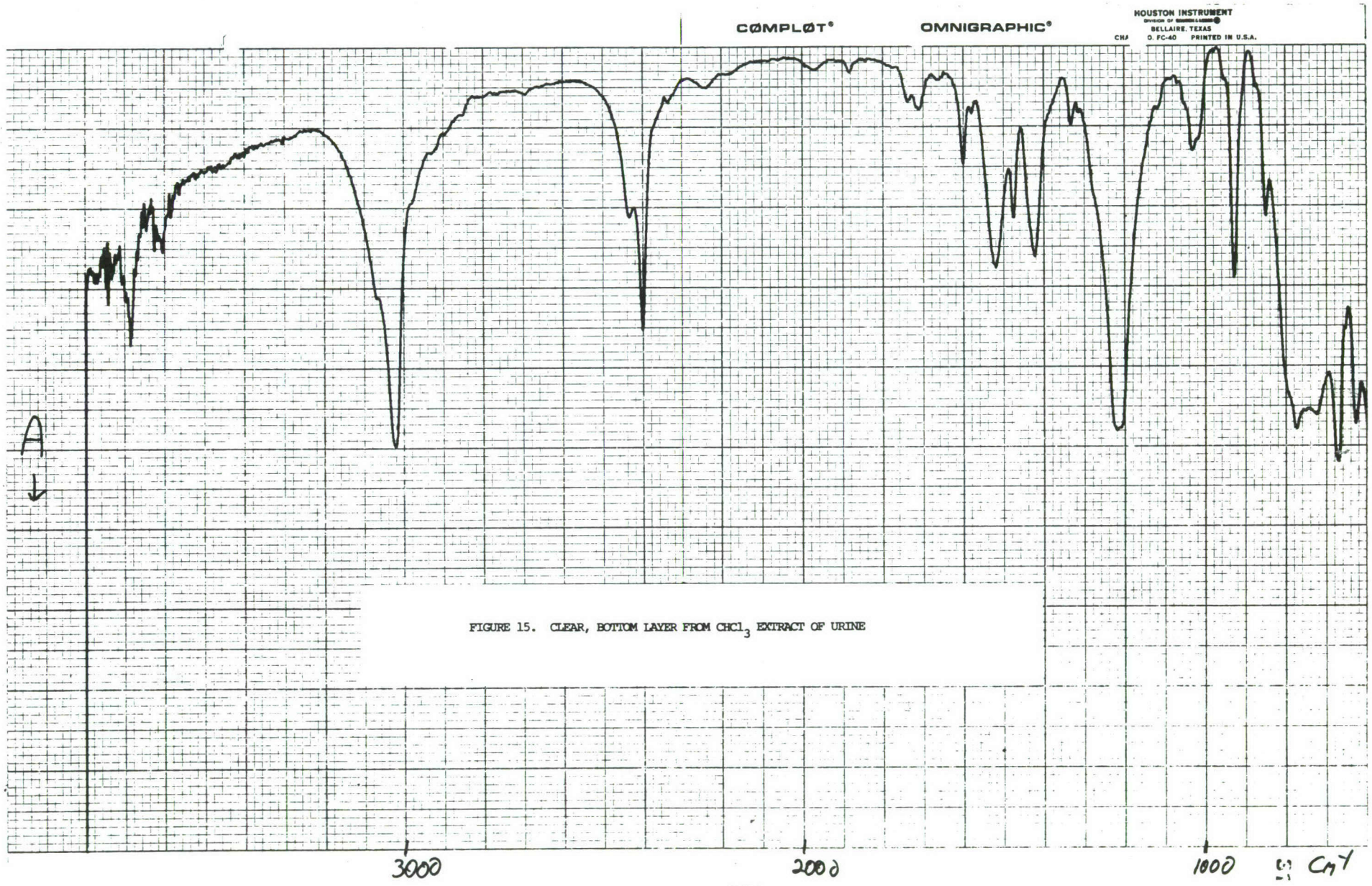


FIGURE 15. CLEAR, BOTTOM LAYER FROM $CHCl_3$ EXTRACT OF URINE

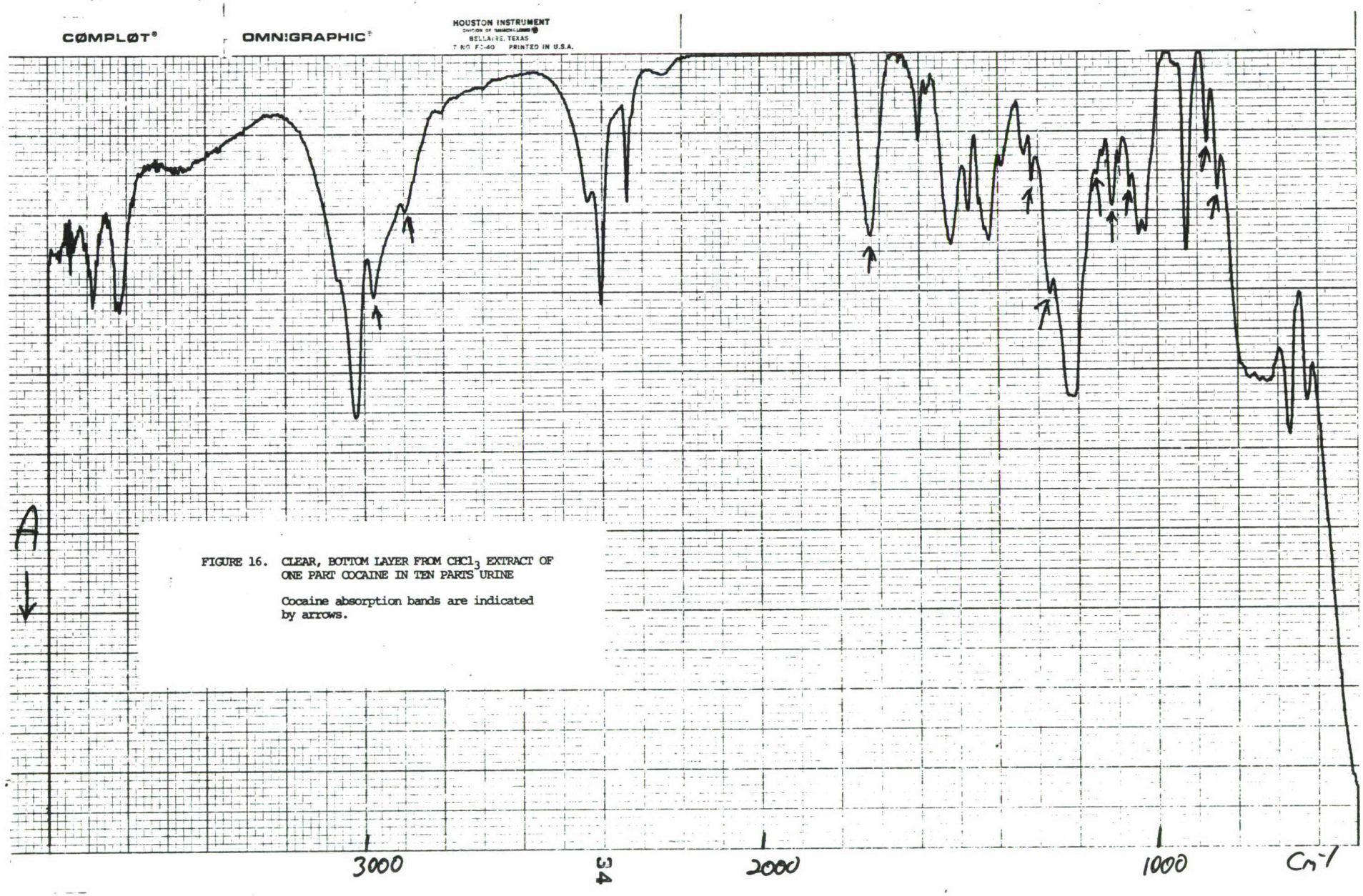


FIGURE 16. CLEAR, BOTTOM LAYER FROM $CHCl_3$ EXTRACT OF ONE PART COCAINE IN TEN PARTS URINE

Cocaine absorption bands are indicated by arrows.

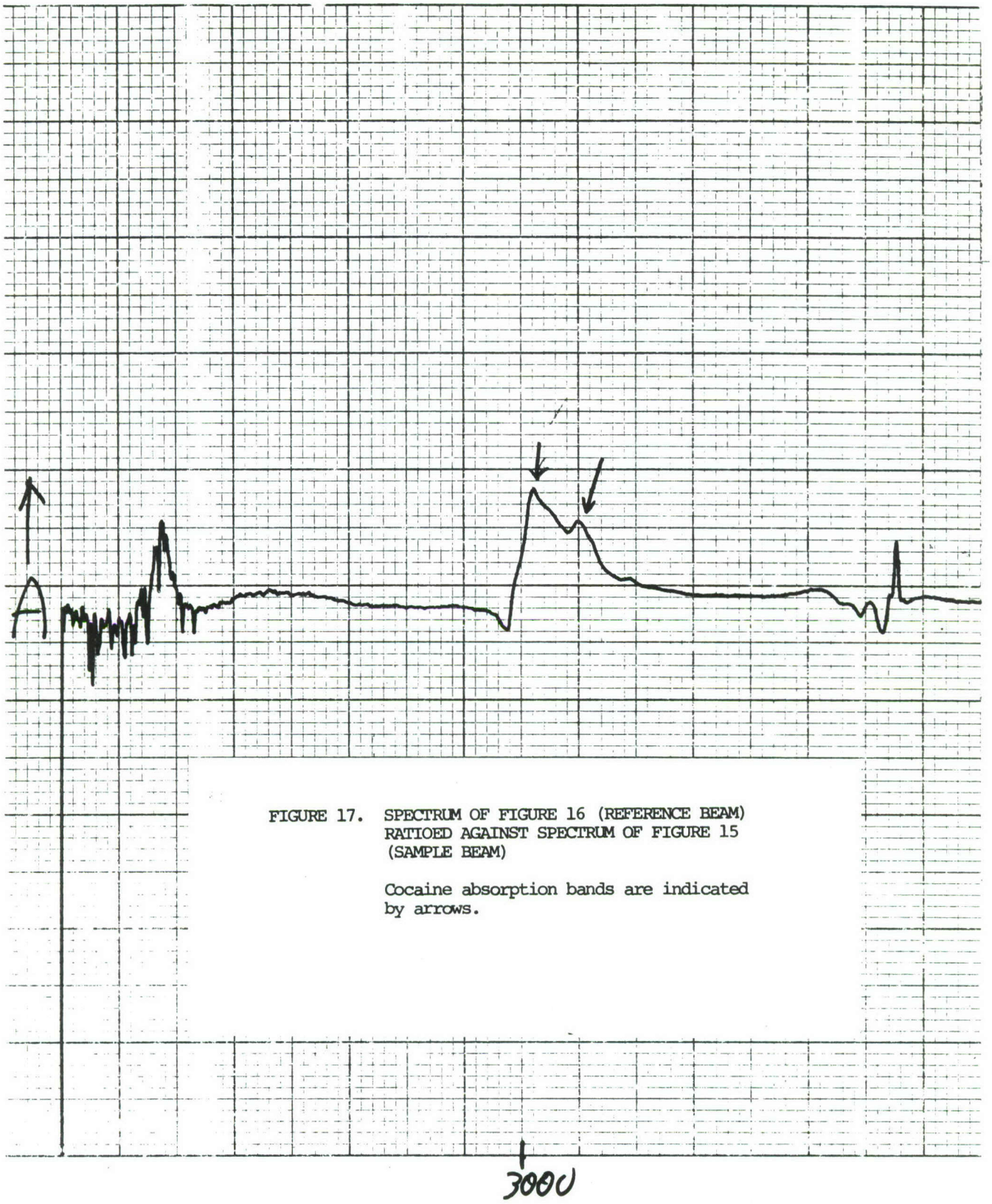
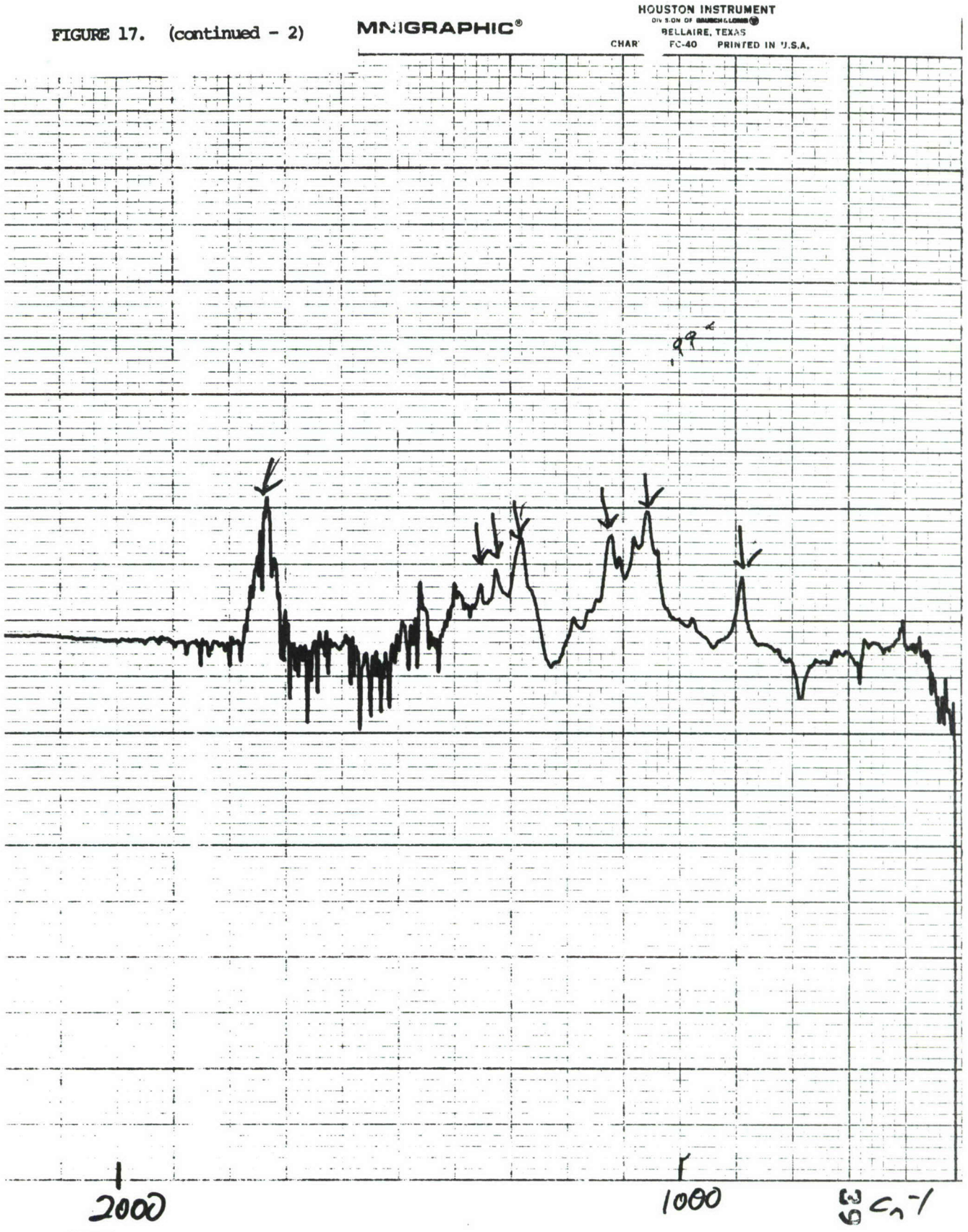


FIGURE 17. SPECTRUM OF FIGURE 16 (REFERENCE BEAM) RATIOED AGAINST SPECTRUM OF FIGURE 15 (SAMPLE BEAM)

Cocaine absorption bands are indicated by arrows.

FIGURE 17. (continued - 2)



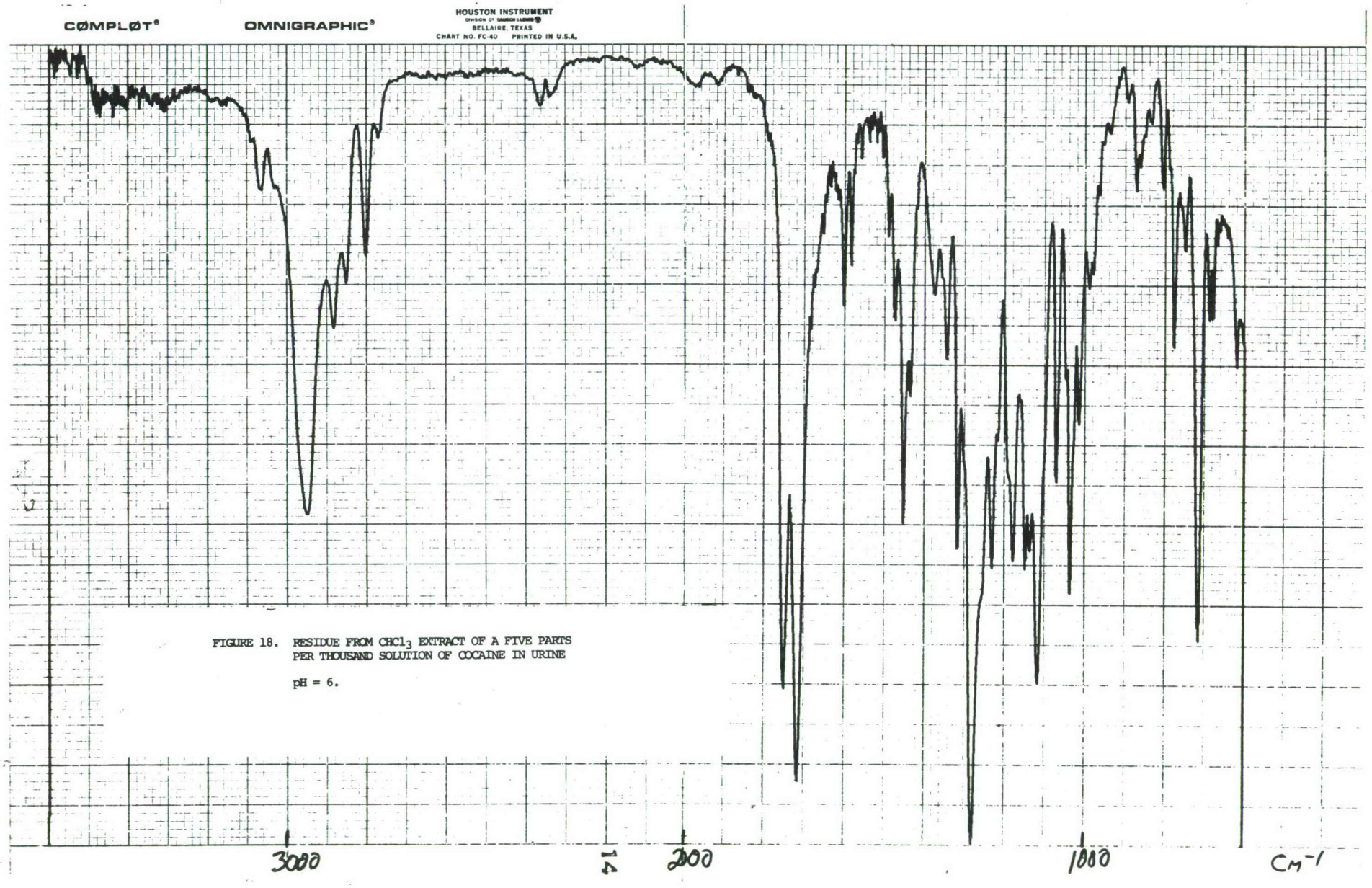


FIGURE 18. RESIDUE FROM $CHCl_3$ EXTRACT OF A FIVE PARTS PER THOUSAND SOLUTION OF COCAINE IN URINE

pH = 6.

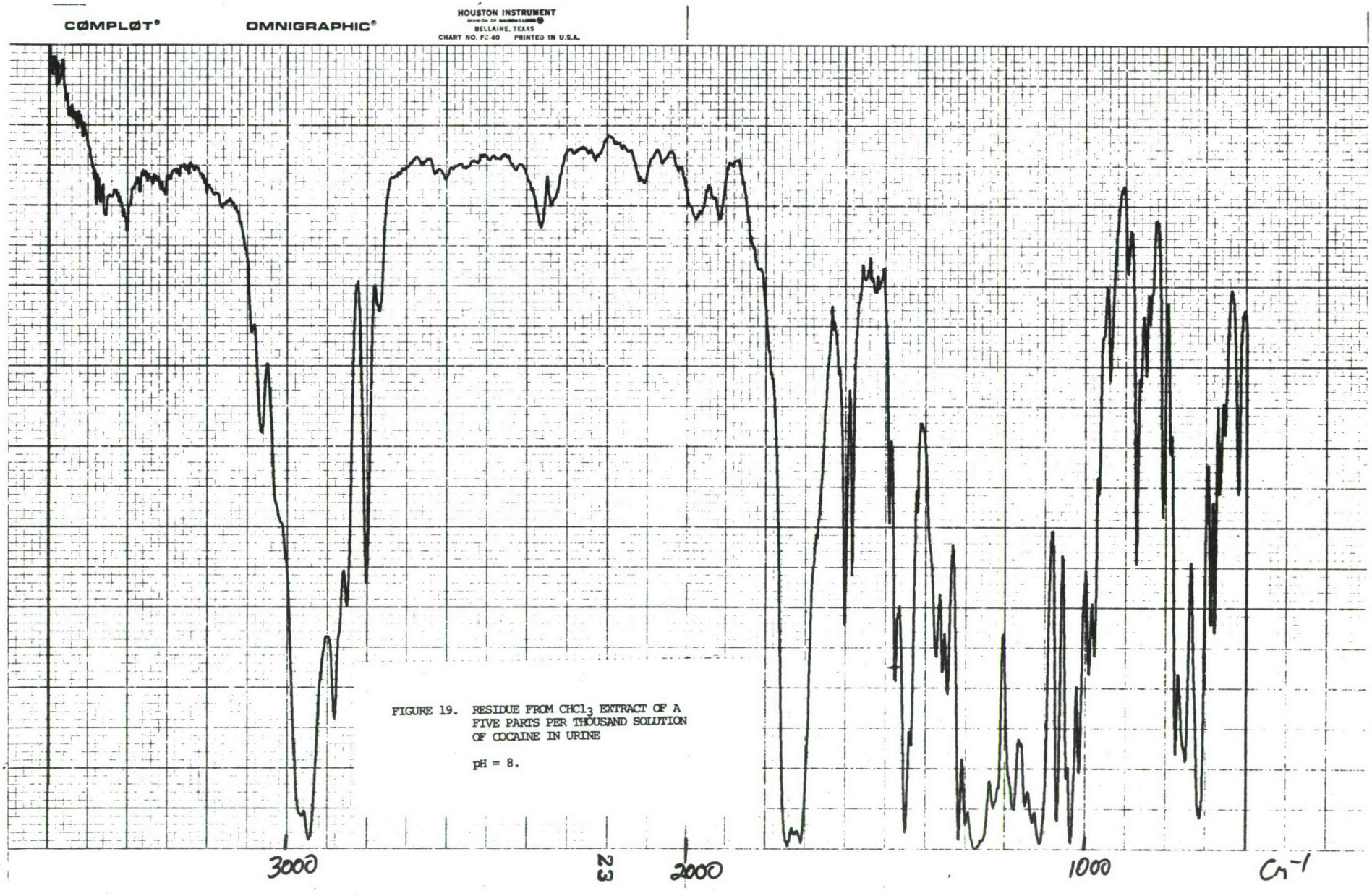


FIGURE 19. RESIDUE FROM $CHCl_3$ EXTRACT OF A FIVE PARTS PER THOUSAND SOLUTION OF COCAINE IN URINE

pH = 8.

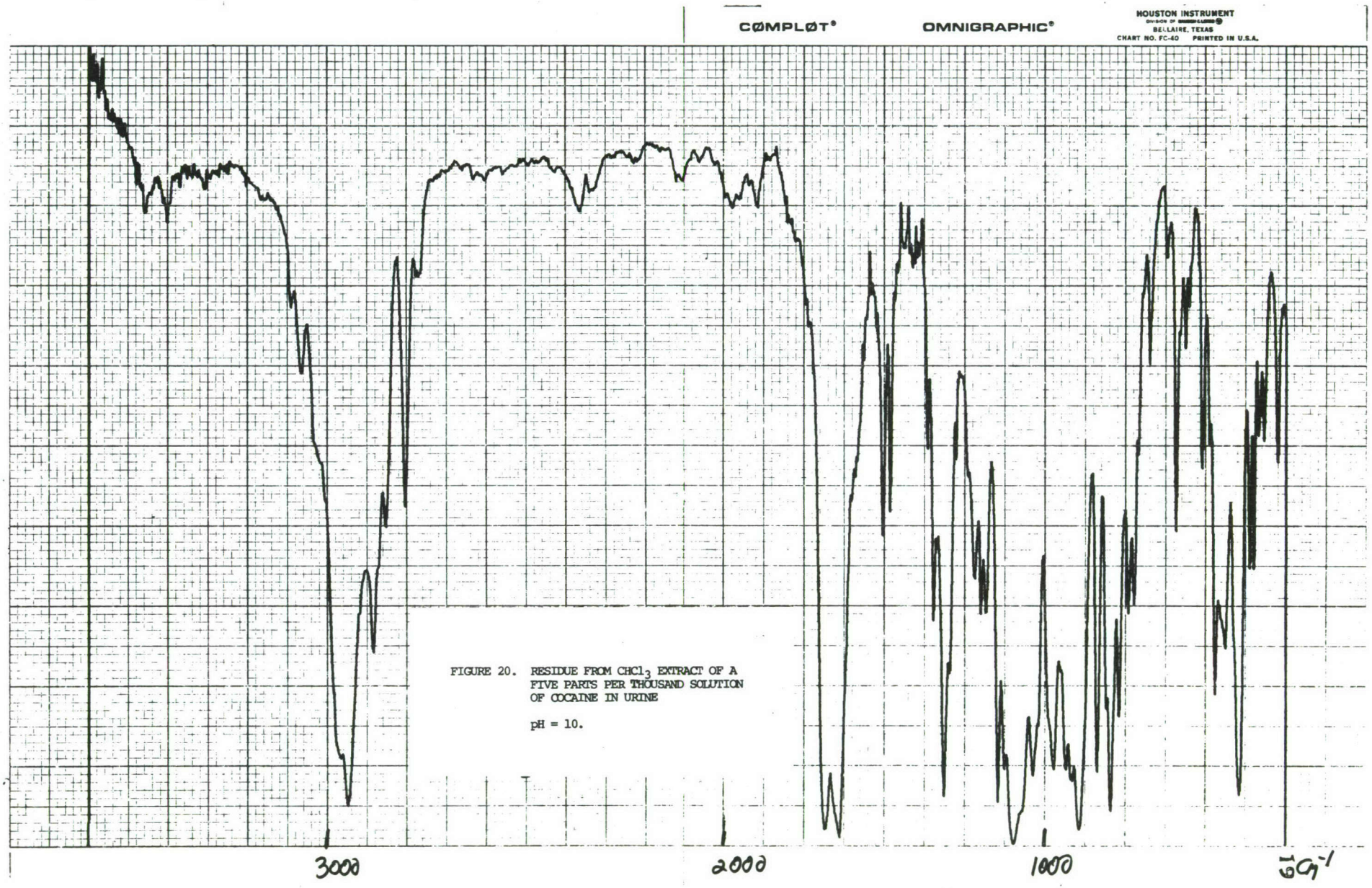


FIGURE 20. RESIDUE FROM $CHCl_3$ EXTRACT OF A FIVE PARTS PER THOUSAND SOLUTION OF COCAINE IN URINE

pH = 10.

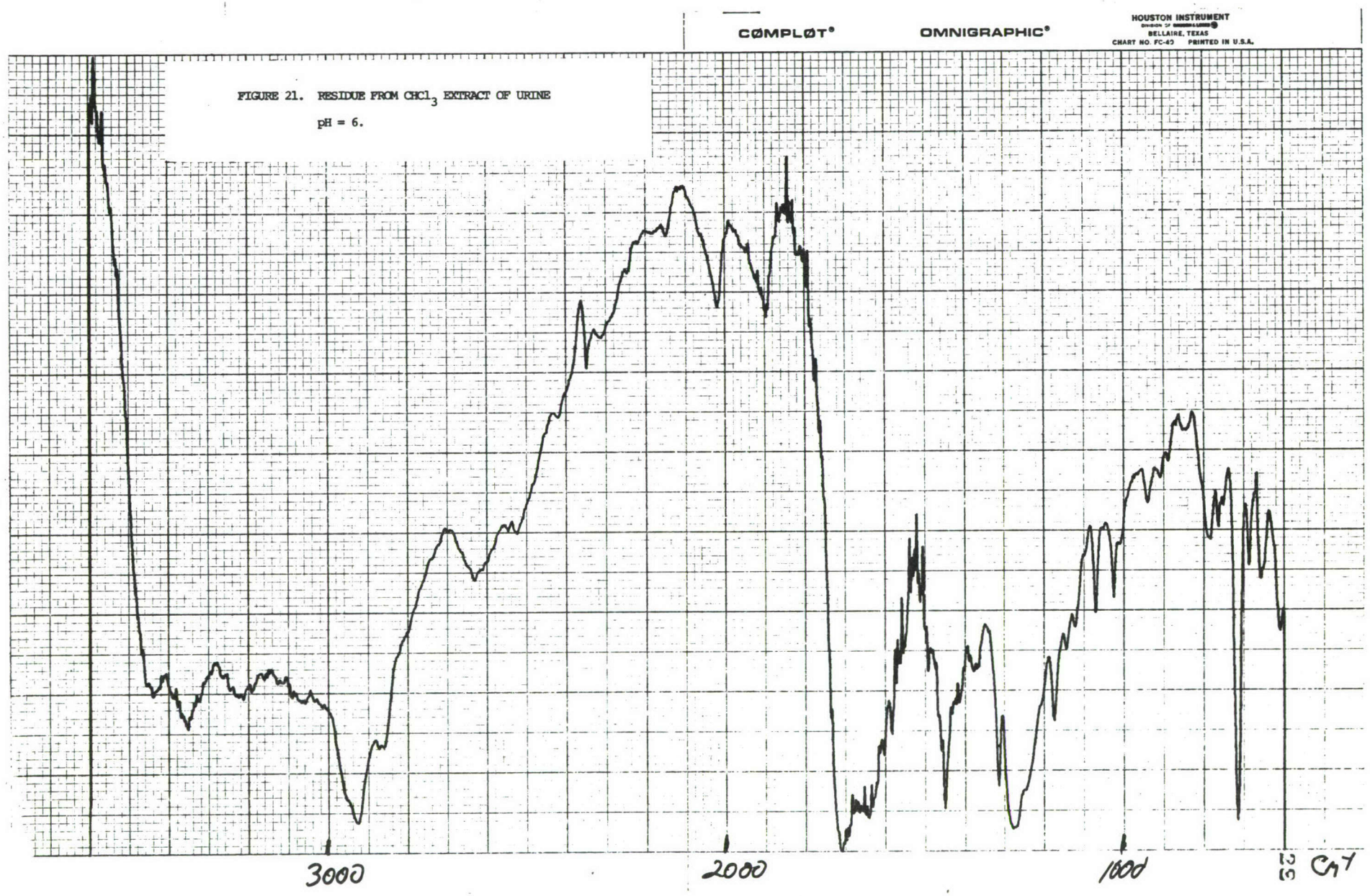

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FIGURE 21. RESIDUE FROM $CHCl_3$ EXTRACT OF URINE
pH = 6.
3000
2000
1000
12 CM

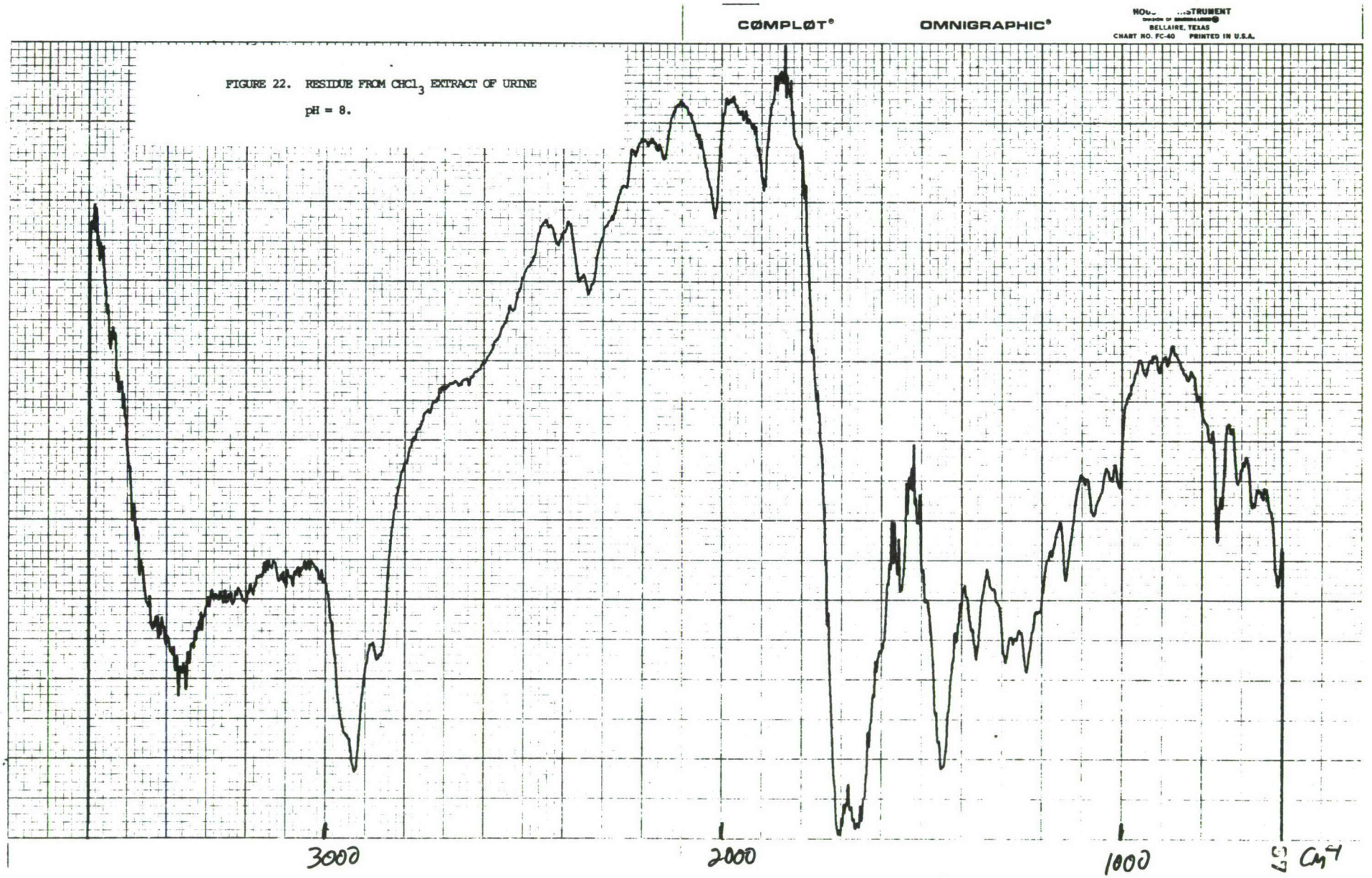

FIGURE 22. RESIDUE FROM $CHCl_3$ EXTRACT OF URINE

pH = 8.

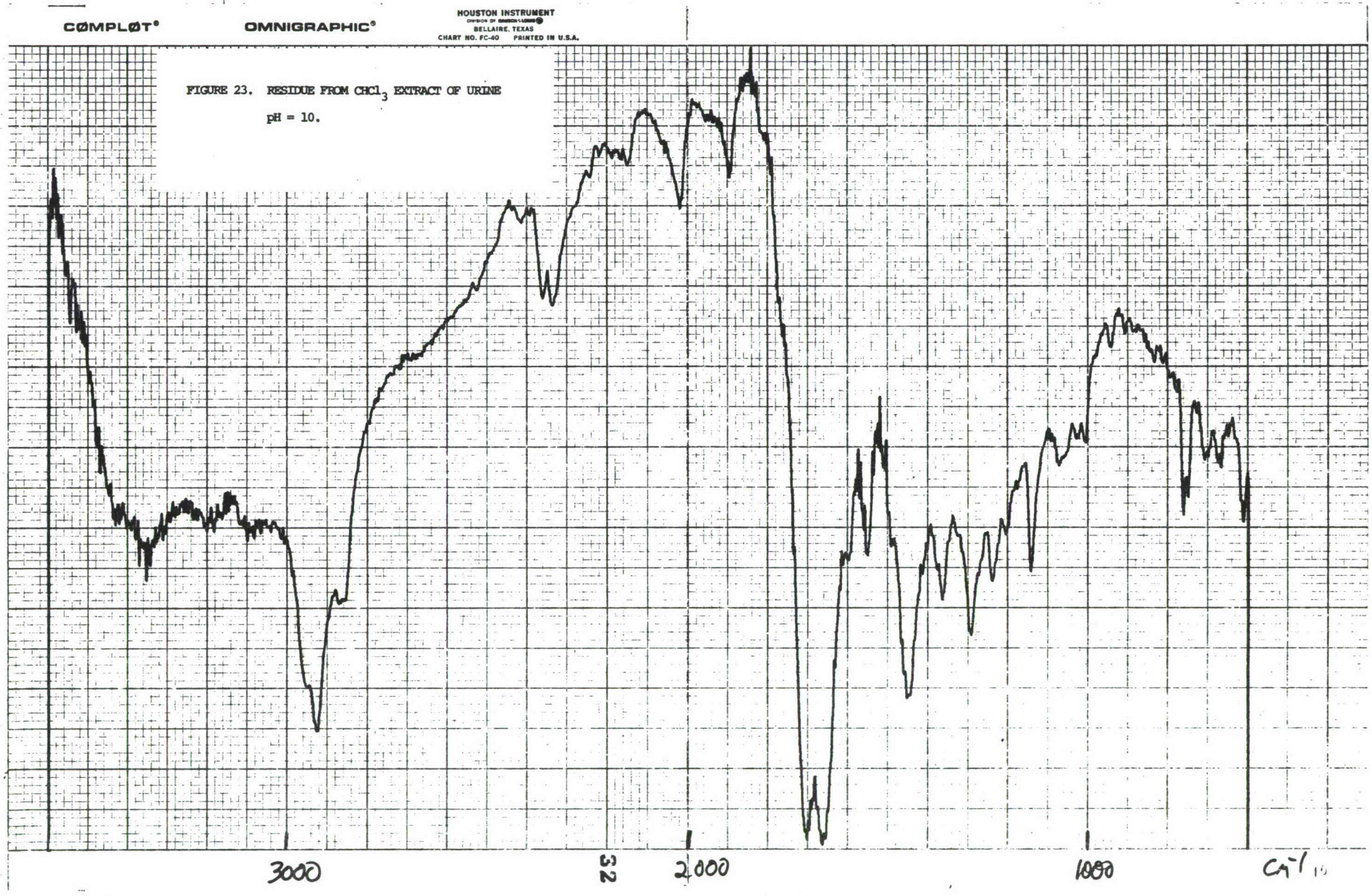
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FIGURE 23. RESIDUE FROM $CHCl_3$ EXTRACT OF URINE
pH = 10.
3000
2000
1000
cm⁻¹

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R. J. Jakobsen, K. C. Brog
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13. ABSTRACT

The parameters pertinent to the development of a compact instrument to detect and reliably identify drugs and related compounds in bulk and in urine were investigated. The program was conducted with emphasis on using correlation interferometry. Studies indicated that the interferometric approach should be complemented with additional enhancement techniques to better assure the success of the proposed instrument.

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