

REFERENCES

- Albrecht, R. Development of antibacterial agents of the nalidixic acid type. Org.Drug.Res. 21(1977) : 9-104.
- Bailey, W.R. and Scott., E.G. Diagnostic Microbiology 7th ed. pp. 173-199 Saint Louis : The C.V. Mosby Company, 1986.
- Blatt, A.H. The Fried' Reaction. Organic Reaction, 1(1942) : 342-365.
- Burger, A. Burger's Medicinal Chemistry 4th ed. pp. 72-80 New York : John Wiley and Sons, 1979.
- Chakravarti, D., Bagchi, P.H. On The Limited Applicability of Kostanecki's Reaction. J.Indian Chem.Soc. 13(1936) : 688 - 696.
- Chakravarti, D., Majumdar, B. Limited Applicability of Kostanecki's Reaction The Influence of Halogen Atom on the Reaction. J.Indian Chem.Soc. 16(1939) : 151 - 158.

Charles, R.H., Frederic, W.S., and Joe, T.A. Acetylation of Ketones to Diketones. Organic Reactions 8(1954) : 90 -95.

Chemence, F., Mortret, O. and Collard, J. New route to N-aryl and N-heteroaryl derivatives of 4-Hydroxy-3-quinoline carboxamide. J. Heterocyclic Chem. 21(1984) : 1345 - 1353.

Crumplin, G.C., Kenwright, M., and Hirst, T., Investigation into the mechanism of action of the antibacterial agent norfloxacin. J. Antimicrob. Chemother. 13(suppl. B) (1984) : 9 - 23.

Domagala, J.M., Hagen, S.E., et al. 7-Substituted 5-amino-1-cyclopropyl-6, 8-difluoro-1,4-dihydro-4-oxo-3-quinoline carboxylic acid. Synthesis and biological activity of a new class of quinolone antibacterials. J.Med.Chem. 31(1988) : 503 - 506.

_____, Hanna, L.D., et al. New structure activity relationships of the quinolone antibacterials using the target enzyme. The development and application of a DNA gyrase assay. J.Med.Chem. 29(1986) : 394 - 404.

Drake, N.L., et al., Synthesis Antimalarials. The Preparation of Certain 4-Aminoquinolines. J.Amer.Chem.Soc. 68(1946) : 1208 - 1213.

Ellis, G.P. The Chemistry of Heterocyclic Compounds, Chromene Chromanone and Chromone pp. 1 - 5, 496 - 547 University of Wales Institute of Science and Technology, Cardiff. John Wiley and Sons. 1977.

Fernandes, P.B., Chu, D.T.W., Claiborne, A.K. Shen, L., and Panet, A.G. Structure-Activity Relationships in Quinolone Antibacterials : Design, Synthesis and Biological Activities of Novel Isothiazoloquinolones. Drug Exptl.Cli.res. 6(1988) : 379 - 383.

Foye, W.O., Principle of Medicinal Chemistry 3 rd. ed. pp. 66 -68. Philadelphia: Lea and Febiger 1989.

Fujeta, T. The role of QSAR in drug design. In G. Jolles and K.R.H. Woolridge (ed.) Drug design : fact or fantasy, pp. 19 - 33. New York : Academic Press, 1984.

Gerllert, M. DNA Topoisomerases. Ann.Rev.Biochem. 50(1981) : 879 - 910.

Hauser, C.R., Swarmer, F.W. and Adam, J.T. The acetylation of ketones to form β -diketones or β -ketoaldehydes. Organic Reactions, 8(1954) : 59-196.

Jack, D.B. Recent advance in pharmaceutical chemistry. The 4-quinolone antibiotics. J.Cli.Hosp.Pharm. 11(1986) : 83.

Jones, G.H., Mackeny, J.B.D., Robinson and Whalley, W.B. The chemistry of fungi. Part II Derivatives of 3,4-dioxophenol. J. Chem. Soc. 1949 : 562-569.

Koga, H., Itoh, A., Murayama, S., Suzue, S., and Irikura, T. Structure Activity Relationships of antibacterial 6,7- and 7,8-disubstituted 1-alkyl-1,4-dihydro-4-oxo quinoline-3-carboxylic acid. J.Med.Chem. 23(1980) :1358 - 1363.

Kruger, J.H., and Walker, G.C. GRO El and DNA K genes of *Escherichia coli* are induced by UV irradiation and nalidixic acid in an HTPR⁺-dependent fashion. Proc.Natl.Acad.Sci. USA 81(1984) : 1499 - 1502.

Leshner, G.Y., Et al. 1,8-Naphthyridine Derivatives A New Class of Chemotherapeutic Agents. J.Pharmaceutic Chem. 5(1962) : 1063 - 1065.



Norhara, A., Umetani, T., and Sanno, Y. A Facial synthesis of 4-oxo-4H-1-Benzopyran-3-carboxaldehyde by Vielsmeier Reagents. Tetrahedron 30(1974) : 3553 - 3561.

Okumura, K., Kondo, K., Oine, T., and Inoue, I. The synthesis of chromone-3-carboxanilides. Chem.Pharm.Bull. 22(1974) : 331 - 336.

Paton, J.H., Reeves, D.S. Fluoroquinolone Antibiotics; Microbiology, Pharmacokinetics and Clinical Used. Drug 36(1988) : 193 - 228.

Pesson, M., De Lajudie, P., and Antovine, M. Synthesis bases on 3-acetyl-4-hydroxy quinolones. C.R.Acad.Sci.Ser.C. 273(1971) : 907 - 910.

Price, C., and Robert, R.M., The synthesis of 4-hydroxyquinolines through ethoxymethylene malonic ester. J.Am.Chem.Soc. 68(1946) : 1204 - 1208.

Sata, K., et al. *In vitro* and *In vivo* activity of Bay 09867 a new quinolone derivative. Antimicrob. Agents Chem. 22(1982) : 548 - 552.

Schentag, J., and domagala, J., Structure-Activity Relationships with the Quinolone Antibiotics. Res.Cli.Forms. 7(1985) : 9 - 13.

Shak, K.J., Coatss, E.A. Design Synthesis, and Correlation Analysis of 7-substituted 4-hydroxyquinoline-3-carboxylic acid as Inhibitor of Cellular Respiration. J.med.Chem. 20(1977) : 1001 - 1006.

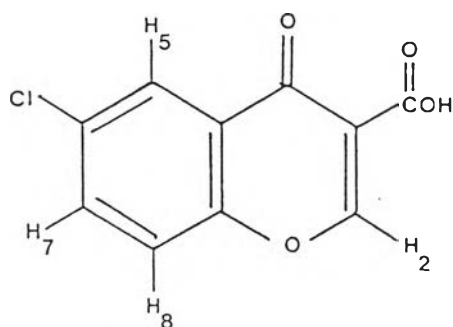
Wentland, et al. Novel Amino Substituted 3-Quinoline Carboxylic Acid Antibacterial Agents Synthesis and Structure-Activity Relationships. J.Med.Chem. 27(1984) : 1103 - 1108.

APPENDICES

Table 2 Physicochemical Properties of Chromone-3-carboxylic Acid derivatives.

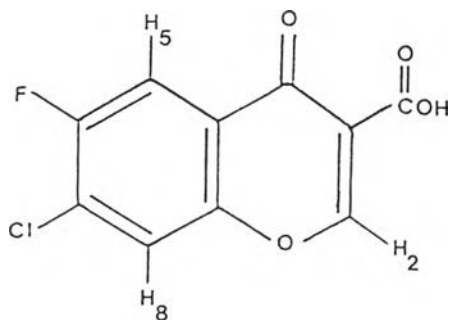
Compounds	Appearance	mp. (°C)	Formular	MW.
I.6-Chlorochromone-3-carboxylic Acid	pale, pink crystal	192-194	$C_9H_5O_4Cl$	224
II.7-Chloro-6-fluorochromone-3-carboxylic Acid	yellow crystal	155	$C_9H_4O_4FCl$	242

Table 3 Spectroscopic Properties of 6-Chlorochromone-3-carboxylic Acid



Position	$^1\text{H-NMR}$		IR (cm^{-1})	MS m/e
	Chemical shift (ppm.)	Coupling constant (Hz)		
H ₂	9.00	-	2600-3150 (O-H, acid)	224
H ₅	8.30	$J_{5,7}=2.5$	1770 (C=O, acid)	
H ₇	7.75	$J_{5,7}=2.5$	1650 (C=O, pyrone)	
		$J_{7,8}=9.0$	1140 (O=C-OH)	
H ₈	7.50	$J_{7,8}=9.0$		

Table 4 Spectroscopic Properties of 7-Chloro-6-fluorochromone-3-carboxylic Acid.



Position	¹ H-NMR		IR (cm ⁻¹)	MS m/e
	Chemical shift (ppm.)	Coupling constant (Hz)		
O-H	12.96	-	2700 (O-H, acid)	242
H ₂	8.96	-	1760 (C=O, acid)	
H ₅	8.00	J _{H5-F} =8.0	1610 (C=O, pyrone)	
H ₈	7.74	J _{H8-F} =6.0		

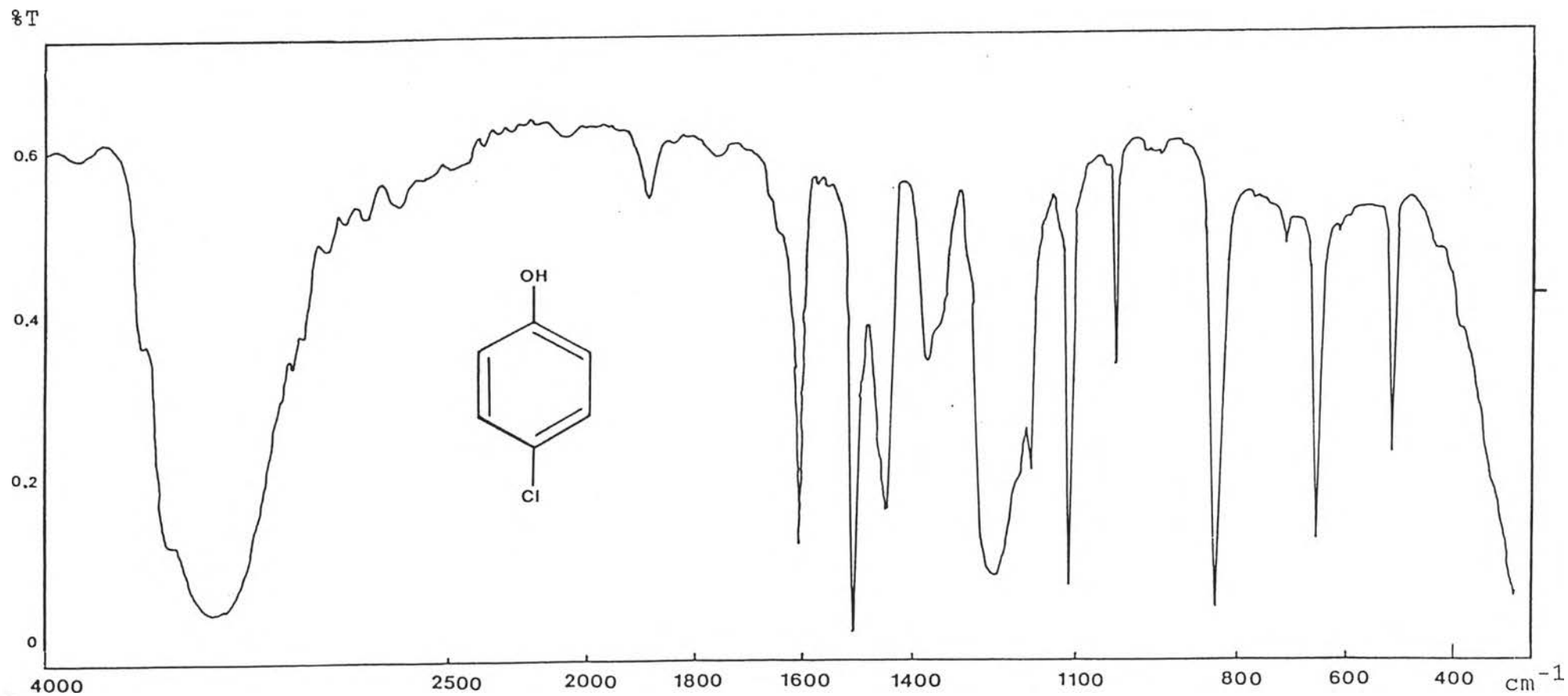


Figure 9 The IR spectrum of 4-Chlorophenol:

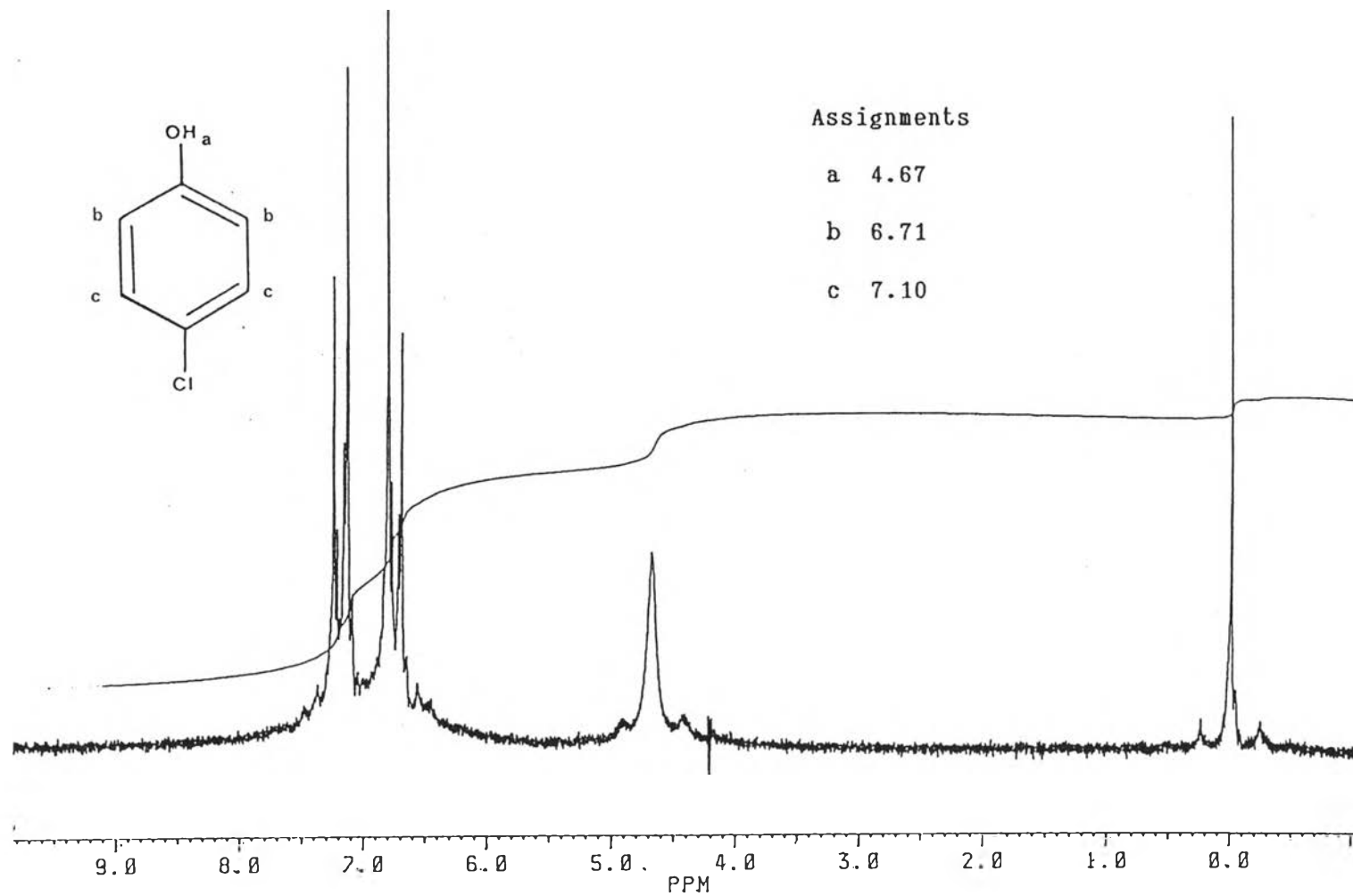


Figure 10 The ^1H -NMR spectrum of 4-Chloro-phenol in CDCl_3

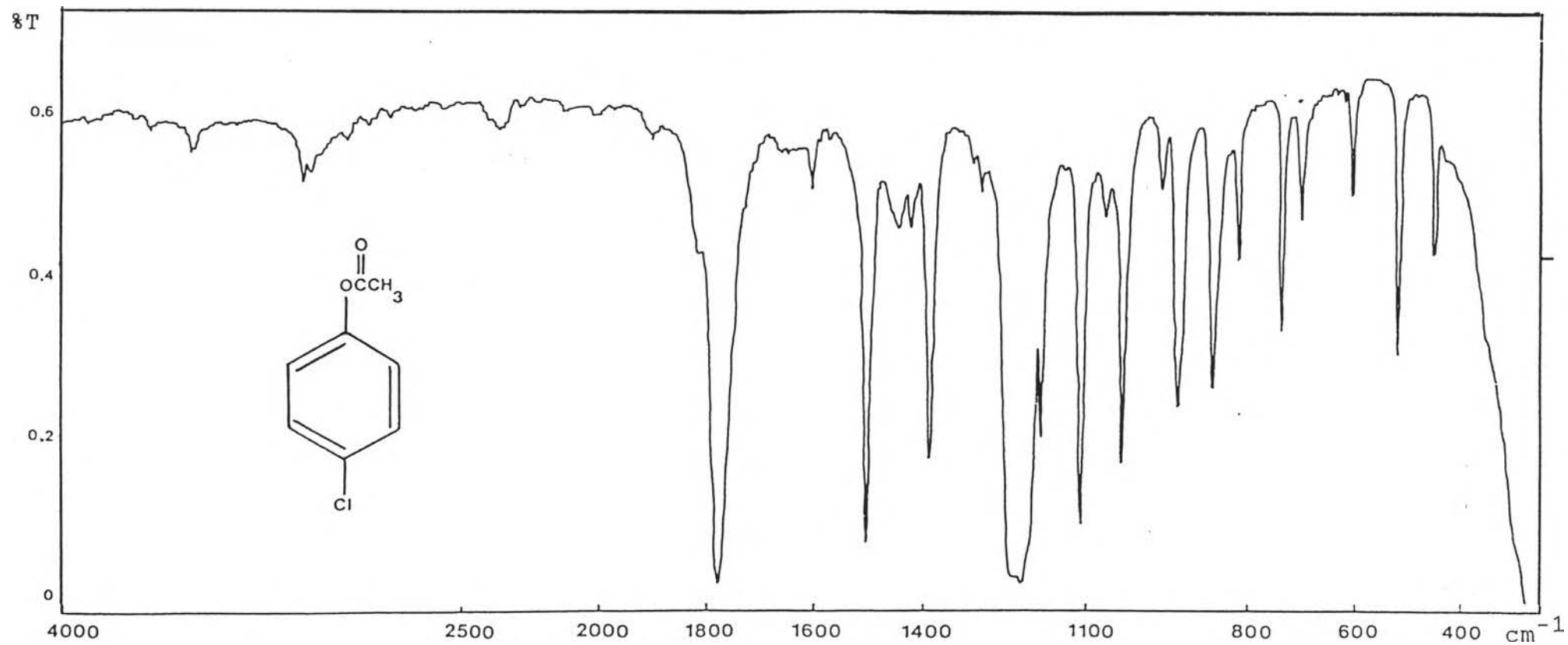


Figure 11 The IR spectrum of 4-Chlorophenyl acetate

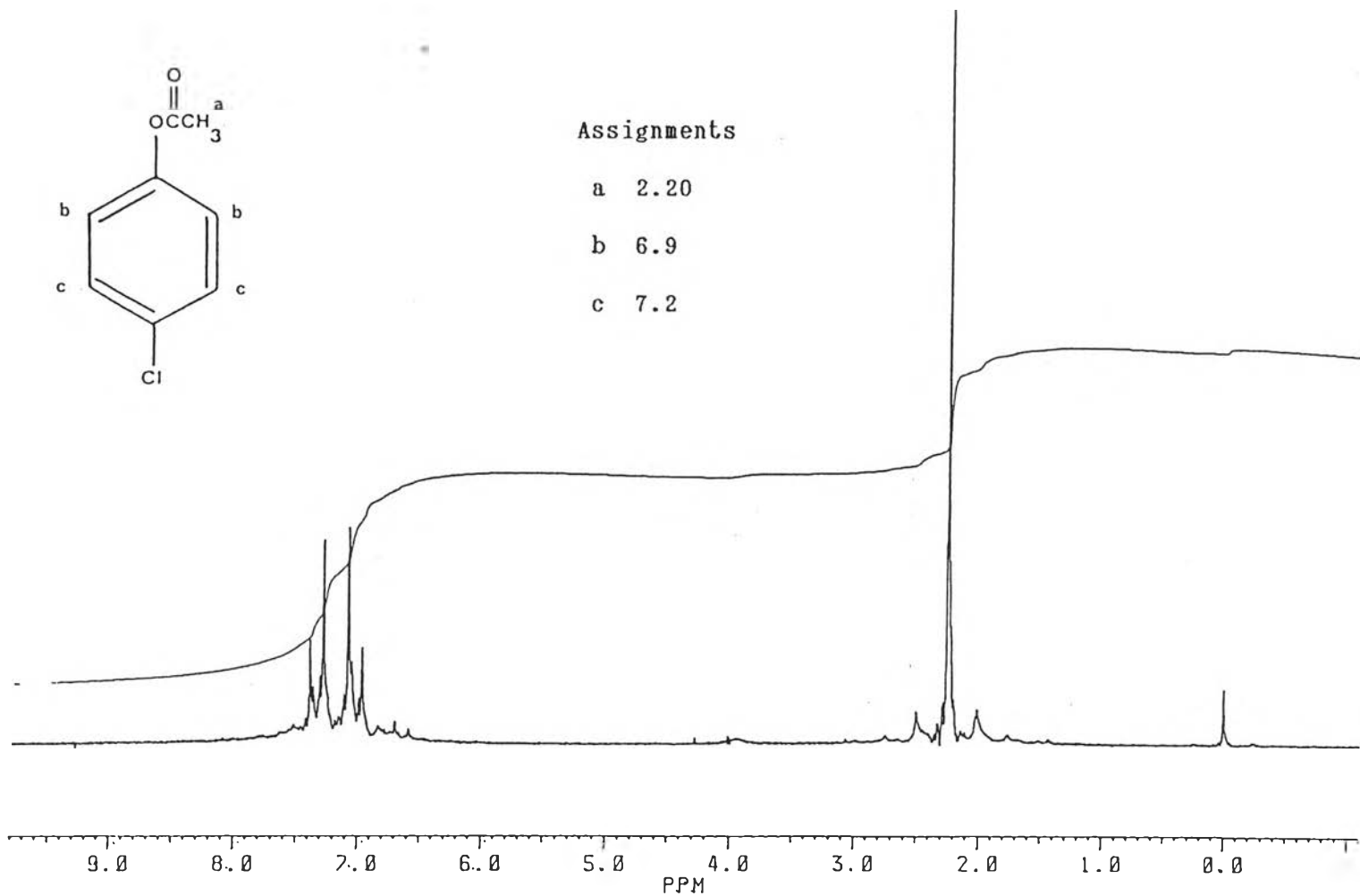


Figure 12 The ^1H -NMR spectrum of 4-Chlorophenyl acetate in CDCl_3

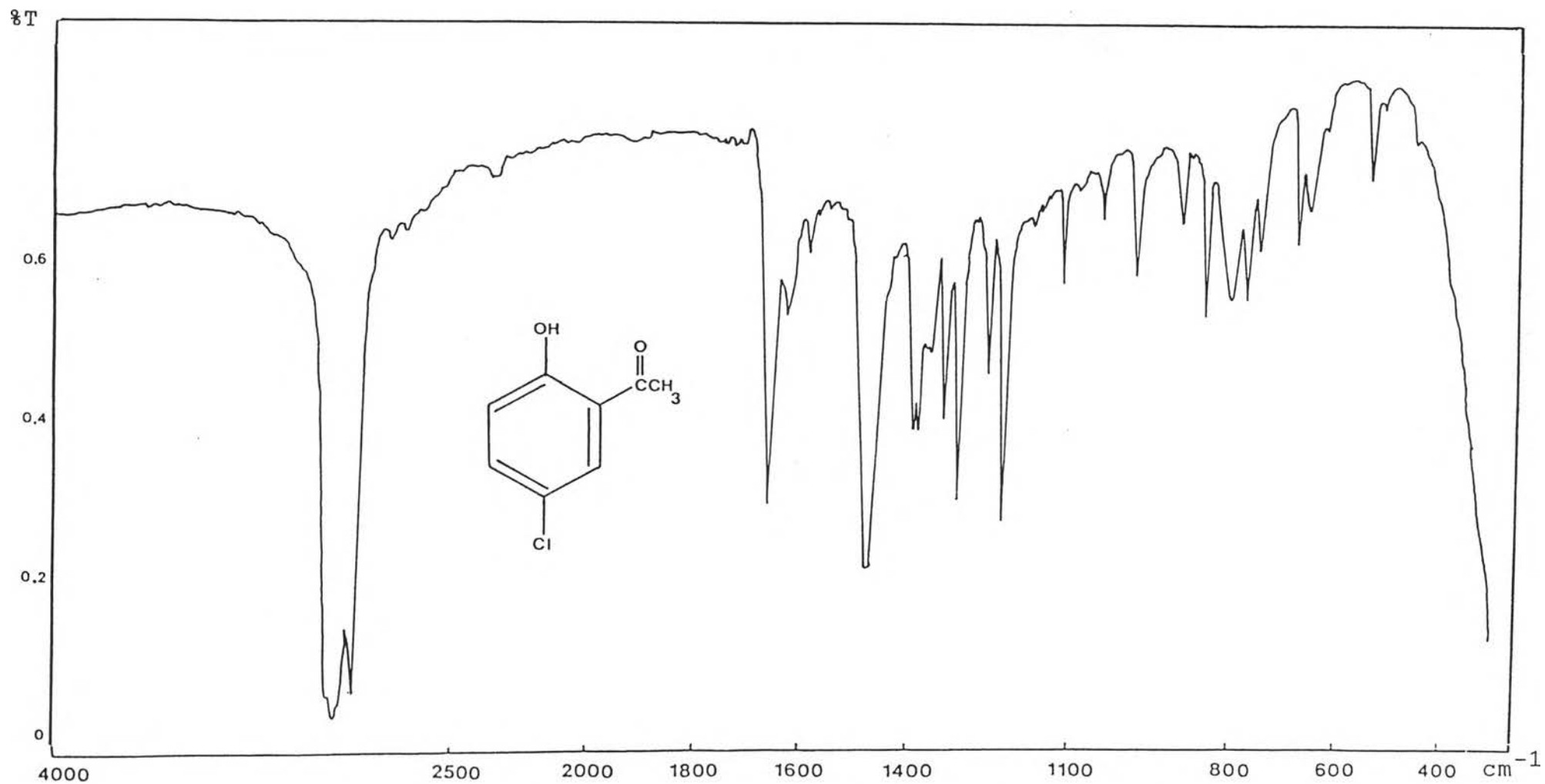


Figure 13 The IR spectrum of 5-Chloro-2-hydroxy
acetophenone

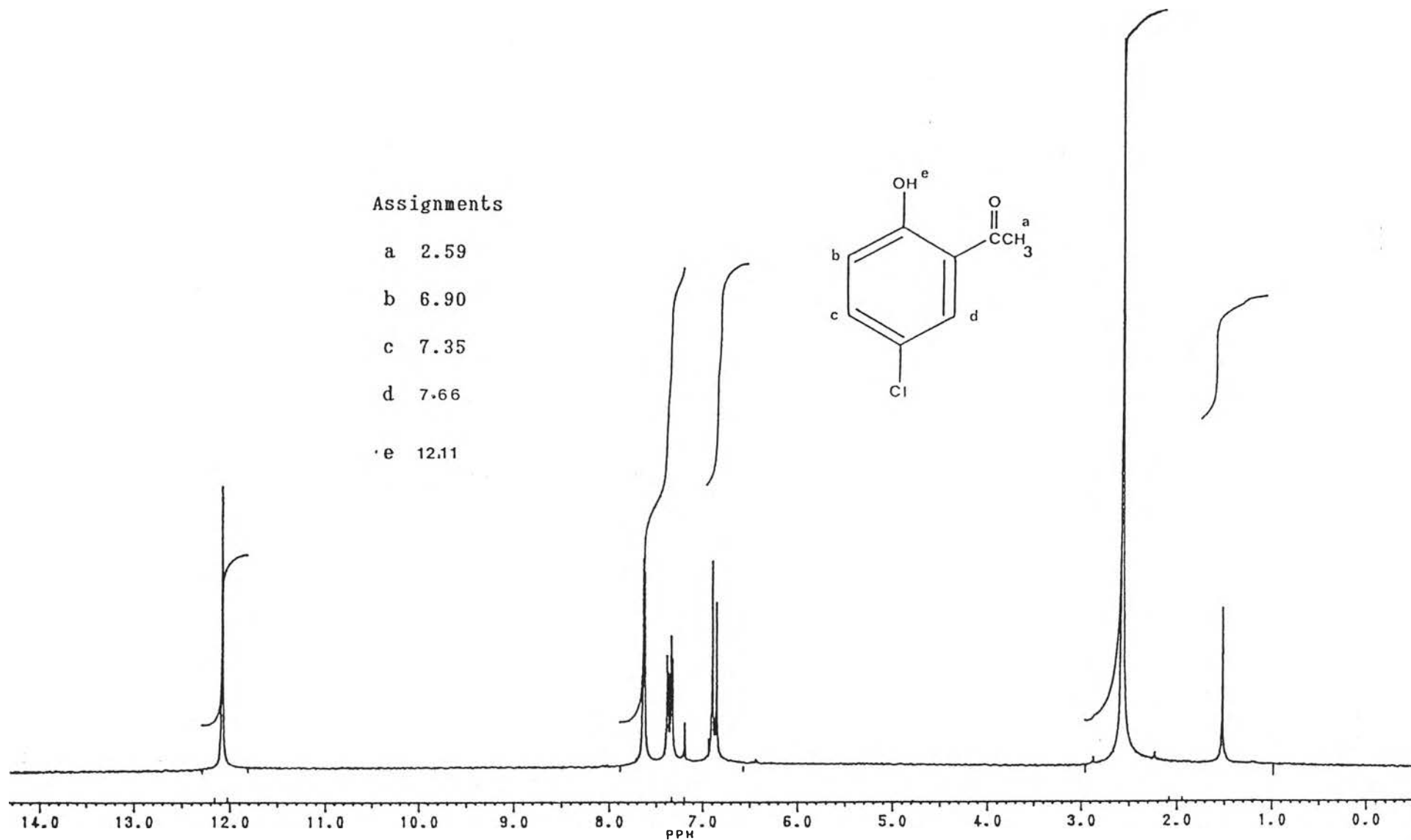


Figure 14 The ^1H -NMR spectrum of 5-Chloro-2-hydroxyacetophenone in CDCl_3

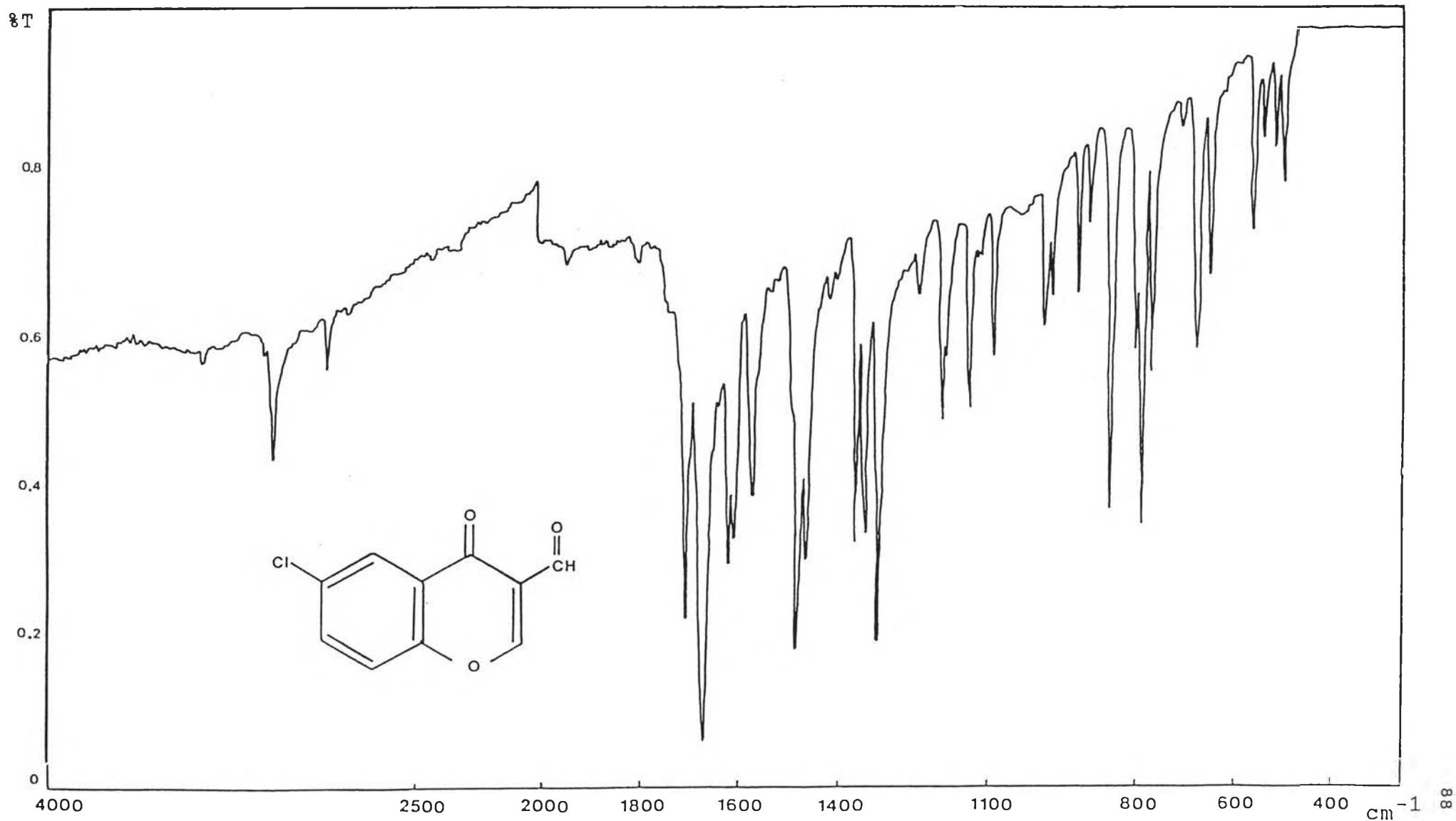


Figure 15 The IR spectrum of 6-Chlorochromone-3-carboxaldehyde

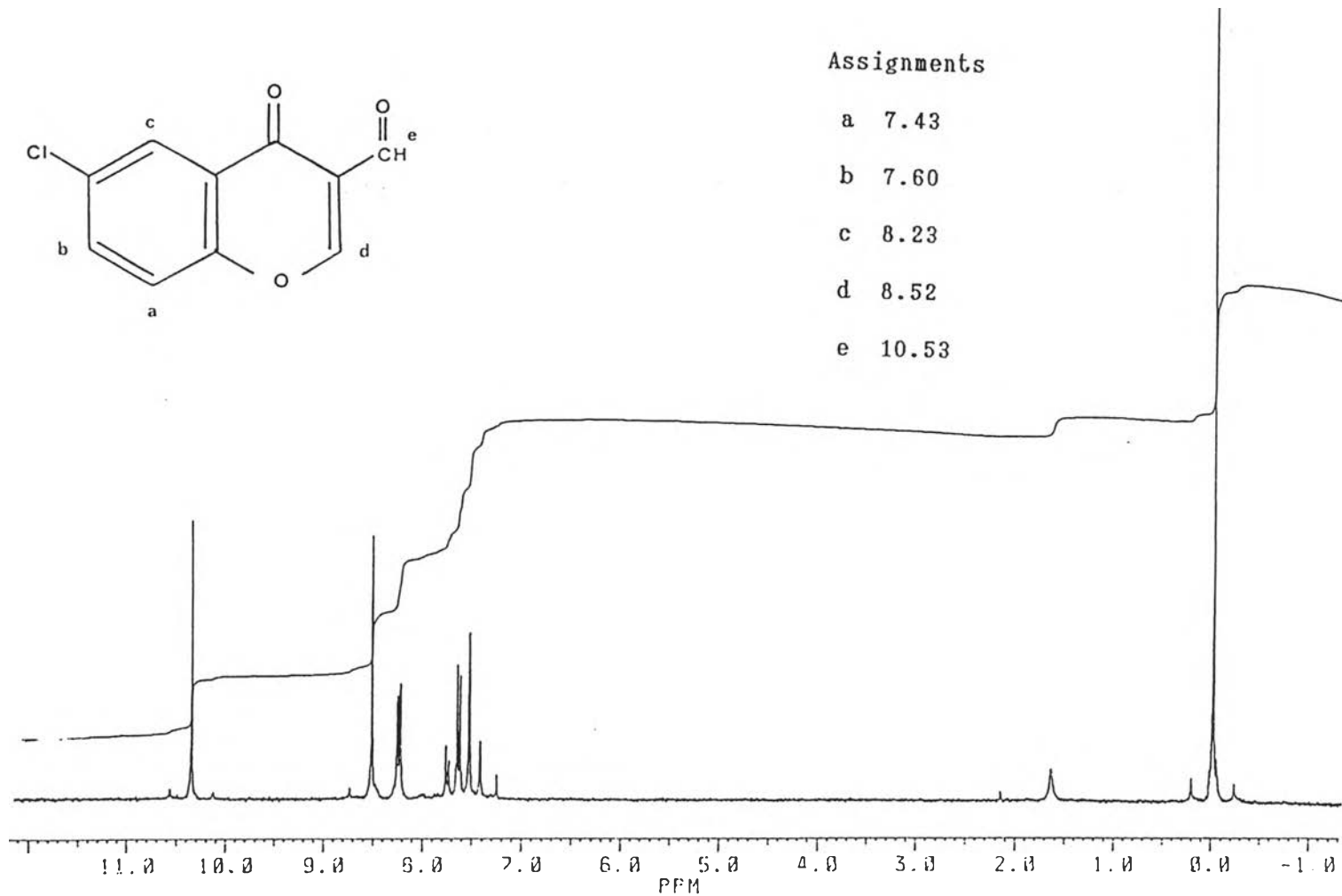


Figure 16 The $^1\text{H-NMR}$ spectrum of 6-Chlorochromone-3-carboxaldehyde in CDCl_3

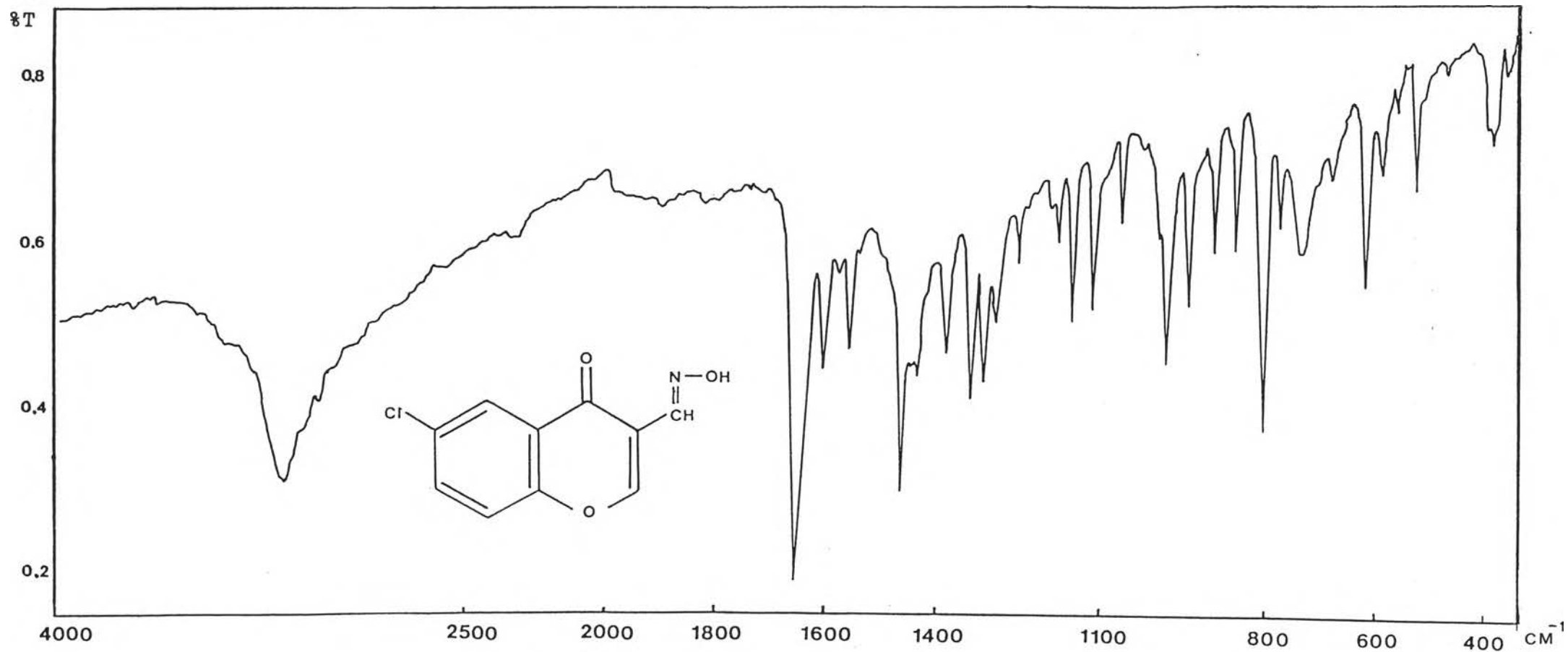


Figure 17 The IR spectrum of 6-Chlorochromone-3-carboaldoxime.

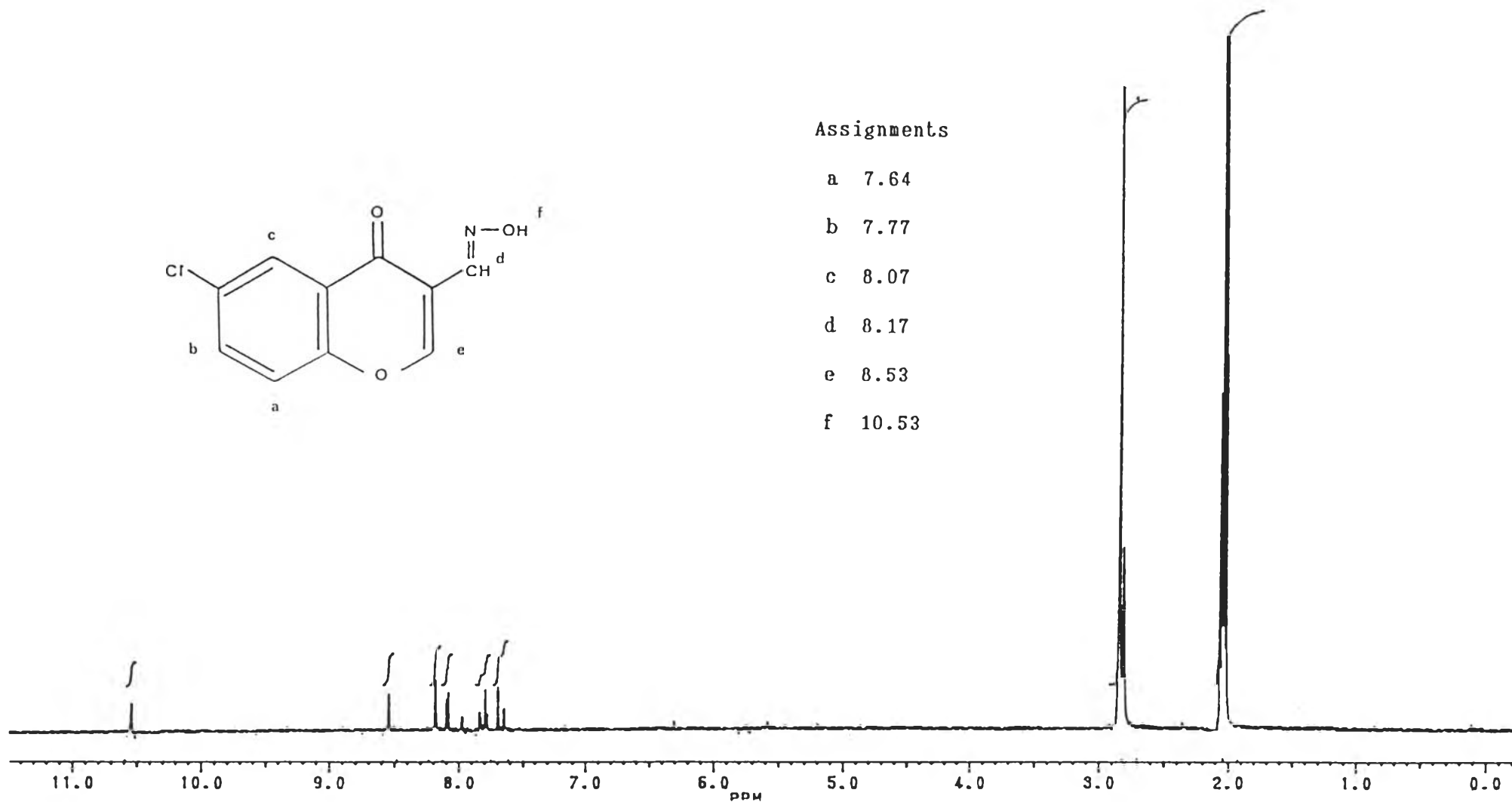
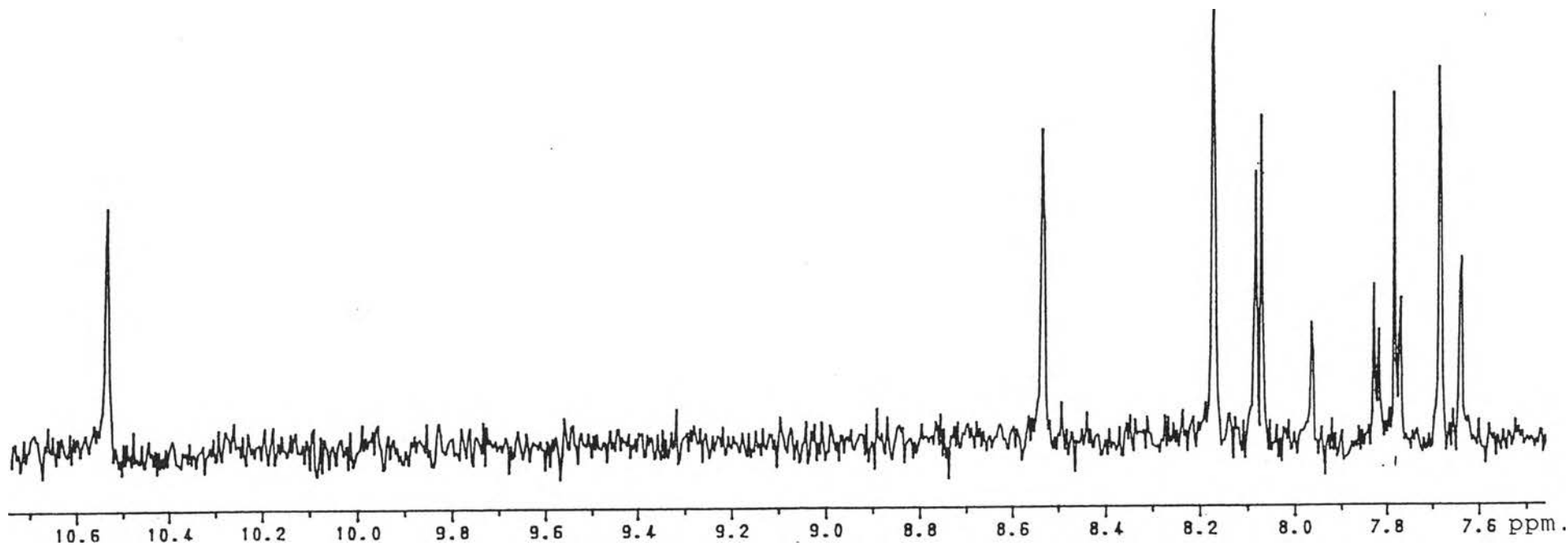


Figure 18 The ^1H -NMR spectrum of 6-Chlorochromone-3-carboaldoxime in acetone- d_6



FIGURES 18 The ^1H -NMR spectrum of 6-Chlorochromone-3-carboaldoxime in acetone- d_6 . (expansion)

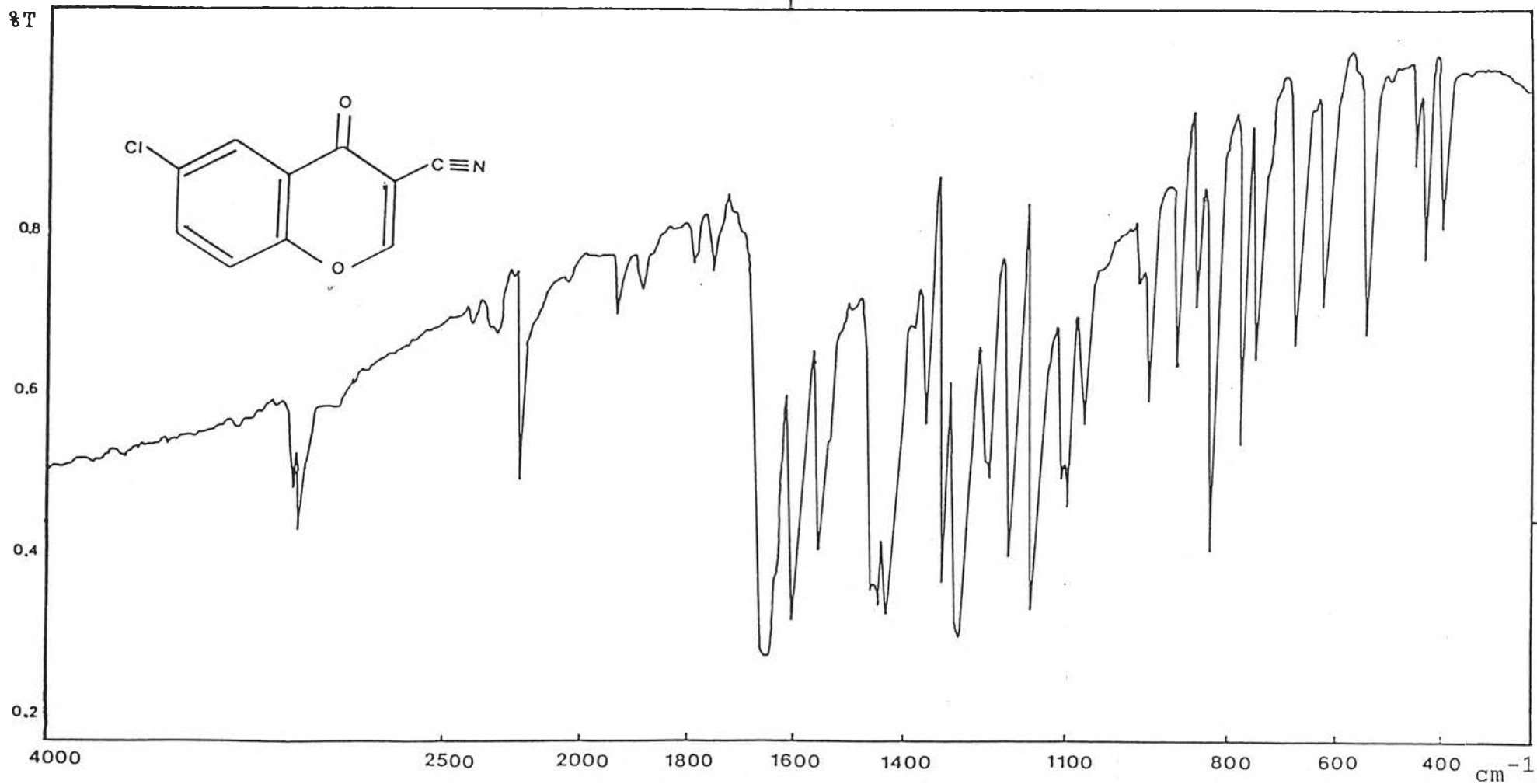
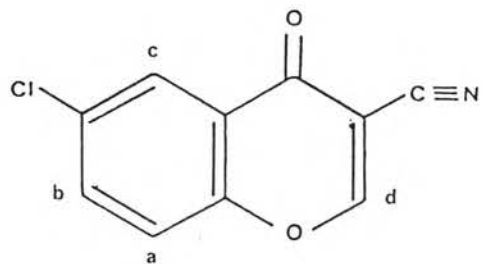


Figure 19 The IR spectrum of 6-Chlorochromone-3-carbonitrile.



Assignments

a 7.73

b 7.85

c 7.92

d 9.17

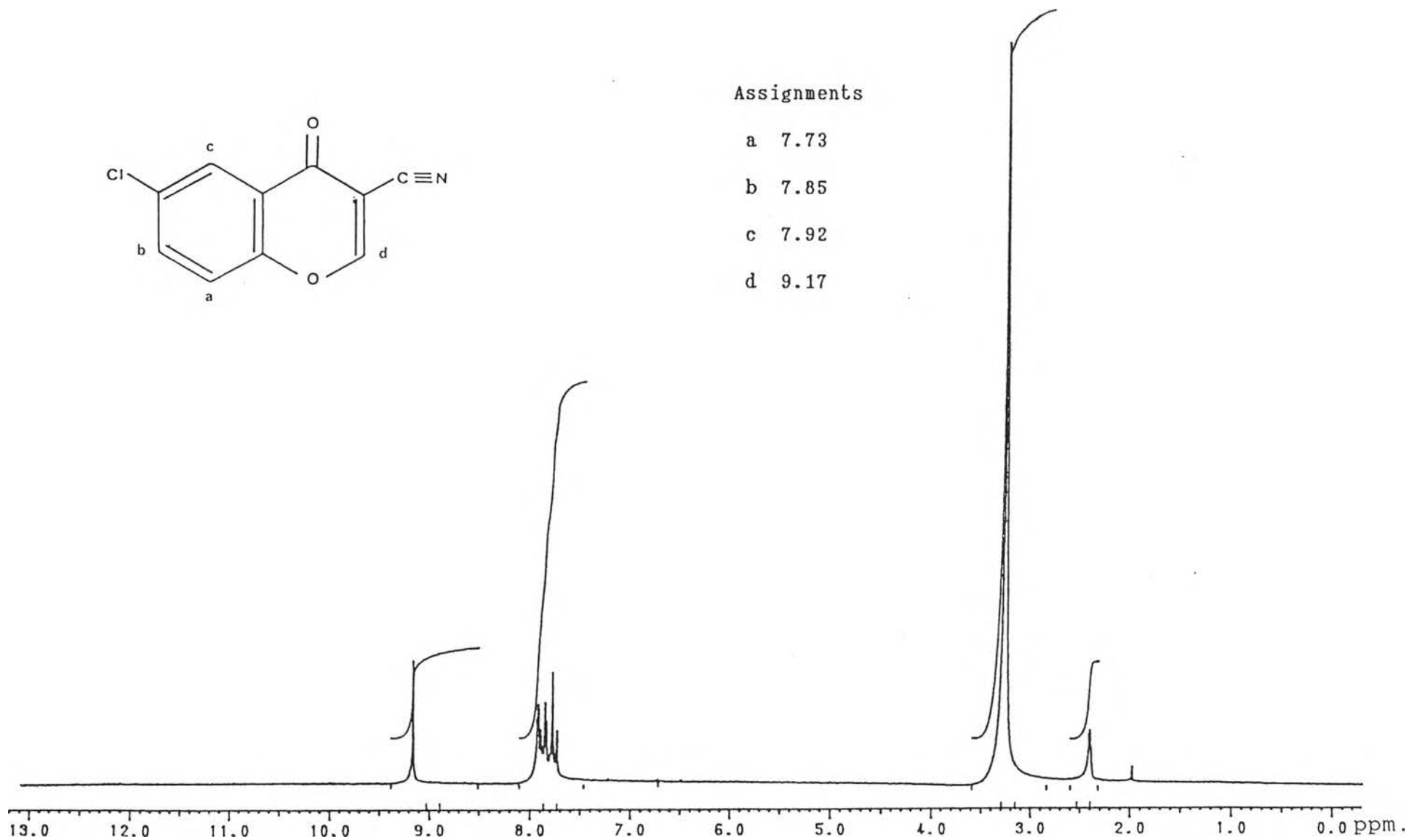


Figure 20 The ¹H-NMR spectrum of 6-Chlorochromone-3-carbonitrile in DMSO-d₆.

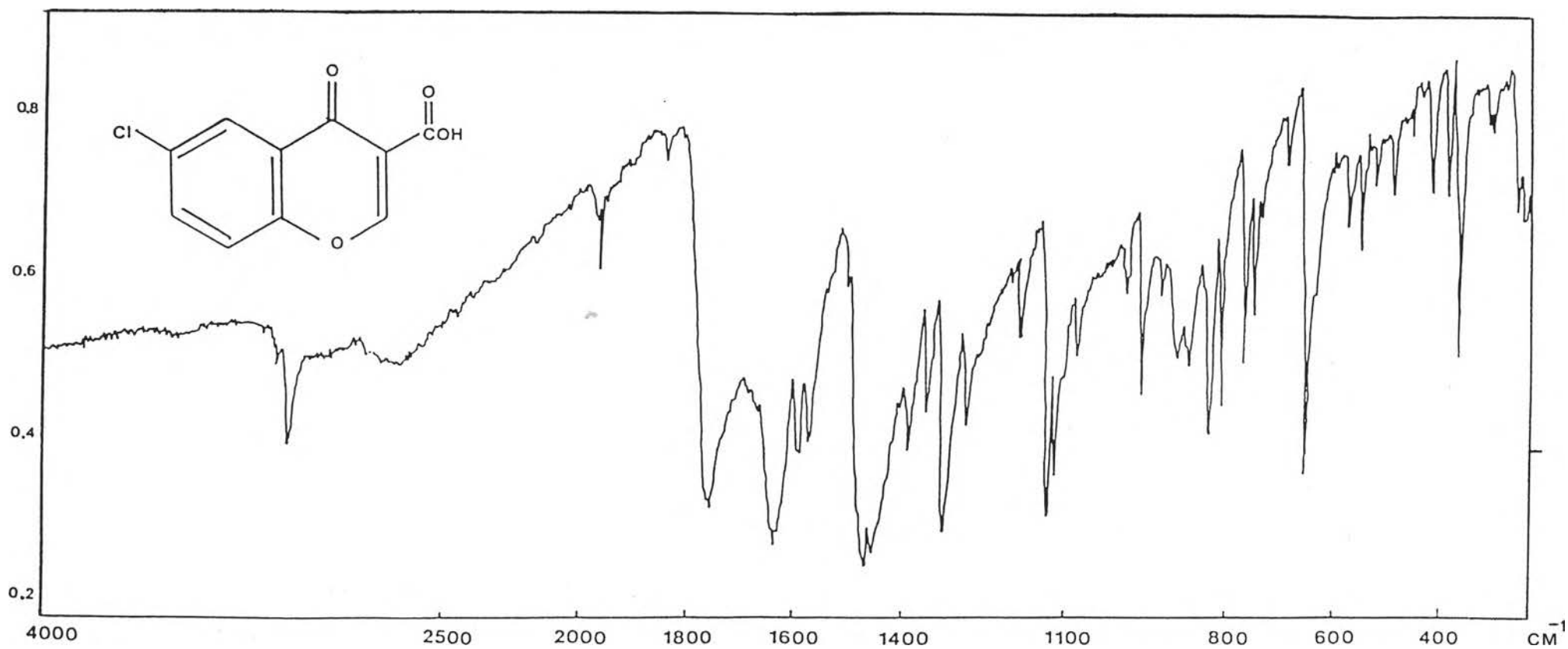


Figure 21 The IR spectrum of 6-Chlorochromone-3-carboxylic acid.

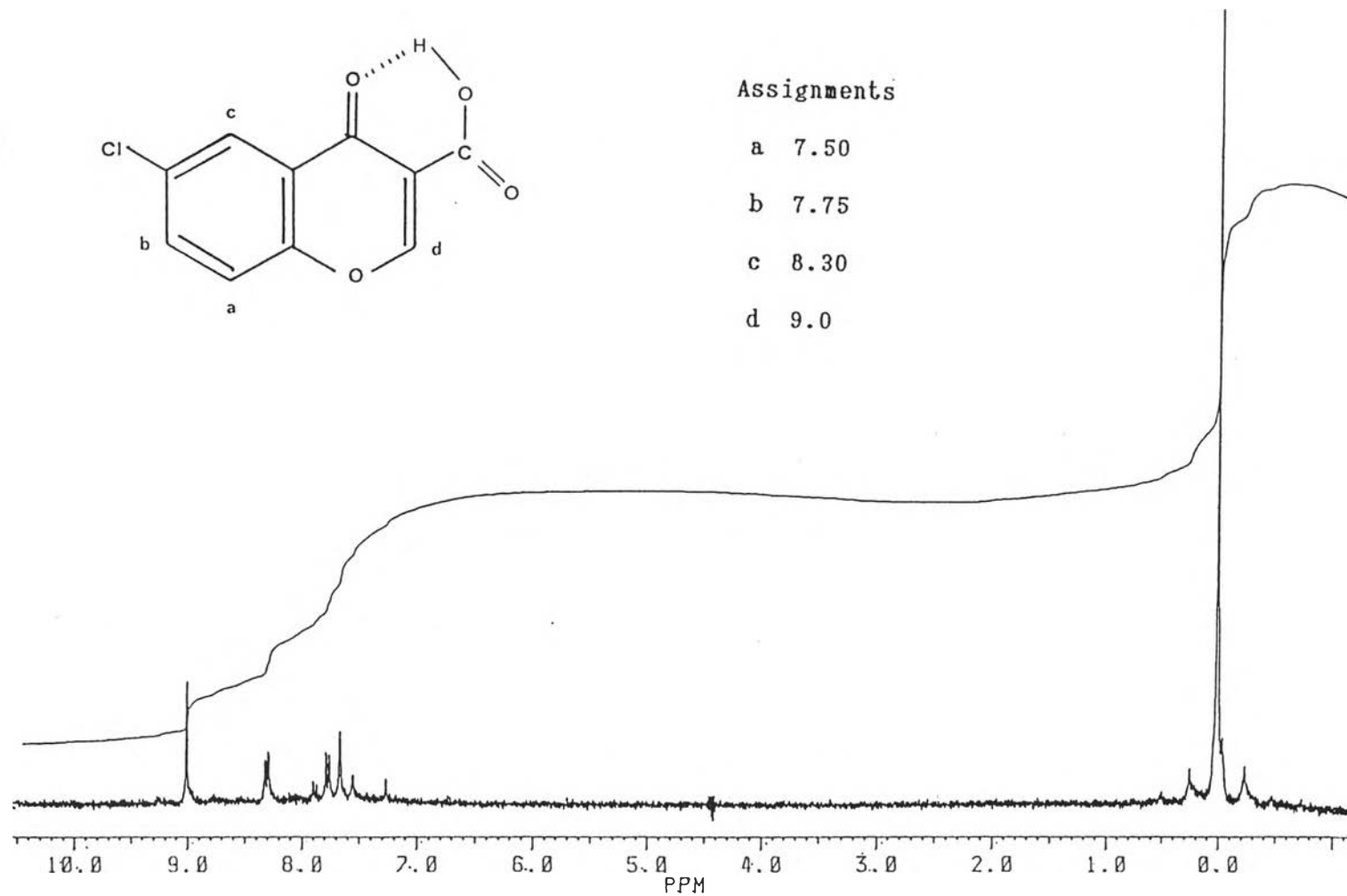


Figure 22 The ^1H -NMR spectrum of 6-Chlorochromone-3-carboxylic acid in CDCl_3 .

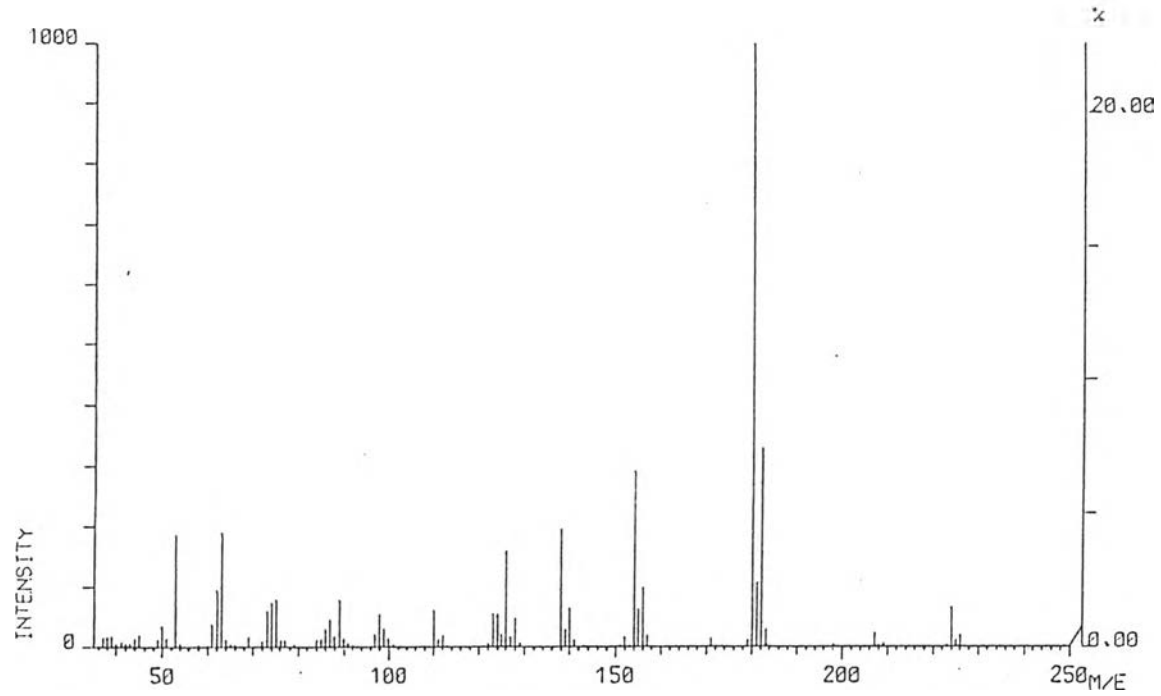


Figure 23 The mass spectrum of 6-Chlorochromone-3-carboxylic acid.

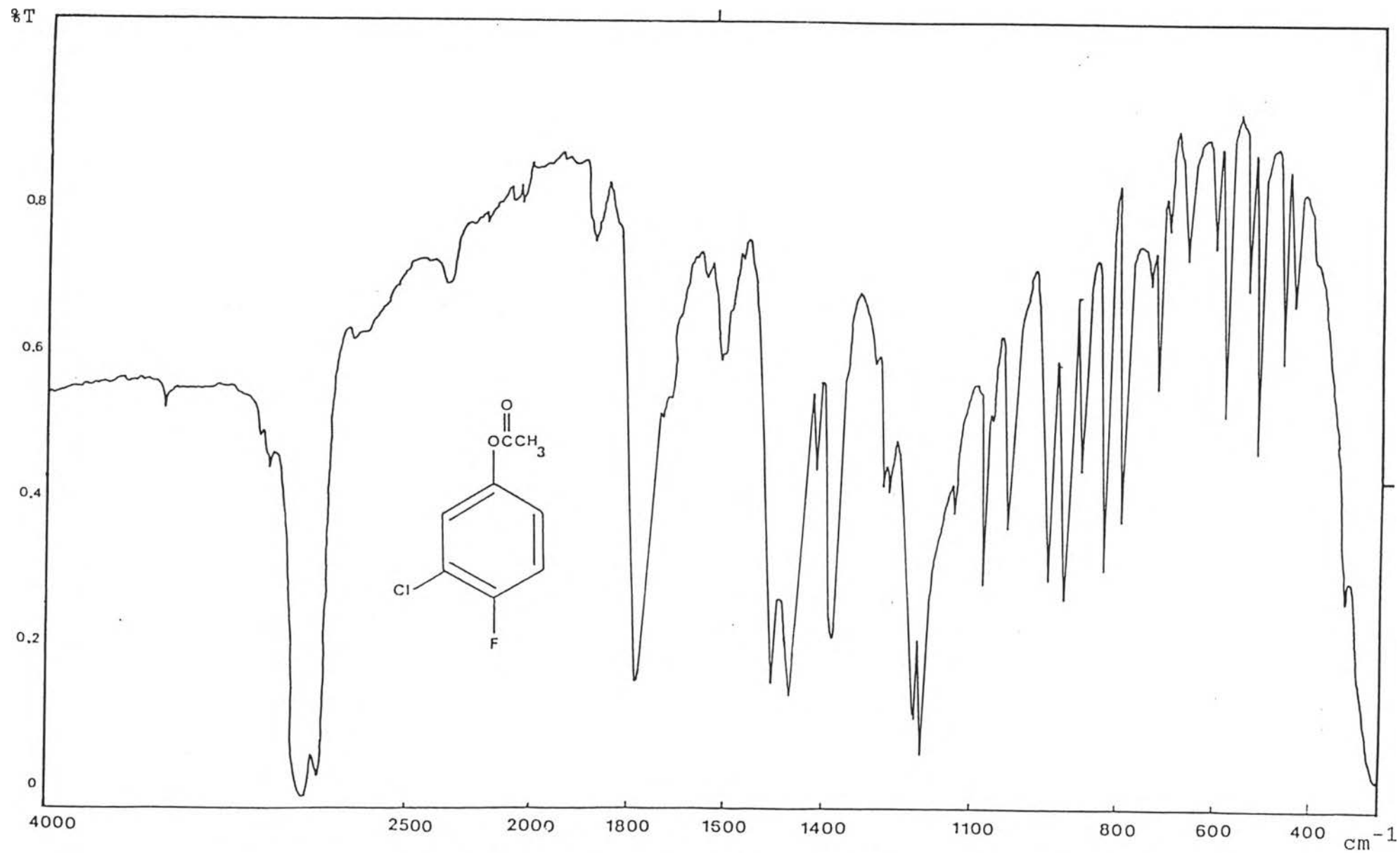


Figure 24 The IR spectrum of 3-Chloro-4-fluoro-phenyl acetate.

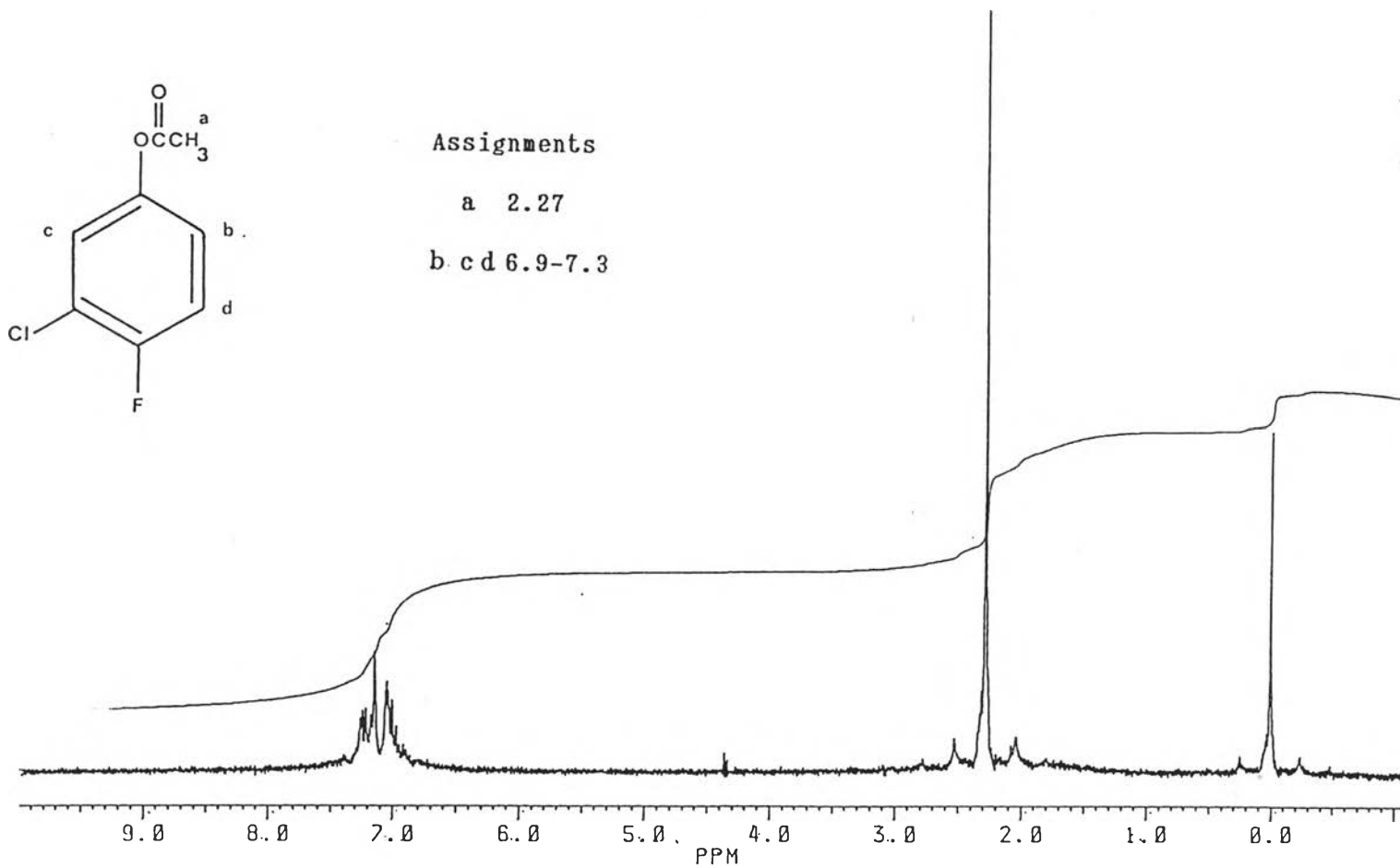


Figure 25 The ^1H -NMR spectrum of 3-chloro-4-fluorophenyl acetate in CDCl_3 .

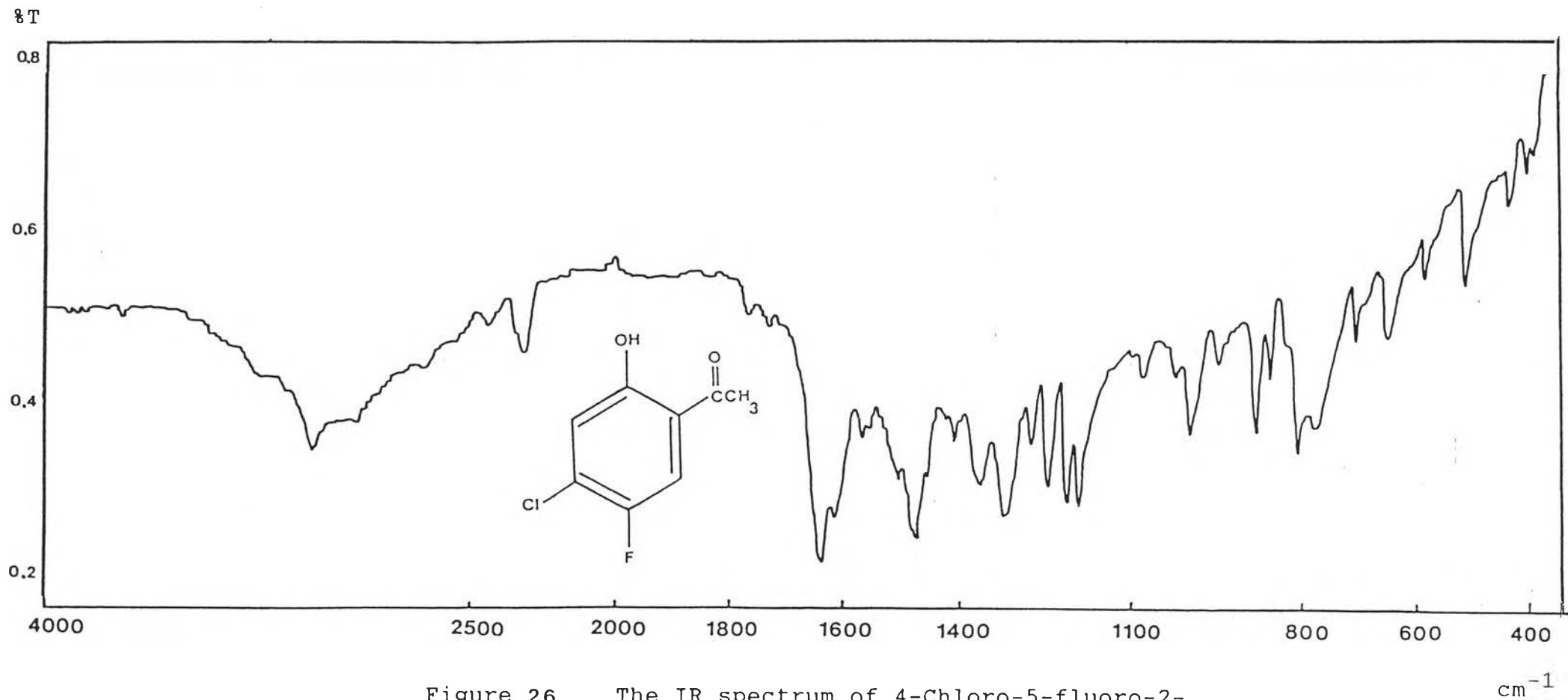


Figure 26 The IR spectrum of 4-Chloro-5-fluoro-2-hydroxyacetophenone.

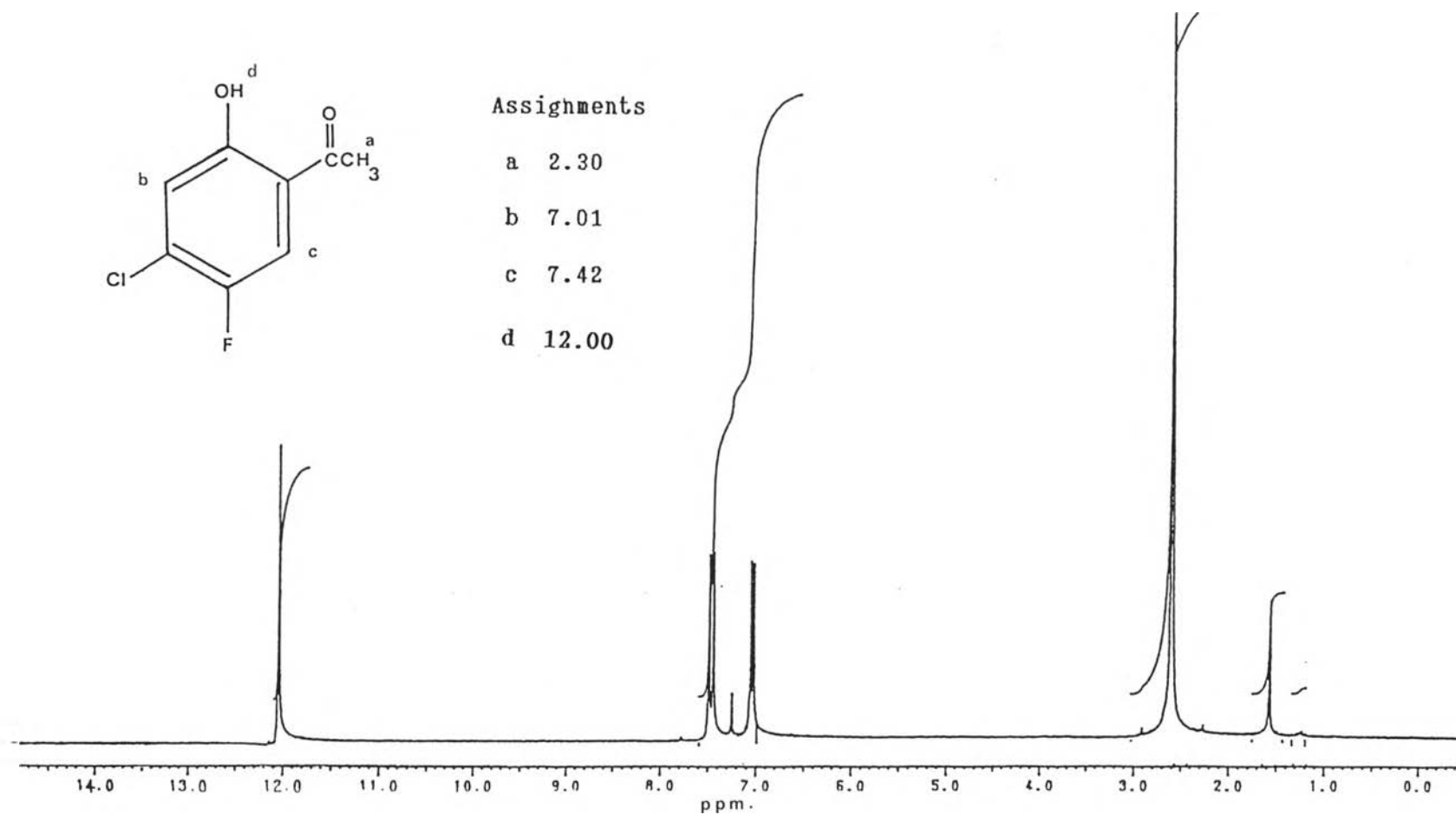


Figure 27 The ^1H -NMR spectrum of 4-Chloro-5-fluoro-2-hydroxyacetophenone in CDCl_3 .

%T

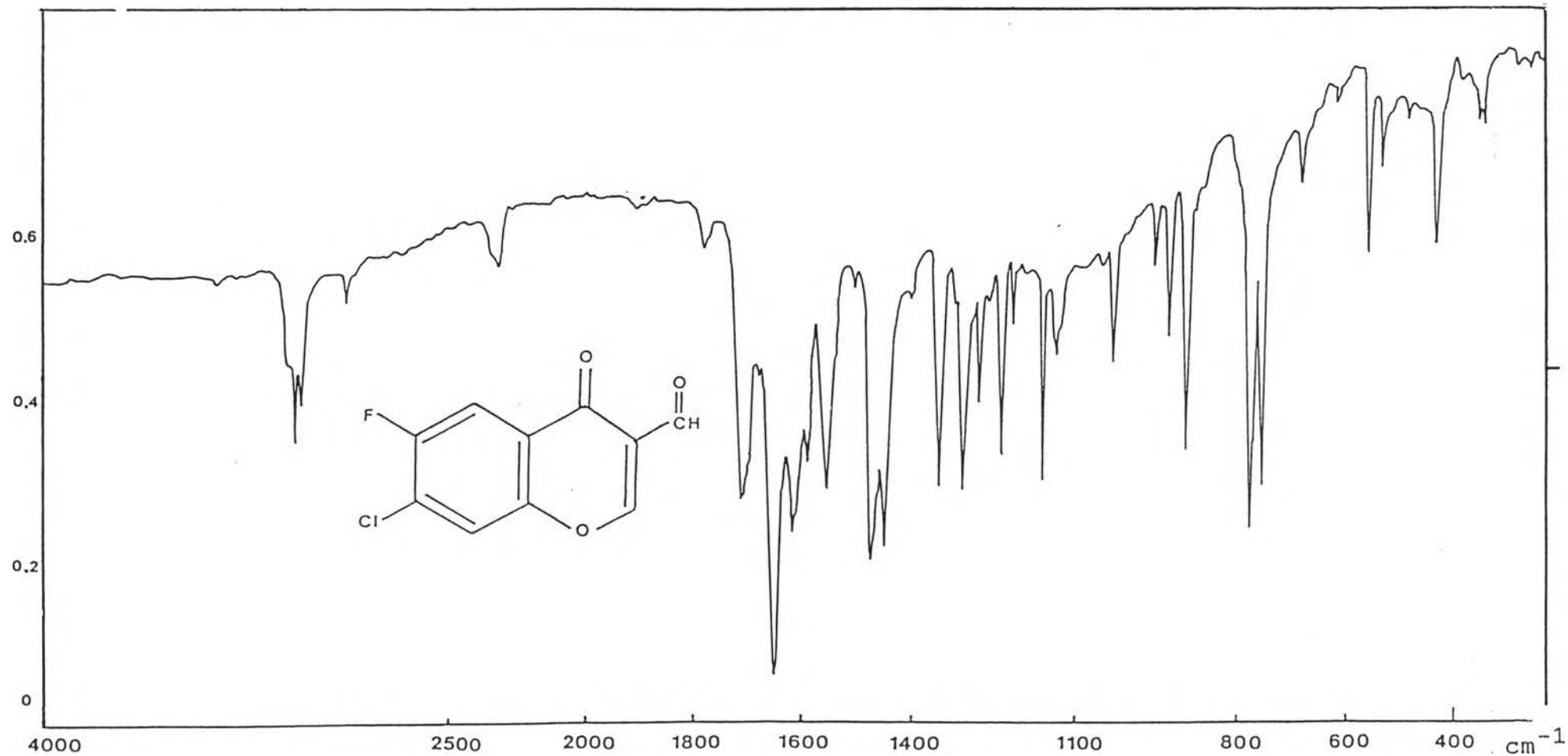


Figure 28 The IR spectrum of 7-Chloro-6-fluoro chromone-3-carboxaldehyde.

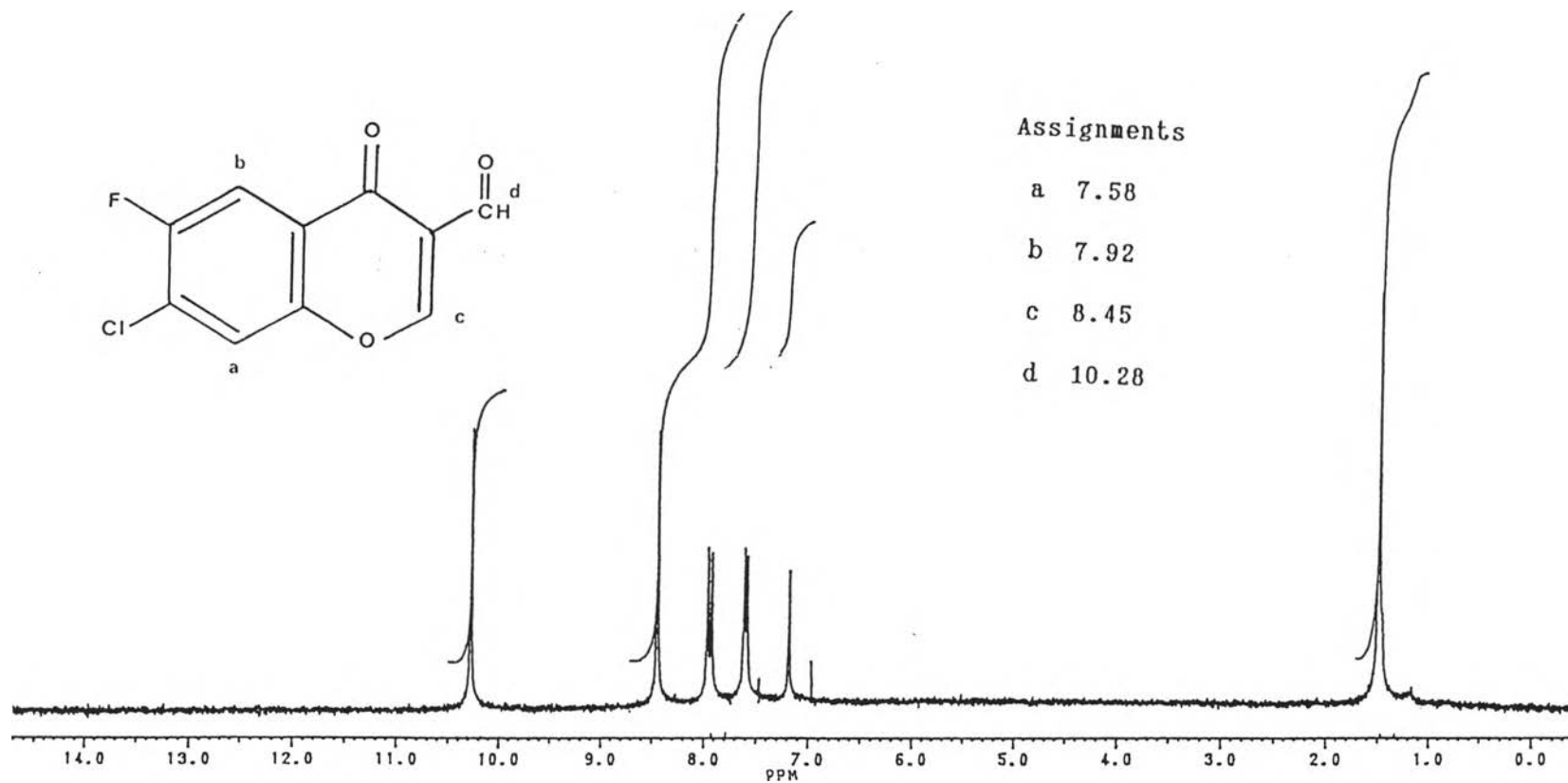


Figure 29 The ^1H -NMR spectrum of 7-Chloro-7-fluoro chromone-3-carboxaldehyde in CDCl_3

8T

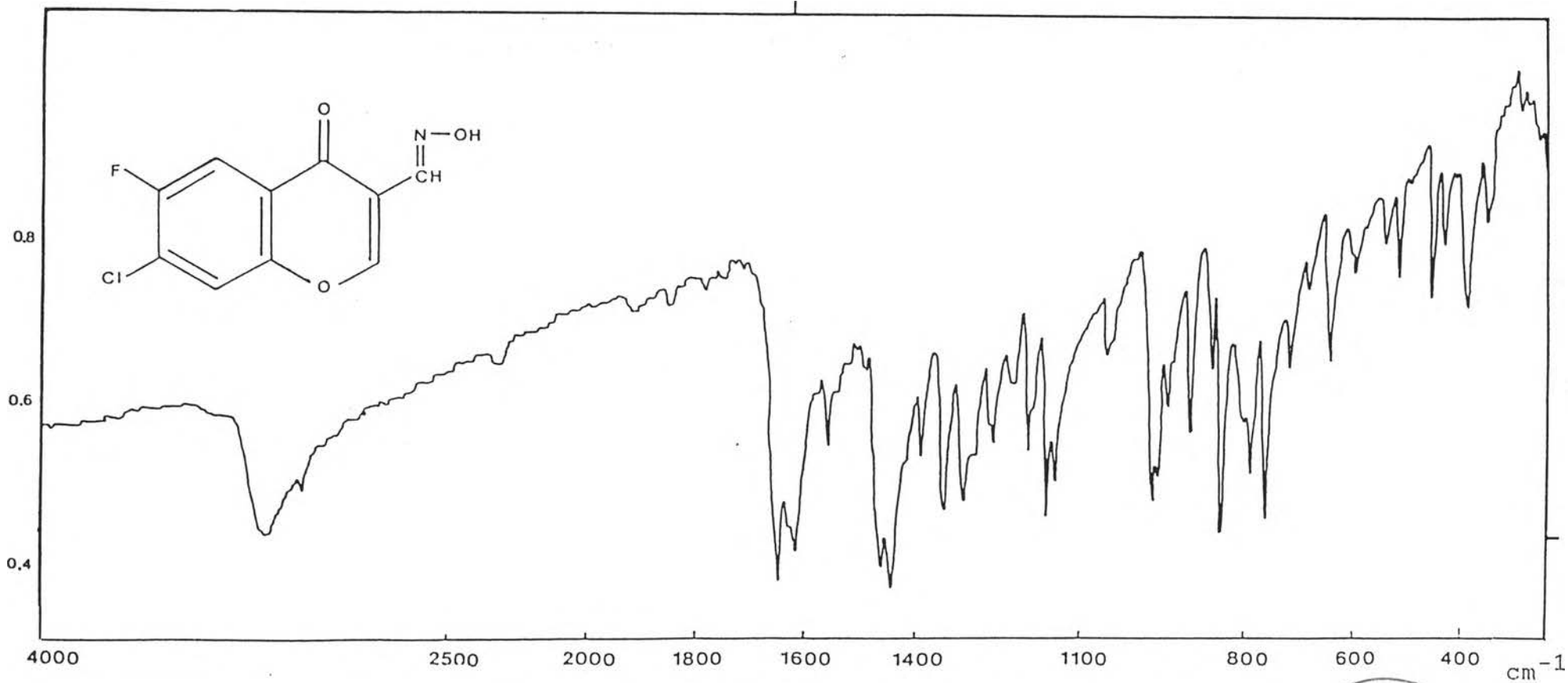


Figure 30 The IR spectrum of 7-Chloro-6-fluoro-chromone-3-carboaldoxime.



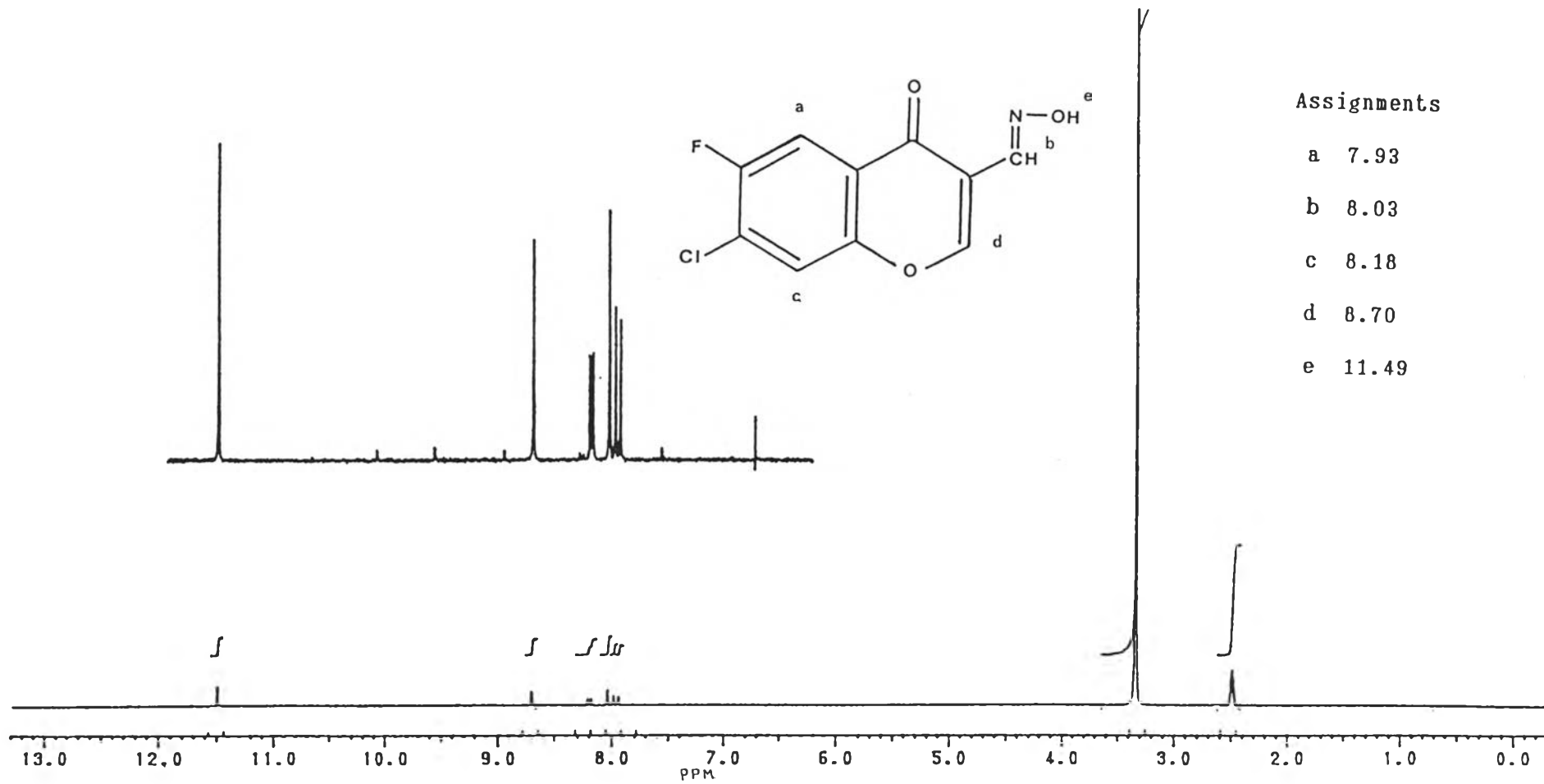


Figure 31 The ¹H-NMR spectrum of 7-Chloro-6-fluoro chromone-3-carboaldoxime in DMSO-d₆

%T

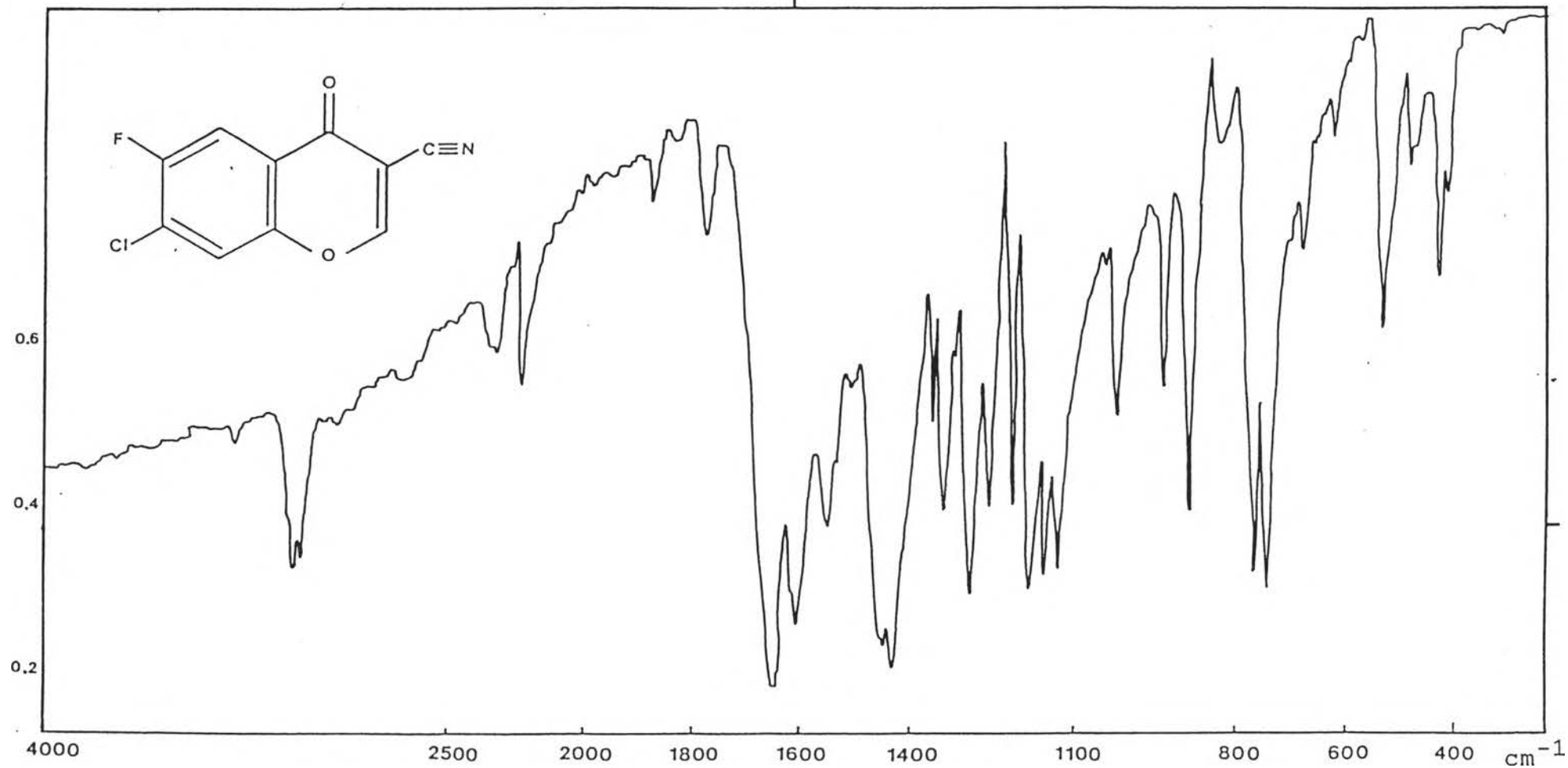
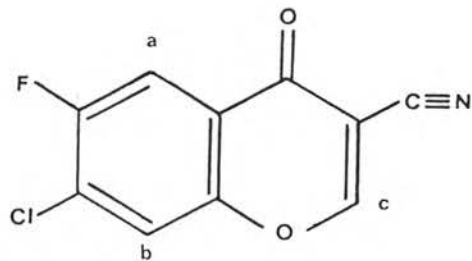


Figure 32 The IR spectrum of 7-Chloro-6-fluoro
chromone-3-carbonitrile



Assignments

- a 7.91
- b 8.23
- c 9.19

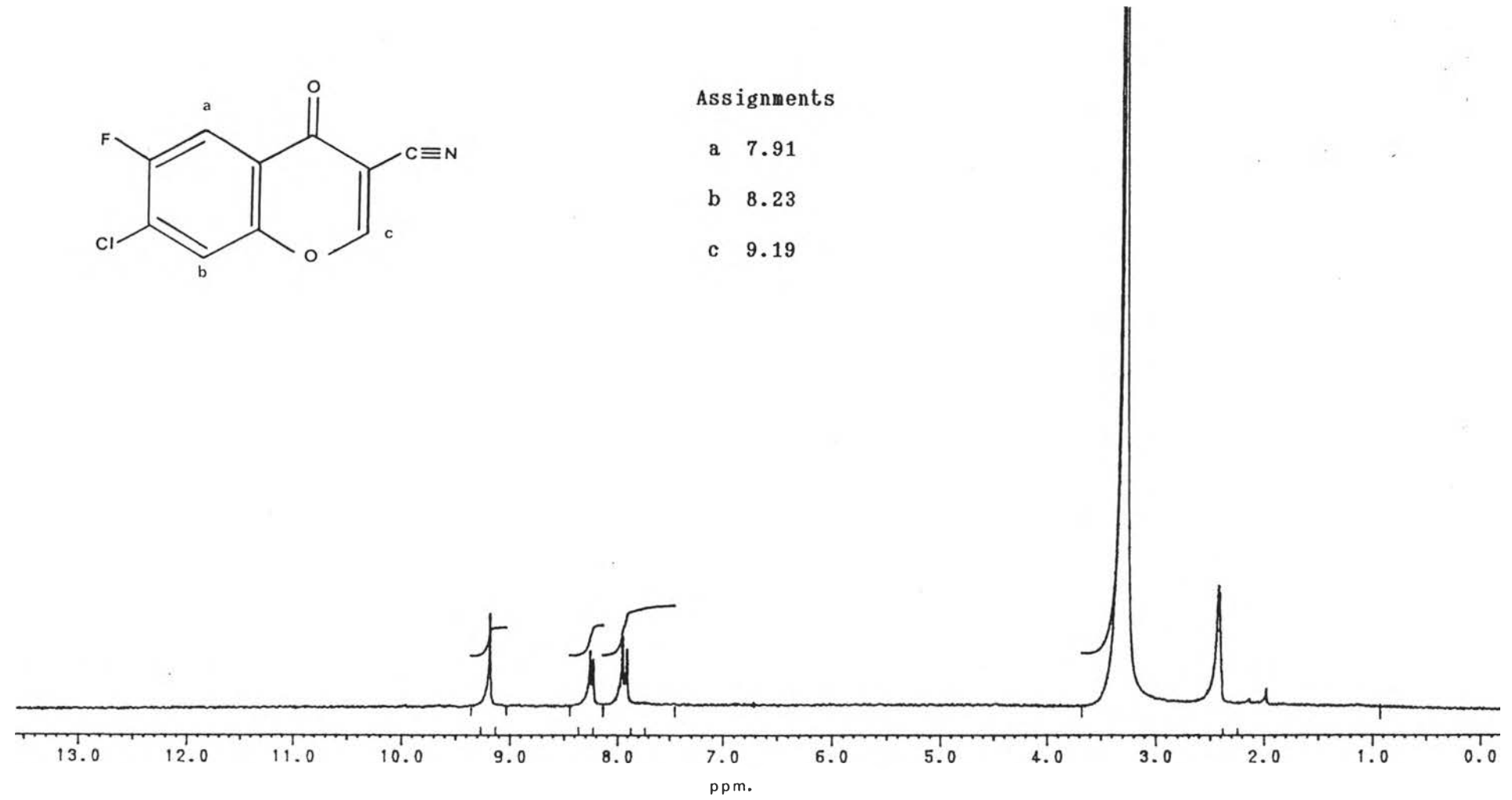


Figure 33 The ¹H-NMR spectrum of 7-Chloro-6-fluoro chromone-3-carbonitrile in DMSO-d₆

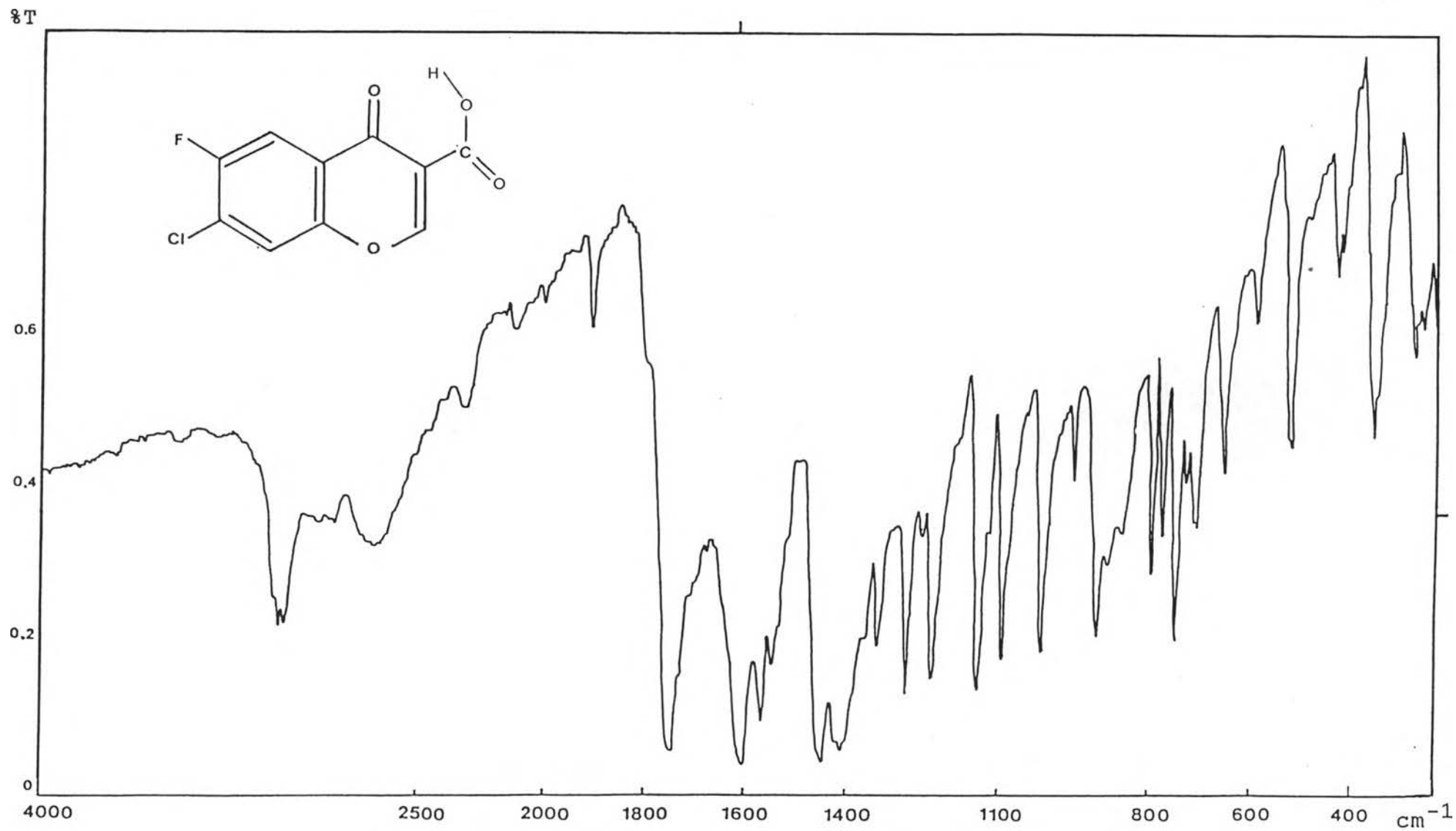


Figure 34 The IR spectrum of 7-Chloro-6-fluoro-chromone-3-carboxylic acid.

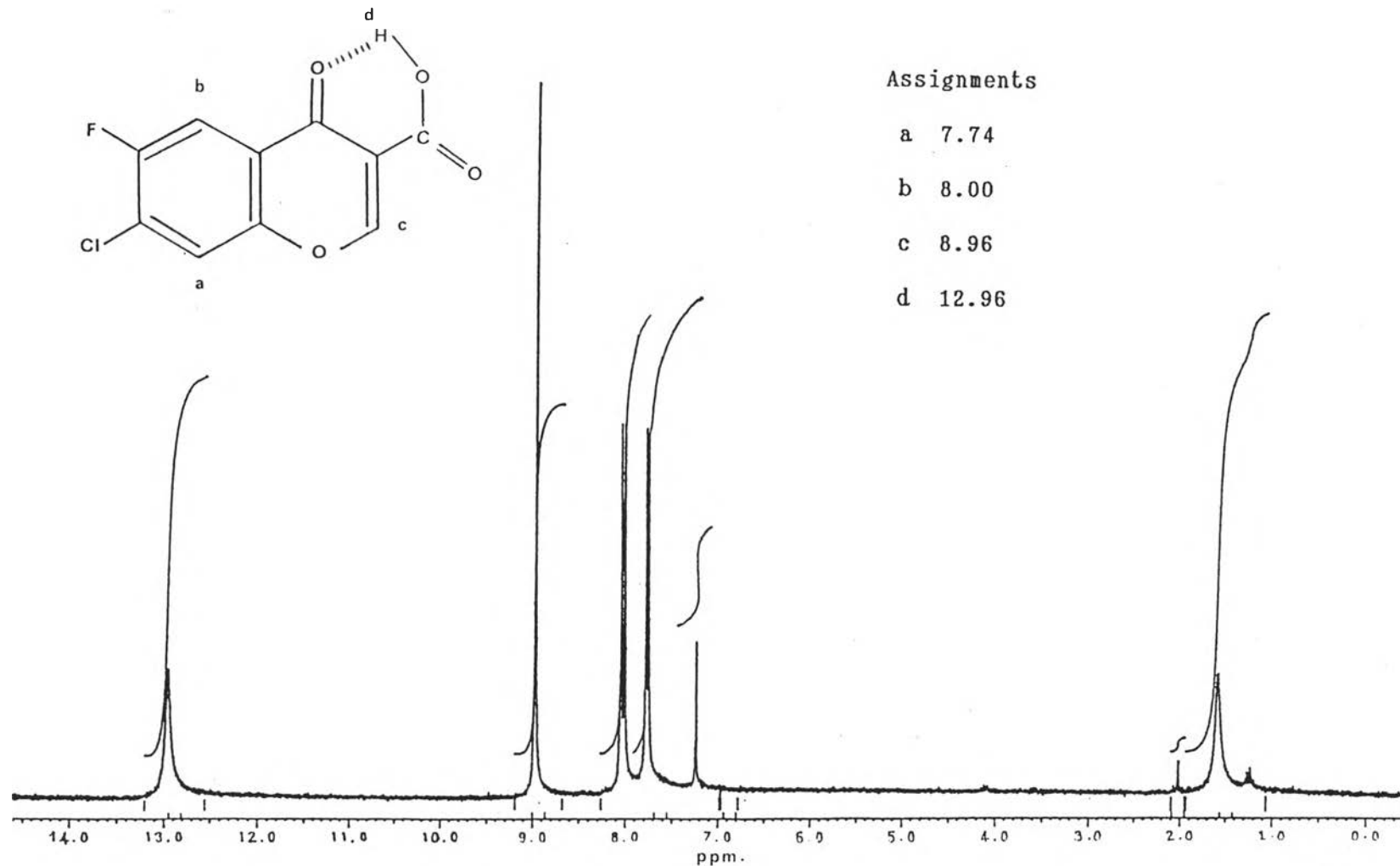


Figure 35 The $^1\text{H-NMR}$ spectrum of 7-Chloro-6-fluoro chromone-3-carboxylic acid in CDCl_3

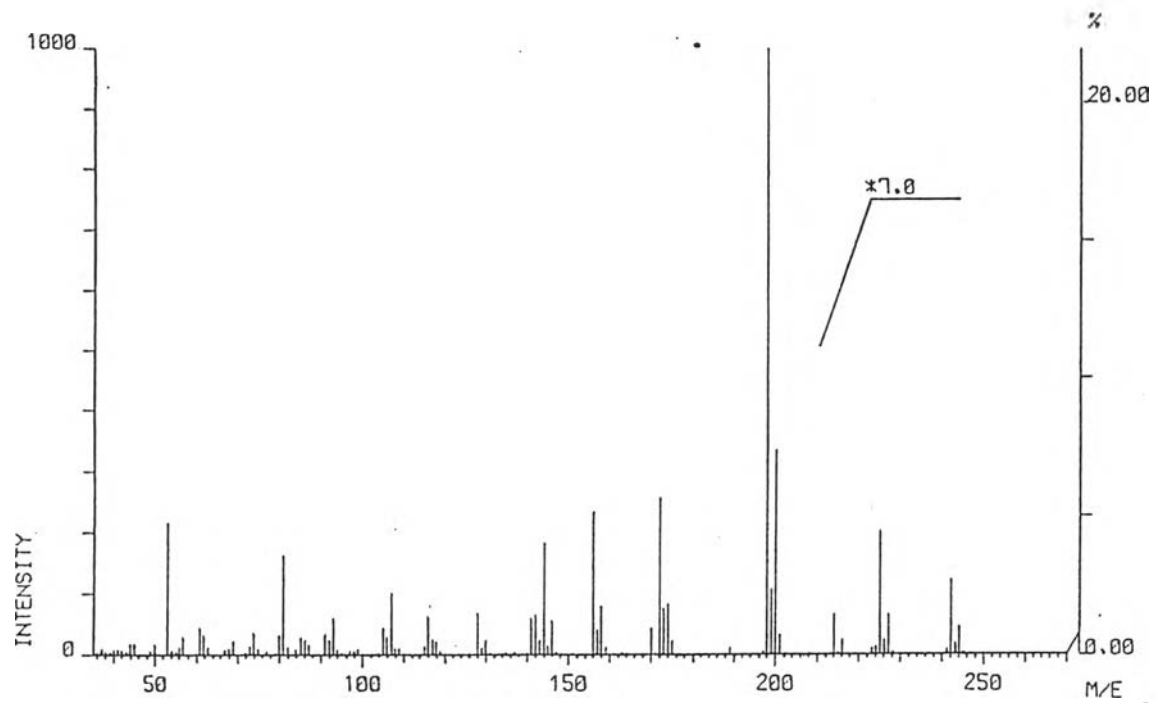


Figure 36 The mass spectrum of 7-Chloro-6-fluoro-chromone-3-carboxylic acid

VITA

Mr. Wiphoosit Limwong was born on November 1967, in Nakornsrihammarat, Southern of Thailand. He graduated with a Bachelor's degree of Pharmaceutical Science from faculty of Pharmaceutical Science, Prince of Songkla University, Songhkla in 1989.

