CHAPTER 2

POLYMER SUPPORTED REACTIONS :
SYNTHESIS OF METHYLENE DIESTERS OF CARBOXYLIC ACIDS

ABSTRACT :

This chapter describes synthesis of methylene diesters prepared by the reaction of polymer supported carboxylate anion with methylene dichloride. The reagent polymer supported carboxylate anion was prepared by treatment of Amberlite IRA-400 with aqueous solution of sodium salt of carboxylic acid.

The method reported here is very efficient for preparation of methylene diesters due to high yields, ease and simplicity. This method is particularly useful to prepare monomers such as methylene diester of cinnamic acid, to prepare bifunctional monomer like methylene diester of o-aminobenzoic acid. In addition to this, methylene diesters of heterocyclic acids such as nicotinic acid, isonicotinic acid have been prepared in quantitative yield and purity.

INTRODUCTION :

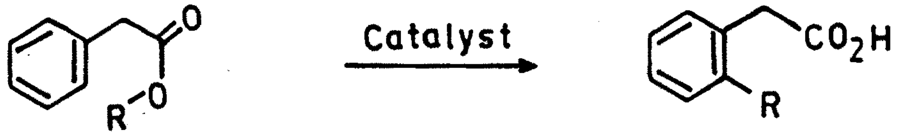
The synthesis of simple esters of carboxylic acids is generally a trivial synthetic transformation due to great variety of methods available (CH_2N_2, $MeOH-H^+$, Me_2SO_4-Base, copper salts alkyl halides[1] and CaO with alkyl halides[2]). Functionalised esters were prepared by Bryson with the purpose to develop methods for intramolecular transfer or intramolecular reaction of the functionalized (R") portion of the carboxylic acid ester (1.1).

Several methods for preparing such sensitive esters have been investigated by Bryson resulting in two successful procedures. The combination of thallium[3] and silver[4] salts of carboxylic acids with corresponding halomethylene effected formation of functionalized esters in generally high yields[5](1.2) A suspension of m-methoxyphenyl acetic acid and metal salt (thallous ethoxide 1 equivalent or silver oxide 1.1 equivalent) in ether was treated with chloromethyl methyl ether (1.1 to 1.3 equivalent) with cooling during the addition of halide. This was followed by heating under reflux for 1 hr under a nitrogen atmosphere. The reaction solution was cooled, filtered, washed with aqueous sodium bicarbonate, dried, concentrated in vacuo and distilled affording m-methoxyphenyl acetate (Tl, 41 %; Ag, 80 %). Symetrical and mixed functionalize esters were prepared by this method are listed in Table (1.3).

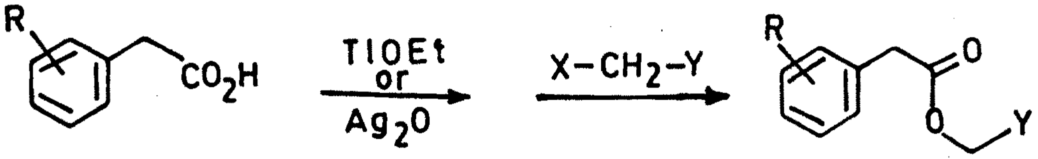
The quantitative conversion of carboxylic acids to esters by reaction of their salts with alkyl bromides or iodides in hexamethyl phosphoramide (HMPA) at room temperature has been reported[6] by J.E. Shaw.

Reaction of mesitoic acid and triethylacetic acid with sodium hydroxide in HMPA followed by addition of ethyl iodide gave the ethyl esters in quantitative yield. In each case the time required for alkylation was less than 5 min at room temperature. The short reaction time, simple procedure and quantitative yield of this reaction make it a valuable method for preparing ethyl esters[7-9]. Other solvent systems such as

CHART-1

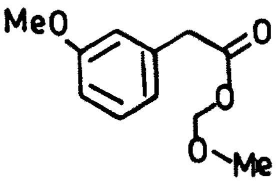
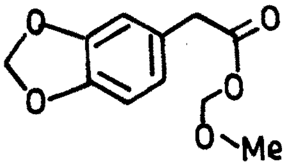
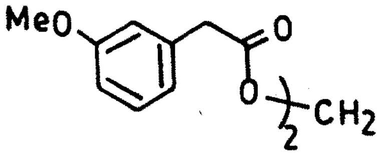
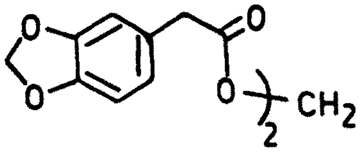
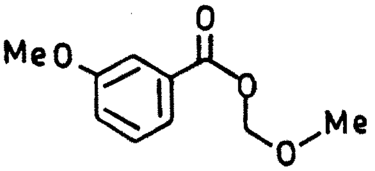
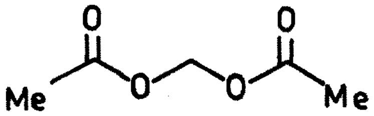


(1)



(2)

Table (3)

Compound	mp/bp °C	Yield %	
		Ag_2O	TlOEt
	112 0·06 mm Hg	80	41
	160 0·025 mm Hg	65	50
	180 0·04 mm Hg	—	75
	55	—	65
	120 0·025 mm Hg	60	—
	80 85 mm Hg	30	35

dimethyl sulphoxide and dimethyl formamide required the use of longer reaction times. Reaction of sodium triethyl acetate with ethyl iodide at room temperature was only two third complete after 5 min in dimethyl sulphoxide and about one third complete after 15 min in dimethylformamide.

Esterification of certain carboxylic acids required the use of unhydrous potassium carbonate as base, since sodium hydroxide caused some decarboxylation. When a solution of malonic acid, sodium hydroxide (aqueous 25 %) and HMPA was stirred for 15 min at room temperature followed by addition of ethyl iodide and continued stirring overnight, only 36 % yield of diethyl-malonate was obtained. The sodium hydroxide caused some decarboxylation of malonic acid as evidenced by the precipitation of sodium carbonate from the solution.

Some decarboxylation was also observed when triphenylacetic acid was treated with sodium hydroxide in HMPA. When a mixture of malonic acid, powdered anhydrous potassium carbonate, ethyl iodide and dry HMPA was stirred for 24 hr at room temperature much higher yield (91 %) of diethyl malonate was obtained. The same procedure used for triphenyl acetic acid gave a 100 % yield of ethyl triphenylacetate[10].

Reaction of sodium salt of 2-ethyl butanoic acid and benzoic acid with dibromomethane in HMPA at room temperature gave 100 % and 86 % yields of corresponding methylene diesters. Sodium benzoate required a longer reaction time (48 hr) than sodium 2-ethylbenzoate (24 hr). This is probably because sodium benzoate, unlike sodium 2-ethyl butanoate is not completely soluble in HMPA[11].

Previously methylene diesters have been prepared from formaldehyde vapour and acid unhydride with H_2SO_4 as catalyst[12] or from paraformaldehyde and acid halide in the presence of $ZnCl_2$[13]. The formation of an aromatic methylene diester by heating a mixture of a carboxylic acid, methylene chloride and triethylamine have been reported[14].

Some of the methylene diesters have been prepared by reaction of paraformaldehyde or polyoxymethylene with an acid unhydride in the presence of mineral or Lewis acid[15-16].

More useful alternative for preparation of methylene diesters of carboxylic acids was reported by K. Holmberg and B. Hansen. Methylene diesters were obtained in good yields from the reaction between TBA (tetrabutyl ammonium) salt of carboxylic acid and dichloromethane. The esters were formed in good yield and purity[17].

Now we found that the reaction between polymer supported carboxylate anion and dichloromethane is still more efficient method than the methods reported yet, for the preparation of methylene diesters.

Polyesters were obtained by base catalysed addition of hydrogen sulfide to α-,β-unsaturated diesters. The polymer formed possess the general formula $(CHR^1\ CHR^2.\ CO\cdot X\cdot R^3\cdot X\cdot CO.\ CHR^2CHR^1S)_n$ wherein R^1 is hydrogen, methyl or phenyl, R^2 is hydrogen or methyl, R^3 is alkylene, aralkylene or oxyalkylene group and X is oxygen, sulpher or imino group. Depending upon the structure, the products are liquids, rubbers or solids. The polymers are obtained with vinyl or sulphahydril termination and efficiency of this termination is very high[18].

The reaction of hydrogen sulphide with diester of unsaturated mono acid produce polyester of thioacids. Thus ethylene diacrylate yields poly (ethylene thiodipropionate)[18].

With the method reported here it is possible to prepare such functionalized α, β unsaturated diesters and one such as methylene dicinnamate reported here, is obtained in very good yields. Our further plan includes polymerisation of such monomers.

Recently chloromethyl esters were prepared from the reaction both chloromethyl chlorosulphate and tetrabutyl ammonium carboxylate. Methylene diesters were prepared from the reaction between tetrabutyl ammonium carboxylate and methylene (bis) chlorosulphate. Fast reaction and quantitative yields are the main features of the reaction[19].

PRESENT WORK :

Generally the polymer support (especially we used here Amberlite IRA-400 (Cl^-) a strongly basic anion exchange resin) causes anionic activation of the anion held. This anionic activation found to be very useful for occurence of some reluctant reactions by traditional methods.

The reaction of polymer supported carboxylate anion with dichloromethane under reflux gave corresponding methylene diesters in quantitative yields and purity.

The reaction times were considerably shortened as compared to that required for reaction between TBA salt of carboxylic acid and dichloromethane[17], owing to the high anionic activation of carboxylate anion.

Dichloromethane act as reactant as well as solvent. Polymeric supports other than Amberlite IRA-400 (Cl^-) were used. Other polymeric supports used were Tulsion A-36, Tulsion A-72 and found to be equally effective as Amberlite IRA-400.

The results are listed in Table (chart 2).

EXPERIMENTAL

General procedure for preparation of polymer supported carboxylate anion :

Commercial strongly basic anion exchange resin in chloride form [Amberlite IRA-400 (Cl^-)] packed in a column was washed with 0.25 N aqueous sodium salt of carboxylic acid until complete removal of chloride ion. The resin was then successively washed with water, alcohol and ether. Finally dried in vacuo at 50°c over P_2O_5 for 10 hr. The exchange capacity was determined by passing 1 M sodium chloride solution 100 ml through the resin (0.3 gm) in a column. The amount of carboxylate anion in the eluent was titrated with 0.01 N hydrochloric acid using methyl orange as an indicator. The exchange capacity was found to be 1.4 - 1.6 mmol/gm of dry resin.

For resins Tulsion A-36 (Cl^-) and Tulsion A-72 (Cl^-), the same procedure was used.

General procedure for preparation of methylene diester of carboxylic acids :

Polymer supported carboxylate anion (5 mmol) was refluxed in 15 ml dichloromethane (Table 2). After completion of reaction, the resin was removed by filteration and washed with some more quantity of dichloromethane. Evaporation of

CHART-2

Reaction

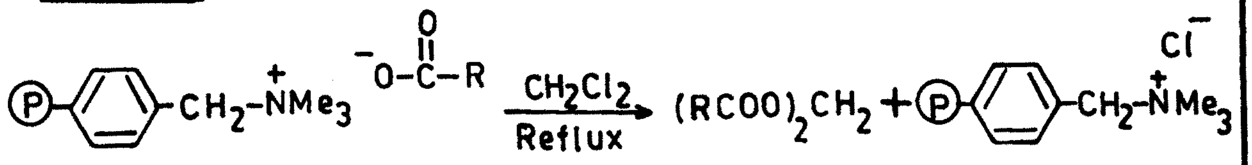
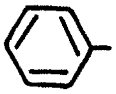
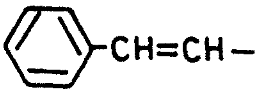
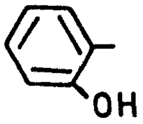
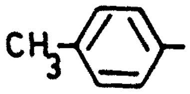
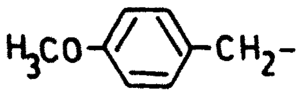
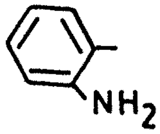
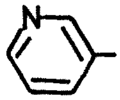
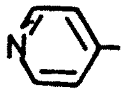
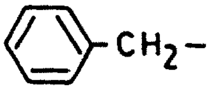
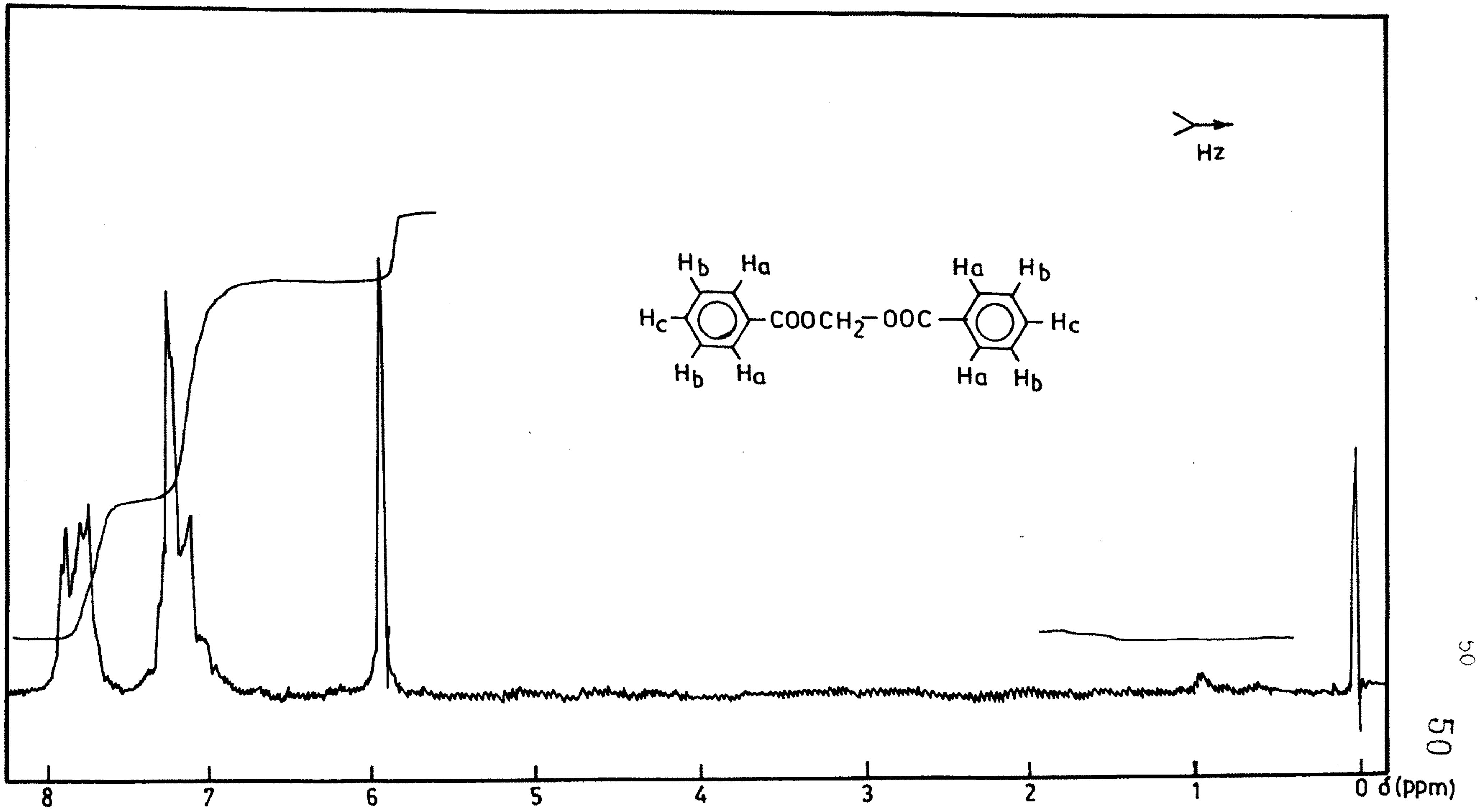


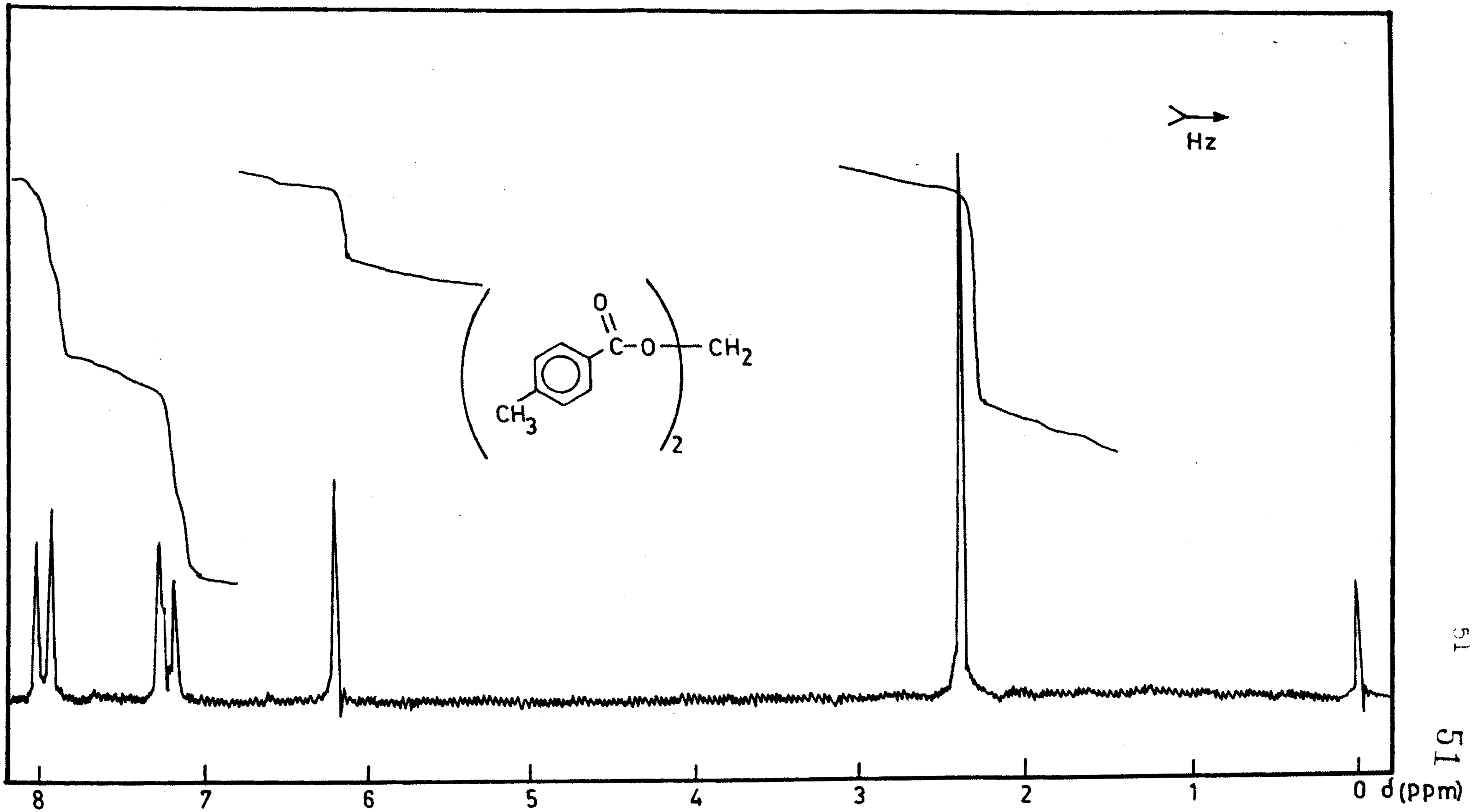
Table : Methylene diesters from carboxylic acids

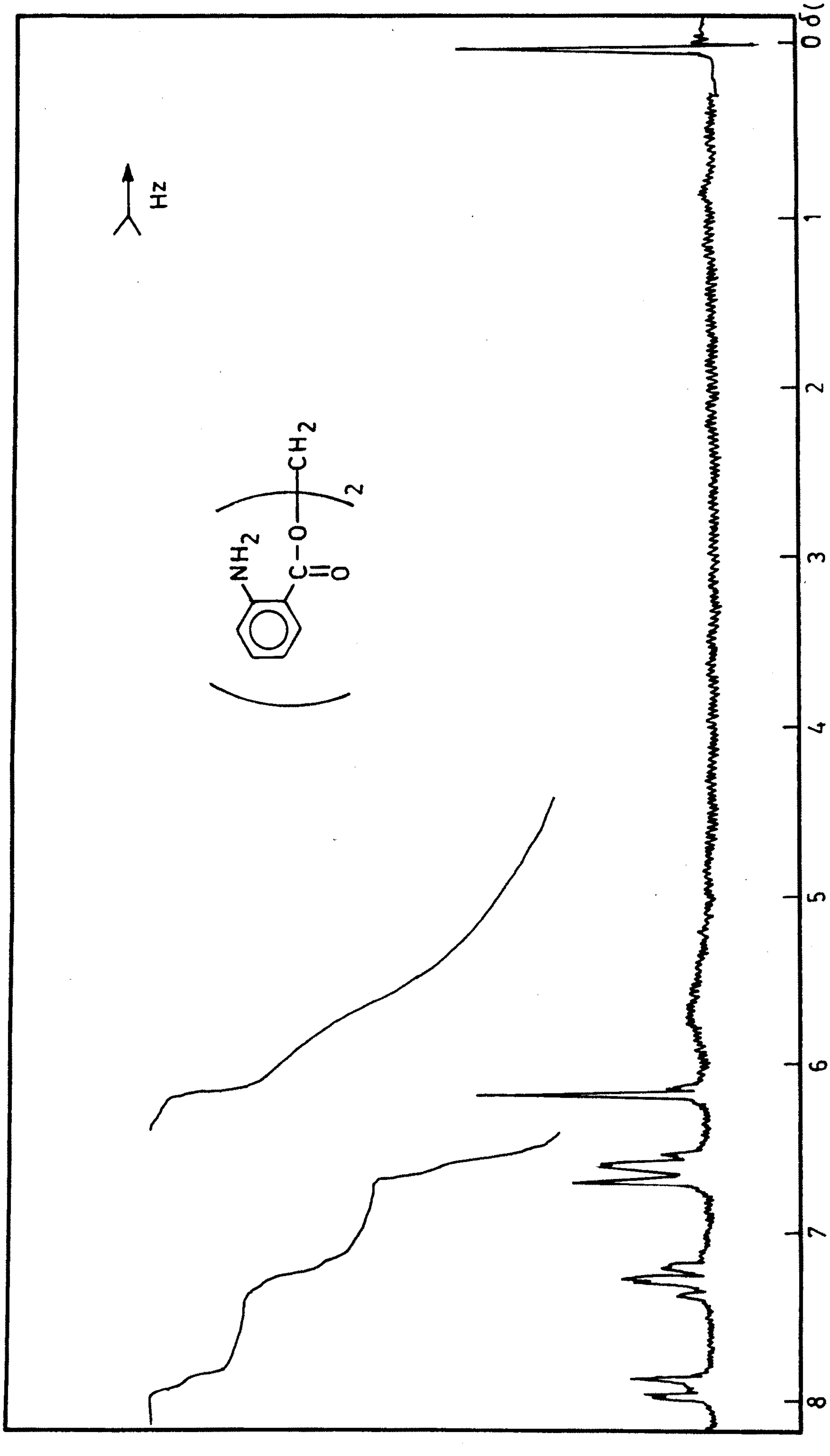
R	Reaction time hr.	Yield %	mp/bp °C
	56	98	96
	56	98	83
	56	90	105
	60	90	96
	90	98	78
	96	50	112
	96	95	190
	96	95	185
	96	90	
$CH_3-CH_2-CH_2-$	56	90	219

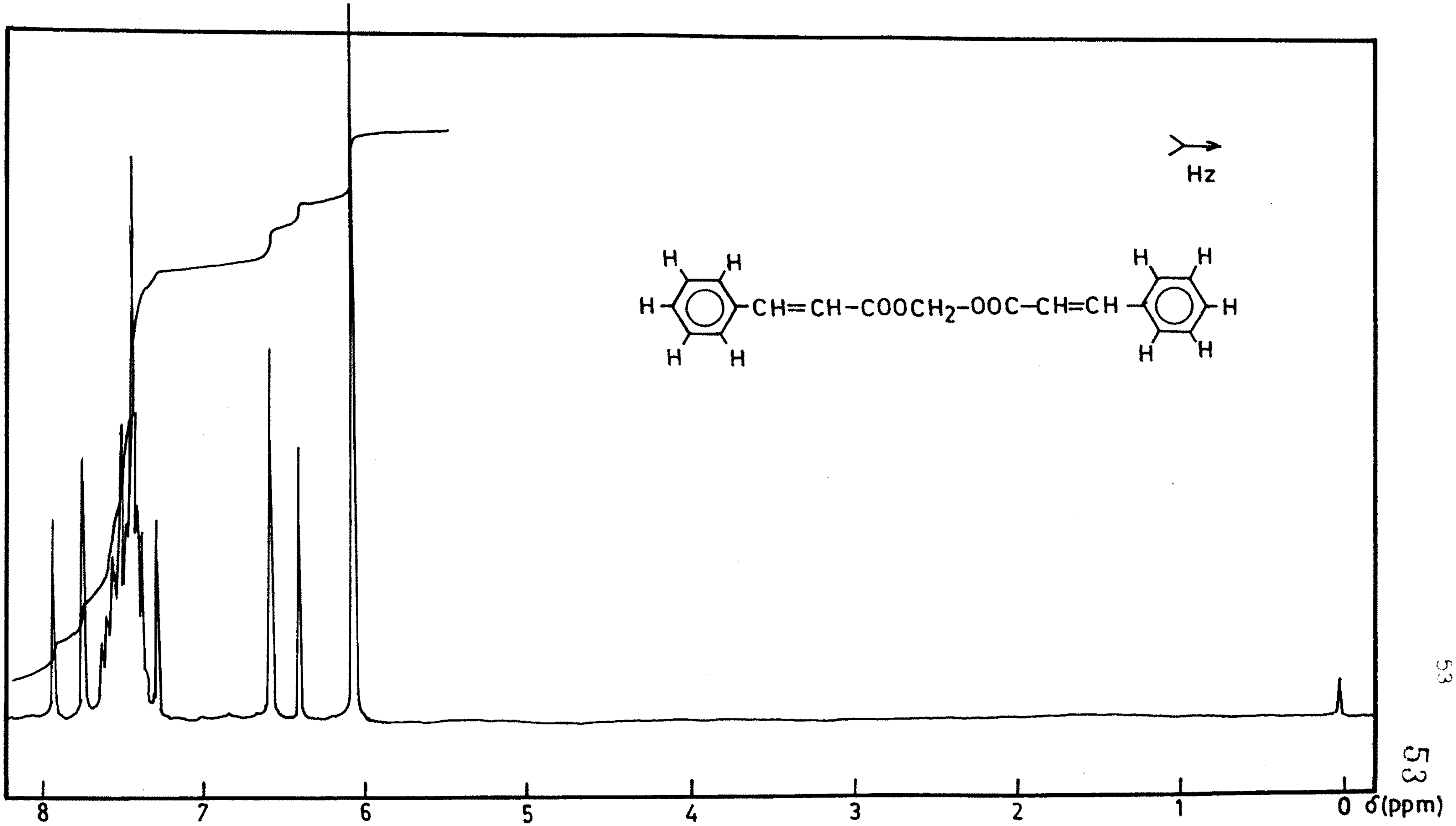
the solvent furnished corresponding methylene diester in quantitative yield and in essentially pure form.

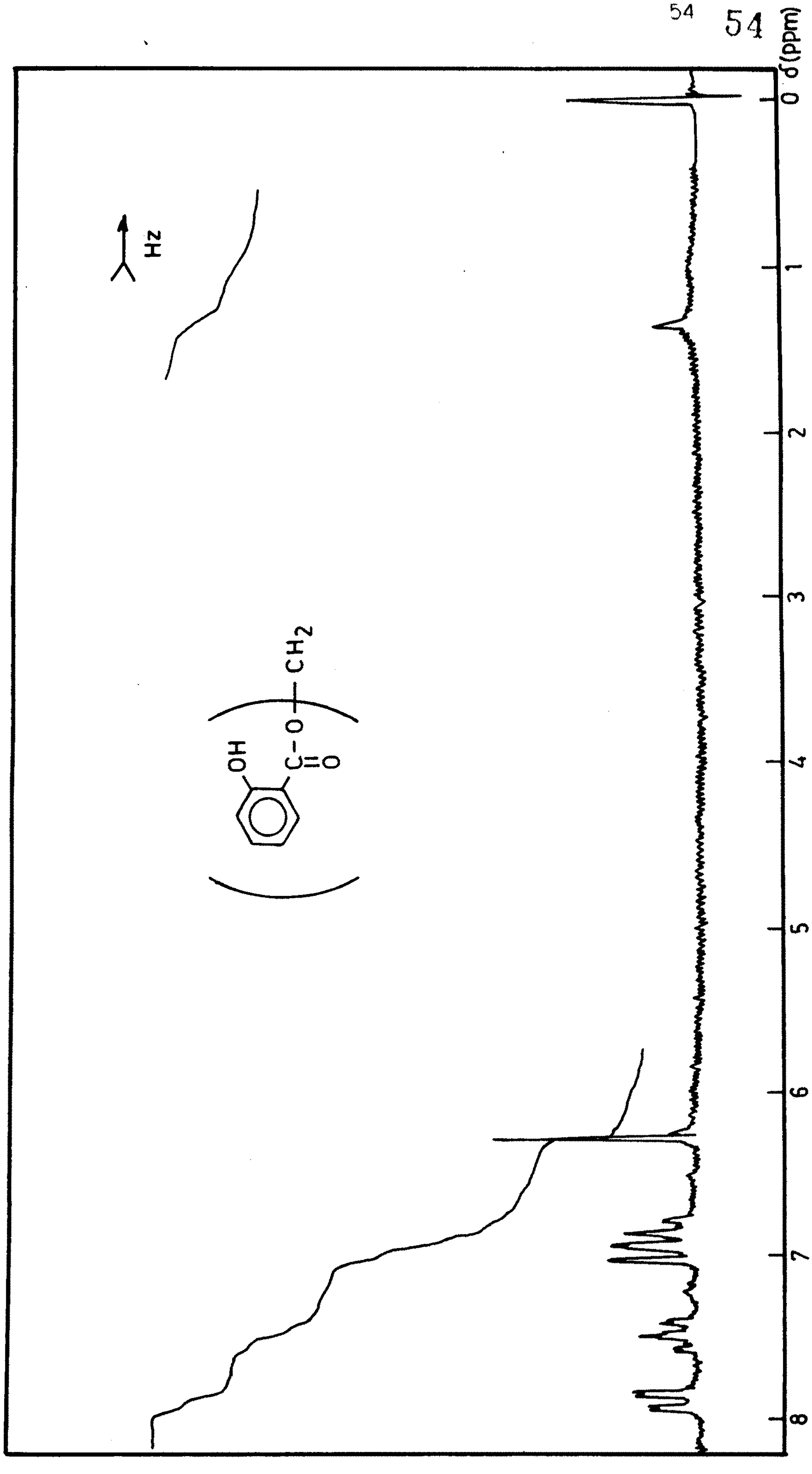
The products were characterised by PMR, IR and TLC. Some of the illustrative PMR spectra are given just after this.

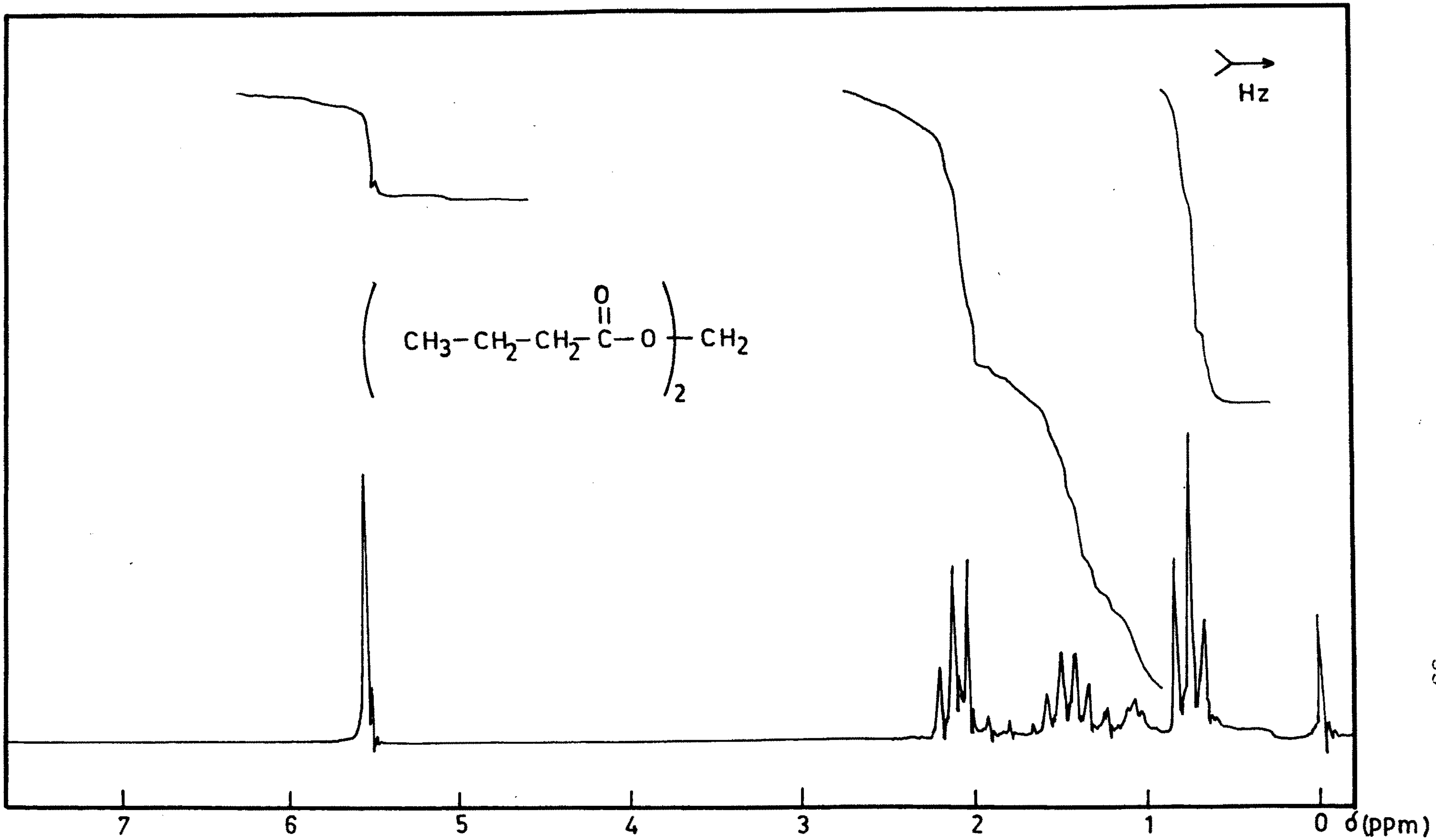

Hz
Hb
Ha
Hc
COOCH2—OOC
Ha
Hb
Hb
Ha
Hc
Ha
Hb
8
7
6
5
4
3
2
1
0 δ(ppm)

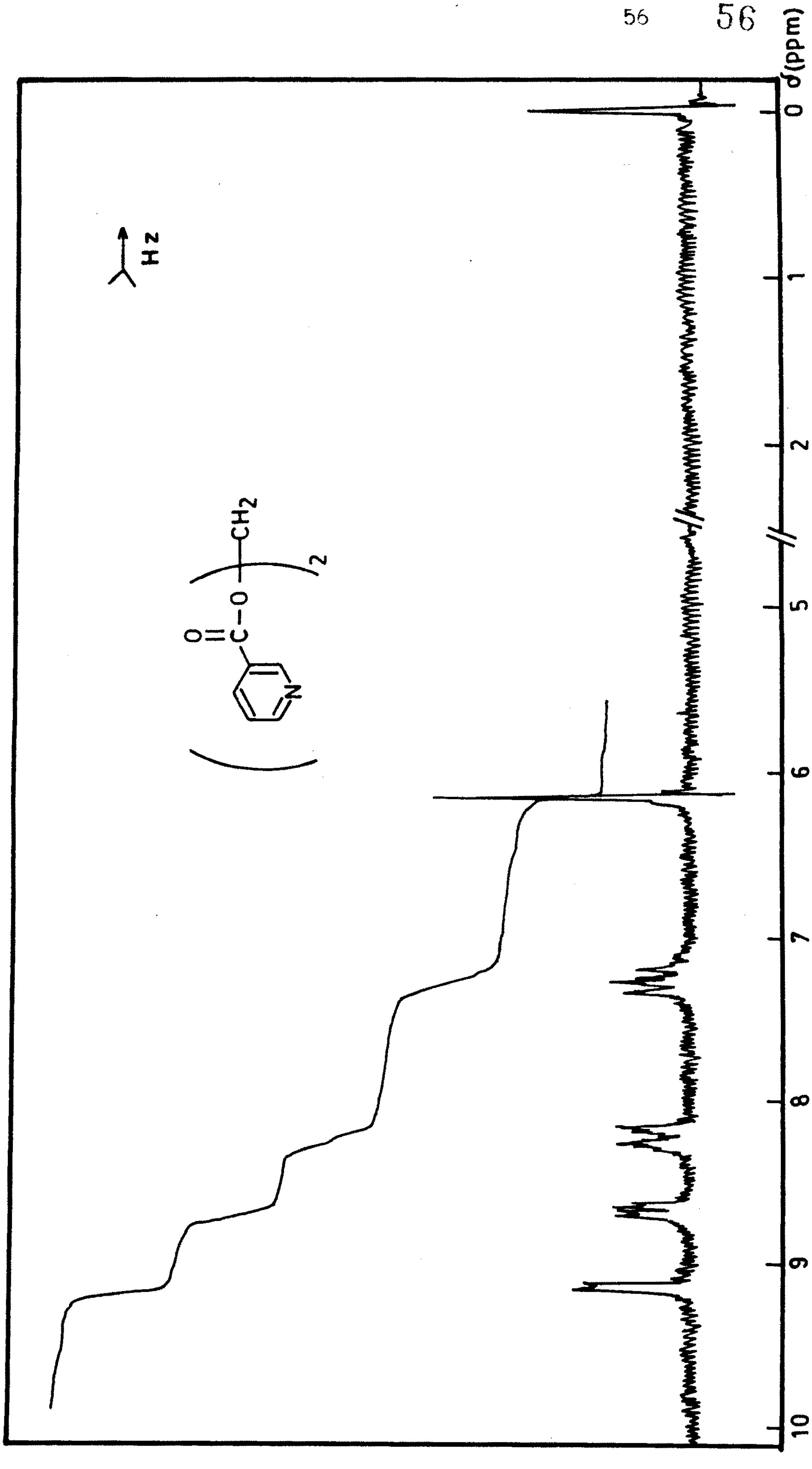

Hz
O
C–O
CH2
CH3
2
8
7
6
5
4
3
2
1
0
δ (ppm)

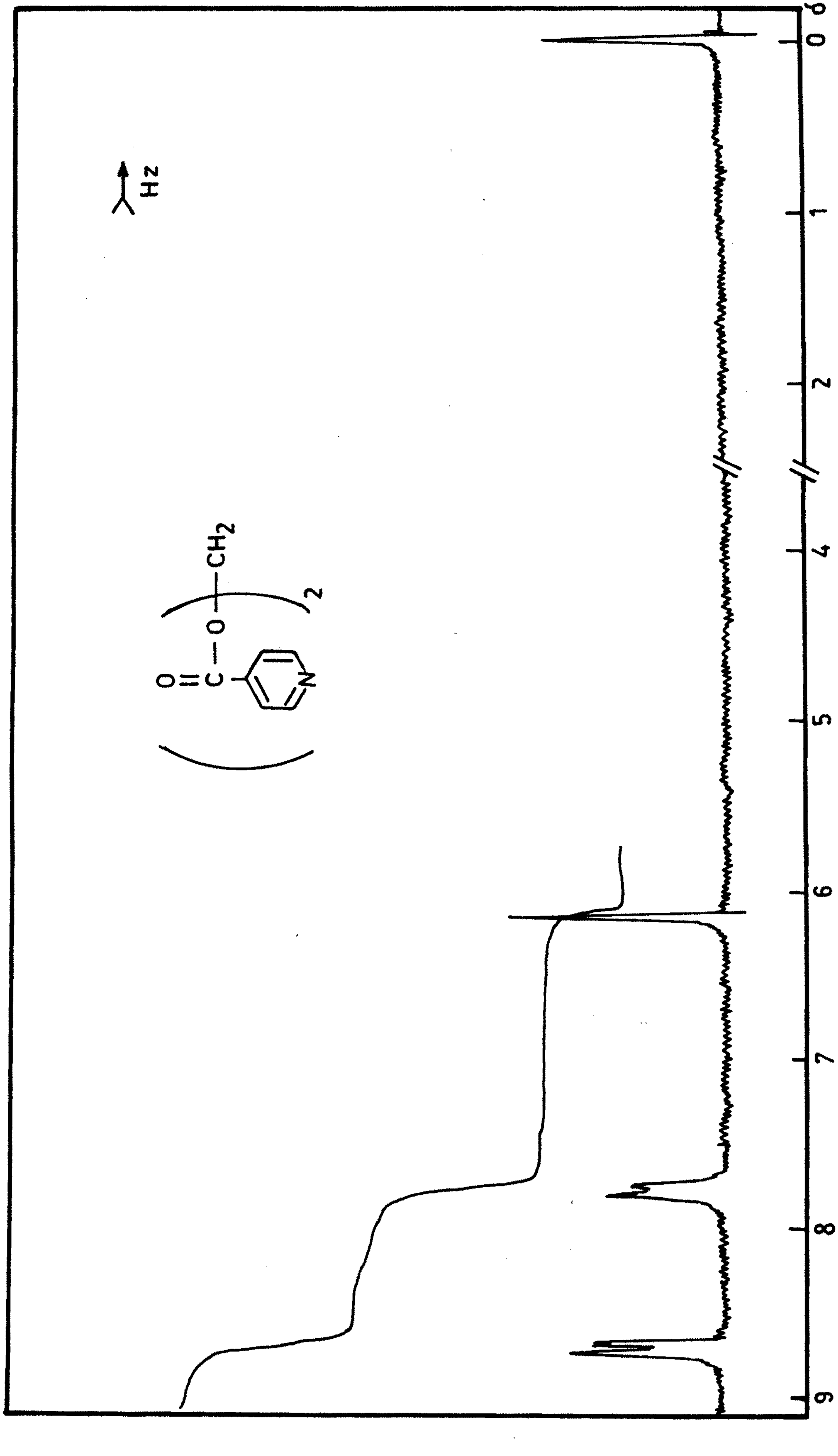

Hz
NH$_2$
C–O
O
CH$_2$
2
0 δ(ppm)
1
2
3
4
5
6
7
8


Hz
CH=CH–COOCH2–OOC–CH=CH
H
8
7
6
5
4
3
2
1
0
δ(ppm)


δ(ppm)
0
1
2
3
4
5
6
7
8
Hz
OH
C-O-CH2
O


Hz
$(CH_3-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-O)_2-CH_2$
7
6
5
4
3
2
1
0
δ(ppm)


Hz
O
C–O
N
CH2
2
δ(ppm)
0
1
2
5
6
7
8
9
10


d(ppm)
0
1
2
4
5
6
7
8
9
Hz
O
C
O
CH$_2$
N
2

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