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OXIDATION OF GLYCEROL USING POLYMER-SUPPORTED IBX

MISS NIPAWAN THADKAD

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By	Miss Nipawan Thadkad
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Accepted by the Faculty of Science, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

..... Dean of the Faculty of Science

(Professor SupotHannongbua, Dr.rer.nat.)

THESIS COMMITTEE

..... Chairman

(Professor Pattarapan Prasassarakich, Ph.D.)

..... Thesis Advisor

(Associate Professor Surachai Pornpakakul, Ph.D.)

..... Examiner

(Amarawan Intasiri, Ph.D.)

..... External Examiner

(Prapas Khorphueng, Ph.D.)

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ไอบีเอกซ์รองรับด้วยพอลิเมอร์รูปแบบใหม่ถูกเตรียมขึ้นในงานวิจัยนี้ เพื่อใช้เป็นตัวออกซิไดส์ในปฏิกิริยาออกซิเดชันของกลีเซอรอล วิธีที่เหมาะสมสำหรับการสังเคราะห์ไอบีเอกซ์รองรับด้วยพอลิเมอร์นี้ประกอบด้วย 8 ขั้นตอน โดยการใช้พาราโทลูอิก แอซิดเป็นสารตั้งต้นสำหรับไอบีเอกซ์ และอะมิโนเมทิลพอลิสไตรีนเป็นวัสดุรองรับ สำหรับการสังเคราะห์ไอบีเอกซ์รองรับด้วยอะมิโนเมทิลพอลิเมอร์นั้น ได้ค้นพบกระบวนการใหม่สำหรับออกซิเดชันพันธะระหว่างไฮโดรเจนที่ต่อกับคาร์บอนของ 3-ไอออโด-4-เมทิลเบนโซอิก แอซิด ปฏิกิริยาออกซิเดชันที่ใช้โซเดียมไฮเปอร์คลอไรด์เป็นตัวออกซิแคนท์นี้ได้ปริมาณการเปลี่ยนแปลงสูงกว่าการใช้โซเดียมเปอร์ไอออเดตเป็นตัวออกซิแคนท์ ไอบีเอกซ์รองรับด้วยพอลิเมอร์รูปแบบใหม่นี้ถูกใช้เพื่อออกซิไดส์เบนซิลแอลกอฮอล์ และกลีเซอรอล และการออกซิเดชันของตัวออกซิแคนท์นี้ถูกนำไปเปรียบเทียบกับการใช้ไอบีเอกซ์ (1) ดีเอ็มพี (2) ไอบีเอกซ์รองรับด้วยอะมิโนเมทิลพอลิเมอร์ (3) N-ฟีนิล-2-ไอออโดซิเบนซาเอไมด์ (4) และ N-ฟีนิล-3-ไอออโดซิเบนโซอิก แอซิด (5) เบนซิลแอลกอฮอล์สามารถถูกออกซิไดส์ได้โดยการใช้ ไอบีเอกซ์ (1) ดีเอ็มพี (2) ไอบีเอกซ์รองรับด้วยอะมิโนเมทิลพอลิเมอร์ (3) และ ไอบีเอกซ์รองรับด้วยอะมิโนเมทิลพอลิเมอร์ (6) เป็นตัวออกซิไดส์ ในทางตรงกันข้ามกลีเซอรอลนั้นไม่สามารถถูกออกซิไดส์ได้ด้วยตัวออกซิไดส์เหล่านี้

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A new polymer-supported IBX was prepared in this research to use as an oxidizing agent in the oxidation reaction of glycerol. The appropriate method for the synthesis of polymer-supported IBX consisted of 8 steps using *p*-toluic acid as a starting material for IBX and aminomethyl polystyrene as a supporting material. For the synthesis of aminomethyl polymer-supported IBX, a new process for oxidation of C-H bond of 3-iodo-4-methylbenzoic acid was discovered. This oxidation using sodium hypochlorite (NaOCl) as an oxidant gave higher conversion than using sodium periodate ($NaIO_4$) as an oxidant. The new polymer-supported IBX was used to oxidize benzyl alcohol and glycerol and its oxidation was also compared with IBX (**1**), DMP (**2**), aminomethyl polymer-supported IBX amide (**3**), N-phenyl-2-iodoxybenzamide (**4**), and N-phenyl-3-iodoxybenzoic acid (**5**). Benzyl alcohol was oxidized with IBX (**1**), DMP (**2**), aminomethyl polystyrene-supported IBX amide (**3**) and aminomethyl polymer-supported IBX amide (**6**) as oxidizing agents while glycerol was not oxidized by those oxidizing agents.

Field of Study : Petrochemistry and Polymer Science Student's Signature Nipawan Thadkad

Academic Year : 2010 Advisor's Signature S. Pornpakakul

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LIST OF ABBREVIATIONS

°C	degree Celsius
cm^{-1}	unit of wavenumber
cm	centimeter
h	hour(s)
min	minute
g	gram(s)
ml	milliliter
mmol	millimole
eq.	mole equivalent
%mol	percent by mole
FT-IR	Fourier Transform Infrared Spectroscopy
NMR	Nuclear Magnetic Resonance Spectroscopy
HPLC	High Performance Liquid Chromatograph
TLC	Thin Layer Chromatography
IBX	2-Iodoxybenzoic acid

CHAPTER I

INTRODUCTION

1.1 Introduction

Nowadays, biodiesel has attracted much attention as a renewable energy to replace diesel oil which is more expensive and its price has the trend to increase continuously.

Glycerol was generated about 10% by-product from biodiesel industry by via the transesterification of vegetables oils. Although pure glycerol has been used in the wide applications for examples food, pharmaceutical and cosmetics industries but its high costly to refine the crude glycerol from biodiesel industry to a high purity that this process isn't sufficient to worth the expense for medium and small biodiesel producers. Many research projects have studied possible ways on the value-added applications of crude glycerol which generate from biodiesel industry. [1] Glycerol has been used as a starting material for synthesis the valuable compounds such as dihydroxyacetone, glyceric acid, and glyceraldehyde. Oxidation reaction is an industrial importance for converting glycerol to the high-value added chemical.

The past decades have reported the use of hypervalent iodine compounds as an oxidizing agent in the oxidation reaction replacing toxic and heavy metal-containing reagents then the reaction has used this reagent to be more environmental friendly reaction condition. [2]

2-Iodoxybenzoic acid (IBX) has been used as a mild oxidizing agent for the oxidation of primary and secondary alcohols to aldehydes and ketones, respectively. In particular, 1,2-diols are converted to α-ketols or α-diketones without any oxidative cleavage of the glycol C-C bond and 1,4-diols are oxidized to γ-lactols. Moreover IBX can oxidize amino alcohols to amino carbonyls without protection of the amino group. [3,4] In the truth, IBX is insoluble in most organic solvents which to dissolve completely in DMSO only. The soluble efficiency of IBX in organic solvents is first account to the application of IBX in the organic synthesis, many projects were synthesized the solid-phase of IBX such as polystyrene- and silica-supported with IBX. [5,6] These solid-phase reagents have attracted much interesting in its qualities that expand the range of viable solvents, simplify separation of byproducts from the reaction mixture, and facilitate recovery and reuse of

the oxidizing agent. Thus polymer-supported IBX has been interested in using as an oxidizing agent for the oxidation reaction of glycerol.

1.2 Objectives

1. To prepare polymer-supported IBX
2. To study the effect of temperature, time and percent of polymer-supported using as an oxidizing agent in the glycerol oxidation

1.3 Scope

The stepwise investigation was carried out as follows.

1. Literature survey for related research work.
2. Preparation of polymer-supported IBX from aminopolystyrene and *p*-toluic acid.
3. Investigation of polymer-supported IBX by FT-IR.
4. Optimization of a condition to use polymer-supported IBX as an oxidizing agent in the glycerol oxidation.
5. Determination of the product from the glycerol oxidation by ^{1}H NMR.

CHAPTER II

THEORY AND LITERATURE REVIEWS

2.1 Basic glycerol chemistry

1,2,3-Propanetriol which to know by name of glycerol is a trihydric alcohol. It is a colorless, odorless, sweet-tasting, and syrupy liquid. It melts at 17.8 °C, boils with decomposition at 290 °C, and is miscible with water and ethanol. The chemical formula for glycerol has showed in figure 2.1.

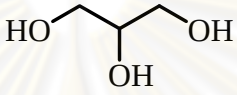


Figure 2.1 The chemical formula of glycerol

It is hygroscopic because it absorbs water from the air then it was used as a moistener in cosmetic. Triglyceride (show in figure 2.2) is ester from glycerol which present in all animal and vegetable fats and oils.

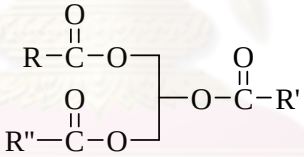
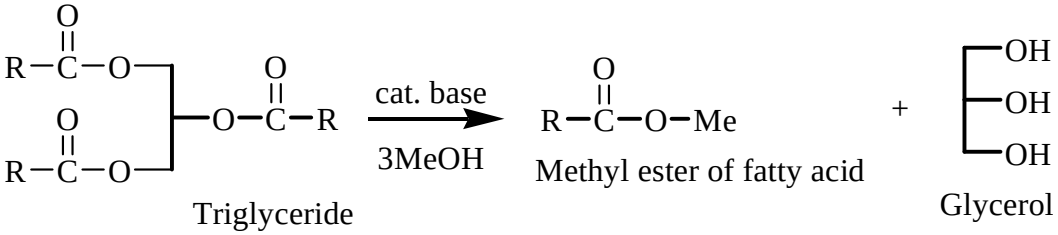


Figure 2.2 The chemical formula of triglyceride

2.2 Glycerol from biodiesel production

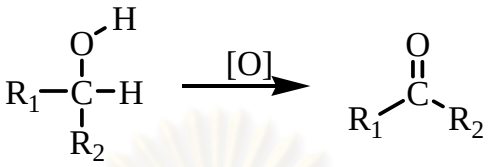
A way to generate glycerol is a by-product from the biodiesel industry. Every 10 kg of biodiesel produced are included about 1 kg of a crude glycerol. The scheme 2.1 shows the reaction for production biodiesel from vegetable oils via the transesterification.



Scheme 2.1 Transesterification of triglyceride

2.3 Oxidation of alcohols

The conversion of alcohols into aldehyde and ketone with the oxidation reaction is an important organic reaction that provides useful intermediates for the preparation of other organic compounds. The pathway of this oxidation reaction showed in scheme 2.2.



Scheme 2.2 The oxidation of alcohol

Dehydrogenation is a synonym for the oxidation of alcohols. The mechanism of this reaction occurs by hydrogen bond of the OH group attached to a carbon atom with least one hydrogen atom from this carbon atom.

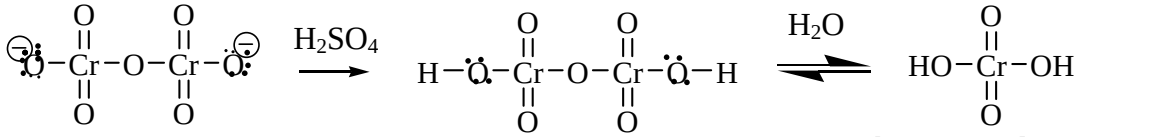
2.4 Oxidizing agent for alcohol oxidation

Oxidizing agents used in the oxidation reaction of alcohols have much variety. The examples of the oxidizing agents are usually used for oxidation of alcohols.

2.4.1 Metal oxyacids

1) Chromium reagents (Chromate)

All forms of Cr(VI) are strong oxidizing agents which oxidize any C-H bonds on a carbon atom without breaking any C-C bonds. Example of the reaction used this reagent as an oxidizing agent is the reaction for the conversion of secondary alcohols to ketones and aldehydes to carboxylic acid. The most common of this reagent type is chromic acid (H_2CrO_4) and pyridinium chlorochromate (PCC). Chromic acid was prepared by treatment of sodium or potassium dichromate with aqueous sulfuric acid which shown in scheme 2.3.

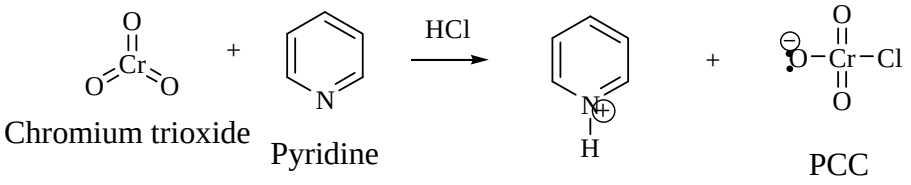


Dichromate ion

Chromic acid (H_2CrO_4)

Scheme 2.3 The process for preparation of chromic acid

Chromic acid is most commonly used to oxidize 2° alcohols to ketones. PCC was produced by mixing chromium trioxide with pyridine and hydrochloric acid as shown in scheme 2.4. The oxidizing component of PCC is the chlorochromate anion ($CrClO_3^-$).



Scheme 2.4 The process for preparation of Pyridinium chlorochromate

PCC was developed especially for the oxidation of 1° alcohols to aldehydes, a transformation which is difficult to accomplish using chromic acid because aldehydes react rapidly with aqueous chromic acid to produce carboxylic acid.

2) Manganese reagents (Permanganate)

Permanganate ion (MnO_4^-) is most commonly used in basic solution. With heat in base, it oxidizes alcohols to carboxylic acid without breaking C-C bonds.

3) Osmium tetroxide

Osmium tetroxide (OsO_4) was used to selectively and stereospecifically oxidize alkenes to 1,2-diols. It was oxidized alkenes to 1,2-diols in cold basic condition and heating the reaction mixture resulted in cleavage of C-C bond.

2.4.2 Nitric acid and nitrous acid

In the commerce, concentrated nitric acid is a 69% aqueous solution which is extremely dangerous because it is a rapid and strong oxidizing agent. In the oxidation reaction which presence of sulfuric acid, it was show in form of NO_2^+ which adds to aromatic rings by lose a hydrogen atom. Moreover, it was used to produce nitrate esters from alcohols. Nitrous acid (HNO_2) can be used to substitute the NO (nitroso) to an aromatic ring with using sulfuric acid as a catalyst in the nitration reaction. Nitration of amines and amides to N-nitroso compounds (R_2-N-N=O) were used nitric acid as a reagent which more famous than nitrous acid.

2.4.3 Halogens

The halogens having the order of the oxidizing ability are $F_2 > Cl_2 > Br_2 > I_2$. They are the strong oxidizing agent for oxidize C-H bonds which the reaction order of various substances are benzyl > alkyl and tertiary > secondary > primary. The most commonly used halogens are Cl_2 and Br_2. In the commerce, Cl_2 which is gas form can be generated in dilute solution that to know in the name of bleach (NaOCl).

2.4.4 Oxygen and peroxides

Dioxygen (O_2) is commonly used in the chemical industry. Usually a catalyst is needed heat or light. It is UV light that makes it possible for dioxygen to dissociate to form oxygen atoms, which react with dioxygen to form ozone; lower energy light will produce an excited state of oxygen which reacts with alkenes. Even without light, oxygen will slowly oxidize aldehydes when they are exposed to air, but most reactions with oxygen at the concentration of the atmosphere are shown at room temperature to be noticed.

Hydrogen peroxide (H_2O_2) is a strong oxidizing agent. Its reactions tend to occur via radical paths. Its reactivity increases if the peroxy (OOH) part of the molecule is linked to an electron withdrawing group, as in peroxyacid. Peroxyacid (RCO_3H) has a peroxy group attached to the carbonyl group. It is a stronger oxidizing agent than hydrogen peroxide itself, converting alkenes into epoxides.

2.5 Oxidation of glycerol

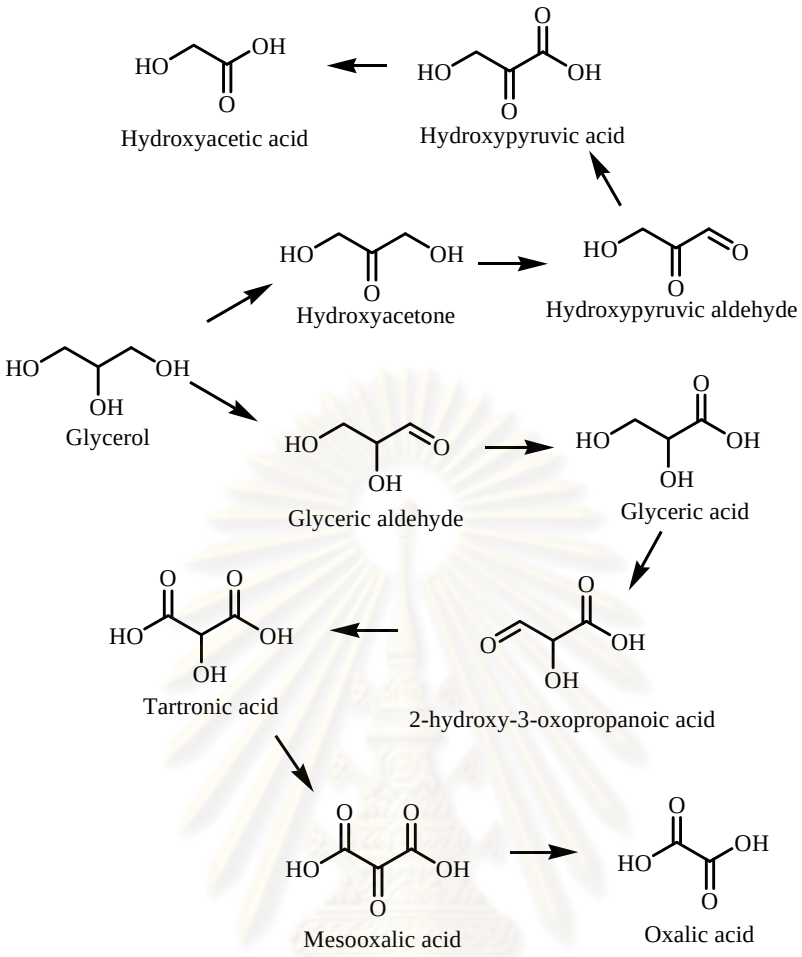
Glycerol has been used as a starting material for syntheses of the high-value chemicals, such as dihydroxyacetone, glyceraldehydes, glyceric acid, glycolic acid, hydroxypyruvic acid, mesoxalic, oxalic acid and tartronic acid, because of its easy availability, low cost and high functionalisation. In the past times, the market for these chemicals has not developed because of their high cost due to their expensive current syntheses. [7,8] For converting glycerol to such a high-value added chemicals with oxidation reaction was shown in scheme 2.5. In the past decade, there are many reports of the oxidation reaction of glycerol. Mostly mono and bimetallics as catalyst and air/oxygen as the oxidizing agents were used.

In 1995, Regis and coworkers studied the oxidation reaction of glycerol by using various metals as the catalyst in this reaction. In case of palladium used as a catalyst 90 % conversion of glycerol was obtained and the reaction gave excellent yield of glyceric acid. Moreover, the reaction used co-metallic of platinium and bismit as a catalyst gave dihydroxy acetone in 37 % yield and 70 % conversion in overall.

In 2004, Porta and coworkers studied the oxidation reaction of glycerol with oxygen in the presence of gold on carbon as the catalyst. They educated the optimize condition to produce glycerate in excellent yield. The best condition that produce 92 % yield of glycerate is the condition at 30 °C using a NaOH/glycerol ratio of 4, a glycerol/Au = 500.

In 2005, Bianchi and coworkers studied the liquid phase oxidation of glycerol with oxygen and a series of monometallic and bimetallic catalysts as the catalysts were used. Moreover, they studied the effect of the metal on the distribution of the products. They found that bimetallic catalysts were more active than monometallic catalysts and the distribution of the products could be controlled by using bimetallic catalysts.

In 2007, Demirel and coworker studied the liquid phase oxidation of glycerol with oxygen using mono and bimetallic supported on carbon as the catalysts. They found that the presence of Pt increases not only the catalyst activity but also the selectivity. The percentage of the dihydroxyacetone could be increased from 26 % (Au/C) to 36 % (Au-Pt/C) when the gold catalyst promoting with platinum as the catalyst was used.



Scheme 2.5 General glycerol oxidation reaction pathways

2.6 Hypervalent iodine

Hypervalent iodine was used as an oxidizing agent in the organic synthesis in the past decade. [9]

2.6.1 Iodine (III) compounds

Iodine (III) compounds, or λ^3-iodines according to the IUPAC nomenclature, are commonly classified according to the type of ligands attached to the iodine atom. The general classes of iodine (III) compounds including:

(1) iodosylarenes ArIO and their acyclic derivatives $ArIX_2$ bearing two non-carbon ligands X

(2) five-memberred iodine heterocycles, benziodoxoles and benziodazoles

(3) iodonium salts $R_2I^+X^-$

(4) iodonium ylides $ArI=CR_2$

(5) iodonium imides ArI=NR [10].

2.6.2 Iodine (V) compounds

Iodine (V) compounds, or λ^5-iodanes according to the IUPAC nomenclature, are substantially less developed in comparison with the chemistry of trivalent iodine. Only several examples of noncyclic λ^5-iodanes with one or more carbon ligands on the iodine atom are known. In contrast, there has been very significant recent interest in the cyclic λ^5-iodanes, mainly iodoxybenzoic acid (IBX) and Dess-Martin periodinane (DMP), which have found broad practical application as mild and selective reagents for the oxidation of alcohols. The classes of iodine (V) compounds including:

(1) Organic Iodyl compounds, RIO_2 or aryl substituted iodoxy derivatives $ArIO_2$

(2) Benziodoxole oxides, the most important representative of benziodoxole oxides is 2-iodoxybenzoic acid (IBX)

(3) Dess-Martin periodinane (DMP; 1,1,1-tris(acetyloxy)-1,1-dihydro-1,2-benziodoxol-3-(1H)-one), it was employed in organic synthesis. [10]

2.7 2-Iodoxybenzoic acid (IBX)

2-Iodoxybenzoic acid (IBX; 1-hydroxy-1,2-benziodoxol-3(1H)-one 1-oxide) as shown in figure 2.3 has been known for more than a century. IBX is different from other valuable oxidants because the process for preparation is easy and inexpensive. Moreover, the reactions using IBX as an oxidizing agent provided very good to excellent yields. IBX and its derivative has attracted much attention as an oxidizing agent in organic synthesis but it has limitation primarily due to its remarkable insolubility in most organic solvents except dimethylsulfoxide (DMSO) which can dissolve IBX completely. Caution! IBX is explosive under impact or heating to > 200 °C. [11]

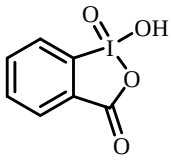
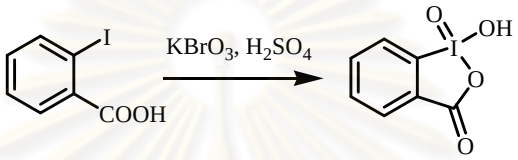


Figure 2.3 The chemical formula of IBX

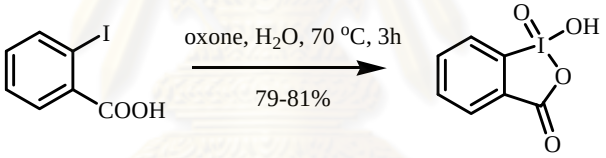
2.7.1 Preparation of IBX

Generally IBX was prepared from the oxidation reaction of 2-iodobenzoic acid with potassium bromated in an aqueous solution of sulfuric acid (scheme 2.6). [3]



Scheme 2.6 The reaction for preparation IBX by used potassium bromated

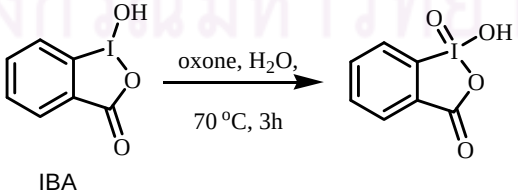
A new way to prepare IBX from 2-iodobenzoic acid is the use of oxone as an oxidizing agent that reported by Santagastino and co-workers (scheme 2.7). [11]



Scheme 2.7 The reaction for preparation IBX by used oxone

2.7.2 Reuse of IBX byproducts

IBX and IBX by-product (iodosylbenzoic acid; IBA) were isolated by filtration from the oxidation of alcohol. The IBX by-product was reused by oxidation with oxone in the water at 70 °C for 3h (scheme 2.8). [12]



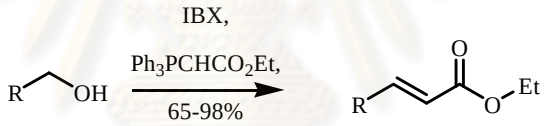
Scheme 2.8 The reaction to reuse the IBX by-product

2.8 Application of IBX

Furthermore, IBX is mild and chemoselective. Primary and secondary alcohols are converted into aldehydes and ketones, repectively, with no over oxidation to acids. 1,2-Diols are converted to α-ketols or α-diketones without oxidative cleavages. Amino alcohols are oxidized to amino carbonyls, without protection of the amino group. Sensitive heterocycles are not affected. Also various other functional groups are compatible with IBX oxidation. [14]

2.8.1 Oxidation of alcohols

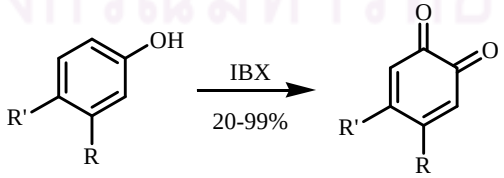
The IBX can be employed as iodine (V) reagents in various oxidations of alcohols to the corresponding carbonyl compounds. Benzylic, allylic, and propargylic alcohols can be oxidized by IBX in the presence of stabilized Wittig ylides to generate α,β-unsaturated esters in a one-pot procedure. This is useful when the intermediate aldehydes are unstable and difficult to isolate. Example of this reaction was shown in scheme 2.9 which was reported by Maiti A. and co-workers. [15]



Scheme 2.9 One-pot oxidation and Wittig reaction to α,β-unsaturated esters

2.8.2 Oxidation of phenolic compounds

An efficient regioselective method for the oxidation of phenols to ortho-quinones can be achieved using 2-iodoxybenzoic acid (IBX). Magdyiak and co-workers reported the preparation of ortho-quinones from phenols by using IBX as an oxidizing agent (scheme 2.10). [16]

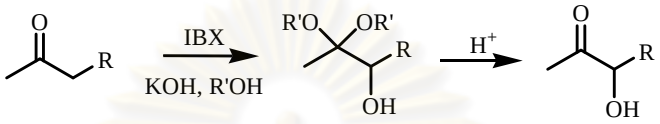


Scheme 2.10 Regioselective oxidation of phenols in the ortho position

2.8.3 Functionalizations of carbonyl compounds

1) Functionalization in the α-position

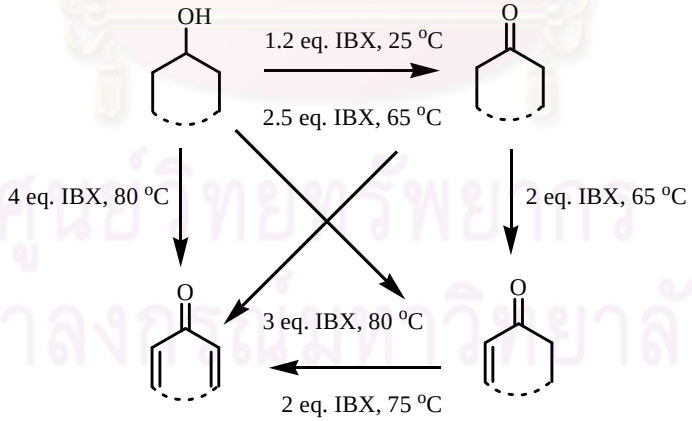
Carbonyl compounds can be functionalized in the α-position under various conditions. Moriarty and co-worker reported that treatment of ketones with 2-iodoxybenzoic acid (IBX) under basic conditions provides efficient routes to α-hydroxylated dialkylacetals. This reaction has also been applied for functionalization in natural product synthesis, because the α-hydroxylated dialkylacetals can be easily hydrolyzed under acidic conditions to α-hydroxy ketones in good overall yields (scheme 2.11). [17]



Scheme 2.11 Synthesis of α-hydroxy dialkylacetals from ketones

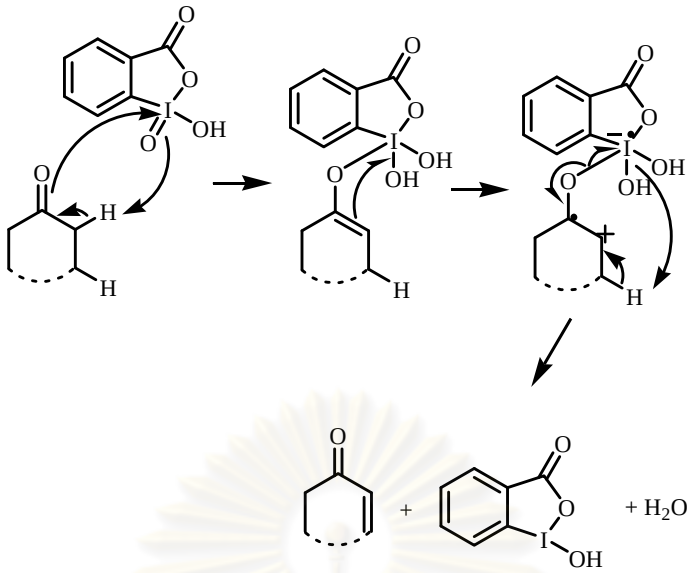
2) Introduction of an α,β-unsaturation

α,β-Unsaturated carbonyl compounds are widely used in organic synthesis and despite of their versatility, their preparation is sometimes a challenging transformation. Depending on the amount of 2-iodoxybenzoic acid (IBX) it is possible to introduce one α,β-unsaturation or even two and generate dienones. Taking into account that one can oxidize alcohols to the corresponding carbonyl compounds with IBX, 4 equivalents of IBX are sufficient for a direct conversion of alcohol into dienones (scheme 2.12).



Scheme 2.12 Synthesis of α,β-unsaturated carbonyl systems

The postulated mechanism for the 2-iodoxybenzoic acid acid (IBX) mediated dehydrogenation reactions described in scheme 2.13 proceeds through enolization with subsequent capture of the enolate moiety.

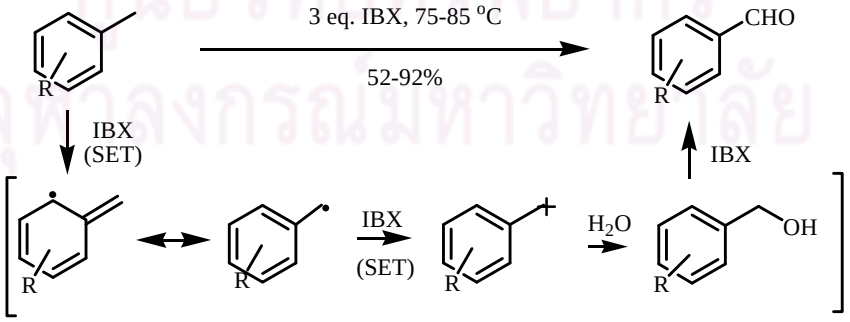


Scheme 2.13 Proposed SET mechanism of the dehydrogenation of carbonyl compound

Although hypervalent iodine compounds are often used as oxidants and sometimes as electrophilic reagents, the dehydrogenation of carbonyl compounds is believed to proceed via a single electron transfer (SET) process. [18,19]

2.8.4 Oxidation of carbon-hydrogen bonds

Recently it was found that iodine (V) compounds like 2-iodoxybenzoic acid (IBX) could be used to affect selective oxidations at carbon atoms adjacent to aromatic systems. The mechanism of this transformation is believed to proceed via a SET (Single-Electron-Transfer) process. A postulated mechanism for the oxidation of benzylic positions is outlined in scheme 2.14. [20]



Scheme 2.14 Oxidation of carbons adjacent to aromatic systems

2.9 Polymer-supported reagents

Because IBX is insolubility in most organic solvents its application in organic synthesis was limited to develop. The IBX is dissolved in DMSO which is the only organic solvent to dissolve this reagent completely. The limitations of DMSO as a solvent are apparent and are sufficient to have motivated two independent syntheses of solid-phase (polystyrene- and silica-bound) analogues of IBX. In each case, these solid-phase reagents expand the range of viable solvents, ease to remove after the end of the reaction by filtration, simplify separation of oxidation byproducts, and facilitate recovery and reuse of the oxidant. However, the elevation of reaction temperature may cause decomposition of starting materials and bring about side reactions.

In 2002, Reed and coworkers have prepared soluble and insoluble polymer supported IBX reagents (figure 2.5). These supports were an insoluble polystyrene gel-type JandaJel resin, a macroporous polystyrene Argo Pore resin, a soluble, non-crosslinked polystyrene resin and soluble poly(ethylene glycol) (PEG 3400) support. Each of the reagents was evaluated for their efficiency in the conversion of benzyl alcohol to benzaldehyde. Results from this study were that the soluble, non-crosslinked polystyrene supported IBX reagent gave the best rate of conversion to benzaldehyde, while the macroporous polymer supported IBX resin provided a superior rate of conversion to benzaldehyde when compared with a gel type resin.

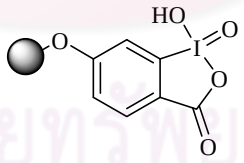
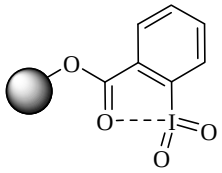
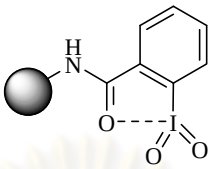


Figure 2.4 The soluble and insoluble polymer-supported IBX

In 2003, Chung and coworkers have prepared polymer-supported IBX esters and amides in two simple steps, which were the coupling of 2-iodoxybenzoic acid to a hydroxyl or amino polystyrene followed by activation of the intermediate product (figure 2.6). These polymer supported reagents were tested as oxidants by the conversion of a series of alcohols to the corresponding aldehydes or ketones. It was found that the polymer-supported IBX amides displayed excellent oxidative activity than the polymer-supported IBX ester in the same condition.



The polymer-supported IBX esters



The polymer-supported IBX amides

Figure 2.5 The polymer-supported IBX esters and amides

In 2003, Lei and coworkers studied the oxidation of a series of alcohols to the corresponding aldehydes by using polymer-supported IBX reagents which were prepared from poly(*p*-methylatyrene). Oxidation of a series of alcohols using polymer supported IBX reagent were carried out at 25 °C in DCM (1 ml/100 mg of oxidant) for 5 h and employed the polymer supported IBX: alcohol ratio of 2:1. All reactions gave excellent yields. The loading of polymer supported was determined to be 0.5 mmol/g.

In 2006, Lie and coworkers studied the factors that mainly influenced the effective loadings of the polymer-supported IBX reagent. They studied the procedure for preparation of the polymer supported 2-iodobenzoic acid. The active component loading of polymer supported IBX (**1-4**) (figure 2.) were analyzed as follows: 0.3, 0.6, 0.4 and 0.8 mmol/g, respectively. Moreover, they investigated 4 oxidation systems for preparation of polymer supported IBX from polymer supported 2-iodobenzoic acid (**4**). The oxidant system using Ba_4NHSO_5/ CF_3COOH provided high loading of polymer supported IBX (0.8 mmol/g).

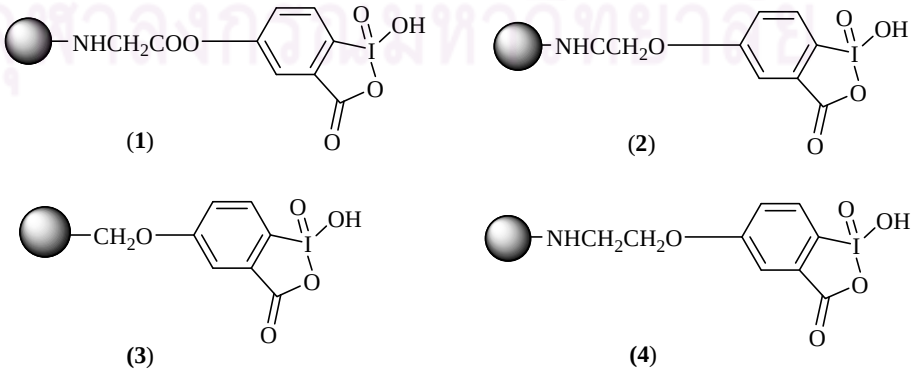


Figure 2.6 Polymer supported IBX (**1-4**)

In 2007, Jang and coworkers have prepared macroporous polystyrene-supported IBX (MPS-IBX) amides (figure 2.8) in two simple steps and studied efficiency of the polymeric reagent in converted a range of alcohols to the corresponding carbonyl compounds in various solvents. It was found that the MPS-IBX amides were compatible with a variety of solvents and had a more efficient oxidation activity toward alkyl alcohols than the gel type polystyrene-supported IBX amides.

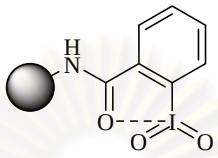


Figure 2.7 Macroporous polystyrene-supported IBX (MPS-IBX) amides

CHAPTER III

EXPERIMENTAL

3.1 Chemicals

All chemicals which were used in this thesis were available from the suppliers as listed in table 3.1

Table 3.1 List of Chemicals

Chemicals	Suppliers
Acetic acid (glacial) (AcOH)	Merck
Aminomethyl polystyrene	Fluka
Aniline	Merck
Calcium bicarbonate	Merck
Calcium hydride	Aldrich
Deterochloroform ($CDCl_3$)	Cambridge Isotope Laboratories (CIL)
Dichloromethane (DCM)	Fisher Scientific
Diethyl ether	Merck
N,N-Dimethylformamide (DMF)	Riedel-de Haen
Dimethylsulfoxide (DMSO)	Riedel-de Haen
Dimethylsulfoxide (DMSO-d_6)	Wilmad Lab Glass
N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide (EDC)	Fluka
Glycerol	Carlo Erba
Hexane	Fisher Scientific
Hydrochloric acid (HCl)	Carlo Erba
Iodine (I_2)	Merck
2-Iodobenzoic acid	Aldrich
Lithium aluminium hydride ($LiAlH_4$; LAH)	Aldrich
Lithium bromide (LiBr)	Sigma-Aldrich
Methanol (MeOH)	Merck
Methanol-d4 (CD_3OD)	Cambridge Isotope Laboratories (CIL)

Chemicals	Suppliers
Oxalyl chloride	Fluka
Oxone®	Riedel-de Haen
Potassium bromide (KBr)	Merck
Potassium hydroxide (KOH)	Merck
Pyridinium chlorochromate (PCC)	Merck
Silica gel (60 mesh)	Merck
Silver oxide (Ag_2O)	BDH Laboratory Reagent
Sodium hydroxide (NaOH)	Merck
Sodium periodate ($NaIO_4$)	Fluka
Sodium thiosulfate (NaS_2O_3)	Univar
Sodium hypochlorite (NaOCl)	Merck
Sodium sulfate (Na_2SO_4)	Merck
Sulfuric acid (H_2SO_4, 95-97 %)	Merck
Tetrahydrofuran (THF)	Merck
p-Toluic acid	Fluka

3.2 Equipments

The equipments used in this thesis were additionally indicated in the details.

3.2.1 Nuclear Magnetic Resonance Spectroscopy (NMR)

^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Model Mercury +400 nuclear magnetic resonance spectrometer and Bruker Model AVANCE operating at 400 MHz for ^{13}C and 100 MHz for ^{1}H. Chemical shifts (δ) are reported in part per million (ppm) relative to tetramethylsilane (TMS) or using the residual protonated solvent signal as a reference (for ^{1}H-NMR; $CDCl_3$ 7.26 ppm, MeOD 3.31 ppm, DMSO-d_6 2.50 ppm and D_2O 4.79 ppm, and for ^{13}C-NMR; $CDCl_3$ 77.16 ppm, MeOD 49.00 ppm and DMSO-d_6 39.52 ppm).

3.2.2 Fourier Transform Infrared Spectrometer (FT-IR)

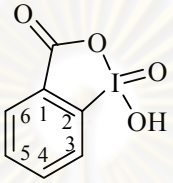
FT-IR spectra were recorded on a Perkin Elmer, Nicolet Impact 410 Fourier transform Infrared Spectrophotometer. Solid samples were formally examined by incorporating the

sample with potassium bromide (KBr) to form a pellet. Liquid sample was coated on the KBr disk.

3.2.3 Mass Spectrometer

HREIMS were recorded on Bruker Model micrOTOF spectrometer and Mass Spectrometer LCT, Micromass UK Limited.

3.3 Synthesis of 2-iodoxybenzoic acid (IBX, 1) from 2-iodobenzoic acid



2-Iodoxybenzoic acid (**1**)

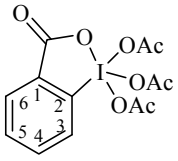
To a solution of Oxone (1.2 eq., 2.97 g, 4.84 mmol) in DI water (20 ml) in a 100 ml round bottom flask, 2-iodobenzoic acid (1 g, 4.03 mmol) was added. The reaction mixture was stirred and warmed to 70-75 °C within 20 minutes. It was stirred at this temperature for 3 hours. When the reaction was complete it was cooled to 5 °C in an ice bath by slow stirring and kept at this temperature for 1.5 hours. The reaction mixture was filtered with suction pump. The solid was washed with water (3 × 20 ml) and acetone (2 × 20 ml) and purified by recrystalization in dichloromethane and hexane to give IBX (0.98 g, 3.50 mmol, 86.85 %):

^{1}H NMR (400 MHz, DMSO-d_6) δ_H 8.14 (1H, d, J = 7.9 Hz, H-6), 8.01 (1H, d, J = 7.8 Hz, H-3), 7.96 (1H, t, J = 7.5 Hz, H-5), 7.70 (1H, t, J = 7.3 Hz, H-4)

^{13}C-NMR (101 MHz, DMSO-d_6) δ_C 166.71 (C=O), 146.54 (C-1), 133.35 (C-2), 132.92 (C-6), 131.08 (C-3), 130.06 (C-5), 124.95 (C-4) ppm.

IR (KBr): υ_{max} 3473, 1628, 541 cm^{-1}

3.4 Synthesis of Dess-Martin Periodinane (DMP, 2) from 2-iodoxybenzoic acid



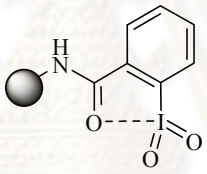
Dess-Martin Periodinane (**2**)

2-Iodoxybenzoic acid (0.5 g, 1.78 mmol) was treated with acetic anhydride (10 ml) and acetic acid (10 ml) under refluxing at 100 °C for 3h. The reaction was cooled to room temperature with slow stirring and white crystal of Dess-Martin Periodinane (DMP) was precipitated. The mixture was filtered and washed with water to give DMP (0.46 g, 1.08 mmol, 60.67 %):

^{1}H NMR (400 MHz, DMSO-d_6) δ_H 8.14 (1H, d, *J* = 7.9 Hz, H-6), 8.03 (1H, d, *J* = 7.2 Hz, H-3), 7.99 (1H, t, *J* = 7.5 Hz, H-5), 7.84 (1H, t, *J* = 7.3 Hz, H-4), 2.50 (3H, s, H-Ac)

^{13}C NMR (101 MHz, DMSO-d_6) δ_C 167.48 (C=O), 146.54 (C-1), 133.36 (C-2), 132.93 (C-6), 131.40 (C-3), 130.06 (C-5), 124.96 (C-4) ppm.

3.5 Synthesis of aminomethyl polystyrene-supported IBX (3) [18]



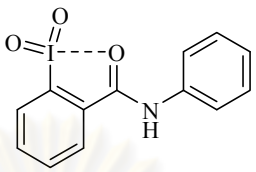
Aminomethyl polystyrene-supported IBX amide (**3**)

Aminomethyl polystyrene (1.1 mmol/g amine loading, 1.2 eq., 1.2 mmol, 1.09 g) was pre-swollen by stirring at room temperature in dimethyl formamide (5 ml). After 1h, 2-iodobenzoic acid (0.25 g, 1 mmol) and N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide (EDC; 3 eq., 0.47 g, 3 mmol) were added to the reaction mixture and continuously stirred at this temperature for 4 h. When the reaction completed, DI water was added to stop the reaction. The polymer-supported 2-iodobenzoic acid was filtered and washed with DI water. To a suspension of the polymer-supported 2-iodobenzoic acid in dichloromethane (20 ml), Oxone (1.5 eq., 0.46 g, 1.5 mmol) and methylsulfonic acid (1 eq., 0.07 ml, 1 mmol) were added. The reaction was stirred at room temperature for about 18-20 h. After that the mixture was filtered and washed with DI water. The polymer-supported IBX was dried in desiccators to give aminomethyl polystyrene-supported IBX amide (**3**) (1.15 g):

IR (KBr)υ_{max}: 3467, 3241, 1633, 1597, 1488, 1446 cm^{-1}.

3.6 Synthesis of N-phenyl-2-iodoxybenzamide (**4**)

The procedure for preparing aminomethyl polystyrene-supported IBX (**3**) was carried out according to Chung and cowerkers (Chung, 2003) and aniline was used instead of aminomethyl polystyrene.

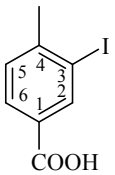


2-iodoxy-N-phenylbenzamide (**4**)

2-Iodobenzoic acid (1 g, 4.03 mmol) was treated with oxalyl chloride (1.5 eq., 0.52 ml, 6.05 mmol) and small amount of DMF in dried DCM (10 ml). The reaction mixture was stirred at room temperature for 1 h under argon. After evaporation of the solvents, a residue was reacted with aniline in dried THF (10 ml) under argon atmosphere. This reaction was stirred at room temperature and the progress of the reaction was monitored by TLC. After 6 h the pH of reaction mixture was adjusted to acidic condition by aqueous hydrochloric acid (1%) and extracted with dichloromethane. After evaporation of the organic solvent, N-phenyl-2-iodobenzamide was obtained. To a solution of N-phenyl-2-iodobenzamide in dichloromethane (10 ml), oxone (1.5 eq., 1.86 g, 6.05 mmol) and methylsulfonic acid (1 eq., 0.29 ml, 4.03 mmol) were added. The reaction was stirred at room temperature for about 18-20 h. After that the reaction mixture was diluted with DI water and extracted with dichloromethane. The organic phase was dried over anhydrous sodium sulfate and evaporated in vacuo to obtain the white solid of N-phenyl-2-iodoxybenzamide (**4**) (1.25 g, 3.52 mmol, 87.34 %).

3.7 Preparation of N-phenyl-2-iodoxybenzoic acid (**5**)

3.7.1 Synthesis of 3-iodo-4-methylbenzoic acid



3-iodo-4-methylbenzoic acid

To a solution of sodium periodate ($NaIO_4$)(0.5 eq., 0.74 g, 3.5 mmol) and iodine (I_2)(1 eq., 1.77 g, 7 mmol) in glacial acetic acid (10 ml), *p*-toluic acid (0.95 g, 7 mmol) was added and stirred at room temperature for 3 h. The mixture was heated to 70 °C within 20 min and stirred at this temperature for 5 h. After the reaction was completed, it was cooled to the room temperature. Iodine excess was filtered and the solution was extracted with dichloromethane. The organic phase was washed with sodium thiosulfate ($Na_2S_2O_3$) and dried over anhydrous sodium sulfate (Na_2SO_4). After evaporation of the solvent, white solid of the product was crystallized from mixture of dichloromethane and hexane to give 3-iodo-4-methylbenzoic acid as white crystal (75%):

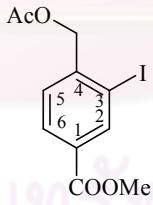
^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.53 (1H, s, H-2), 7.97 (1H, d, J = 7.9 Hz, H-6), 7.33 (1H, d, J = 7.9 Hz, H-5), 2.50 (4H, s, H-Me)

^{13}C NMR (101 MHz, $CDCl_3$): δ_C 170.03 (C=O), 148.04 (C-1), 140.80 (C-2), 130.03 (C-6), 129.79 (C-3), 128.48 (C-5), 100.68 (C-4), 28.64 (C-Me)

IR (KBr)υ_{max}: 3431, 1668, 1426, 1375, 1307, 1258, 534 cm^{-1}.

HRMS (ESI-TOF) *m/z* 261.9485 $[M+H]^+$ calcd for $C_8H_7O_2I$ 262.04.

3.7.2 Synthesis of 3-iodo-4-(acetoxymethyl)benzoate



3-iodo-4-(acetoxymethyl)benzoate

3-Iodo-4-methylbenzoic acid was oxidized using NaOCl and $NaIO_4$ as oxidizing agent and using LiBr and KBr as halogen sources. The reaction mixture was heated at temperature 65-110 °C (using an oil bath) for 6-24 h in acetic acid. NaOCl was added after the reaction mixture was heated to this temperature (65-110 °C) for the case that using NaOCl as an oxidizing agent. The reaction mixture was diluted with water and extracted with DCM. Organic phase was washed with sodium bicarbonate ($NaHCO_3$) solution and dried with sodium sulfate (Na_2SO_4). It was evaporated with vacuum evaporator.

3.7.2.1 Study on the optimum conditions for the oxidation reaction of 3-iodo-4-methylbenzoic acid

To optimize the condition for oxidation of 3-iodo-4-methylbenzoic acid in acetic acid was studied. The yield of all products was analyzed by 300 MHz ^{1}H NMR spectroscopy.

1) Effect of reaction temperature

The oxidation was carried out as described in the general procedure, but the reaction temperature was varied (80, 95, and 110 °C).

2) Effect of reaction time

The oxidation was carried out as described in the general procedure, but the reaction time was varied (8, 12 and 24 h).

3) Effect of halogen source

The oxidation was carried out as described in the general procedure, but the halogen source was varied; lithium bromide (LiBr), and potassium bromide (KBr).

4) Effect of mole equivalent of sodium hypochlorire

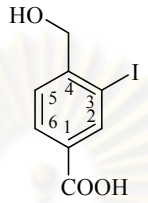
The oxidation was carried out as described in the general procedure, but the mole equivalent of the oxidizing agent was varied (0.5, 1 eq.).

Since isolation of 3-iodo-4-hydroxymethylbenzoic acid and 3-iodo-4-acetoxymethylbenzoic acid from the oxidation of 3-iodo-4-mehylbenzoic acid was unsuccessful, compounds in methyl ester from were easy to be isolated by silica gel column chromatography. After oxidation of 3-iodo-4-benzoic acid, the reaction mixture was treated with a solution of diazomethane (CH_2N_2) in Et_2O at room temperature and the process of the reaction was monitored by TLC. After the reaction was completed, the solvent was evaporated. A residue was extracted and subjected to silica gel column chromatography eluting with 50% dichloromethane: hexane to give 3-Iodo-4-(acetoxymethyl)benzoate as white crystal in quantitative yield:

^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.50 (1H, s, H-2), 8.01 (1H, d, J = 8.0 Hz, H-6), 7.43 (1H, d, J = 8.0 Hz, H-5), 5.14 (2H, s, H-CH_2), 3.92 (3H, s, H-Ac), 2.17 (3H, s, H-Me)

^{13}C NMR (101 MHz, $CDCl_3$): δ_C 170.82 (C=O), 165.72 (C=O), 143.60 (C-1), 140.89 (C-2), 131.76 (C-6), 129.86 (C-3), 128.93 (C-5), 97.42 (C-4), 70.05 (C-Ac), 52.89 (C-Me), 21.29 (C-CH_2); IR (KBr)υ_{max}: 3454, 1694, 1636, 1429, 1387, 1287, 1256, 1203, 534 cm^{-1}.

3.7.3 Synthesis of 3-iodo-4-(hydroxymethyl)benzoic acid



3-iodo-4-(hydroxymethyl)benzoic acid

3-Iodo-4-(acetoxymethyl)benzoate and 3-iodo-4-(hydroxymethyl)benzoate were hydrolyzed by a solution of sodium hydroxide solution in methanol by stirring at room temperature for 12 h. After the reaction was completed, the mixture was extracted with dichloromethane and dried over anhydrous sodium sulfate. The organic phase was evaporated to give white crystal of 3-iodo-4-(hydroxymethyl)benzoic acid in quantitative yield:

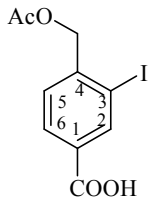
^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.39 (1H, s, H-2), 7.96 (1H, d, J = 8.0 Hz, H-6), 7.50 (1H, d, J = 8.0 Hz, H-5), 4.57 (2H, s, H-CH_2)

^{13}C NMR (101 MHz, $CDCl_3$): δ_C 167.00 (C=O), 147.95 (C-1), 140.23 (C-2), 131.00 (C-6), 129.57 (C-3), 127.48 (C-5), 95.34 (C-4), 68.66 (C-CH_2)

IR (KBr)υ_{max}: 3434, 1701, 1416, 1203, 534 cm^{-1}.

HRMS (ESI-TOF) *m/z* 277.9442 $[M+H]^+$ calcd for $C_8H_7O_3I$ 278.04.

3.7.4 Synthesis of 3-iodo-4-(acetoxymethyl)benzoic acid



3-iodo-4-(acetoxymethyl)benzoic acid

3-Iodo-4-(hydroxymethyl)benzoic acid was acetylated with acetic anhydride in a presence of conc. sulfuric acid (H_2SO_4). The reaction mixture was refluxed at 80 °C for 5 h and then extracted with dichloromethane. The organic phase was dried over anhydrous sodium sulfate and evaporated to give a residue. The residue was subjected to silica gel column chromatography eluting with 50% dichloromethane and hexane to give 3-iodo-4-(acetoxymethyl)benzoic acid as white crystal in quantitative yield:

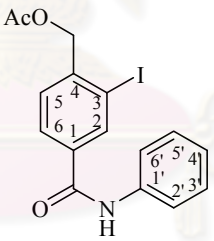
^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.57 (1H, s, H-2), 8.08 (1H, d, J = 8.9 Hz, H-6), 7.47 (1H, d, J = 8.0 Hz, H-5), 5.16 (2H, s, CH_2-OAc), 2.19 (3H, s, CH_3CO-)

^{13}C NMR (101 MHz, $CDCl_3$): δ_C 170.42 (C=O), 169.43 (C=O), 143.76 (C-1), 140.65 (C-2), 130.67 (C-6), 129.91 (C-3), 128.54 (C-5), 97.01 (C-4), 69.67 (CH_2-OAc), 20.84 (CH_3CO-)

IR (KBr)υ_{max}: 3444, 1703, 1694, 1423, 1371, 1294, 1252, 1232, 496 cm^{-1}.

HRMS (ESI-TOF) *m/z* 319.9542 $[M+H]^+$ calcd for $C_8H_7O_2I$ 320.08.

3.7.5 Synthesis of N-phenyl-3-iodo-4-(acetoxymethyl)benzoic acid



N-phenyl-3-iodo-4-(acetoxymethyl)benzoic acid

3-Iodo-4-(acetoxymethyl)benzoic acid was treated with oxalyl chloride in small amount of DMF in dried DCM. The reaction mixture was stirred at room temperature for 1 h under argon. After evaporation of the solvent, a residue was dissolved in dried THF and aniline was then added. This reaction was stirred at room temperature and the progress of the reaction was monitored by TLC. After 6 h, pH of the reaction mixture was adjusted to acidic condition by aqueous hydrochloric acid (1%) and extracted with dichloromethane. Evaporation of the organic solvent afforded N-phenyl-3-iodo-4-(acetoxymethyl)benzoic acid as brown crystal (85%):

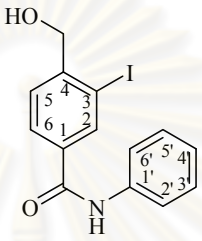
^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.32 (1H, s, H-2), 7.90 (1H, s, H-N), 7.83 (1H, d, J = 8.0 Hz, H-6), 7.63 (2H, d, J = 7.9 Hz, H-2', 6'), 7.45 (1H, d, J = 8.0 Hz, H-

5), 7.37 (2H, t, *J* = 7.9 Hz, H-3', 5'), 7.17 (1H, t, *J* = 7.4 Hz, H-4'), 5.15 (2H, s, CH_2-OAc), 2.18 (3H, s, CH_3CO-)

^{13}C NMR (101 MHz, $CDCl_3$): δ_C 170.46, 163.73, 142.07, 138.02, 137.58, 136.24, 129.15, 128.91, 126.94, 124.92, 120.34, 97.70, 69.32, 20.86

IR (KBr)υ_{max}: 3445, 3305, 1731, 1642, 1592, 1529, 1436, 1323, 1243, 532 cm^{-1}.

3.7.6 Synthesis of N-phenyl-3-iodo-4-(hydroxymethyl)benzoic acid



N-phenyl-3-iodo-4-(hydroxymethyl)benzoic acid

N-Phenyl-3-iodo-4-(acetoxymethyl)benzoic acid was hydrolyzed with potassium hydroxide in the solution mixture of methanol and water (1:1). The reaction mixture was heated at 50 °C and the progress of the reaction was monitored by TLC. After 4h the reaction mixture was extracted with dichloromethane and dried over anhydrous sodium sulfate. The organic solvent was evaporated in vacuo to afford N-phenyl-3-iodo-4-(acetoxymethyl)benzoic acid as brown crystal in quantitative yield:

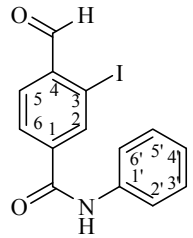
^1H NMR (400 MHz, $CDCl_3$): δ_H 8.92 (1H, s, H-2), 8.22 (1H, s, H-N), 7.77 (1H, d, *J* = 8.0 Hz, H-6), 7.61 (2H, d, *J* = 7.9 Hz, H-2', 6'), 7.47 (1H, d, *J* = 8.0 Hz, H-5), 7.31 (2H, t, *J* = 7.9 Hz, H-3', 5'), 7.11 (1H, t, *J* = 7.4 Hz, H-4'), 4.56 (2H, s, CH_2-OH)

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C 164.89, 146.74, 137.84, 137.76, 135.32, 129.23, 128.95, 127.38, 127.07, 124.71, 120.61, 96.24, 68.41, 29.64

IR (KBr)υ_{max}: 3438, 3324, 1649, 1601, 1542, 1491, 1436, 1323, 1239, 508 cm^{-1}.

HRMS (ESI-TOF) *m/z* 352.9910 $[M+H]^+$ calcd for $C_8H_7O_2I$ 353.16.

3.7.7 Synthesis of N-phenyl-3-iodo-4-(formyl)benzoic acid



N-phenyl-3-iodo-4-(formyl)benzoic acid

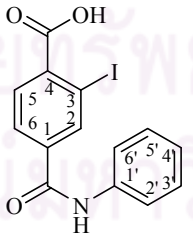
N-Phenyl-3-iodo-4-(acetoxymethyl)benzoic acid was oxidized with pyridinium chloro chromate (PCC) in dried DCM. The reaction mixture was stirred over 3 h at room temperature and monitored by TLC. After the reaction was completed, it was filtered through silica gel 60 and washed with diethyl ether. The organic phase was evaporated to afford N-phenyl-3-iodo-4-(formyl)benzoic acid as brown crystal in quantitative yield:

^{1}H NMR (400 MHz, $CDCl_3$): δ_H 10.11 (1H, s), 8.43 (1H, s, H-N), 7.94 (1H, d, J = 8.0 Hz, H-6), 7.90 (2H, d, J = 8.0 Hz, H-2', 6'), 7.63 (1H, d, J = 7.9 Hz, H-5), 7.39 (2H, t, J = 7.9 Hz, H-3', 5'), 7.20 (1H, t, J = 7.4 Hz, H-4')

^{13}C NMR (101 MHz, $CDCl_3$): δ_C 194.87, 140.96, 139.44, 137.24, 130.37, 129.24, 127.03, 125.31, 120.44, 100.34

IR (KBr)υ_{max}: 3441, 3309, 1688, 1646, 1533, 1442, 1323, 508 cm^{-1}.

3.7.8 Synthesis of N-phenyl-3-iodo-4-(carbonyl)benzoic acid



N-Phenyl-3-iodo-4-(carbonyl)benzoic acid

N-Phenyl-3-iodo-4-(formyl)benzoic acid was added to the mixture of sodium hydroxide (NaOH) and silver oxide (Ag_2O) in DI water. The reaction was heated at 60 °C for 20 min. The reaction mixture was filtered and washed with hot water. The filtrate was poured into 1:1 hydrochloric acid solution with vigorous stirring. The reaction mixture was cooled to 20°C in an ice-bath and N-phenyl-3-iodo-4-(carbonyl)benzoic acid was crystallized. The

crystals were filtered and washed with ice water to give the title compound as white crystal (80%)

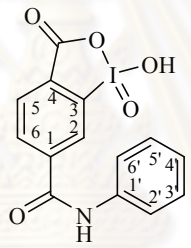
^{1}H NMR (400 MHz, CD_3OD): δ_H 8.52 (1H, s, NH), 7.98 (1H, d, *J* = 9.6 Hz, H-6), 7.88 (1H, d, *J* = 8.0 Hz, H-5), 7.69 (2H, d, *J* = 7.7 Hz, H-2', 6'), 7.37 (2H, t, *J* = 8.0 Hz, H-3', 5'), 7.16 (1H, t, *J* = 7.4 Hz, H-4')

^{13}C NMR (101 MHz, MeOD): δ_C 169.70, 166.29, 141.17, 140.97, 139.64, 139.56, 131.32, 129.87, 128.20, 125.95, 122.45, 122.30, 93.93

IR (KBr)υ_{max}: 3438, 3292, 1694, 1639, 1529, 1446, 491 cm^{-1}.

HRMS (ESI-TOF) *m/z* 367.9781 $[M+H]^+$ calcd for $C_8H_7O_2I$ 367.14.

3.7.9 Synthesis of N-phenyl-3-iodoxybenzoic acid (5)



N-Phenyl-2-iodoxybenzoic acid (**5**)

N-Phenyl-3-iodo-4-(carbonyl)benzoic acid was added to the solution of oxone in DI water. The reaction was stirred at room temperature about 30 minutes and then the reaction was warmed to 70-75 °C within 20 minutes. The reaction was stirred at this temperature for 3 h. When the reaction was completed, it was cooled to 5 °C in an ice-bath by slow stirring and kept at this temperature for 1.5 h. The reaction mixture was filtered and washed with cool water to give N-phenyl-2-iodoxybenzoic acid as white crystal (75%):

^{1}H-NMR (400 MHz, MeOD): δ_H 8.45 (1H, s, N-H), 8.26 (1H, s, H-2), 7.79 (1H, d, *J* = 7.5 Hz, H-6), 7.57 (2H, d, *J* = 7.9 Hz, H-2', 6'), 7.35 (1H, d, *J* = 9.3 Hz, H-5), 7.26 (2H, t, *J* = 7.8 Hz, H-3', 5'), 7.06 (1H, t, *J* = 5.9 Hz, H-4')

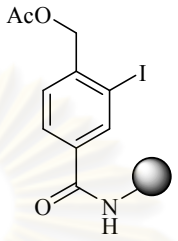
^{13}C NMR (101 MHz, MeOD): δ_C 180.37, 139.57, 129.83, 128.05, 125.78, 122.42, 73.86, 64.42, 33.06, 30.74, 30.45, 24.20

IR (KBr)υ_{max}: 3434, 1639, 1562, 1410, 1381, 489 cm^{-1}.

HRMS (ESI-TOF) *m/z* 399.31 $[M+H]^+$ calcd for $C_8H_7O_2I$ 399.14.

3.8 Synthesis of aminomethyl polymer-supported IBX amide (**6**)

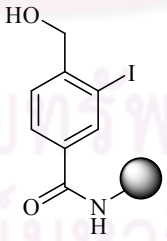
3.8.1 Preparation of polymer-supported 3-iodo-4(acetoxymethyl)benzoic acid



Polymer-supported 3-iodo-4-(acetoxymethyl)benzoic acid

3-Iodo-4-(acetoxymethyl)benzoic acid was treated with oxalyl chloride in small amount of DMF in dried DCM. The reaction mixture was stirred at room temperature for 1 h under argon. After evaporation of the solvent, a residue was dissolved in dried THF and aminomethyl polystyrene was then added. This reaction was stirred at room temperature. After 6 h, pH of the reaction mixture was adjusted to acidic condition by aqueous hydrochloric acid (1%). The polymer was filtered and washed with DCM to afford polymer-supported 3-iodo-4-(acetoxymethyl)benzoic acid.

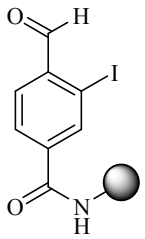
3.8.2 Preparation of polymer-supported 3-iodo-4-(hydroxymethyl)benzoic acid



Polymer-supported 3-iodo-4-(hydroxymethyl)benzoic acid

Polymer-supported 3-iodo-4-(acetoxymethyl)benzoic acid was pre-swollen in DCM about 3 h and then the solution of potassium hydroxide in DI water was added. The reaction was heated to 50 °C. After 4 h the reaction was filtered and washed with dichloromethane to afford polymer-supported 3-iodo-4-(acetoxymethyl)benzoic acid.

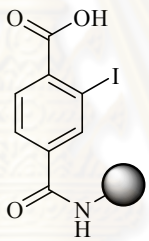
3.8.3 Preparation of polymer-supported 3-iodo-4-(formyl)benzoic acid



Polymer-supported 3-iodo-4-(formyl)benzoic acid

Polymer-supported 3-iodo-4-(acetoxymethyl)benzoic acid was pre-swollen in DCM about 3 h and then pyridinium chloro chromate (PCC) was added. The reaction was stirred over 3 h at room temperature. The reaction was filtered and washed with DCM to afford polymer-supported 3-iodo-4-(formyl)benzoic acid.

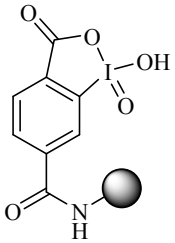
3.8.4 Preparation of polymer-supported 3-iodo-4-(carbonyl)benzoic acid



Polymer-supported 3-iodo-4-(carbonyl)benzoic acid

Polymer-supported 3-iodo-4-(formyl)benzoic acid was pre-swollen in DCM about 3 h. Silver oxide (Ag_2O) and the solution of sodium hydroxide (NaOH) in DI water were added to the reaction and heated to 60°C for 3 h. The reaction was filtered and washed with hot water. The polymer was poured into 1:1 hydrochloric acid solution with vigorous stirring. The reaction was cooled to 20°C in an ice-bath. The polymer was filtered and washed with ice water to give polymer-supported 3-iodo-4-(carbonyl)benzoic acid.

3.8.5 Preparation of aminomethyl polymer-supported IBX amide (**6**)



Aminomethyl polymer-supported IBX amide (**6**)

Polymer-supported 3-iodo-4-(carbonyl)benzoic acid was pre-swollen in DCM about 3 h. The solution of oxone in DI water was added to the reaction. The reaction was stirred at room temperature about 30 minutes and warmed to 70-75 °C within 20 minutes. The reaction was stirred at this temperature for 3 h. Then the reaction was cooled to 5 °C in an ice-bath by slow stirring and kept at this temperature for 1.5 h. The reaction was filtered and washed with cool water to give aminomethyl polymer-supported IBX amide (**6**).

3.9 Oxidation of benzyl alcohol and glycerol with oxidizing agents (1) to (6)

3.9.1 Oxidation of benzyl alcohol with IBX (1), DMP (2), 2-iodoxy-N-phenylbenzamide (4) or 2-iodoxy-4-(phenylcarbanoyl)benzoic acid (5)

Benzyl alcohol was added to the reaction mixture of oxidizing agent (IBX (**1**), DMP (**2**), 2-iodoxy-N-phenylbenzamide (**4**) or 2-iodoxy-4-(phenylcarbanoyl)benzoic acid (**5**)) in DMSO. The reaction was stirred at room temperature for 24 h. DI water was added to stop the reaction and appeared the white crystal of oxidizing agent. The crystal was filtered and washed with DCM. Filtrate was extracted with DCM. The organic phase was evaporated to give the mixture of benzyl alcohol substrate and benzaldehyde as product. The product was examined by ^{1}H-NMR spectroscopy.

3.9.2 Oxidation of benzyl alcohol with aminomethyl polystyrene-supported IBX amide (3) or aminomethyl polymersupported IBX amide (6)

Benzyl alcohol was added to the reaction mixture of oxidizing agent (aminomethyl polystyrene-supported IBX amide (**3**) or aminomethyl polymersupported IBX amide (**6**)) in DCM. The reaction was stirred at room temperature for 24 h. The polymer was filtered and washed with DCM. The filtrate was evaporated to give the mixture of benzyl alcohol substrate and benzaldehyde as product. The product was examined by ^{1}H-NMR spectroscopy.

3.9.3 Oxidation of glycerol with IBX (1), DMP (2), aminomethyl polystyrene-supported IBX amide (3), 2-iodoxy-N-phenylbenzamide (4), 2-iodoxy-4-(phenylcarbanoyl)benzoic acid (5) or aminomethyl polymersupported IBX amide (6)

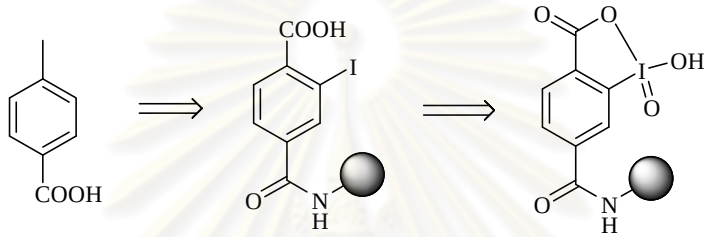
Glycerol was added to the reaction mixture of oxidizing agent (IBX (**1**), DMP (**2)**, aminomethyl polystyrene-supported IBX amide (**3**), 2-iodoxy-N-phenylbenzamide (**4**), 2-iodoxy-4-(phenylcarbanoyl)benzoic acid (**5**) or aminomethyl polymersupported IBX amide (**6**)) in MeCN:H_2O (2:1). The reaction was heated at 70 °C for 5 h. DI water was added to stop the reaction and appeared the white crystal of oxidizing agent. The crystal was filtered and washed with water. Aqueous phase was evaporated to give the mixture of product. The product was examined by ^{1}H-NMR spectroscopy.

CHAPTER IV

RESULTS AND DISCUSSION

4.1 Processes for synthesis of oxidizing agent

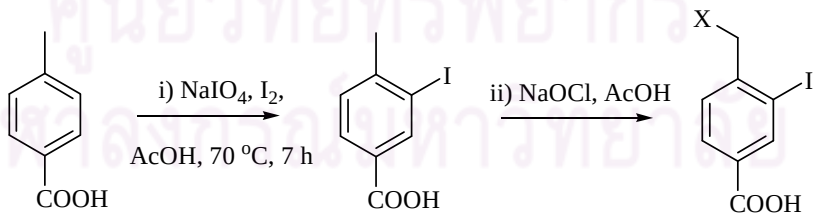
The new polymer-supported IBX was prepared in this research by using *p*-toluic acid as a starting material for IBX and aminomethyl polystyrene as a supporting material (scheme 4.1).



p-toluic acid (**7**) (**8**) (**6**)

Scheme 4.1 Processes for synthesis of new polymer-supported IBX

This process was started with iodination of *p*-toluic acid using sodium periodate and iodine in a mixture of acetic acid, conc. sulfuric acid and dichloromethane at 70 °C for about 7 h. The reaction mixture was recrystallized from dichloromethane/hexane to afford 3-iodo-4-methylbenzoic acid (**9**). Oxidation of C-H bond of 3-iodo-4-methylbenzoic acid (**9**) was performed using $NaIO_4$ as an oxidizing agent to give 3-iodo-4-(acetoxymethyl)benzoic acid (**11**) in poor yield (see in table 4.1 entry 1-2).



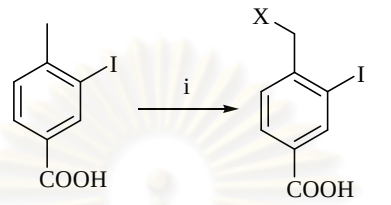
(7) **(9)** **(10)** X = OH **(11)** X = OAc

Scheme 4.2 Processes for oxidation of 3-iodo-4-methylbenzoic acid (**9**)

The oxidation of 3-iodo-4-methylbenzoic acid (**9**) to 3-iodo-4-(acetoxymethyl)benzoic acid (**11**) was studied by using sodium hypochlorite (NaOCl) as an oxidizing agent The reactions were carried out in acid condition. It was found that the reaction using NaOCl as an

oxidizing provided higher yield than using $NaIO_4$ as an oxidizing agent. We also studied the effect of temperature, reaction time and halide sources on the oxidative of C-H bond. The results were shown in table 4.1.

Table 4.1 NaOCl-mediated oxidative bromination and acetoxylation of 3-iodo-4-methylbenzoic acid[a]



(10) X = OAc

(11) X = OH

Entry	Metal halide (mol eq.)	Temp. (°C)	Time (h)	Oxidizing agent (mol eq.)		Yield[b] (%)	
				NaOCl	$NaIO_4$	(**10**)	(**11**)
1	LiBr (1)	80	24	1	-	11	1
2	LiBr (1)	80	24	-	1	4	1
3	LiBr (1)	95	24	1	-	56	9
4	KBr (1)	95	24	1	-	48	5
5	LiBr (1)	95	24	0.5	-	69	11
6	LiBr (1)	95	6	1	-	24	1
7	LiBr (1)	95	12	1	-	28	1
8	LiBr (1)	110	24	-	1	6	1
9	KBr (1)	110	24	-	1	8	2
10	KBr (5)	110	8	2.5	-	10	1
11	LiBr (5)	110	8	2.5	-	14	-
12	KBr (5)	110	8	-	2.5	16	1
13	KBr (10)	95	8	1	-	29	-

[a] Condition: substrate (0.1 mmol), glacial acetic acid (10mL).

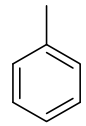
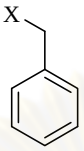
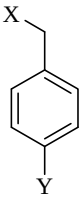
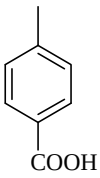
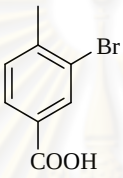
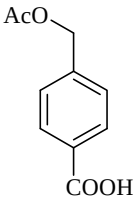
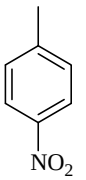
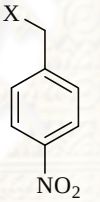
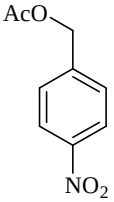
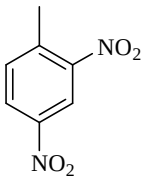
[b] The yield of all products were analyzed by ^{1}H-NMR.

The yields of this reaction were found to be high in the case that heating at 95 °C (entry 1,3). Percentage yield of 3-iodo-4-(acetoxymethyl)benzoic acid (**10**) was increased when increasing the reaction time (entry 3,6,7). In comparison between lithium bromide (LiBr) and potassium bromide (KBr) as halogen source, the reaction using LiBr as halogen sources gave better yield of 3-iodo-4-(acetoxymethyl)benzoic acid (**10**) than the reaction using KBr (entry 3,4). Surprising, this reaction using 3-iodo-4-methylbenzoic acid as substrate and NaOCl as oxidizing agent was found to be higher yield than the reaction using $NaIO_4$ as oxidant at the same mole equivalent of oxidant (entry 1,2). The reaction using NaOCl (0.5 mol eq.) and LiBr (1 mol eq.) was critical in achieving high levels of the conversion of the 3-iodo-4-methylbenzoic acid at 95 °C for 24 h (entry 5).

Moreover, NaOCl and $NaIO_4$ were used as oxidizing agent in oxidative bromination and acetoxylation of toluene, *p*-toluic acid, *p*-toluenesulfonic acid, *p*-nitrotoluene and dinitrotoluene. LiBr was used as the halogen source by reflux at 95 °C for 24 h in acetic acid. The results were shown in table 4.2.

Toluene was oxidized by NaOCl to benzyl alcohol and benzyl acetate in 32 and 23 %yield, respectively while toluene was oxidized by $NaIO_4$ to benzyl acetate and 4-bromotoluene in 10 and 56 %yield, respectively. Oxidation of *p*-toluic acid with NaOCl gave 3-bromo-4-methylbenzoic acid as a product in good yield and did not give other by-product in the reaction. For oxidation of *p*-toluic acid with $NaIO_4$ was obtained 4-hydroxymethyl benzoic acid as a major product. Oxidation of *p*-nitrotoluene with NaOCl gave *p*-nitrobenzyl alcohol and *p*-nitrobenzyl acetate as products. Oxidation of *p*-nitrotoluene with $NaIO_4$ as an oxidizing agent was gave *p*-nitrobenzyl acetate as a product in excellent yield. Moreover, dinitrotoluene was not oxidized by NaOCl and $NaIO_4$.

Table 4.2 Results of oxidative bromination and acetoxylation with NaOCl and $NaIO_4$[a]

substrates	Oxidizing agent (% yield)[b]	
	NaOCl	$NaIO_4$
	 P_1 (X = OH) 32 % P_2 (X = OAc) 23 %	 P_1 (X = OAc, Y = H) 10 % P_2 (X = H, Y = Br) 56 %
	 63 %	 37 %
	 P_1 (X = OH) 76 % P_2 (X = OAc) 23 %	 95 %
	No reaction	No reaction

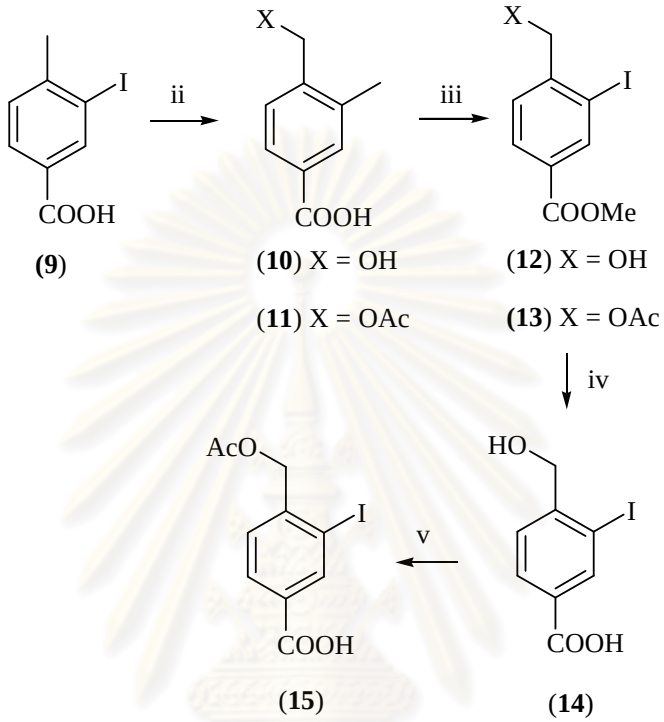
[a] Condition; substrate:oxidant (1:1), 95 °C, 24 h, AcOH

[b] The yield of all products were analyzed by ^{1}H-NMR.

In conclusion the oxidative bromination of alkylbenzoic acid to the corresponding carboxylic acids in good yields was obtained by using NaOCl/LiBr/95 °C/24 h/ AcOH. In comparison of sodium periodate ($NaIO_4$) and sodium hypochlorite (NaOCl), the reaction of alkylbenzoic acid using NaOCl as an oxidizing agent provided higher yield than using $NaIO_4$ as an oxidizing agent.

Isolation of (**10**) and (**11**) from the oxidation of 3-iodo-4-mehylbenzoic acid was unsuccessful. Their methyl ester (**12**) and (**13**) were easy to isolate by silica gel column chromatography. Treatment of (**10**) and (**11**) with diazomethane (CH_2N_2) followed by column

chromatography gave (**12**) and (**13**). Compound (**14**) was prepared by hydrolysis of the mixture of (**12**) and (**13**) with aqueous NaOH in MeOH. 3-Iodo-4-(hydroxymethyl)benzoic acid was acetylated with acetic anhydride in a presence of conc. sulfuric acid to give 3-iodo-4-(acetoxymethyl)benzoic acid (**15**).



Scheme 4.3 Processes for synthesis of 3-iodo-4-(acetoxymethyl)benzoic acid (**15**)

ii) NaOCl, KBr, AcOH, reflux, 110 °C, 8h

iii) Diazomethane, ether, stir, rt. 3h

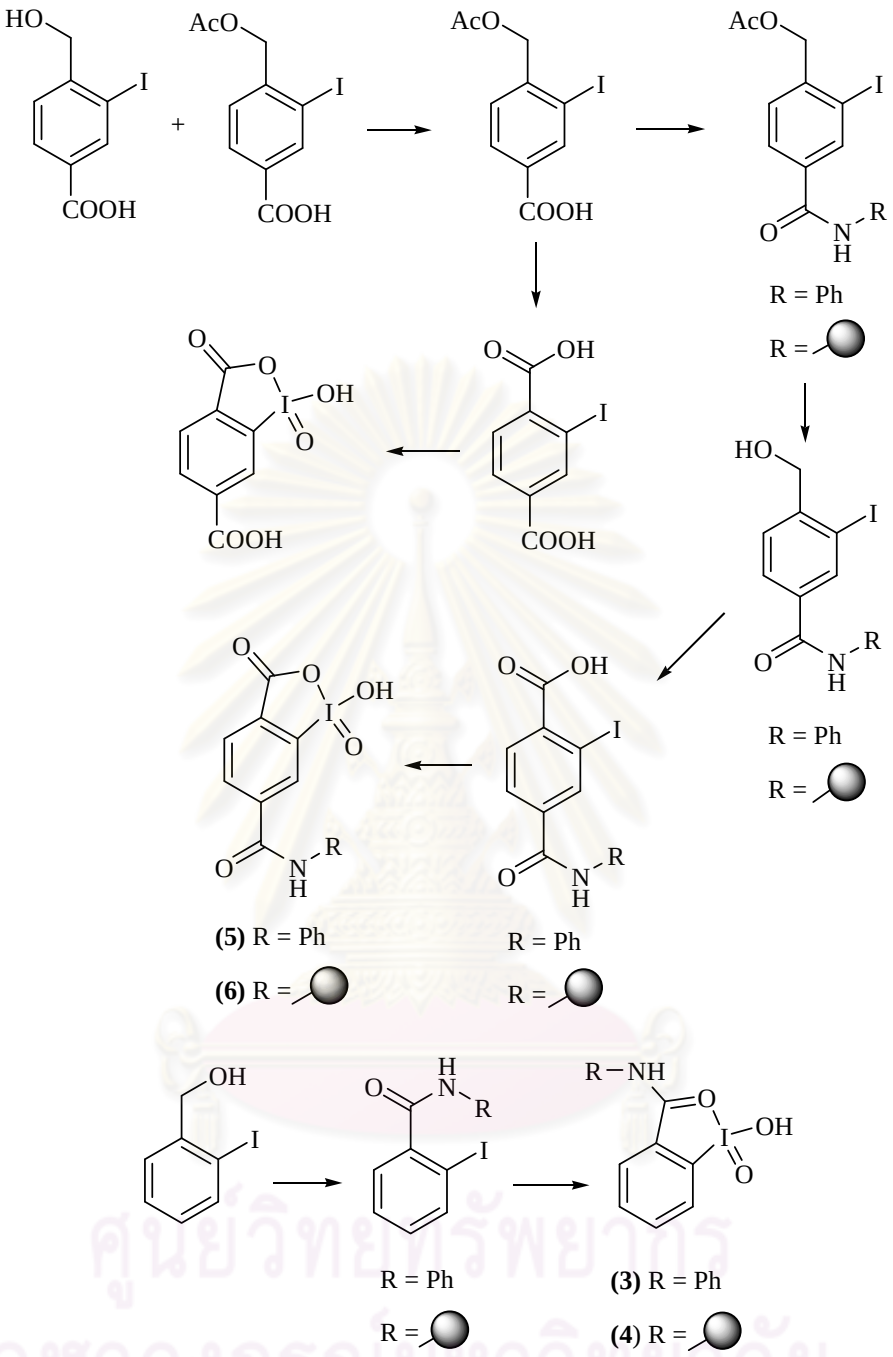
iv) NaOH, MeOH, stir, rt.

v) Ac_2O, H_2SO_4, reflux, 80°C, 5h

Compound (**15**) was used as starting material for preparation of IBX compound (**5**) and polymer-supported IBX (**6**) (see scheme 4.4). 3-Iodo-4-(acetoxymethyl)benzoic acid (**15**) was treated with oxalyl chloride and small amount of DMF in dried DCM. The reaction was stirred at room temperature for 1 h under argon. After evaporation of the solvent, a residue was reacted with aniline in dried THF at room temperature for 2 h to afford N-phenyl-3-iodo-4-(acetoxymethyl)benzoic acid. N-phenyl-3-iodo-4-(acetoxymethyl)benzoic acid was hydrolyzed with aqueous potassium hydroxide in methanol at 50 °C for 4 h. The reaction mixture was extracted with dichloromethane and dried over anhydrous sodium sulfate. The organic phase was evaporated in vacuo to give N-phenyl-3-iodo-4-(hydroxymethyl)benzoic acid. It was oxidized with pyridinium chlorochromate (PCC) in dried DCM at room

temperature for about 3 h. The product was filtered through silica gel and washed with diethyl ether. The organic phase was dried over anhydrous Na_2SO_4. After filtration and evaporation, 3-iodo-4-(formyl)-N-phenylbenzamide was obtained. 3-Iodo-4-(formyl)-N-phenylbenzamide was oxidized with silver oxide (Ag_2O) in the solution of sodium hydroxide (NaOH) at 60°C for 30 min. The reaction mixture was filtered and washed with hot water. The filtrate was poured onto hydrochloric acid: DI water (1:1) with vigorous stirring and then cooled to 20°C in an ice-bath. N-Phenyl-3-iodo-4-(carbonyl)benzoic acid was crystallized. The white crystals were filtered and washed with ice water. N-Phenyl-3-iodo-4-(carbonyl)benzoic acid was oxidized with oxone in DI water at 70 °C for 3 h and then cooled to 5 °C in an ice-bath. The solid was filtered and washed with cool water to afford N-phenyl-3-iodoxybenzoic acid (**5**). For synthesis of aminomethyl polymer-supported IBX amide (**6**) aminomethyl polystyrene polymer was used instead of aniline.

Processes for synthesis of aminomethyl polystyrene-supported IBX amide (**3**), 2-iodoxy-N-phenylbenzamide (**4**), N-phenyl-3-iodoxybenzoic acid (**5**) and aminomethyl polymer-supported IBX amide (**6**) were shown in scheme 4.4.



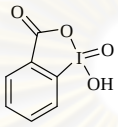
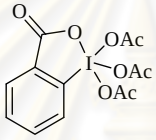
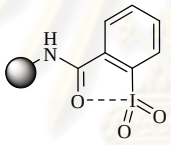
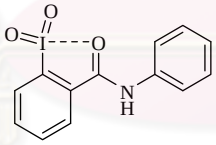
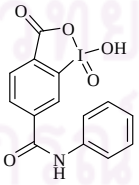
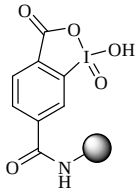
Scheme 4.4 Processes for synthesis oxidizing agent (**3-6**)

4.2 Oxidation of benzyl alcohol and glycerol with oxidizing agent (**1**) to (**6**)

IBX (**1**), DMP (**2**), aminomethyl polystyrene-supported IBX amide (**3**), 2-iodoxy-N-phenylbenzamide (**4**), 2-iodoxy-4-(phenylcarbanoyl)benzoic acid (**5**) and aminomethyl polymer-supported IBX amide (**6**) were used as the oxidizing agents in the oxidation of benzyl alcohol and glycerol.

Benzyl alcohol was oxidized with those oxidants at room temperature for 24 h to afford benzaldehyde and it was monitored by ^{1}H NMR to measure the percentage yield (Table 4.3).

Table 4.3 Results from oxidation of benzyl alcohol using oxidants (**1**-**6**) [a]

Entry	oxidant	solvent	Benzaldehyde (% yield) [b]
1	IBX (**1**) 	DMSO	92
2	DMP (**2**) 	DMSO	98
3	aminomethyl polystyrene-supported IBX amide (**3**) 	DCM	9.9 %
4	2-iodoxy-N-phenylbenzamide (**4**) 	DMSO	No reaction
5	2-iodoxy-4-(phenylcarbanoyl)benzoic acid (**5**) 	DMSO	No reaction
6	aminomethyl polymersupported IBX amide (**6**) 	DCM	1.9 %

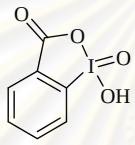
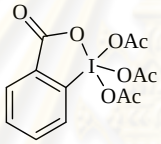
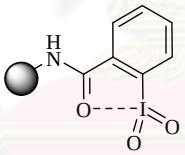
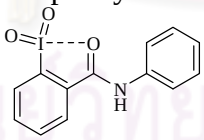
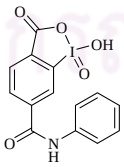
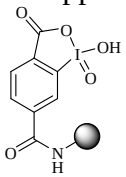
[a]All reactions were performed at 25 °C for 24 h.

[b]The reaction product was determined by ^{1}H NMR spectroscopy.

IBX (**1**), DMP (**2**), aminomethyl polystyrene-supported IBX amide (**3**) and aminomethyl polymer-supported IBX amide (**6**) were used in oxidation of benzyl alcohol. Aminomethyl polymer-supported IBX amide (**3**) and (**6**) could oxidize benzyl alcohol to benzaldehyde in poor yield because they had low loading of amino group (0.1 mmol/g).

Glycerol was oxidized with these oxidants at 70 °C for 5 h. The product from oxidation was monitored by ^{1}H NMR to measure the conversion of the reaction. (Table 4.4)

Table 4.4 Results of glycerol oxidation using all oxidants [a]

Entry	oxidant	solvent	Conversion (%) [b]
1	IBX (**1**) 	MeCN:H_2O (2:1)	No reaction
2	DMP (**2**) 	MeCN:H_2O (2:1)	No reaction
3	aminomethyl polystyrene-supported IBX amide (**3**) 	MeCN:H_2O (2:1)	No reaction
4	2-iodoxy-N-phenylbenzamide (**4**) 	MeCN:H_2O (2:1)	No reaction
5	2-iodoxy-4-(phenylcarbanoyl)benzoic acid (**5**) 	MeCN:H_2O (2:1)	No reaction
6	aminomethyl polymer-supported IBX amide (**6**) 	MeCN:H_2O (2:1)	No reaction

[a]All reactions were performed at 70 °C for 5 h.

[b]The reaction product was determined by ^{1}H NMR spectroscopy.

Glycerol was not oxidized by all oxidizing agents (**1-6**). Because aminomethyl polystyrene could not be swollen in MeCN:H_2O.

CHAPTER V

CONCLUSION

The new polymer-supported IBX was prepared in this research using *p*-toluic acid as a starting material for IBX and aminomethyl polystyrene as supporting material. The appropriate method for synthesis of aminomethyl polymer-supported IBX amine (**6**) consisted of 8 steps. *p*-Toluic acid was iodinated with iodine and sodium periodate in acetic acid to afford 3-iodo-4-methylbenzoic acid. A new process for oxidation of C-H bond of 3-iodo-4-methylbenzoic acid was discovered. It was found that the use of sodium hypochlorite (NaOCl) as an oxidant for the oxidation of such acid gave higher conversion than using sodium periodate ($NaIO_4$) as an oxidant. We suggested that the oxidation of alkylbenzoic acid using NaOCl/LiBr/95 °C/24 h/AcOH was an easy procedure which gave the corresponding carboxylic acids in good yields. The polymer-supported IBX amide (**6**) was compared with IBX (**1**), DMP (**2**), aminomethyl polymer-supported IBX amide (**3**), N-phenyl-2-iodoxybenzamide (**4**), and N-phenyl-3-iodoxybenzoic acid (**5**) in oxidation of benzyl alcohol and glycerol. Benzyl alcohol could be oxidized with IBX (**1**), DMP (**2**), aminomethyl polystyrene-supported IBX amide (**3**) and aminomethyl polymer-supported IBX amide (**6**) while glycerol could not be oxidized by those oxidizing agents.

Suggestion for future work

1) Study the oxidation of 3-bromo-4-methylbenzoic acid, 2-iodobenzoic acid and 4-iodobenzoic acid by using NaOCl as oxidizing agent and LiBr as the halogen source in acetic acid at 95 °C for 24 h.
2) Study the oxidation of glycerol by using IBX as oxidizing agent in THF or THF/H_2O.

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APPENDIX

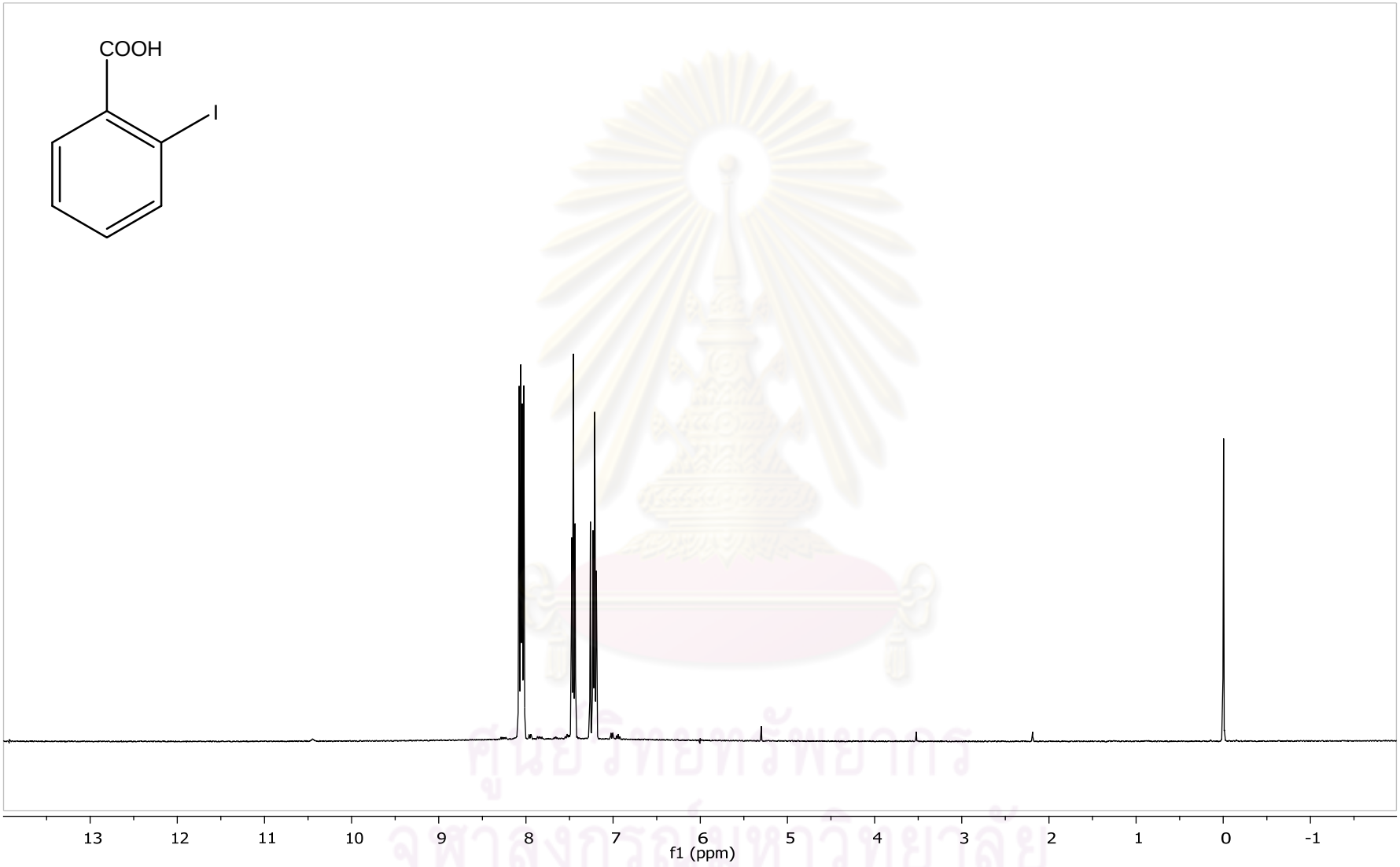

Figure A1 The ^{1}H-NMR spectrum of 2-iodobenzoic acid

48

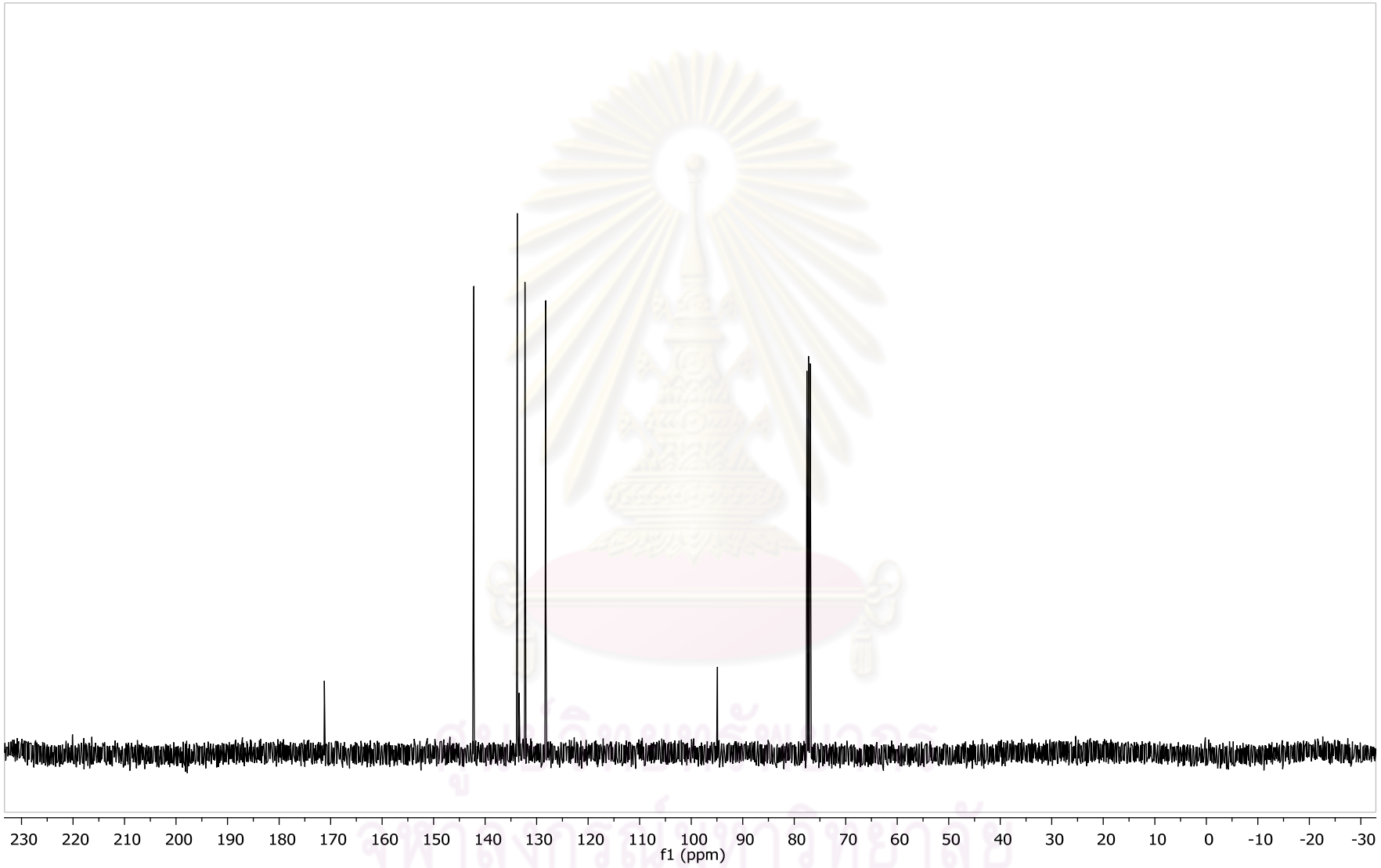

Figure A2 The ^{13}C-NMR spectrum of 2-iodobenzoic acid

49

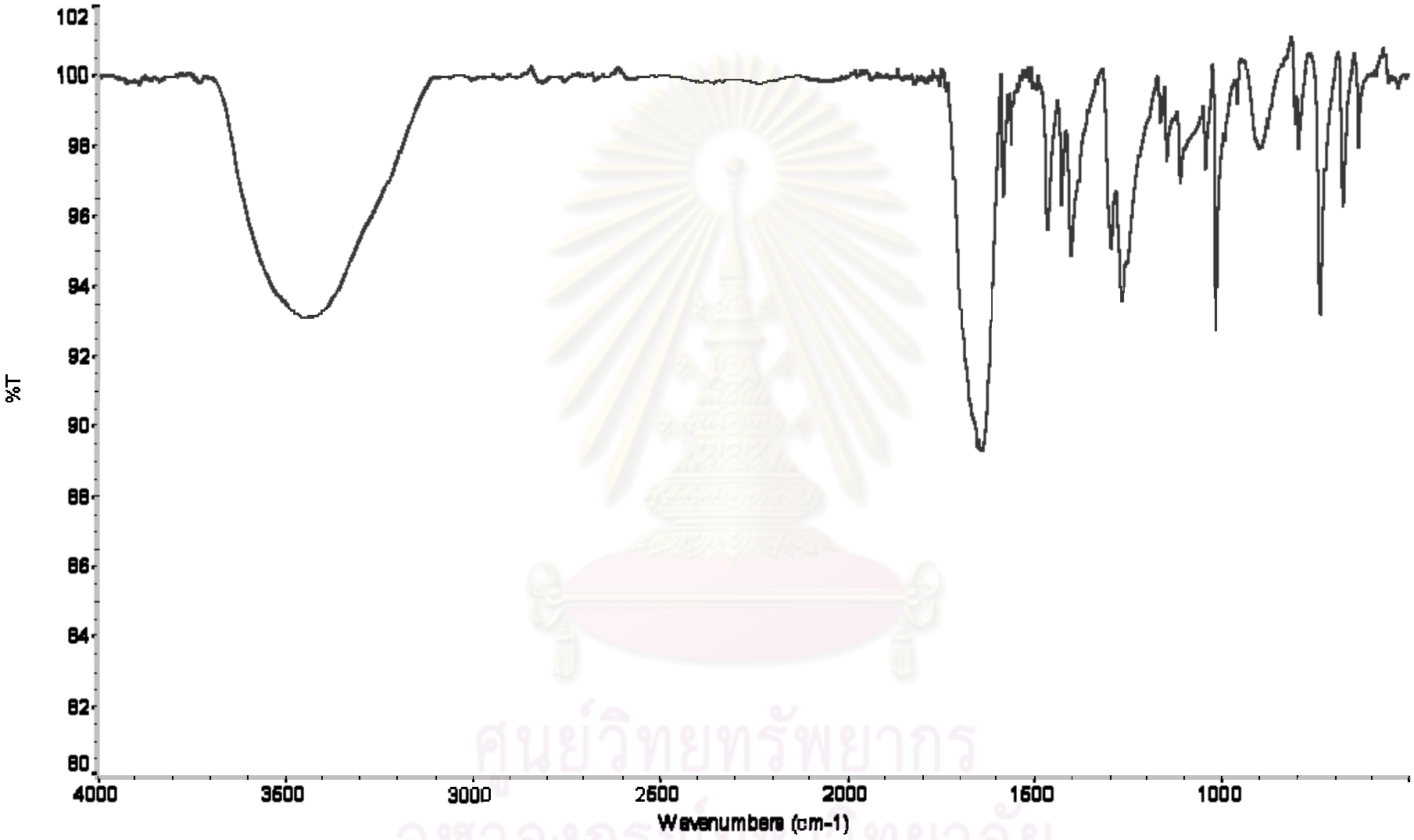

Figure A3 The FT-IR spectrum of 2-iodobenzoic acid

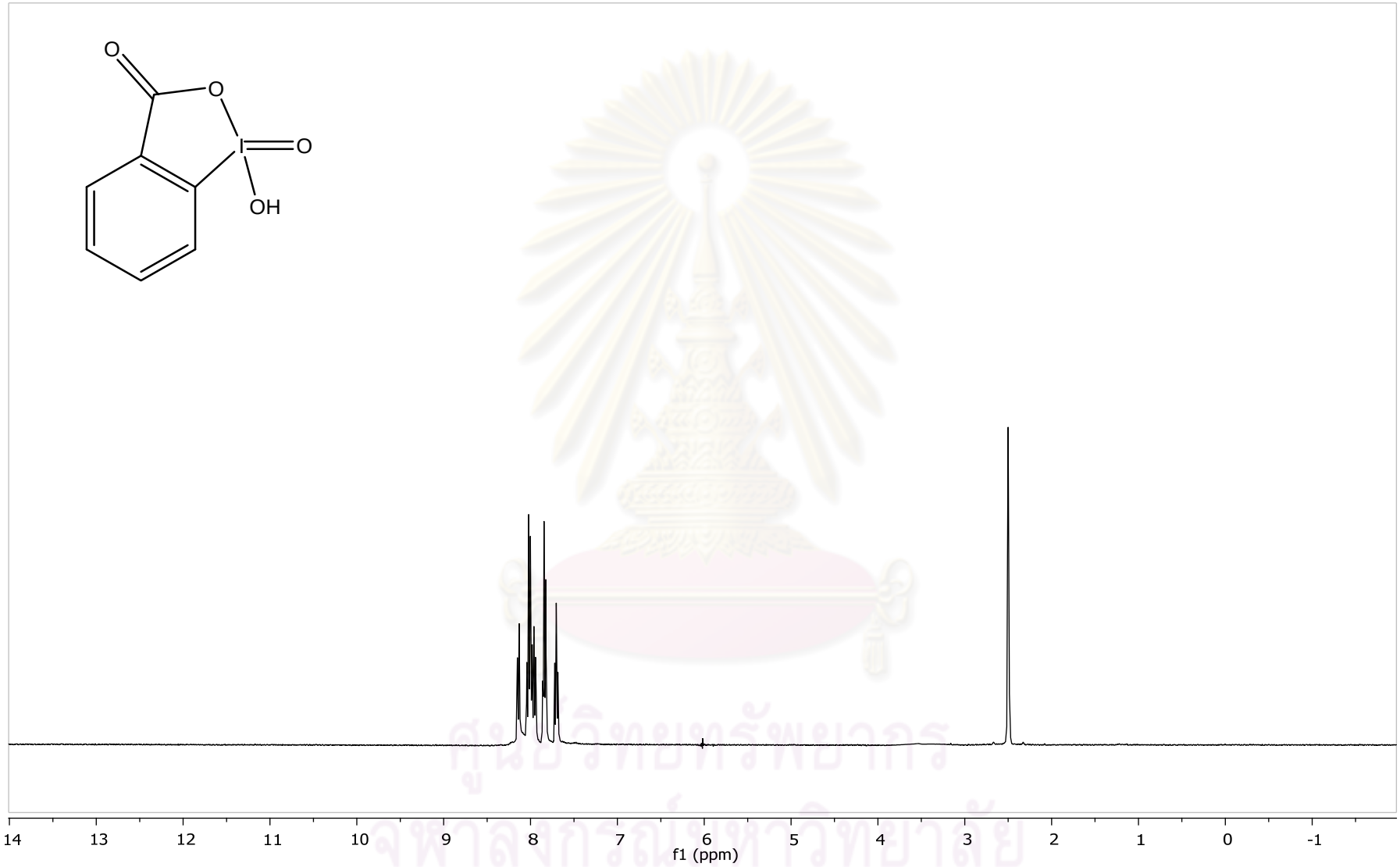

Figure A4 The ^{1}H-NMR spectrum of 2-iodoxybenzoic acid (IBX)

51

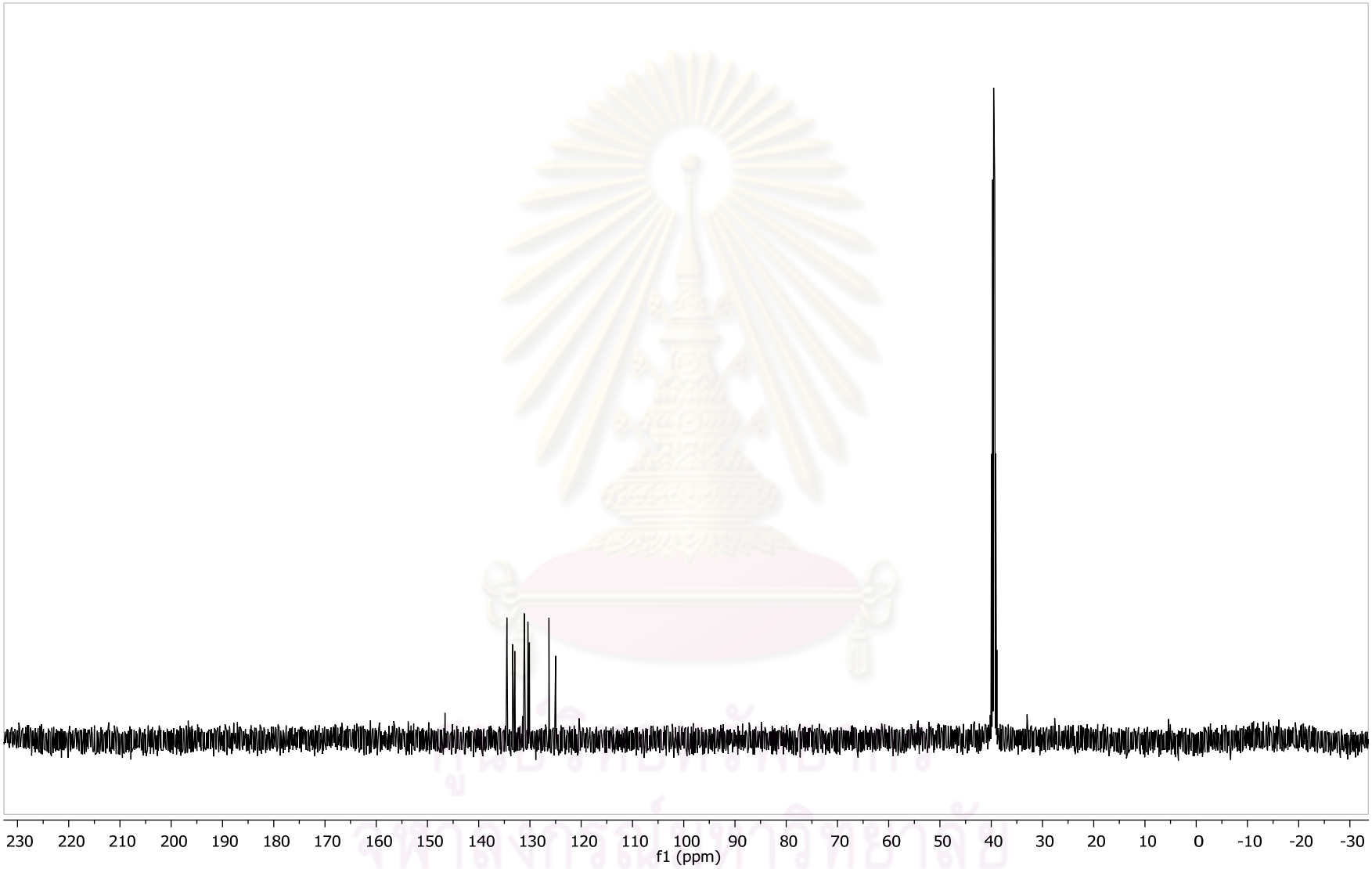

Figure A5 The ^{13}C-NMR spectrum of 2-iodoxybenzoic acid (IBX)

52

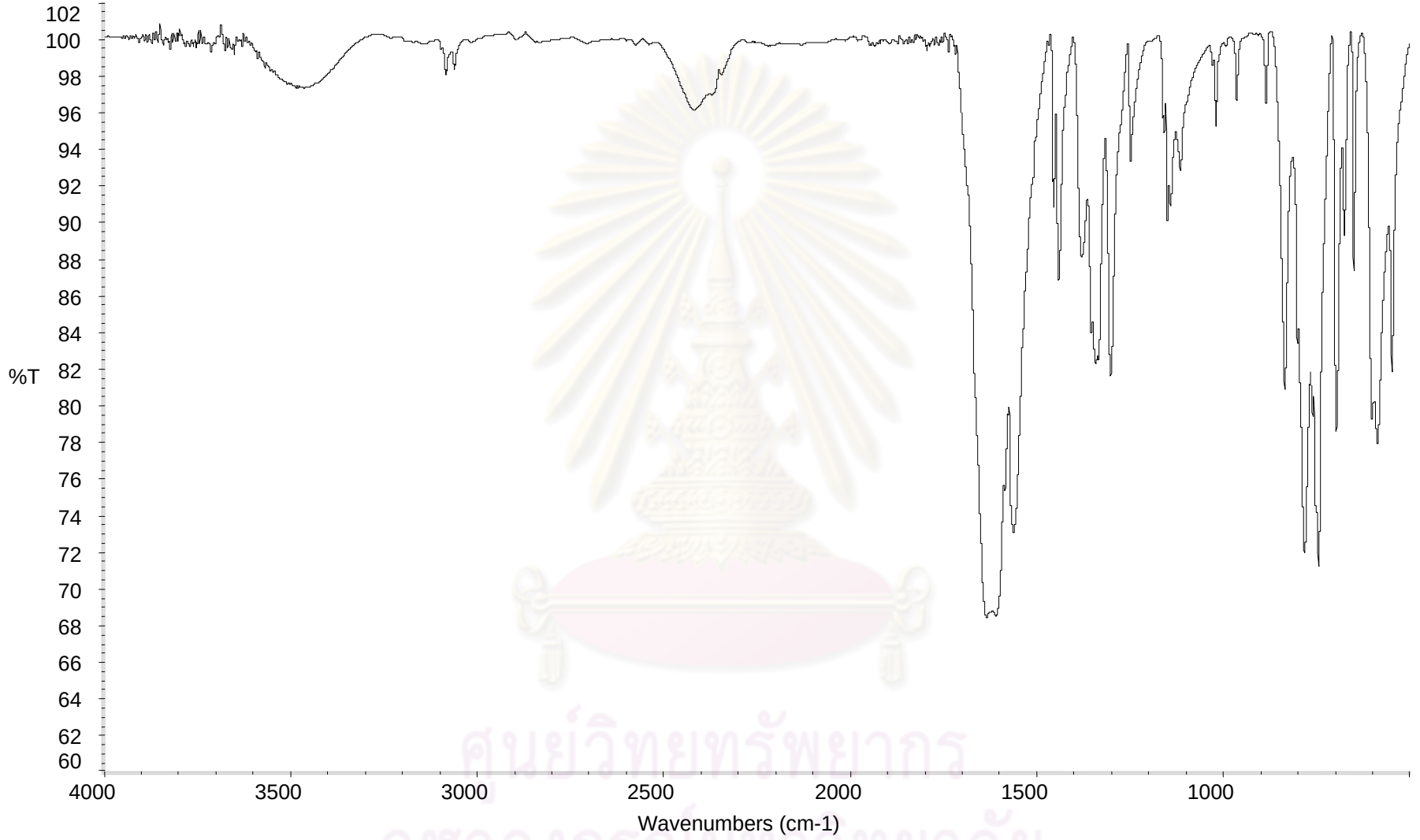

Figure A6 The FT-IR spectrum of 2-iodoxybenzoic acid (IBX)

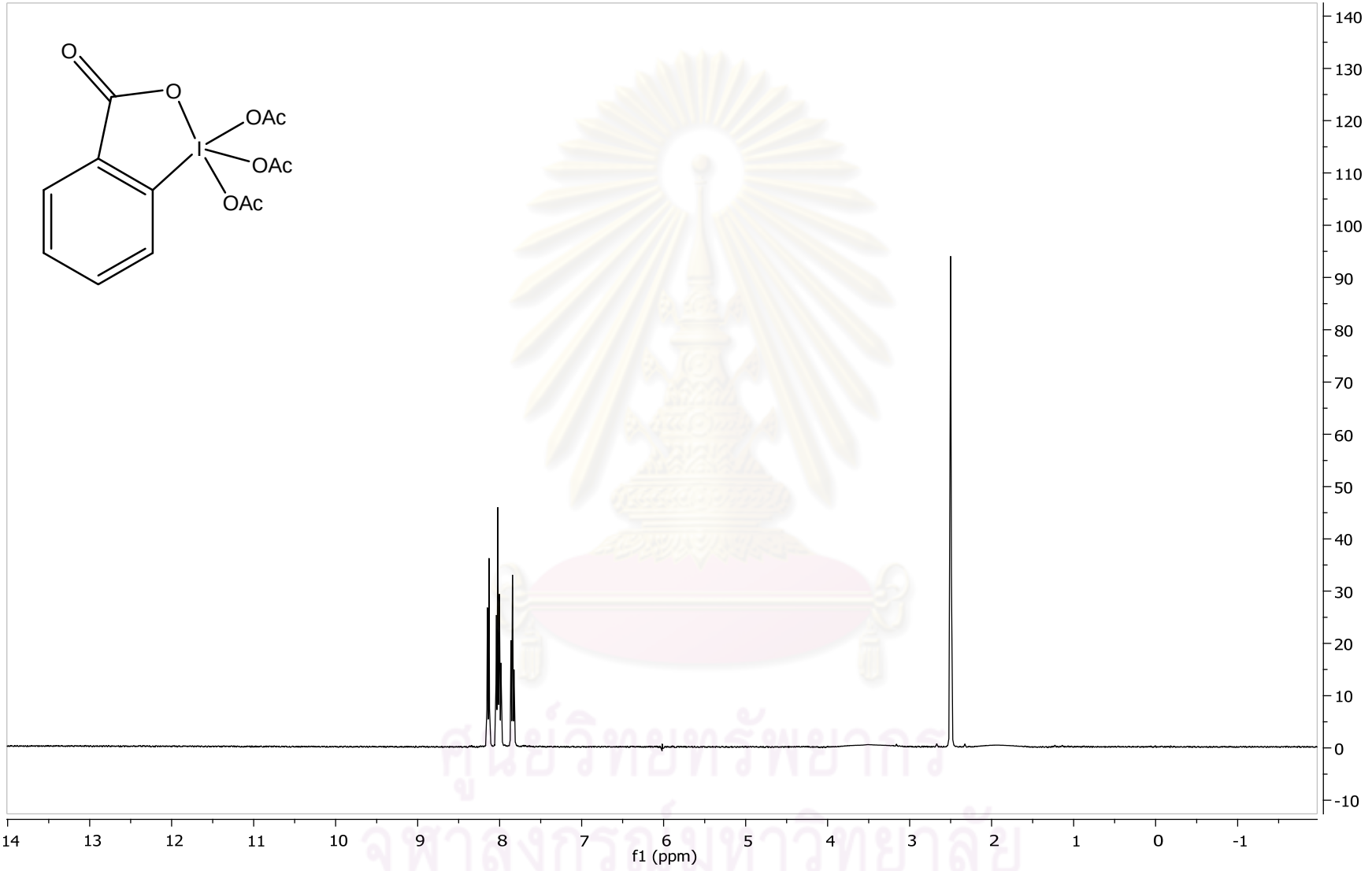

Figure A7 The ^{1}H-NMR spectrum of Dess-Martin Periodinane (DMP)

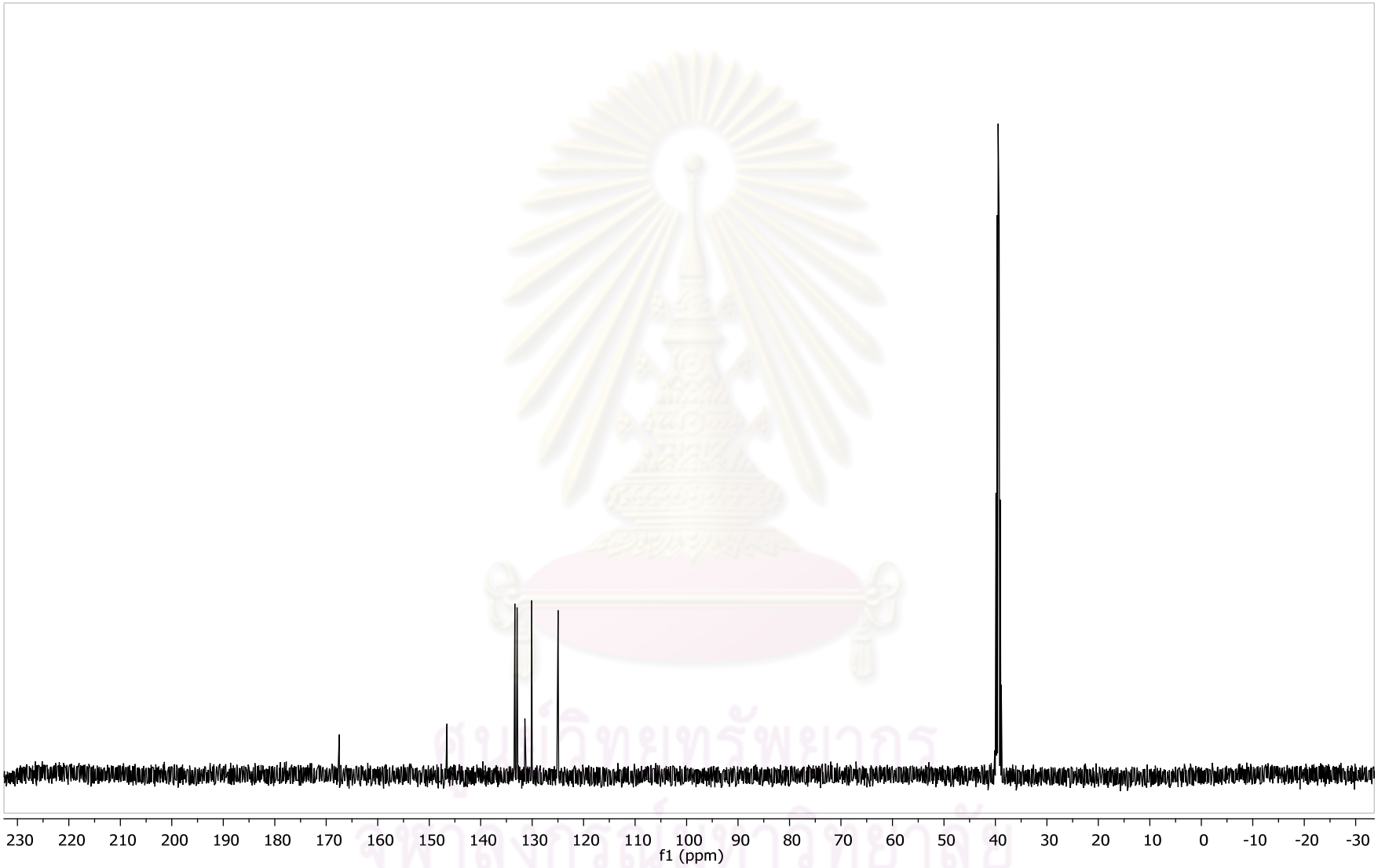

Figure A8 The ^{13}C-NMR spectrum of Dess-Martin Periodinane (DMP)

55

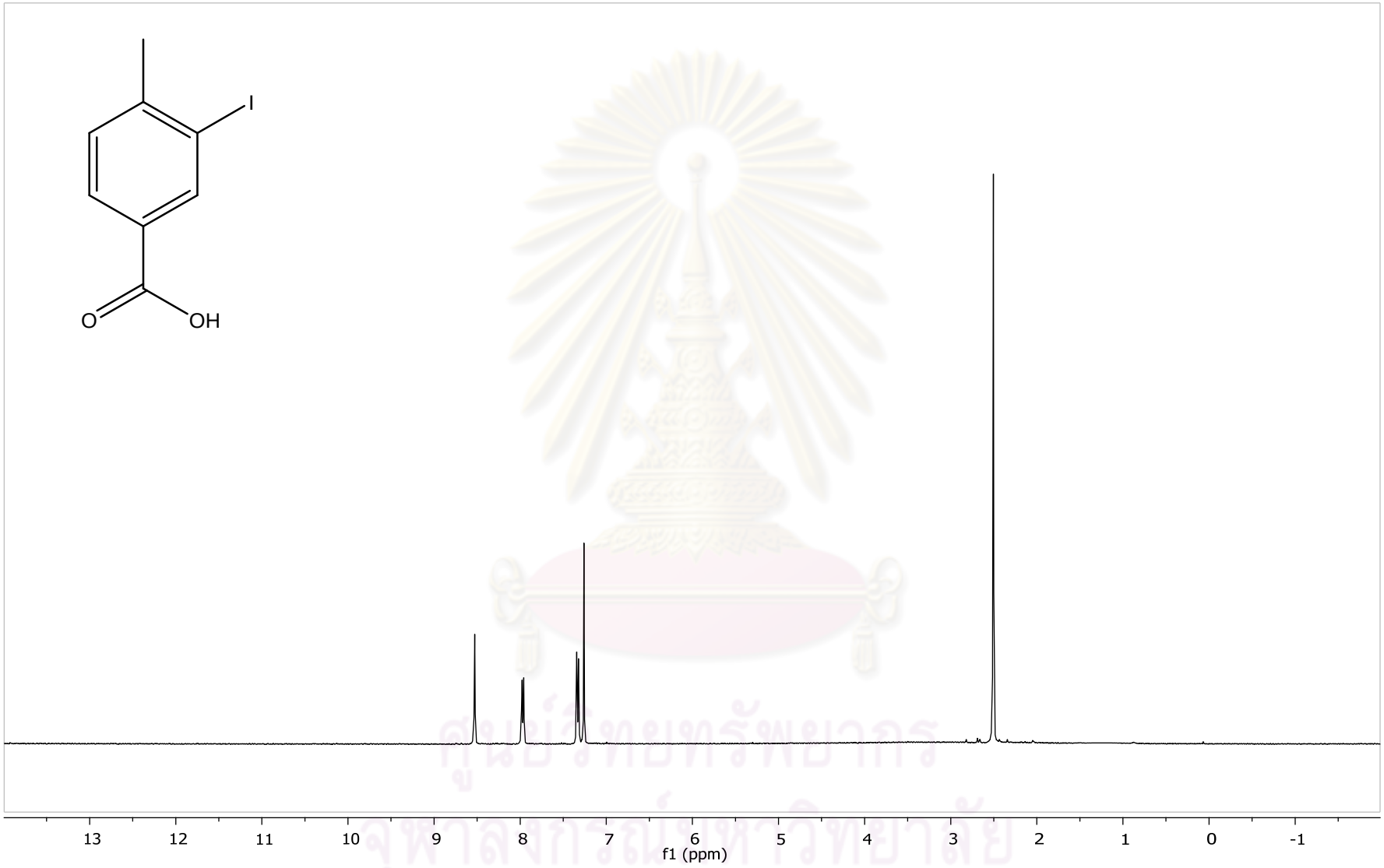

Figure A9 The ^{1}H-NMR spectrum of 3-iodo-4-methylbenzoic acid

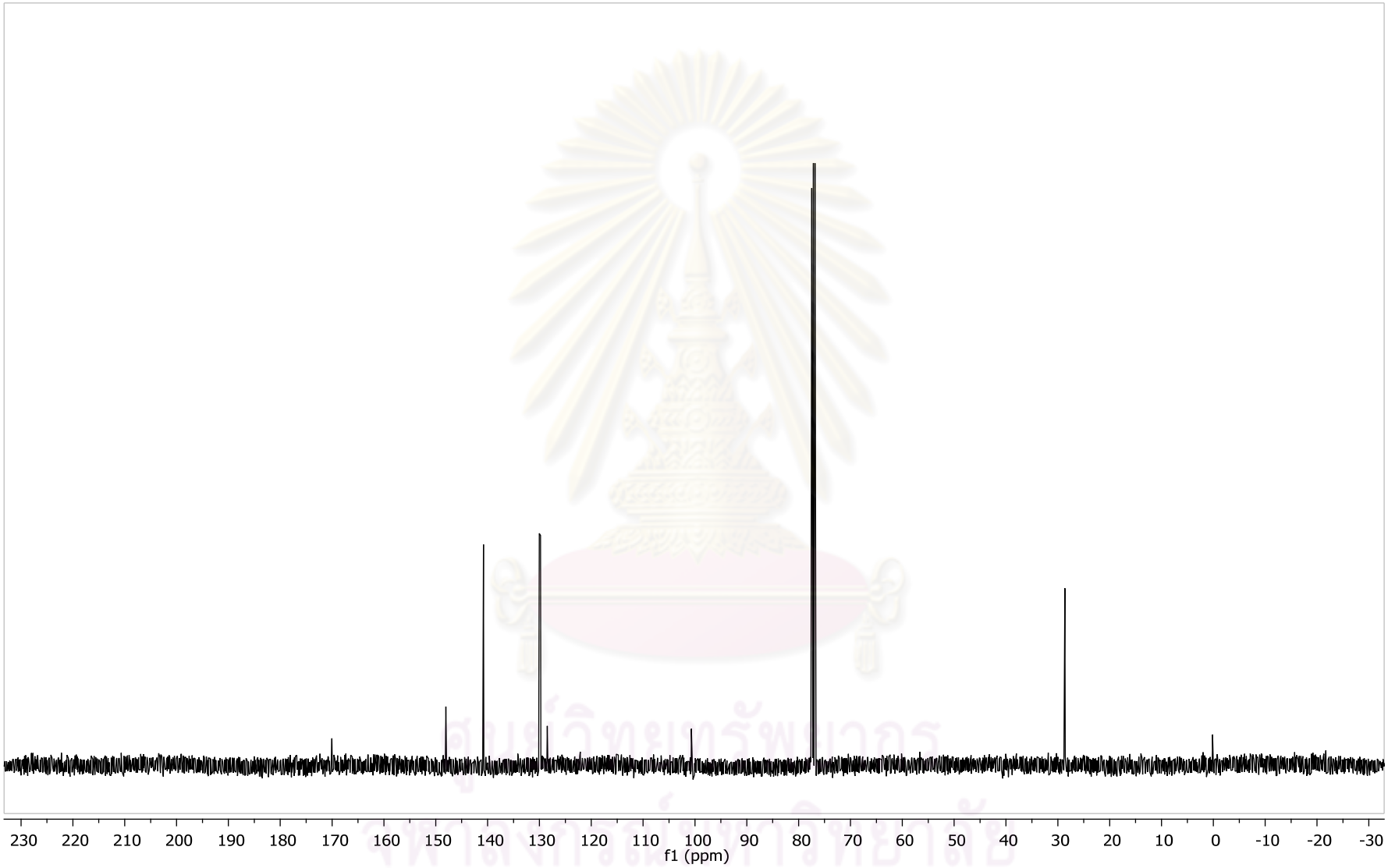

Figure A10 The ^{13}C-NMR spectrum of 3-iodo-4-methylbenzoic acid

57

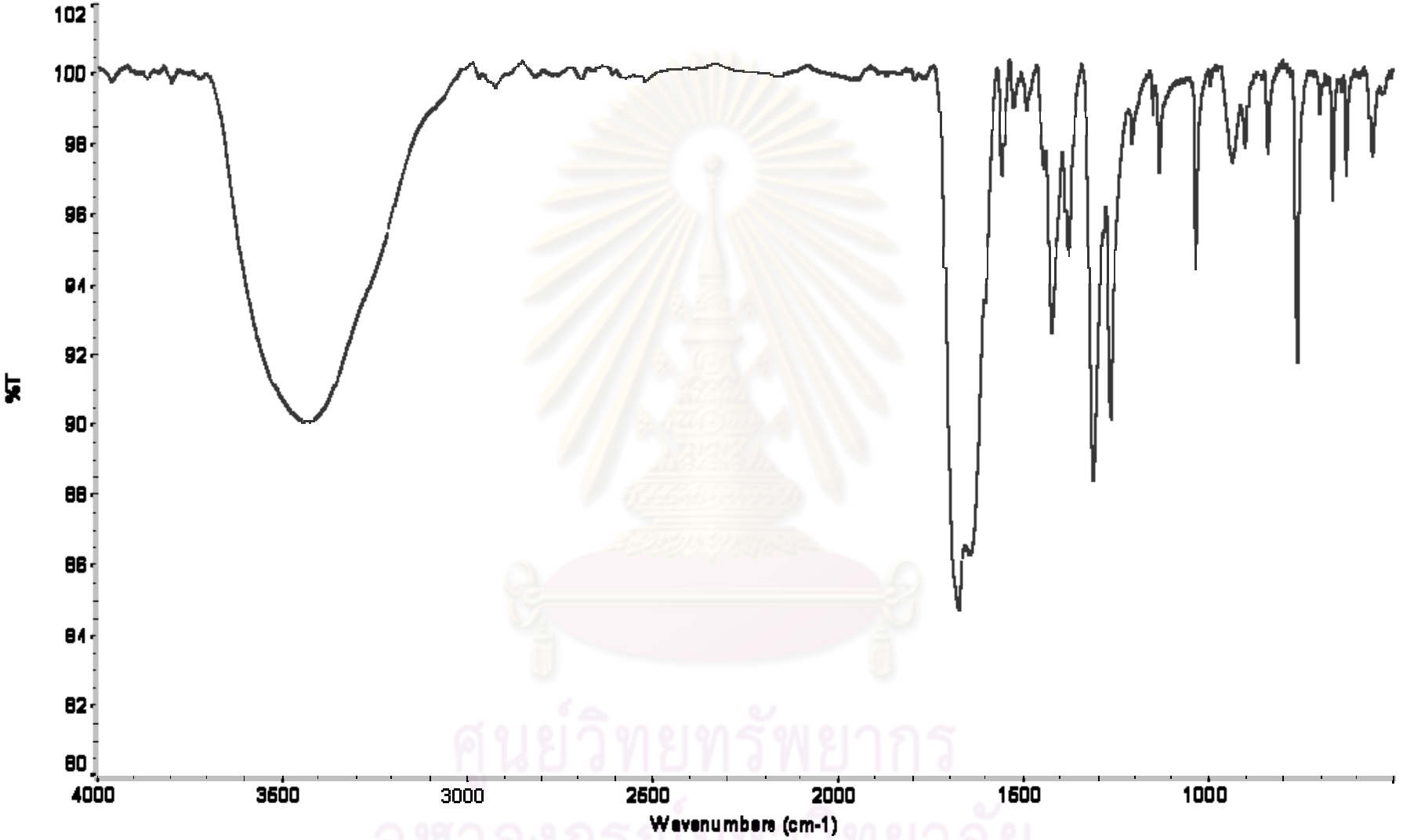

Figure A11 The FT-IR spectrum of 3-iodo-4-methylbenzoic acid

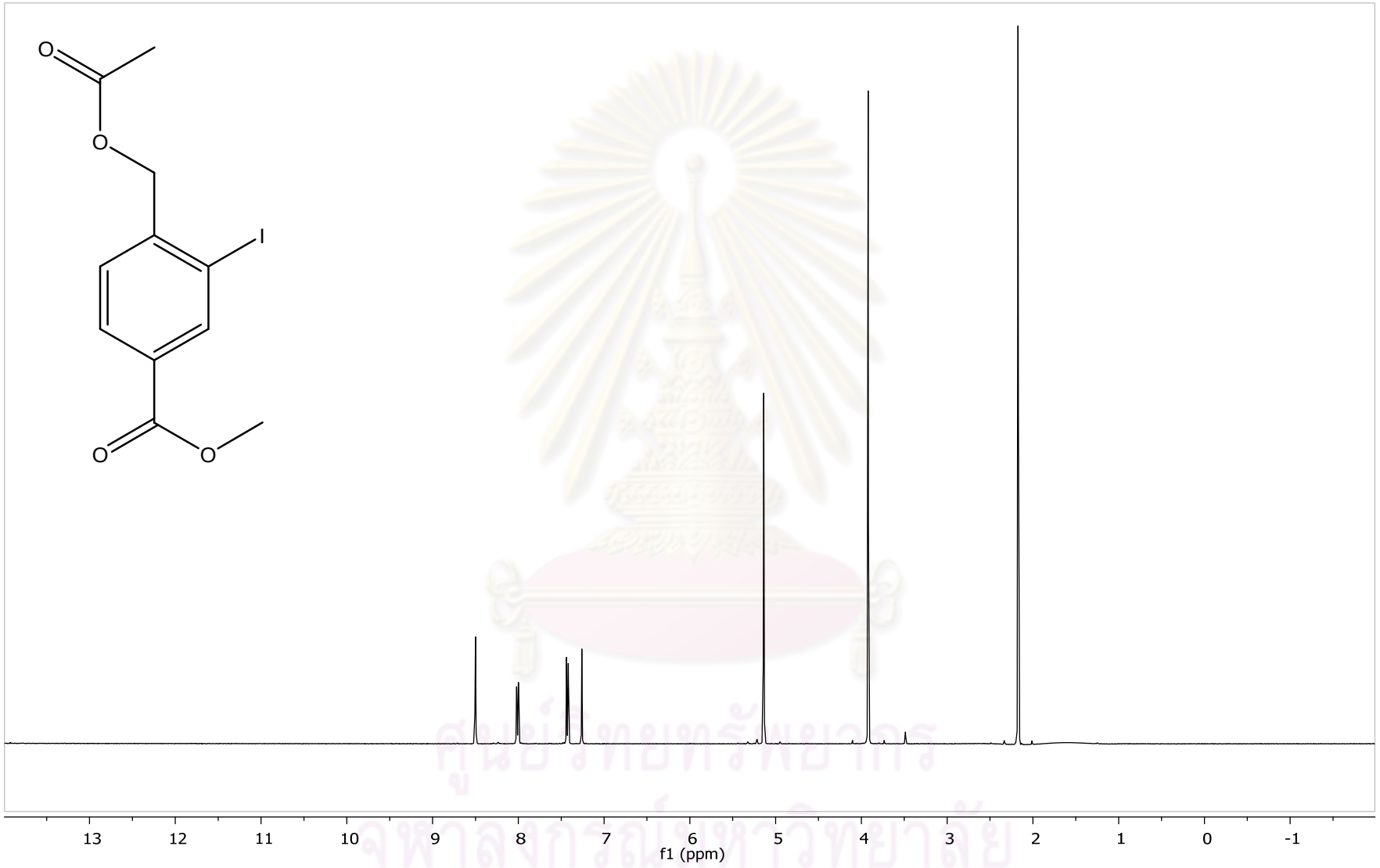

Figure A12 The ^{1}H-NMR spectrum of 3-iodo-4-(acetoxymethyl)benzoate

59

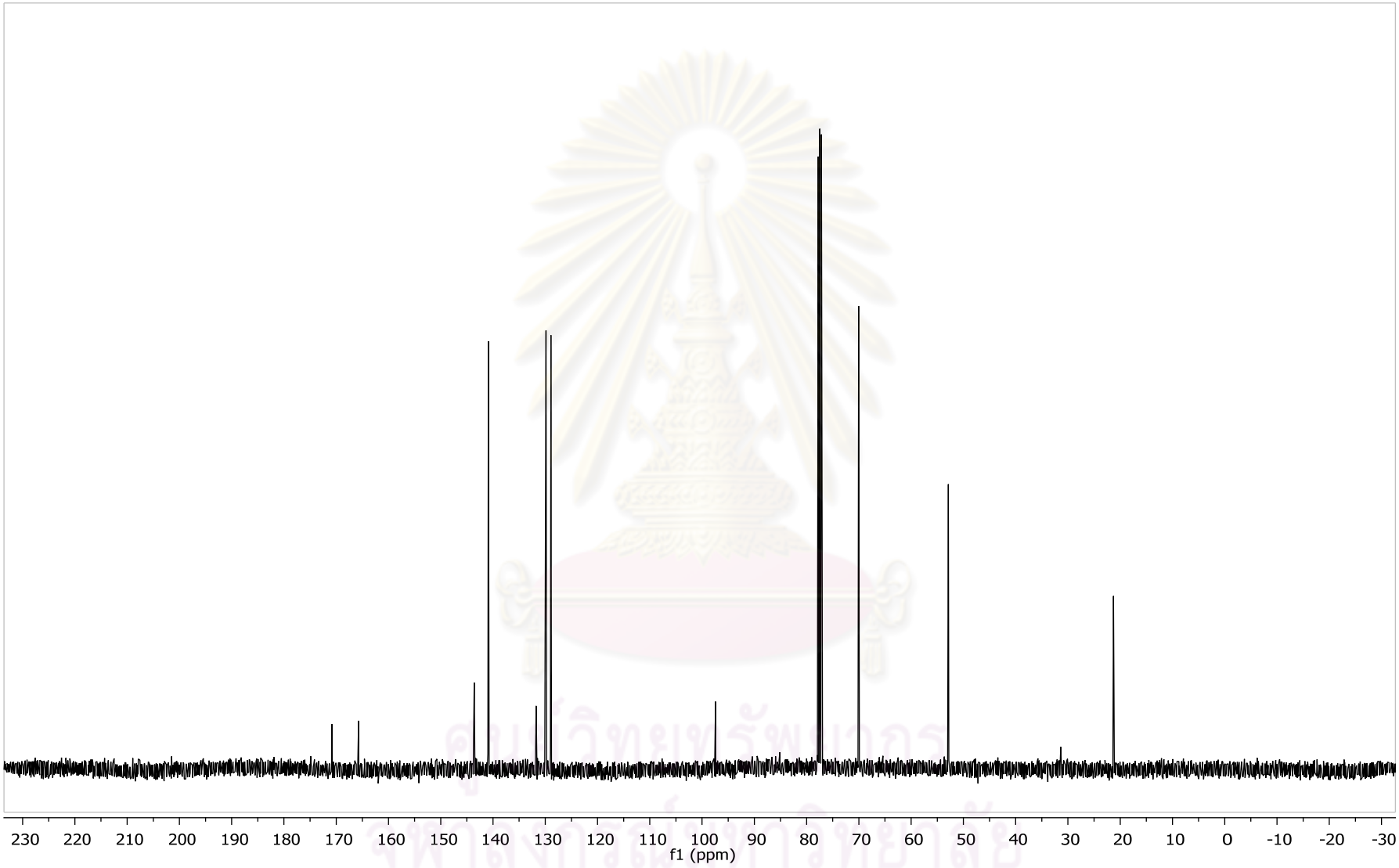

Figure A13 The ^{13}C-NMR spectrum of 3-iodo-4-(acetoxymethyl)benzoate

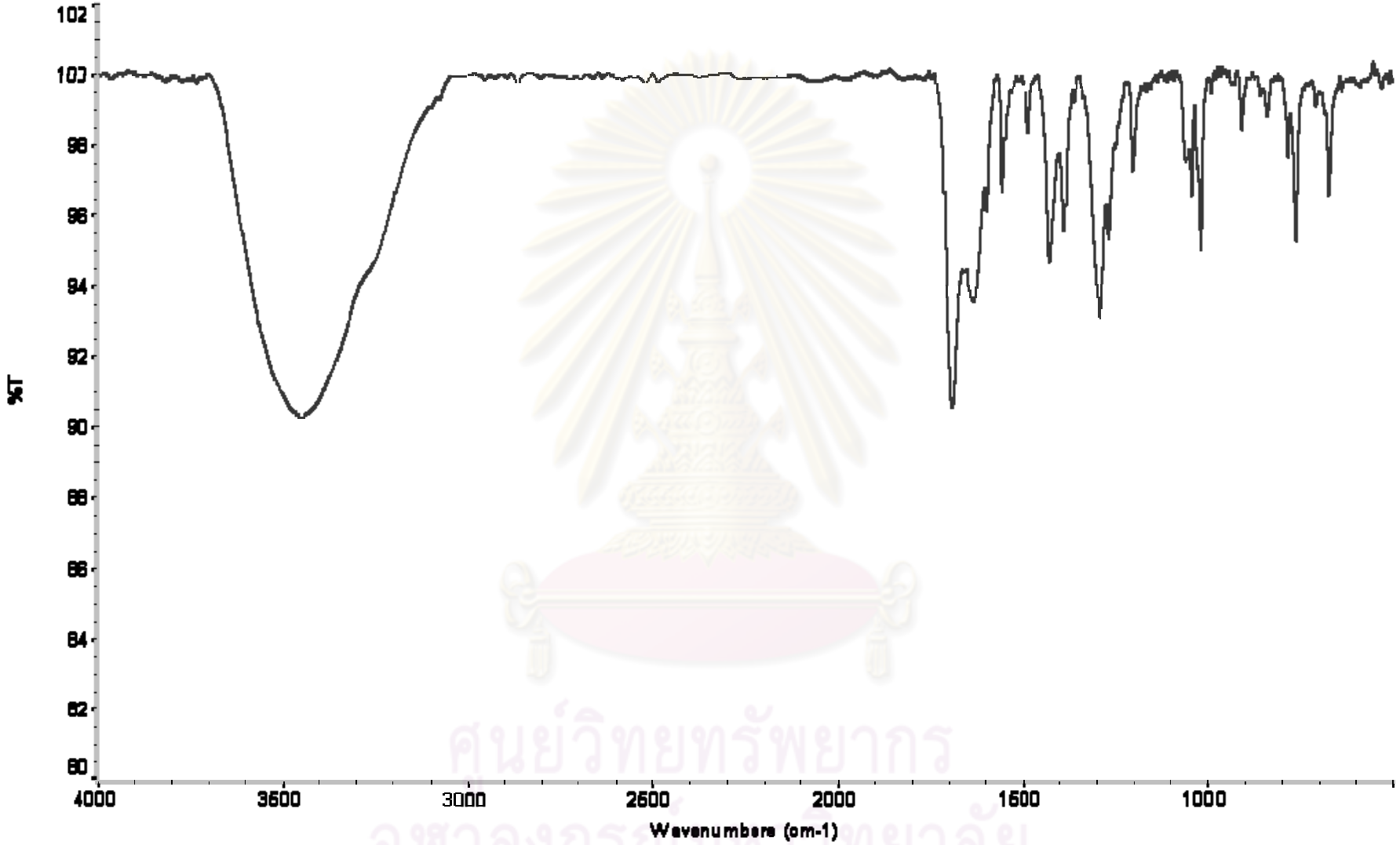

Figure A14 The FT-IR spectrum of 3-iodo-4-(acetoxymethyl)benzoate

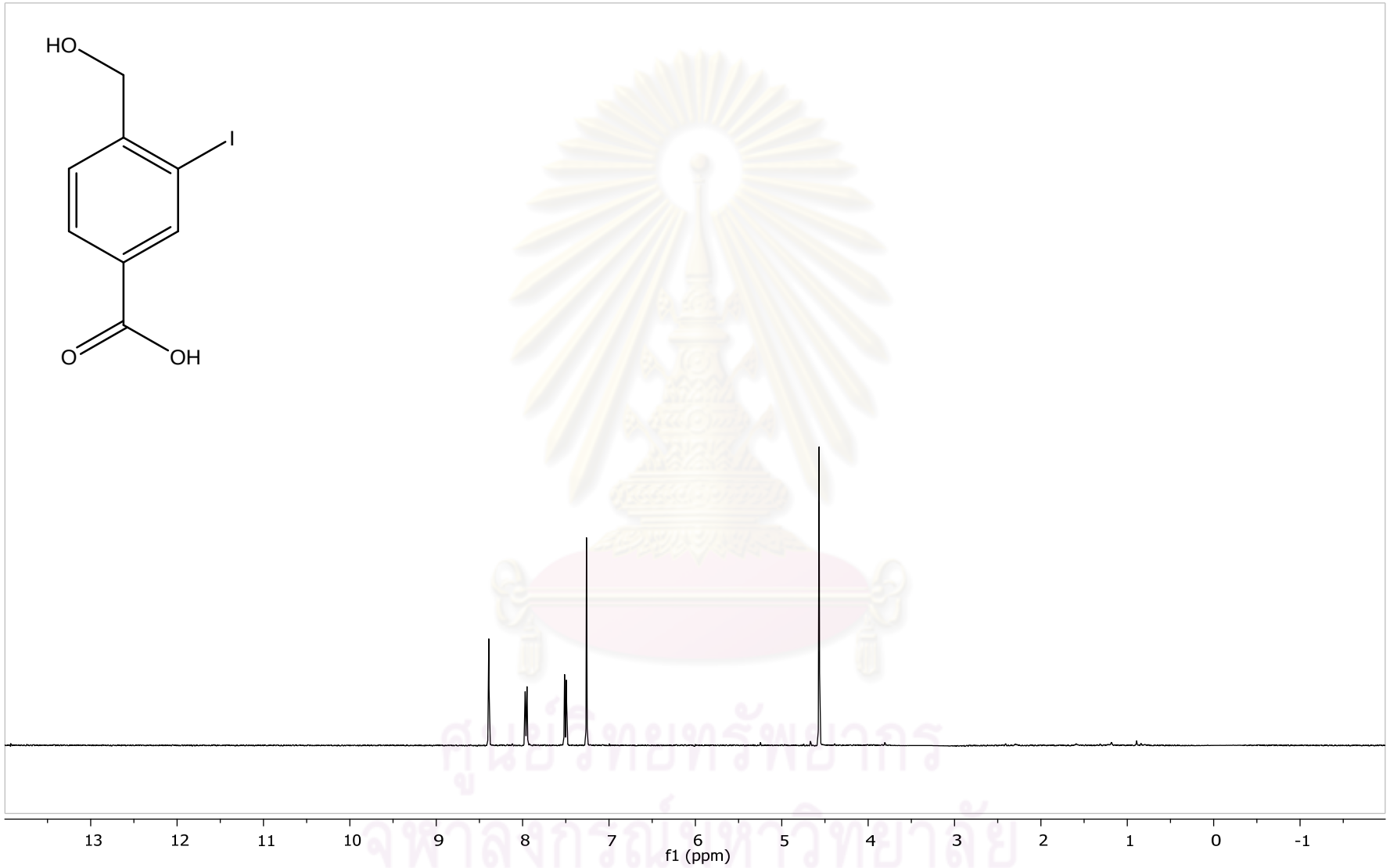

Figure A15 The ^{1}H-NMR spectrum of 3-iodo-4-(hydroxymethyl)benzoic acid

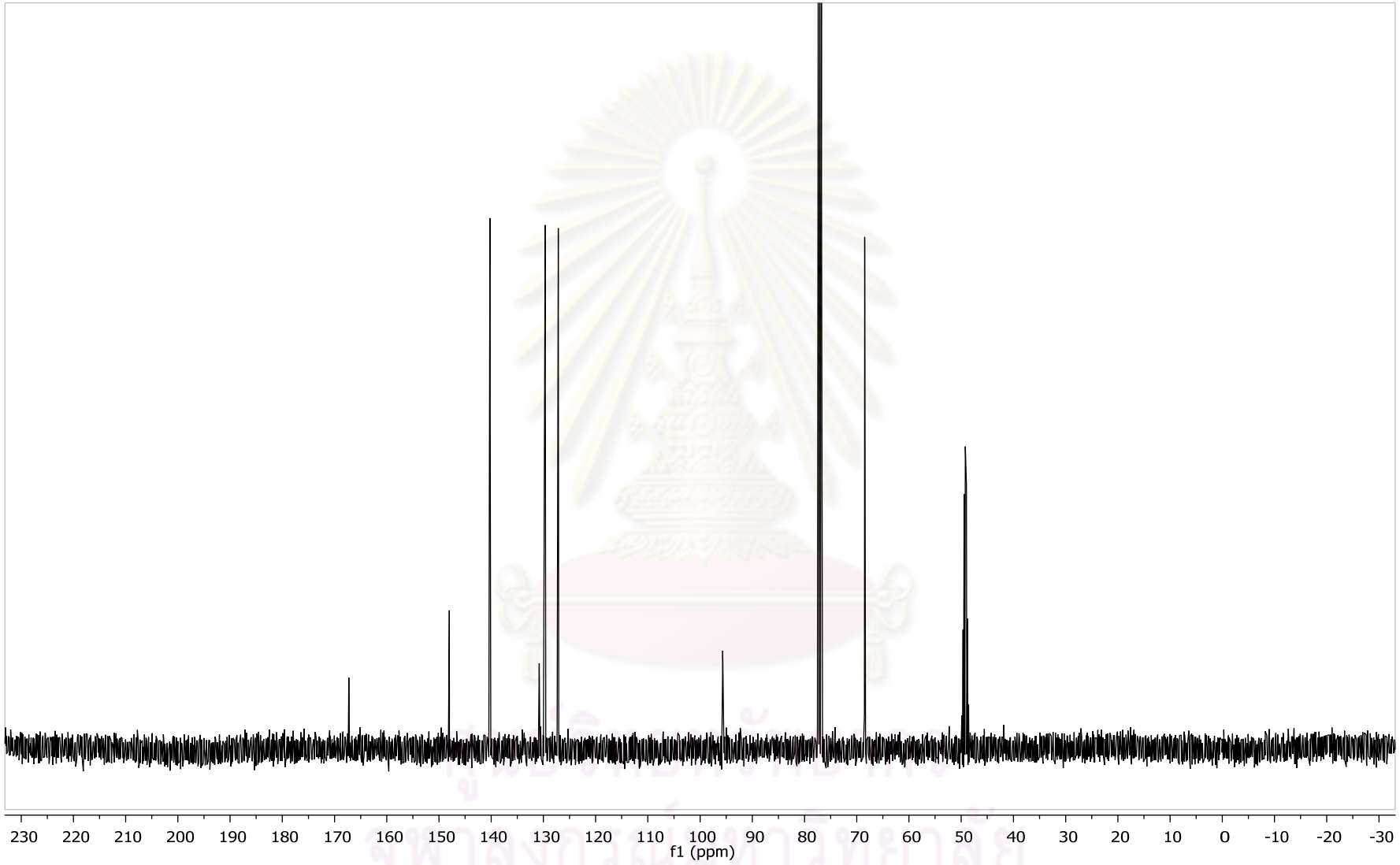

Figure A16 The ^{13}C-NMR spectrum of 3-iodo-4-(hydroxymethyl)benzoic acid

63

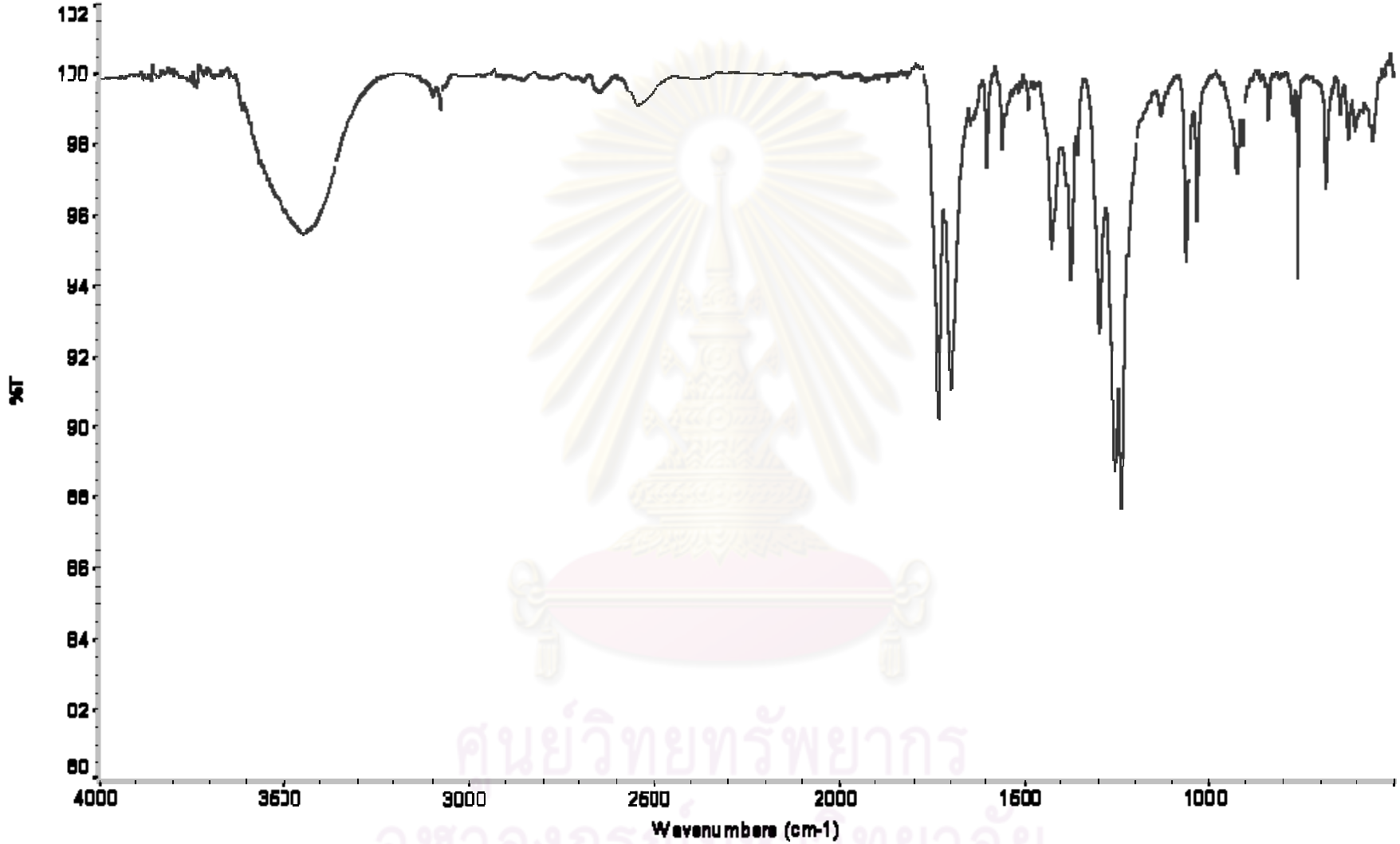

Figure A17 The FT-IR spectrum of 3-iodo-4-(hydroxymethyl)benzoic acid

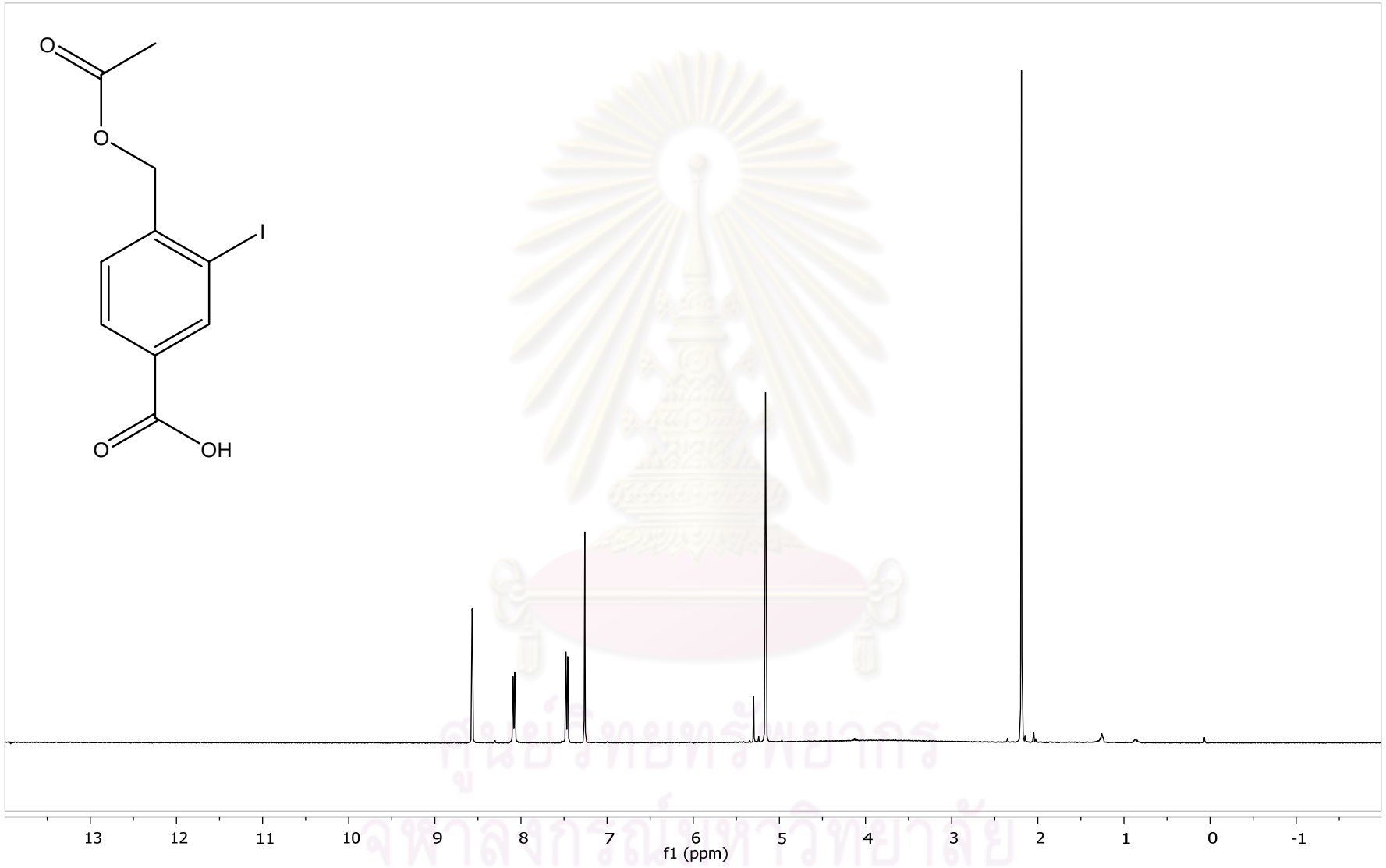

Figure A18 The ^{1}H-NMR spectrum of 3-iodo-4-(acetoxymethyl)benzoic acid

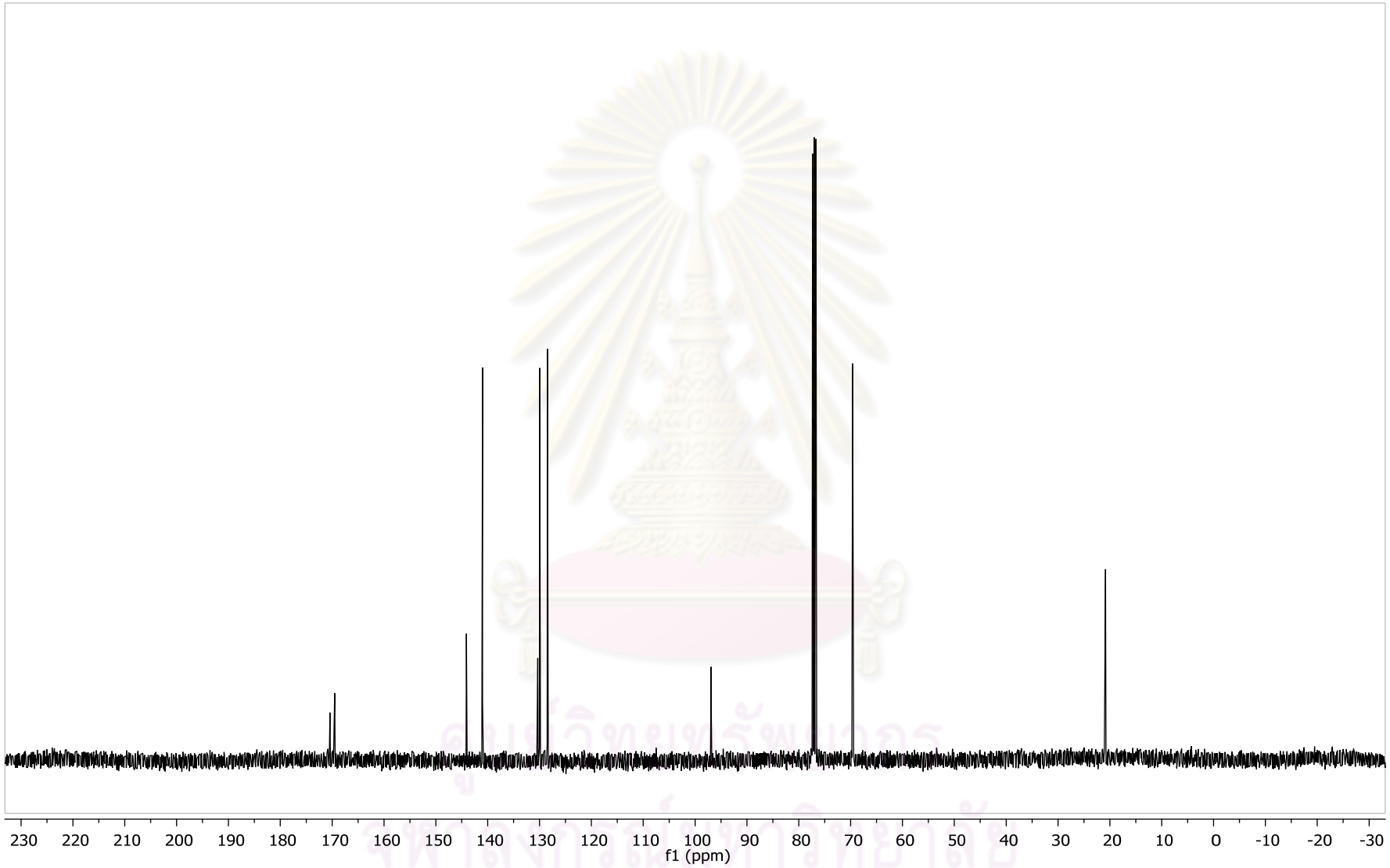

Figure A19 The ^{13}C-NMR spectrum of 3-iodo-4-(acetoxymethyl)benzoic acid

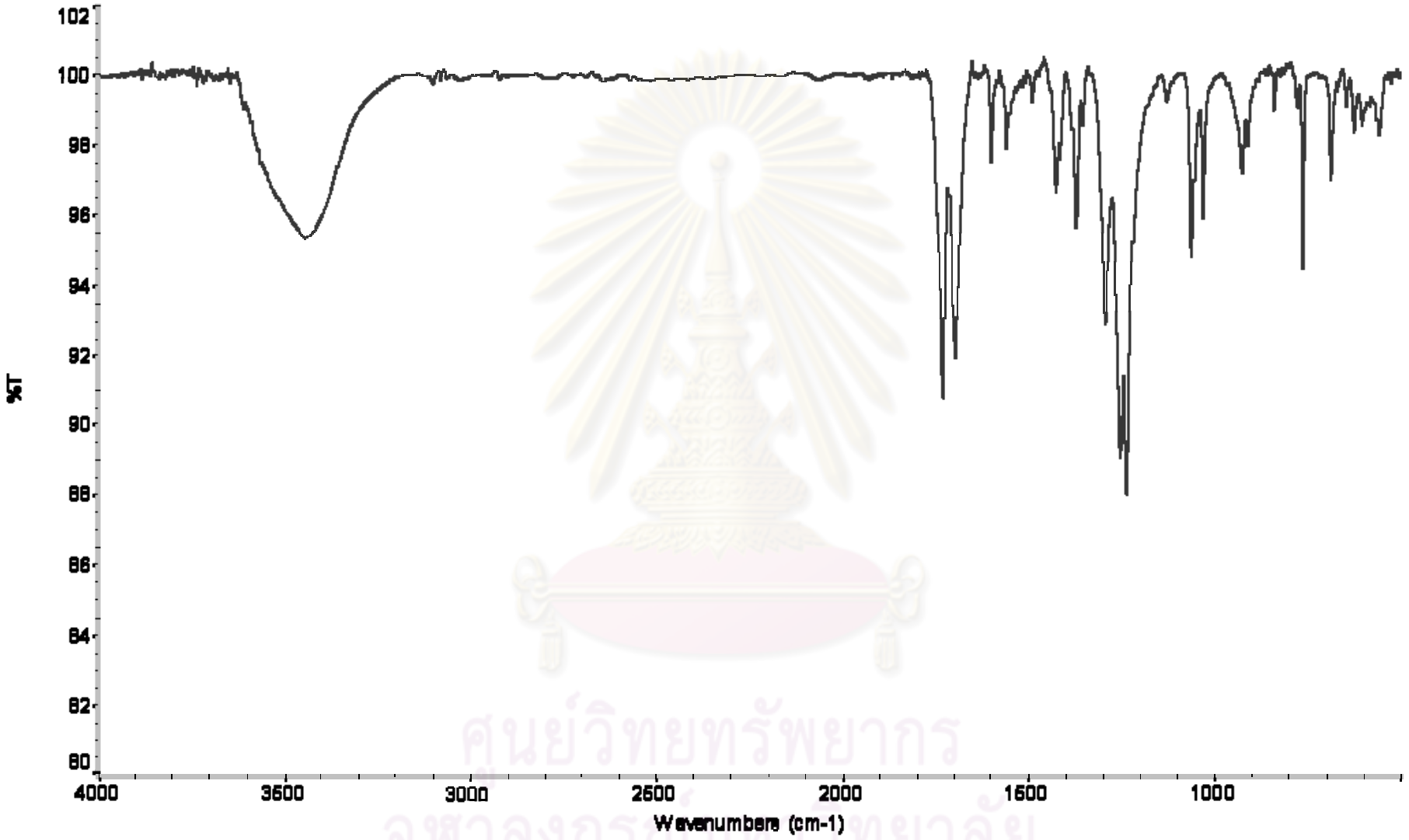

Figure A20 The FT-IR spectrum of 3-iodo-4-(acetoxymethyl)benzoic acid

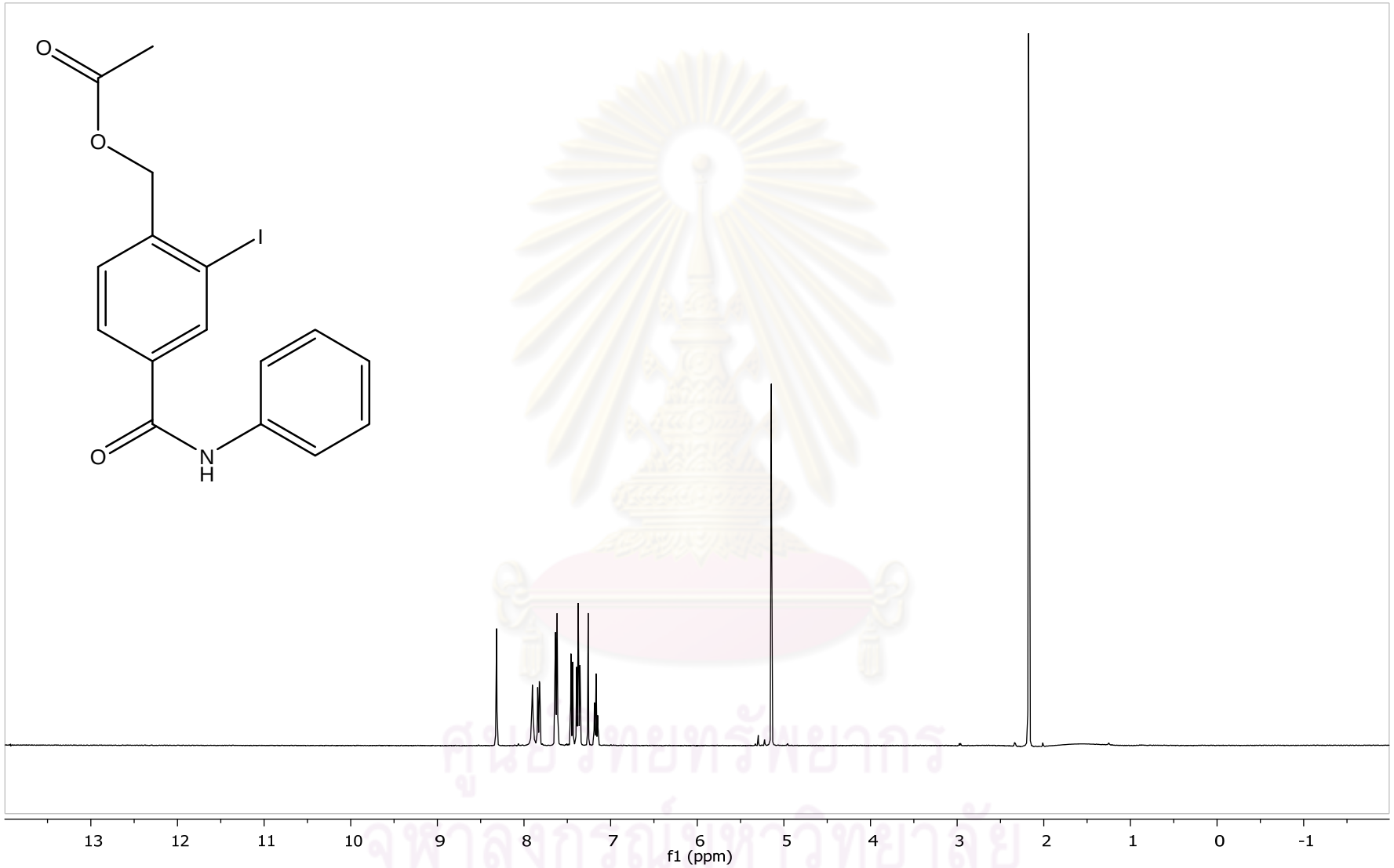

Figure A21 The ^{1}H-NMR spectrum of 2-iodo-4-(phenylcarbamoyl)benzyl acetate

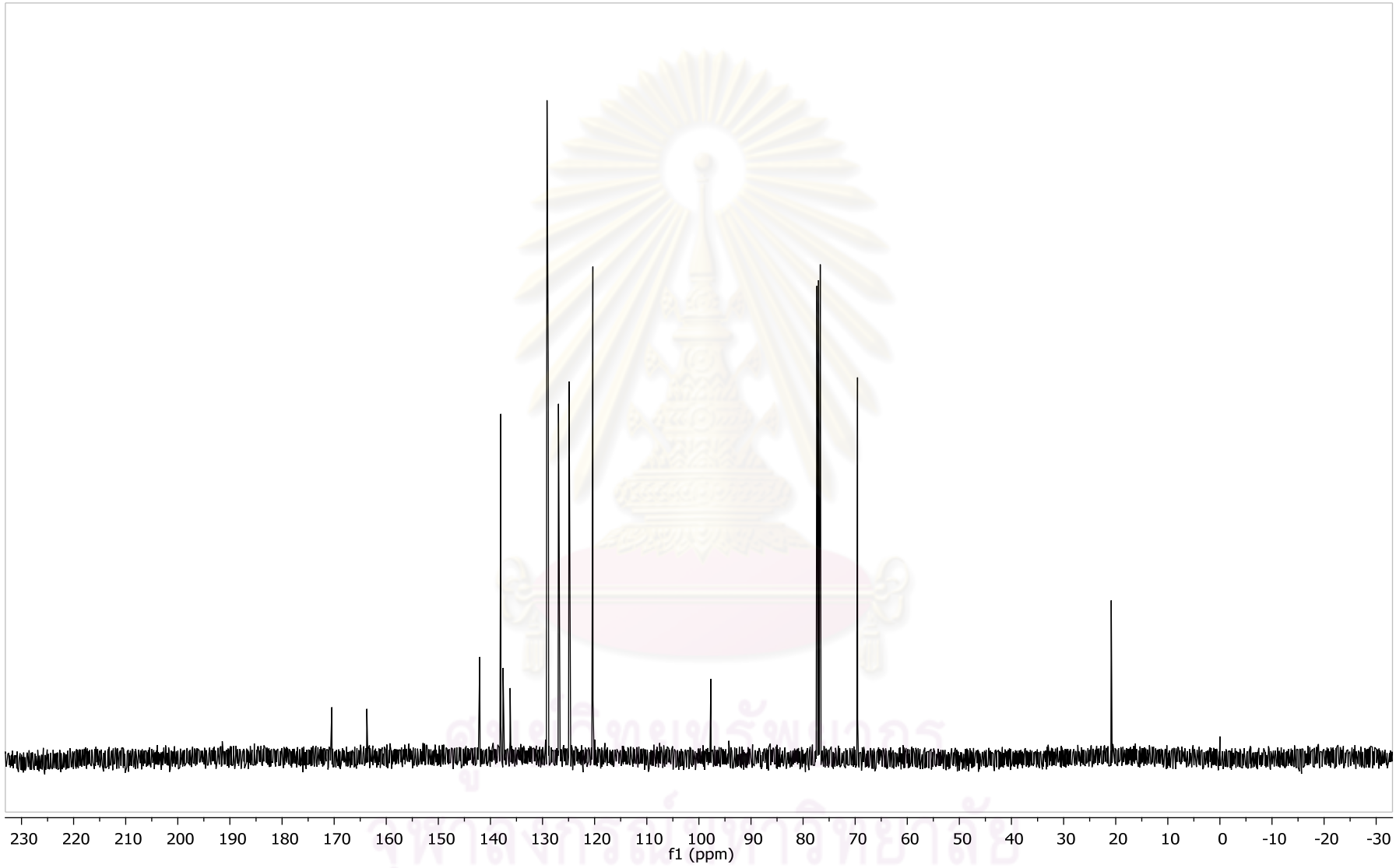

Figure A22 The ^{13}C-NMR spectrum of 2-iodo-4-(phenylcarbamoyl)benzyl acetate

69

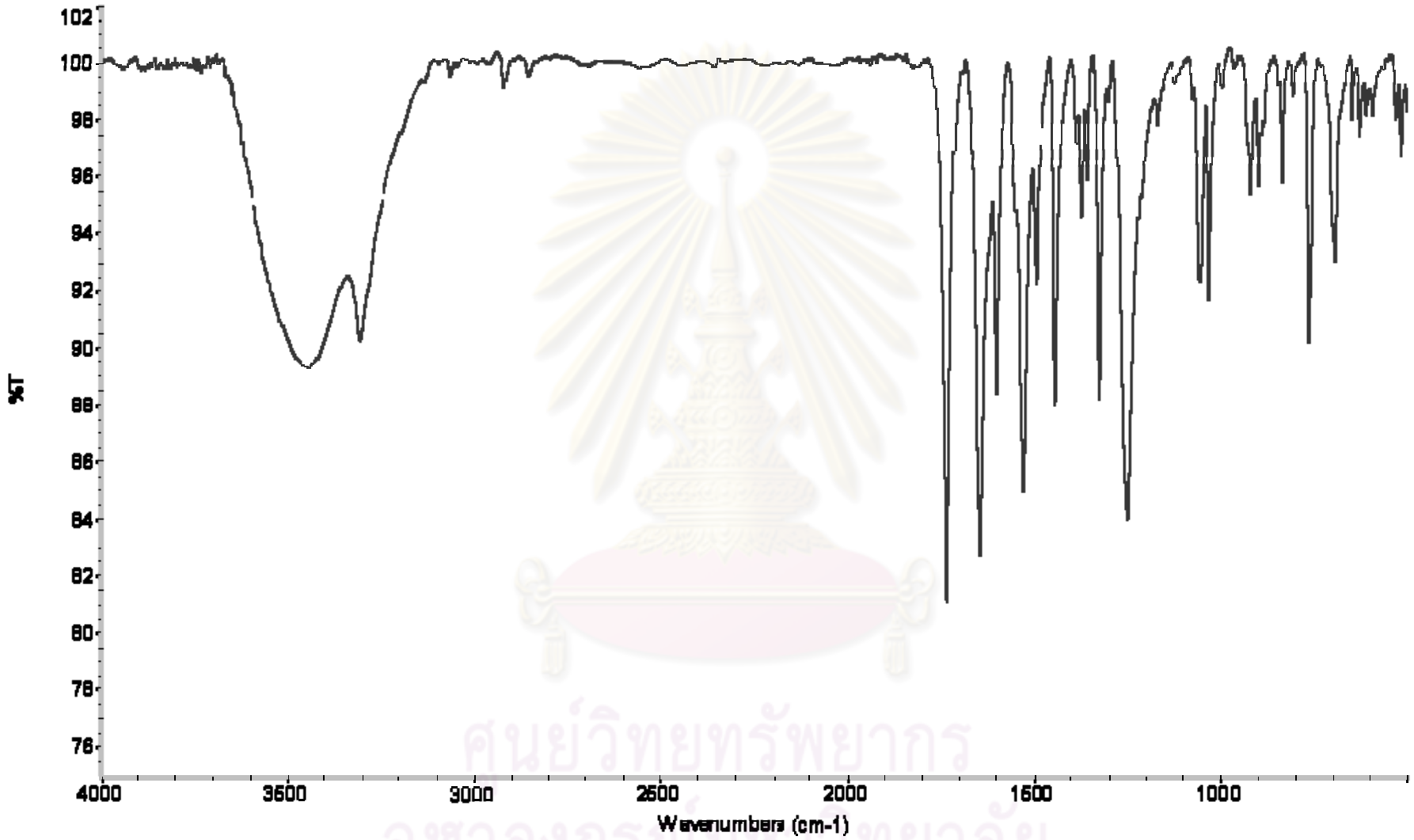

Figure A23 The FT-IR spectrum of 2-iodo-4-(phenylcarbamoyl)benzyl acetate

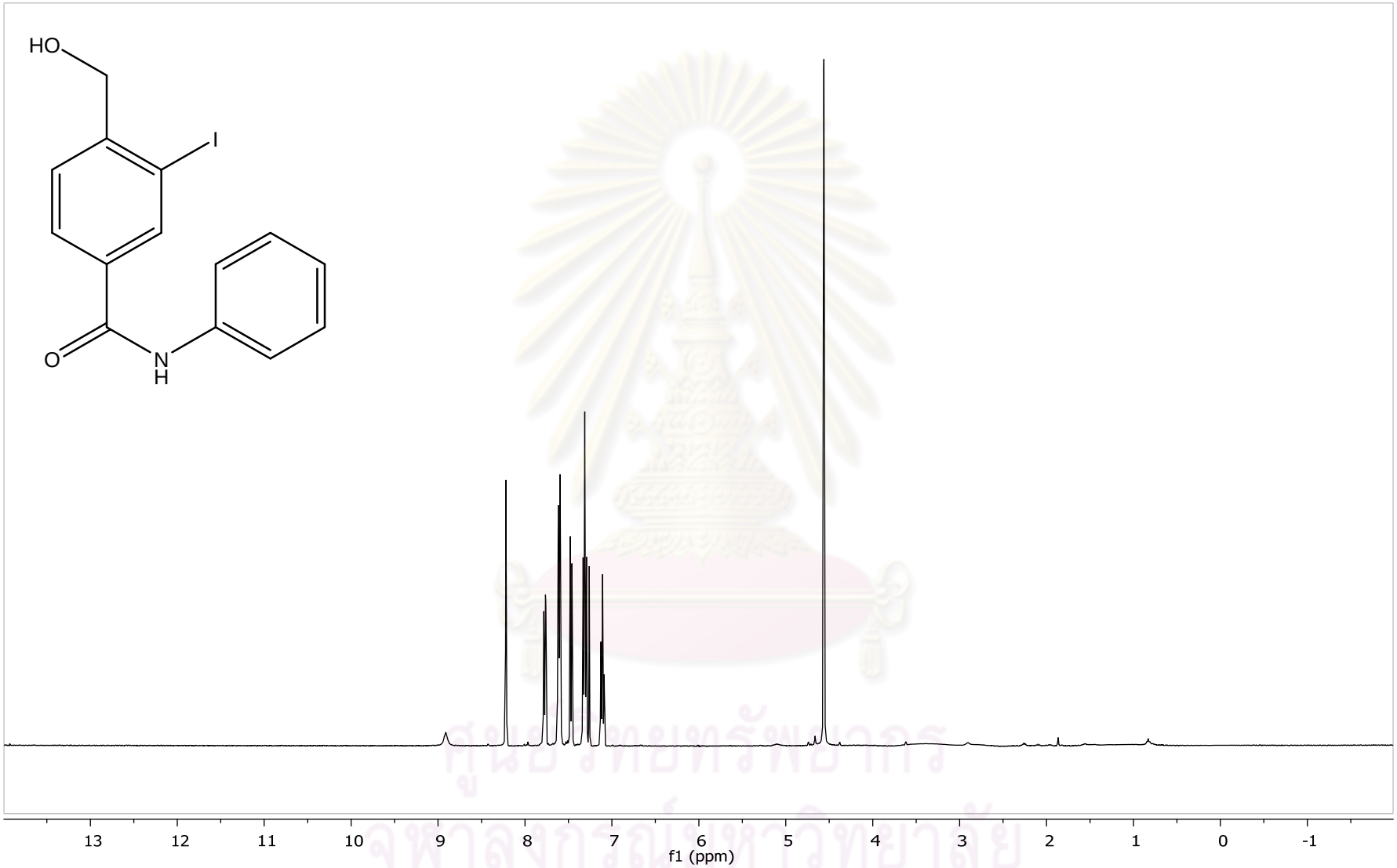

Figure A24 The ^{1}H-NMR spectrum of 3-iodo-4-(hydroxymethyl)-N-phenylbenzamide

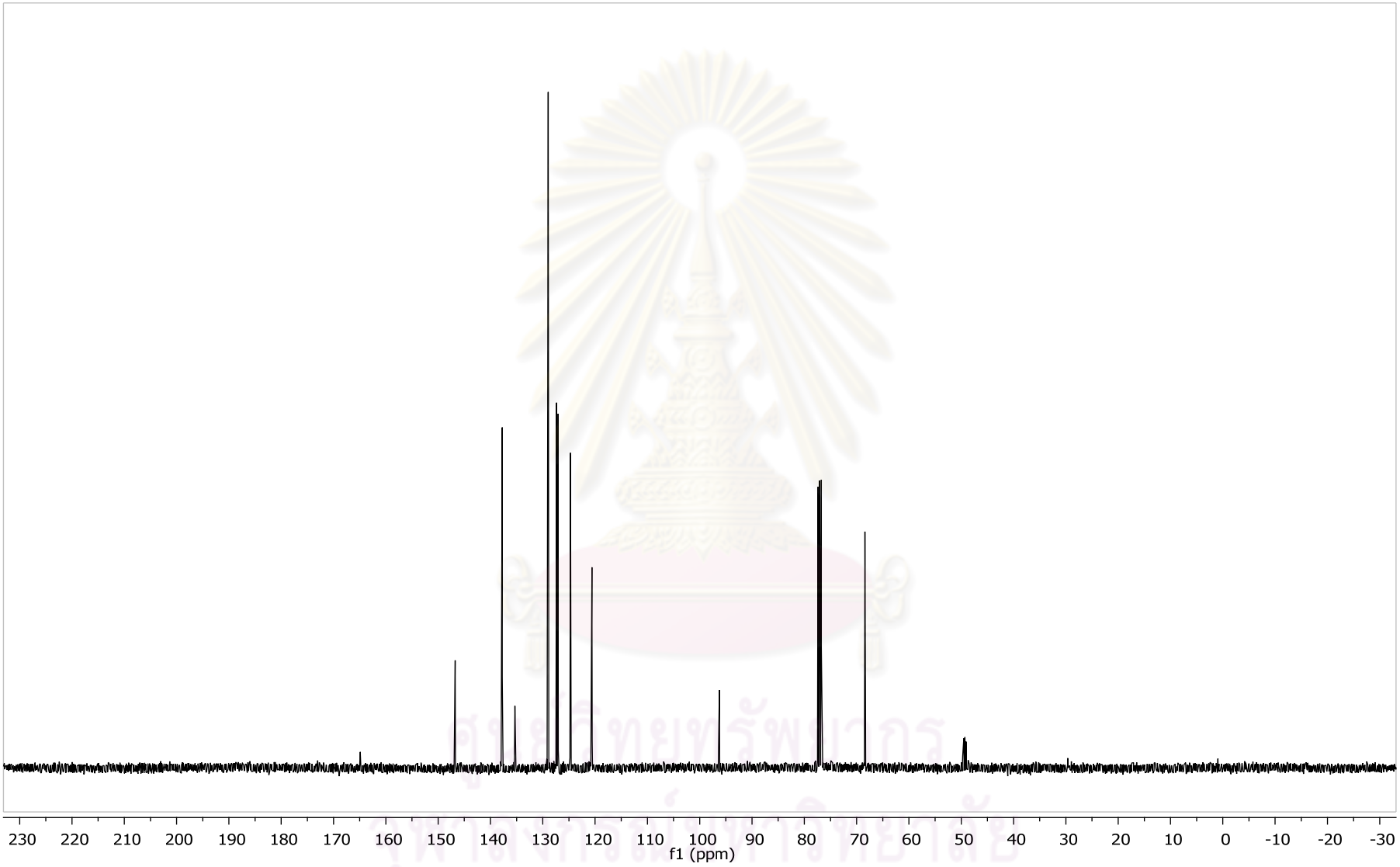

Figure A25 The ^{13}C-NMR spectrum of 3-iodo-4-(hydroxymethyl)-N-phenylbenzamide

72

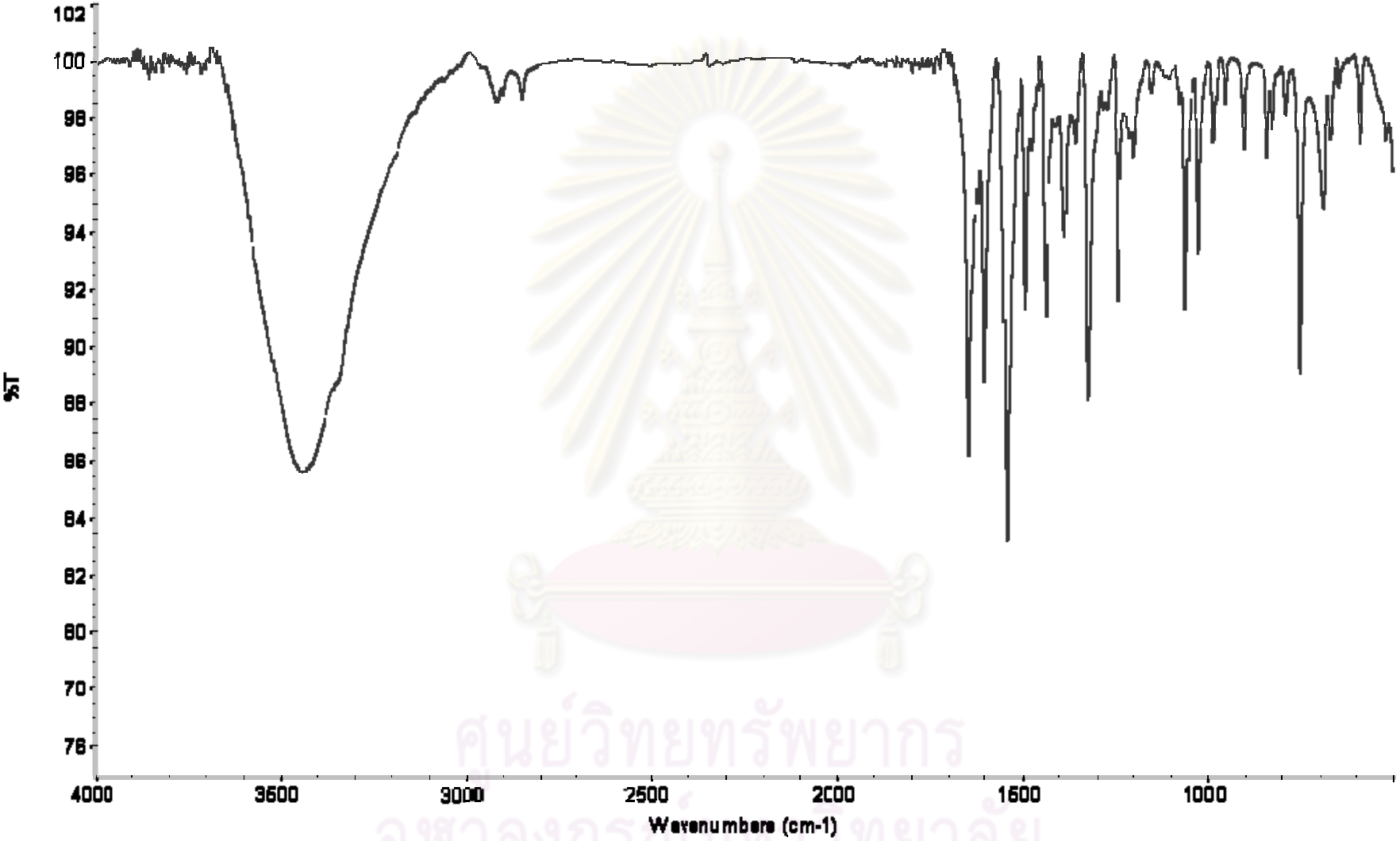

Figure A26 The FT-IR spectrum of 3-iodo-4-(hydroxymethyl)-N-phenylbenzamide

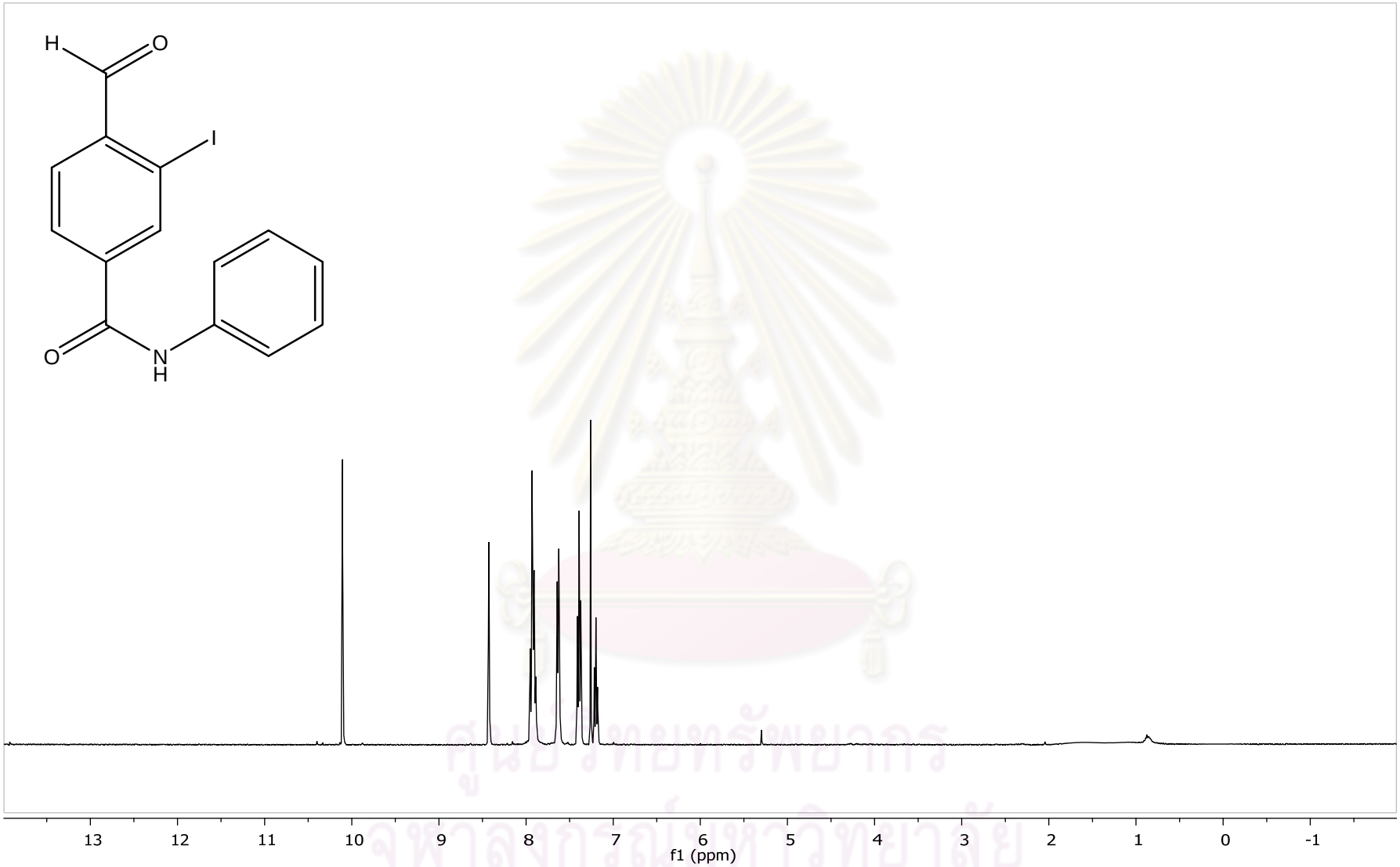

Figure A27 The ^{1}H-NMR spectrum of 3-iodo-4-(formyl)-N-phenylbenzamide

74

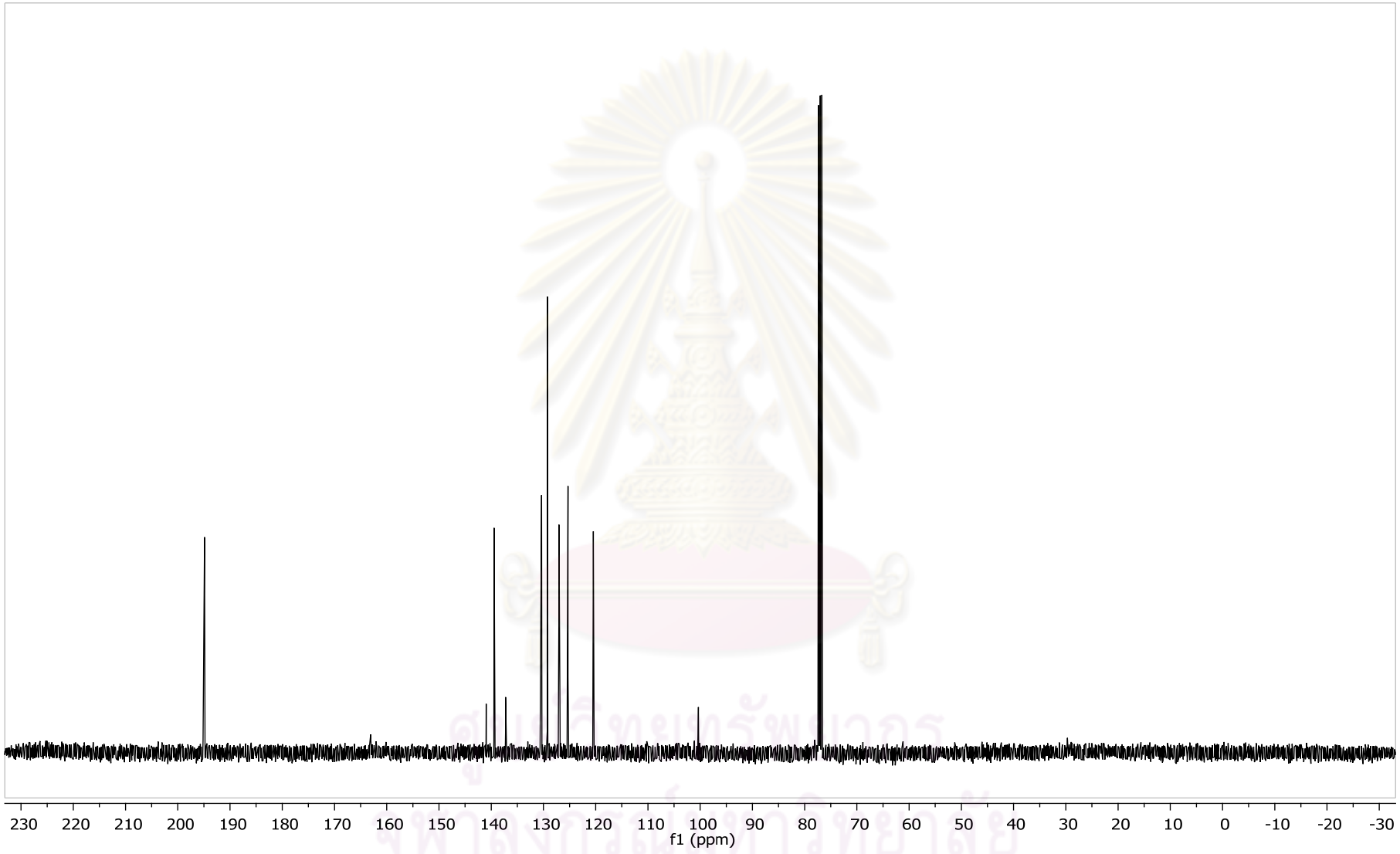

Figure A28 The ^{13}C-NMR spectrum of 3-iodo-4-(formyl)-N-phenylbenzamide

75

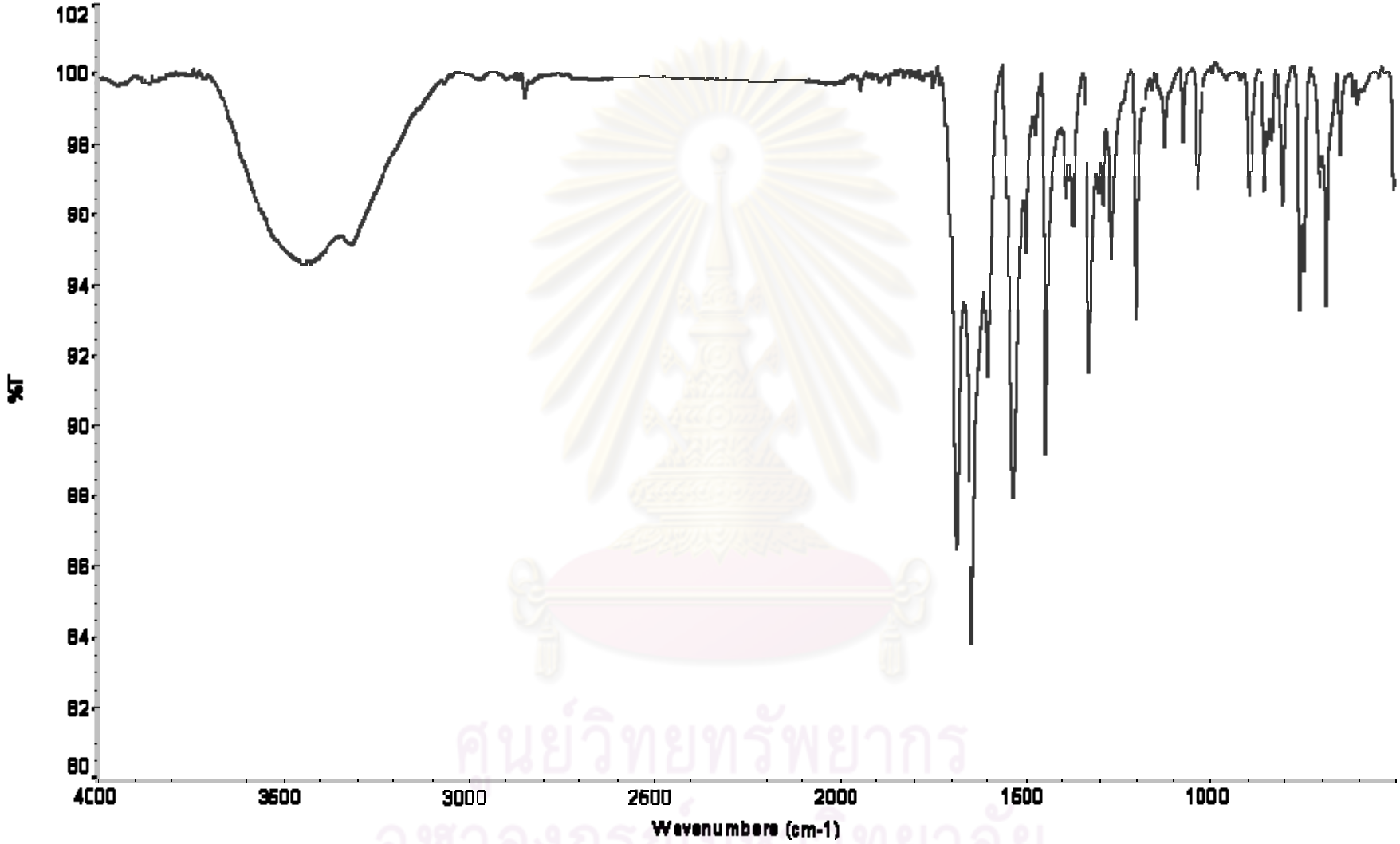

Figure A29 The FT-IR spectrum of 3-iodo-4-(formyl)-N-phenylbenzamide

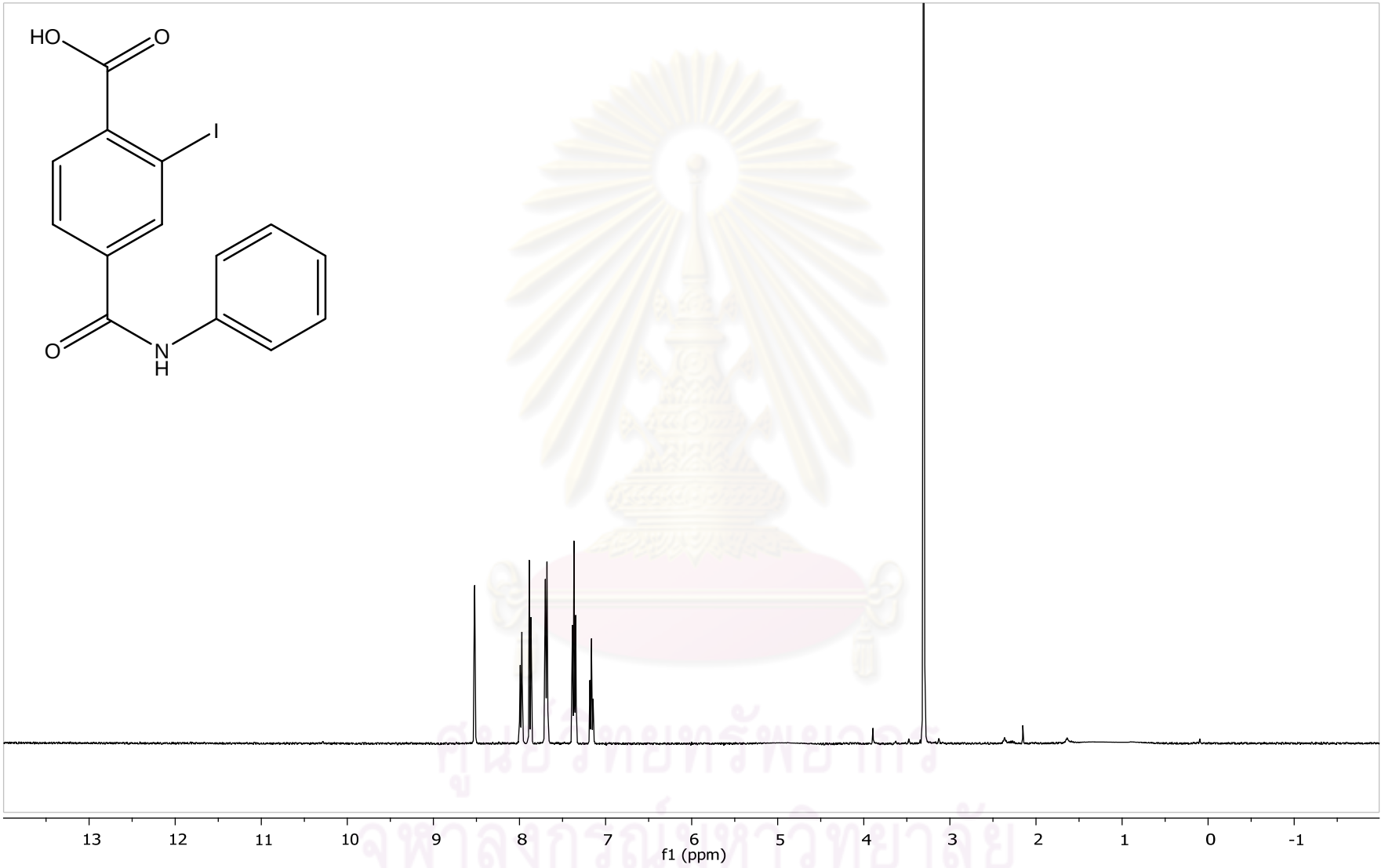

Figure A30 The ^{1}H-NMR spectrum of 3-iodo-4-(carbonyl)-N-phenylbenzamide

77

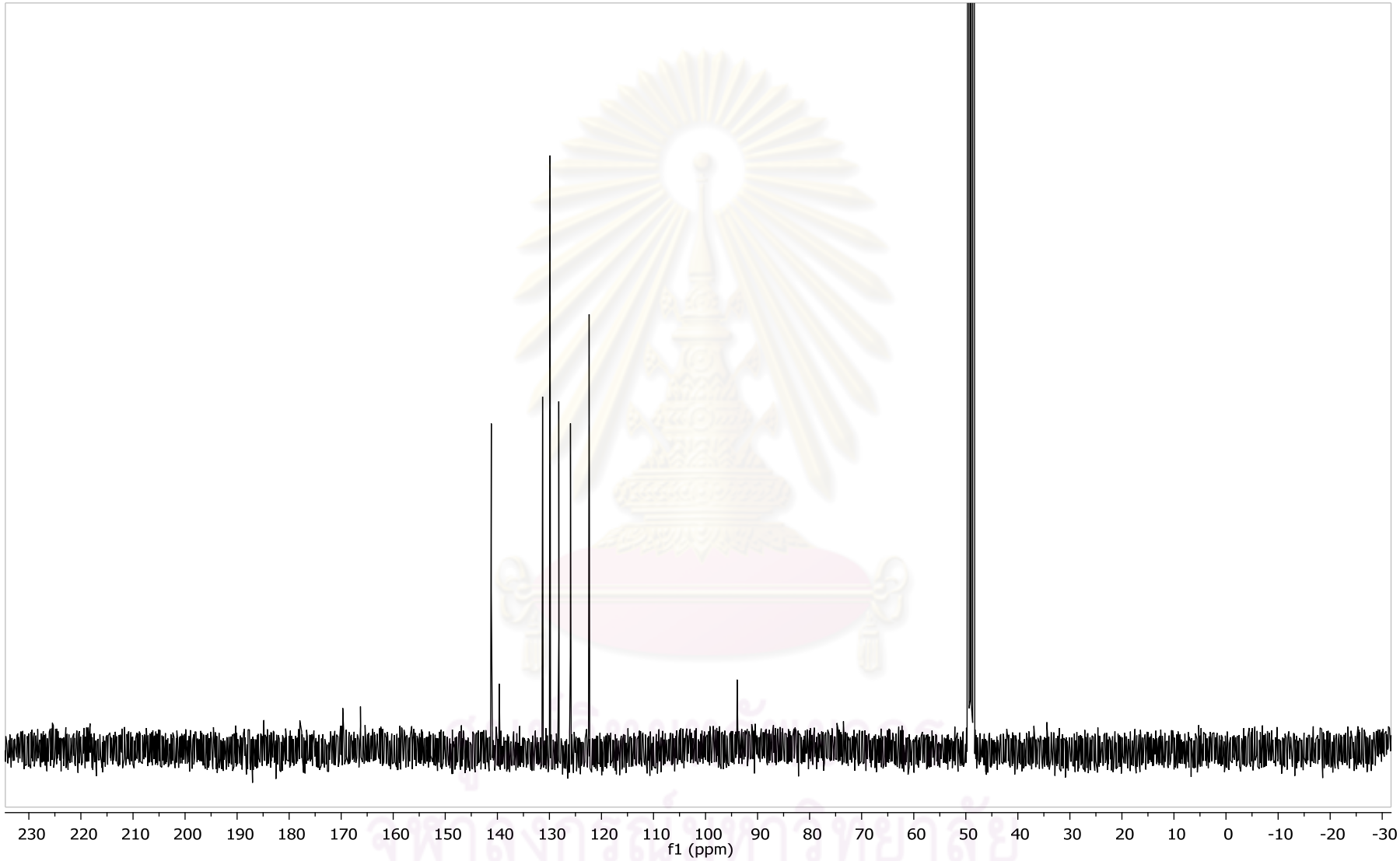

Figure A31 The ^{13}C-NMR spectrum of 3-iodo-4-(carbonyl)-N-phenylbenzamide

78

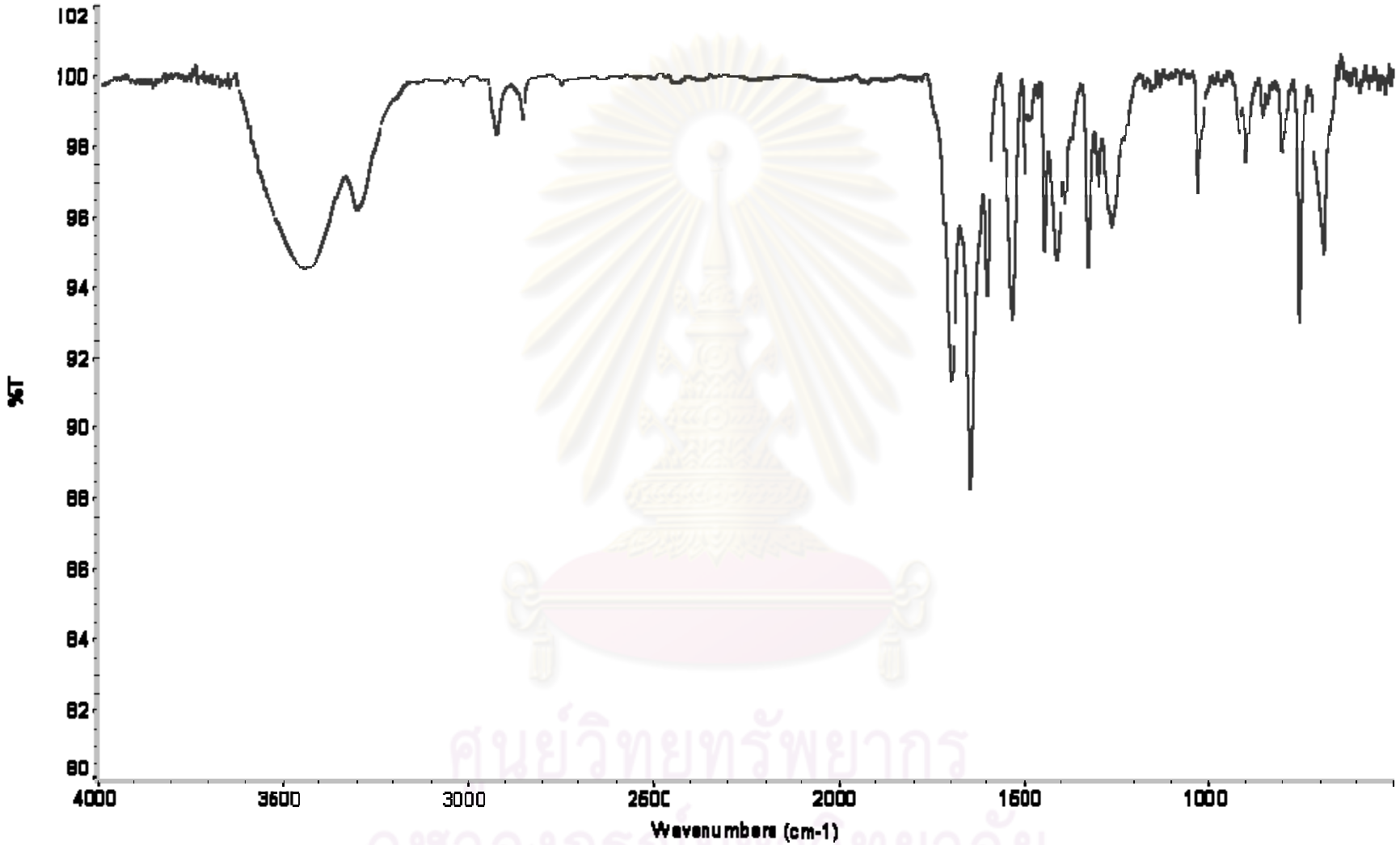

Figure A32 The FT-IR spectrum of 3-iodo-4-(carbonyl)-N-phenylbenzamide

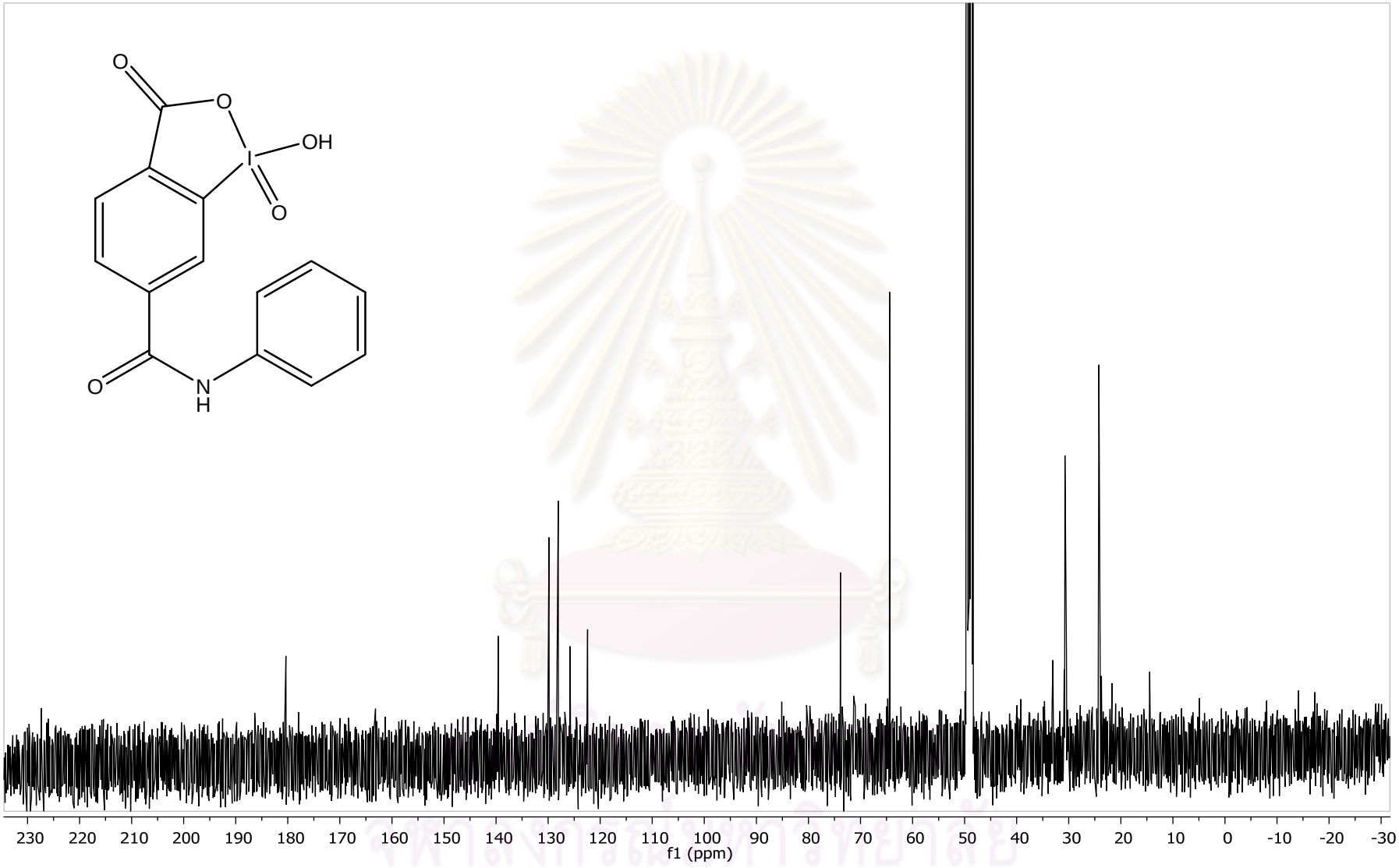

Figure A33 The ^{13}C-NMR spectrum of 2-iodoxy-4-(phenylcarbanoyl)benzoic acid

80

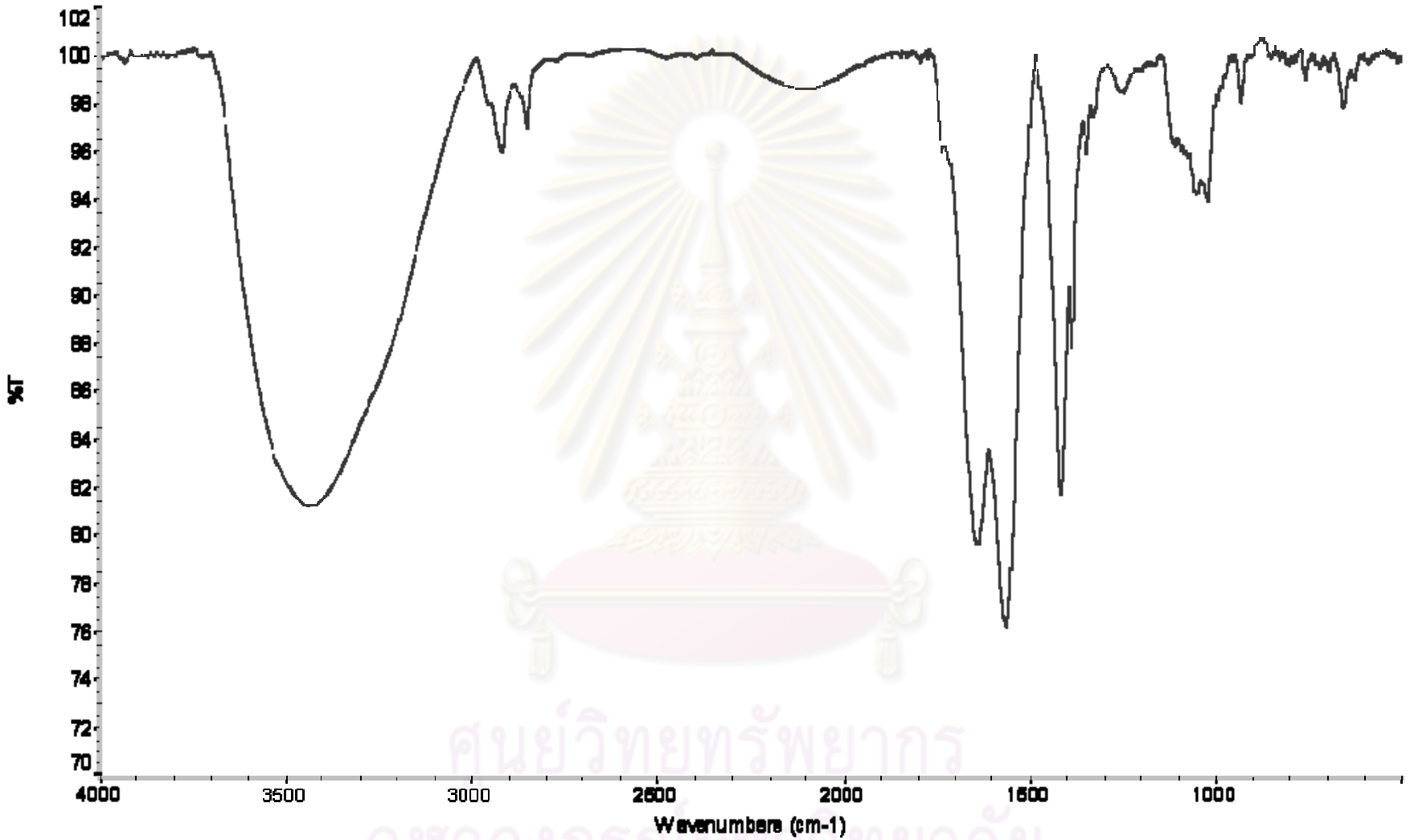

Figure A34 The FT-IR spectrum of 2-iodoxy-4-(phenylcarbanoyl)benzoic acid

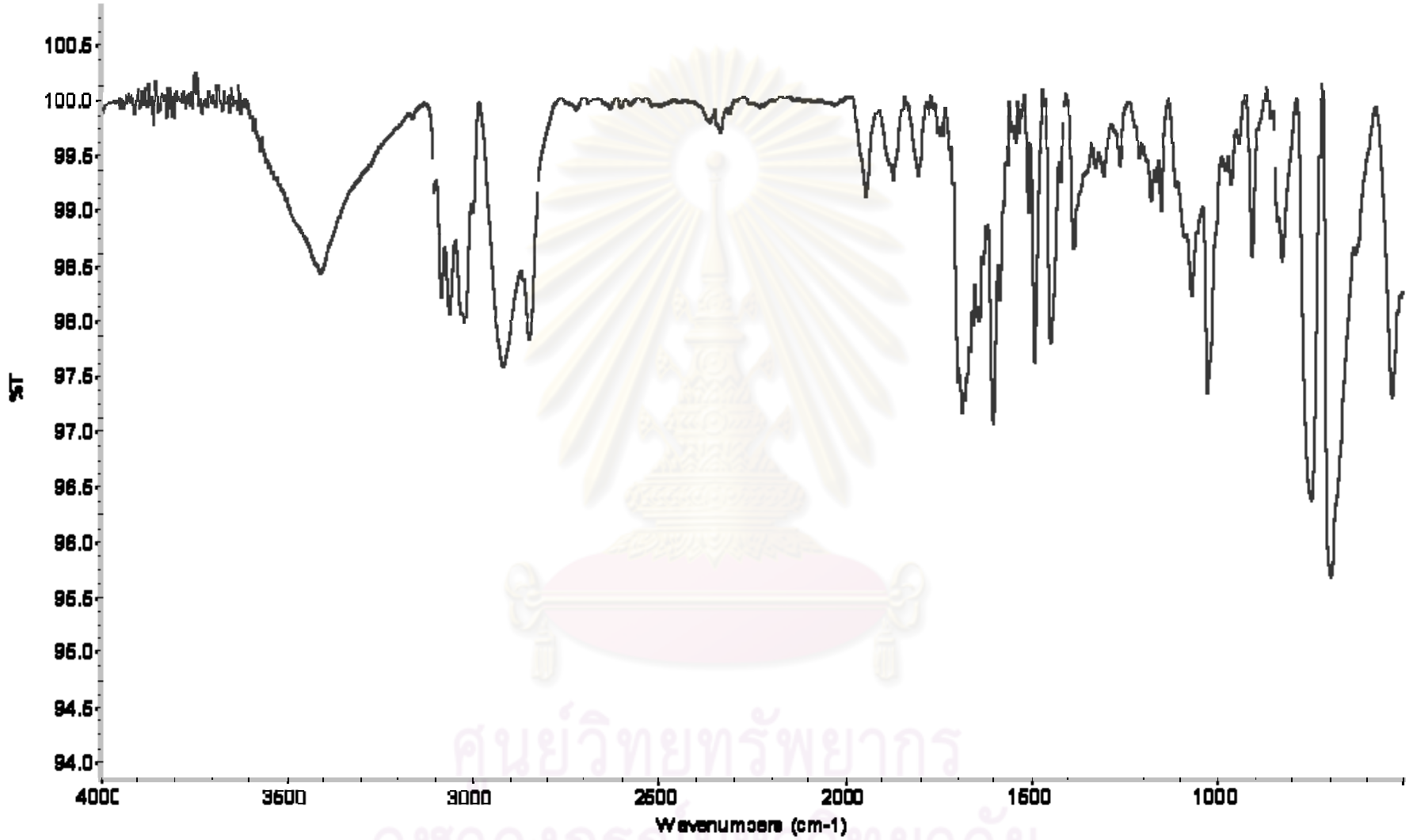

Figure A35 The FT-IR spectrum of aminomethyl polystyrene

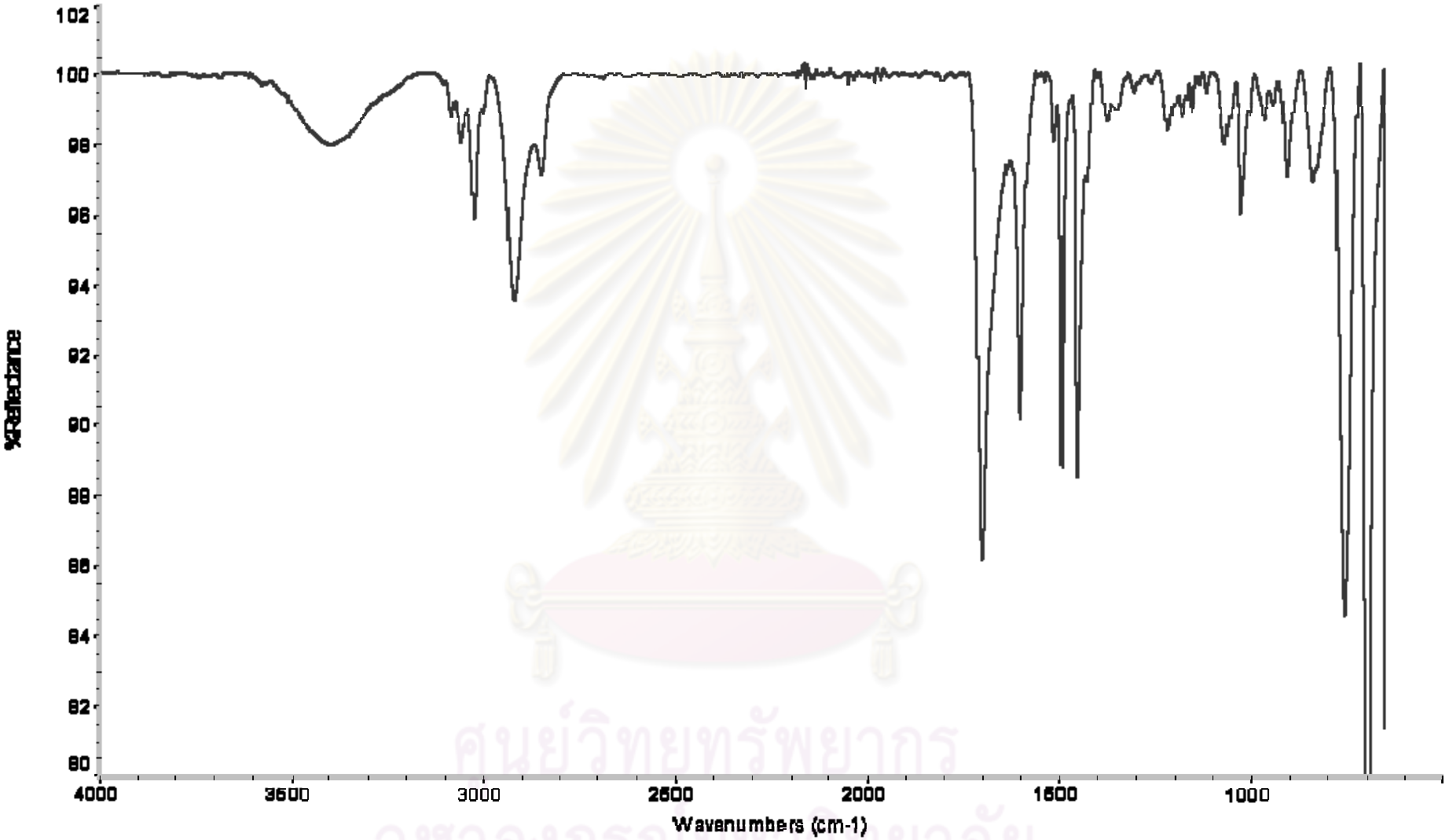

Figure A36 The FT-IR spectrum of polymer-supported 3-iodo-4-(acetoxymethyl)benzoic acid

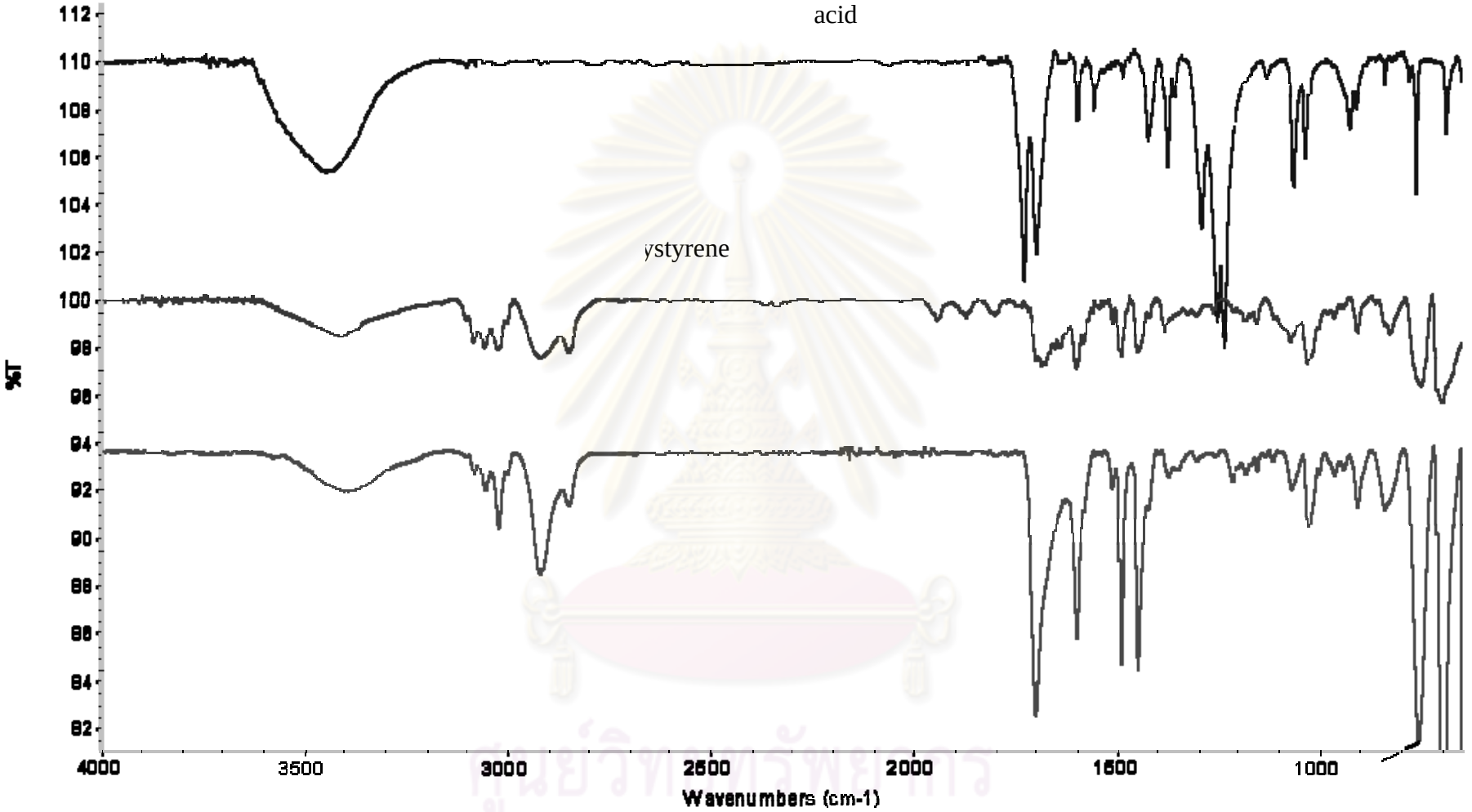

Figure A37 The FT-IR spectrum of 3-iodo-4-(acetoxymethyl)benzoic acid, aminomethyl polystyrene and Polymer-supported 3-iodo-4-(acetoxymethyl)benzoic acid

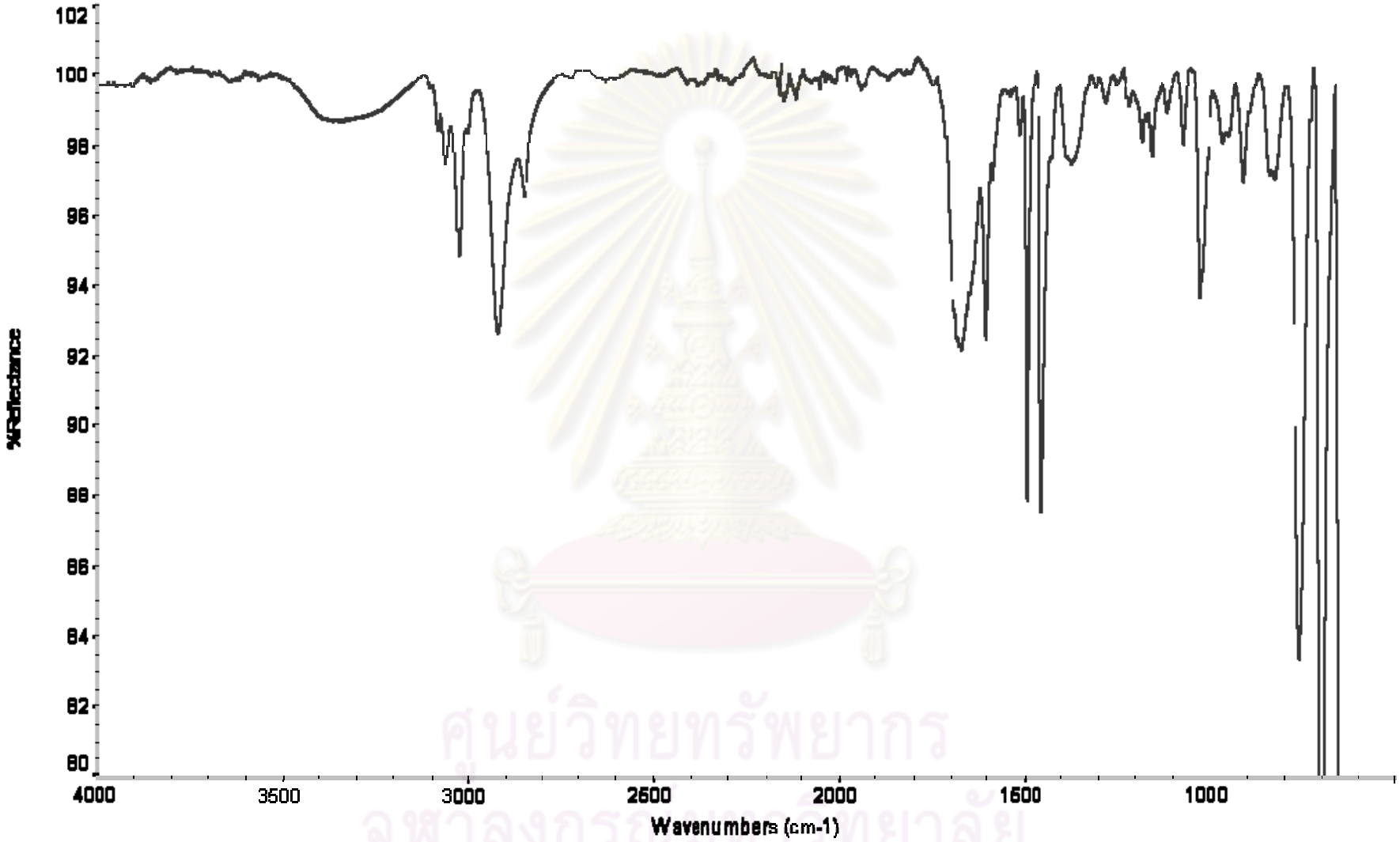

Figure A38 The FT-IR spectrum of polymer-supported 3-iodo-4-(formyl)benzoic acid

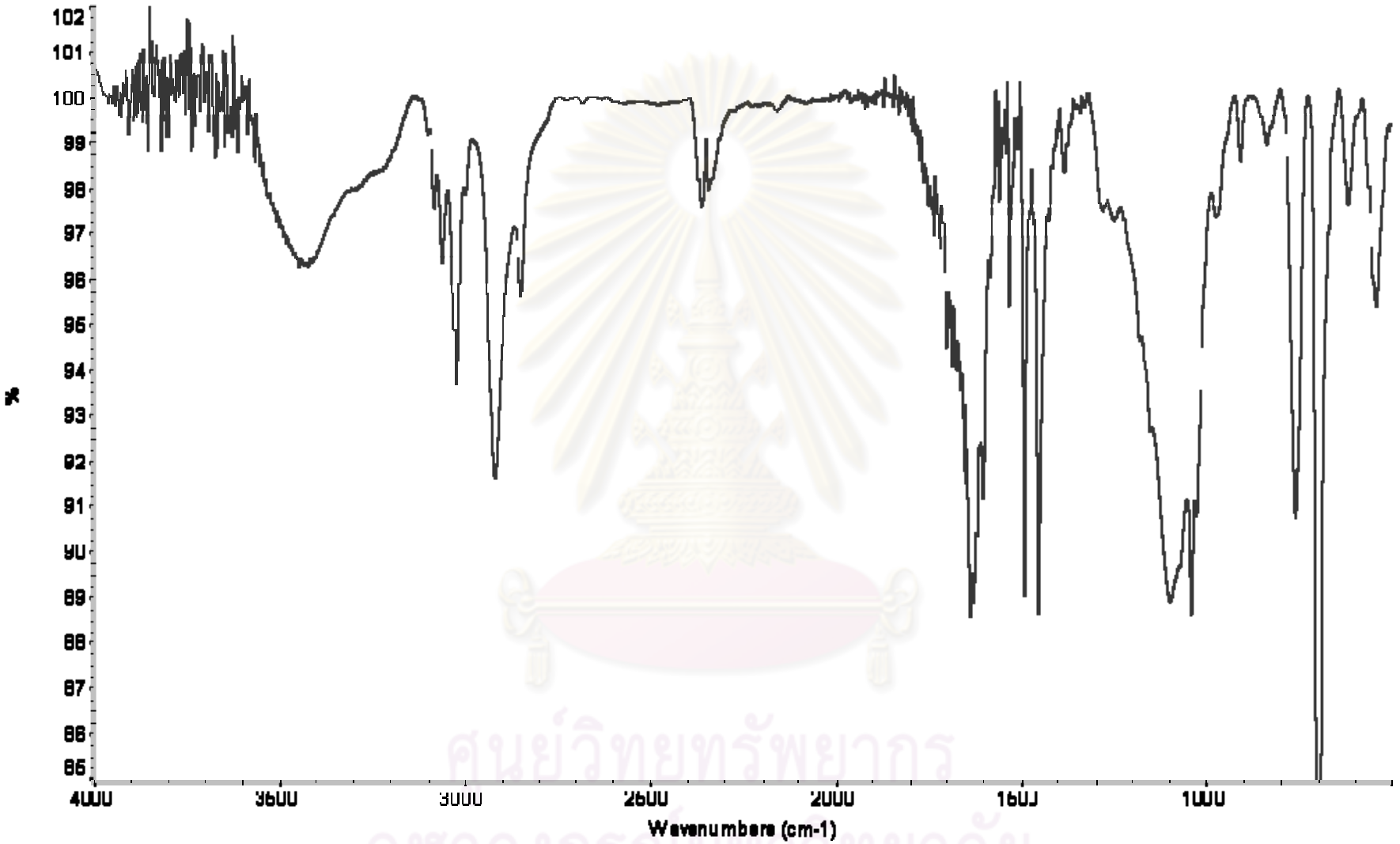

Figure A38 The FT-IR spectrum of aminomethyl polymer-supported IBX amide (**6**)

VITA

Miss Nipawan Thadkad was born on January 27, 1985 in Nonthaburi, Thailand. She graduated at Chonphathan wittaya School in 2002. She received the Bachelor Degree of Science in chemistry, Prince of Songkar University in 2007. She continued her Master study in program of Petrochemistry and Polymer Science, Faculty of Science, Chulalongkon University in 2007 and completed the program in 2010.