SELECTIVITY OF THE POLYMER-SUPPORTED WILKINSON'S CATALYST

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ABSTRACT

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WILKINSON'S CATALYST

By

Sawit Phisanbut

In order to study the selectivity of the polymer-supported Wilkinson's catalyst, which had been proved to catalyze the hydrogenation of substrates of different sizes with different reduction rates, the Δ^2-steroid links by an ester linkage with different kinds of unsaturated fatty acid were used as the substrates for the reduction. The results seem to indicate that in benzene solution, the steric effect of the polymer is the factor that determines the selectivity of the catalyst. As the polarity of the solvent increases the length of the side chain of the steroid, instead of the steric effect, becomes an important factor in determining the selectivity of the supported catalyst.

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Sawit Phisanbut

A THESIS

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To my parents

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INTRODUCTION

In the past decade, the development of transition metal complexes which act as homogeneous catalysts has interested many researchers.[1] The first rapid and practical system developed for homogeneous hydrogenation of alkene and alkyne at 25°C and 1 atmospheric pressure was Wilkinson's catalyst [$RhCl(P\emptyset_3)_3$] in benzene solution.[2] Most homogeneous catalysts have proved to be more selective and operate under milder condition than a corresponding heterogeneous system. Although the heterogeneous catalyst reactions are exceedingly difficult to study in detail, the important advantage of the heterogeneous over a homogeneous catalyst is the difficulty in the separation of the homogeneous catalyst from the solution after reactions without the loss of catalytic activities.

Merrifield[3] reported the solid-phase peptide synthesis in which a peptide chain can be synthesized within the insoluble matrix in a stepwise manner from one end while the other end is attached to the insoluble polymer (styrene-divinylbenzene) by a covalent bond. The reaction inside the polymer beads are similar to the reactions in

the solution. Since that time rapid advances have been made in using insoluble polymer-supported for synthetic[4] and catalytic[5] purposes. Several attempts have been made to combine the advantages of homogeneous and heterogeneous catalysis; for example, Manassen[5a] prepared the heterogeneous hydroformylation catalyst by heating copolymer p-diphenylphosphinostyrene-divinylbenzene beads at 100°C with rhodium chloride or cobolt chloride under a carbon monoxide atmosphere to prepare a catalyst which can be removed after reactions by filtration and reused again. Capka[5b] and co-workers used an insoluble polymer-supported rhodium (I) complex as a hydrosilylation catalyst for alkene.

One of the most successful areas of research has involved the preparation of the polymer-supported Wilkinson's catalyst[6] which converts the homogeneous catalyst into a heterogeneous system. This catalyst can be easily removed from the solution and reused many times without significant loss of activity. As pointed out by Collman,[7] most of the homogeneous catalyst must have a vacant coordination site on the metal in order to bring the substrate into the coordination sphere of the metal to catalyze reactions. This vacant coordination site is generally destroyed by dimerization of the two metals into an insoluble precipitate which is no longer active in catalysis. For example, Wilkinson's catalyst $[RhCl(P\emptyset_3)_3]$ (I) in benzene solution loses a ligand (tri-phenylphosphine)

to form an active complex (II) and catalyze reactions or dimerize as an insoluble precipitate (III) as in Scheme 1.

Scheme 1

$$\underset{(I)}{RhCl(P\emptyset_3)_3} \overset{-P\emptyset_3}{\rightleftharpoons} \underset{(II)}{RhCl(P\emptyset_3)_2} \rightleftharpoons \text{catalysis}$$

$$\Downarrow$$

$$\underset{(III)}{[RhCl(P\emptyset_3)_2]_2}$$

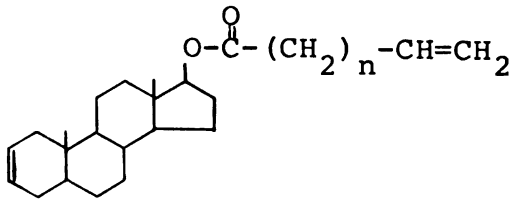
The attachment of Wilkinson's catalyst to the random sites of a fairly rigid insoluble polymer tends to minimize the probability of the metals being within bonding distance. Therefore, the removal of a ligand from the catalyst on the polymer-support to form an active complex to catalyze reactions would be less likely to result in dimerization of two active complexes. Consequently, the catalytic activity of the catalyst might be increased by polymer attachment.

The research reported in this thesis is the result of the selectivity of the supported Wilkinson's catalyst. This catalyst has been shown to have selectivity based on olefin size.[6b] For example, the relative rate of reduction of 1-hexene is many times faster than the relative rate of reduction of a Δ^2-cholestene in benzene solution.[8] It is known that most of the reactions are inside the polymer[9] and the pore size of the polymer is determined by the

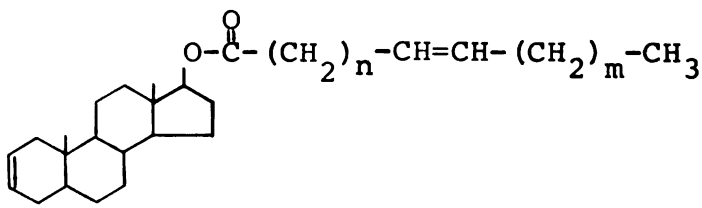
percentage of cross-linking of divinylbenzene. Therefore, the ability of a large molecule to diffuse into the catalytic center should be small while the smaller molecule that fits the pore size of the polymer can easily diffuse into the catalytic center. If the size of the carbon-carbon double bond is determined by the distance parallel to the double bond and this factor determines the relative rate of reduction, the supported catalyst might be useful in the selective reduction of two or more double bonds with different sizes in the same molecule. It might be used to reduce the side chain of steroid which is usually long and acyclic and can diffuse into the center of reaction while the double bond in the steroid nucleus is not affected.

Since the side chain of the steroid might be the part that diffuses into the catalytic center and the steroid nucleus is outside the polymer beads, the steroid that has a fairly long side chain should diffuse into the catalytic center easier than the corresponding shorter one. Therefore, the selectivity might also depend on the length of the side chain and the position of the double bonds (terminal and internal double bond) in the side chain. The latter is due to the steric and electronic factors of the bulky group that are attached to the double bond. It has been shown that Wilkinson's catalyst reduces the terminal olefin faster than the internal olefin.[2a]

In order to study the selectivity of this supported catalyst on the side chain of a steroid, a Δ^2-steroid linked by an ester linkage to different kinds of straight chain unsaturated fatty acid were chosen to be the substrates for reductions (see Figure 1).



n = 1, 2, 3, 8.



n = 7, m = 7 (trans)

n =11, m = 7 (cis)

Figure 1.

After reduction, the steroid esters will be hydrolyzed to the sterol and fatty acid to analyze the amounts of products being reduced individually.

Some of the Δ^2-steroid esters mentioned above will be used to study the effect of the polarity of the solvent

on the selectivity of the supported catalyst. Since the catalyst is attached to the non-polar polymer, the non-polar substrate should tend to diffuse into the polymer faster than the polar substrate. Increasing the solvent polarity should have two effects on the reaction:

(1) it decreases the pore size of the polymer

and (2) increases the diffusion rate of non-polar substrate to the catalytic center.

As a result, the supported catalyst might increase the selectivity for the side chain of the steroid, since there should be a larger size restriction on the steroid nucleus to diffuse into the polymer while the side chain will have a smaller size requirement and be influenced by a large polar gradient.

By the same arguments, Wilkinson's catalyst and the polymer beads alone might be used to reduce the double bond in the steroid nucleus and leave the double bond in the side chain un-reduce. If the polar solvent is used to push the side chain into the polymer beads while the steroid nucleus is reduced by the homogeneous Wilkinson's catalyst outside the polymer beads.

RESULTS AND DISCUSSION

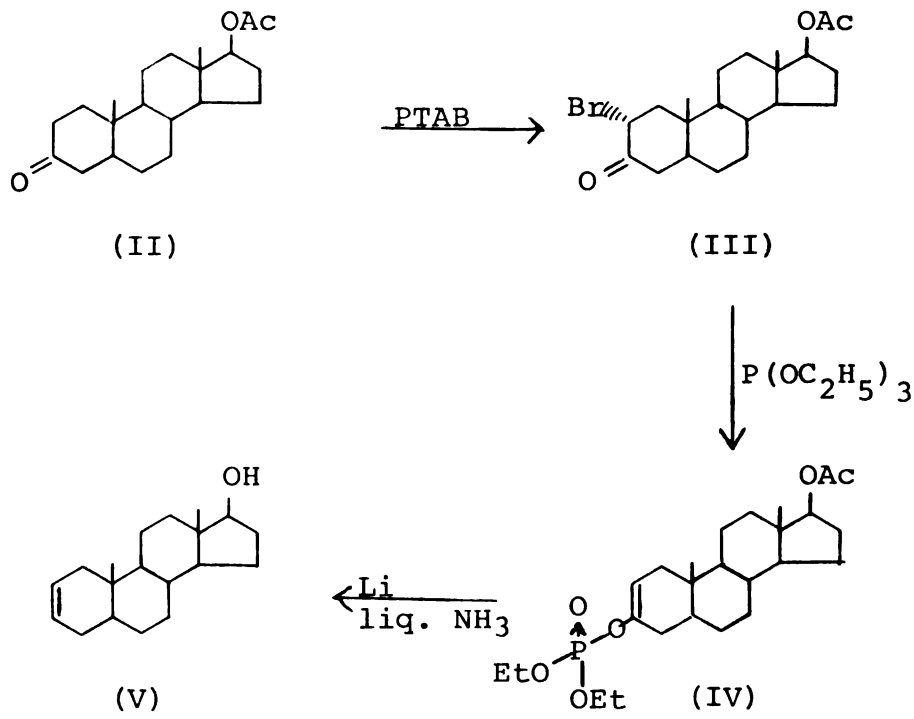
Preparation of the Δ^2-steroid esters

In order to prepare the Δ^2-steroid ester substrates for the proposed reductions, the 5α-androst-2-ene, 17β-ol was prepared by the method of M. Fetizon, et al.,[10] as shown in Scheme 2. The dihydrotestosterone acetate (II) was prepared in 62% yield by the reduction of testosterone acetate with lithium in liquid ammonia.[11] The product was re-acetylated with acetic anhydride and pyridine, as partial de-acetylation had occurred. Bromination of (II) with phenyltrimethyl ammonium tribromide (PTAB)[12] gave the 2α-bromo, keto steroid (III) in 80% yield. This compound underwent a Perkow reaction[13] to the enol diethyl phosphate (IV) in 72% yield on refluxing with triethyl phosphite. The enol phosphate (IV) was then reduced with a slight excess of lithium and liquid ammonia to give 62% yield of the 5α-androst-2-ene, 17β-ol (V) mp 161-163°C.

The fatty acids, 3-butenoic acid (bp 73-75°C @ 15 mmHg) and 5-hexenoic acid (bp 61-63°C @ 1 mmHg) were prepared by oxidation of 3-butene, 1-ol and 5-hexene, 1-ol respectively with Jone's reagent.[14] After the fatty acids

were separated from the aqueous mixture, the acids were dried with the molecular sieve (No. 4A) and purified by distillation under reduced pressure.

Scheme 2



The acids were converted to the corresponding acid chlorides with excess thionyl chloride and used immediately for esterification with the Δ^2-steroid. The heat sensitive acid chlorides (10-undecenoyl, 9-octadecenoyl and 13-docosenoyl chloride) were used without distillation after the excess thionyl chloride and benzene has been removed. The Δ^2-steroid esters were prepared in fair yield (listed in Table 3), by using a slight excess of the acid chloride,

since increasing the amounts of the acid chloride did not significantly improve the yield of the esters.

Hydrogenation with the supported Wilkinson's catalyst

Approximately one gram of the supported catalyst was used in the reductions. The beads were first tested for their catalytic activity, using cyclohexene as a substrate for the reduction. These beads were then used in a series of reductions with one or two mmol of the Δ^2-steroid esters (listed in Table 1) in benzene solution. The reduction was stopped after an equimolar amount of hydrogen had been consumed. The recovered steroid and fatty acid of each hydrogenated esters after hydrolyses was analyzed by NMR to determine the percentage of the products reduced. The results are in Table 1.

The results indicated that the supported catalyst has a selectivity based on the size of the olefin. This is especially true for the terminal olefin of the side chain of the steroid which easily diffused inside the polymer. The side chain is most easily reduced while the larger double bond in the steroid nucleus which has difficulty diffusing into the catalytic center is not reduced. The results also indicated that the selectivity of the supported catalyst is independent of the length of the side chain, as the difference in the selectivity between the fairly long side chain and the shorter one is small.

Table 1.--The Percentage[a] of Acids and Steroid Being Reduced with Supported Wilkinson's Catalyst and Wilkinson's Catalyst in Benzene Solution.

Esters	Beads		$RhCl(P\emptyset_3)_3$	
	% fatty acid	% steroid	% fatty acid	% steroid
3-butenoic acid	84	15	64	37
4-pentenoic acid	87	12	65	34
5-hexenoic acid	86	13	66	35
10-undecenoic acid	90	11	71	29
9-octadecenoic acid (trans)	69	32	52	49
13-docosenoic acid (cis)	74	27	60	39

(a) The percentage $\pm$ 4% of the numbers given for the fatty acid

$\pm$ 5% of the numbers given for the steroid

This is probably due to the increased steric effect of the supported catalyst, since the Wilkinson's catalyst is attached to the polymer which is a large molecule. This effect does prevent the complexation of the steroid nucleus in the coordination sphere of the metal while the side chain with less steric bulk can enter into the catalytic site more easily.

The selectivity of the supported catalyst decreased when an internal olefin was used as a substrate for the reduction. This is due to the steric and electronic effects of the substrate as shown by Wilkinson,[2a] for the homogeneous Wilkinson's catalyst, the rate of reductions are: terminal olefin > cis olefin > trans olefin. This result is also most consistent with the greater selectivity being due to the increase bulk of the catalyst.

Hydrogenation with homogeneous Wilkinson's catalyst

In order to determine the selectivity of the supported catalyst in contrast to the homogeneous catalyst, the same number of substrates were used in the reduction with homogeneous Wilkinson's catalyst. The results (also shown in Table 1) indicate that the supported catalyst has higher selectivity than the corresponding homogeneous catalyst. This is probably due to the greater size restriction of the ligand of the supported catalyst than the homogeneous catalyst. Figure 2 shows that the selectivity difference of the terminal olefin on the

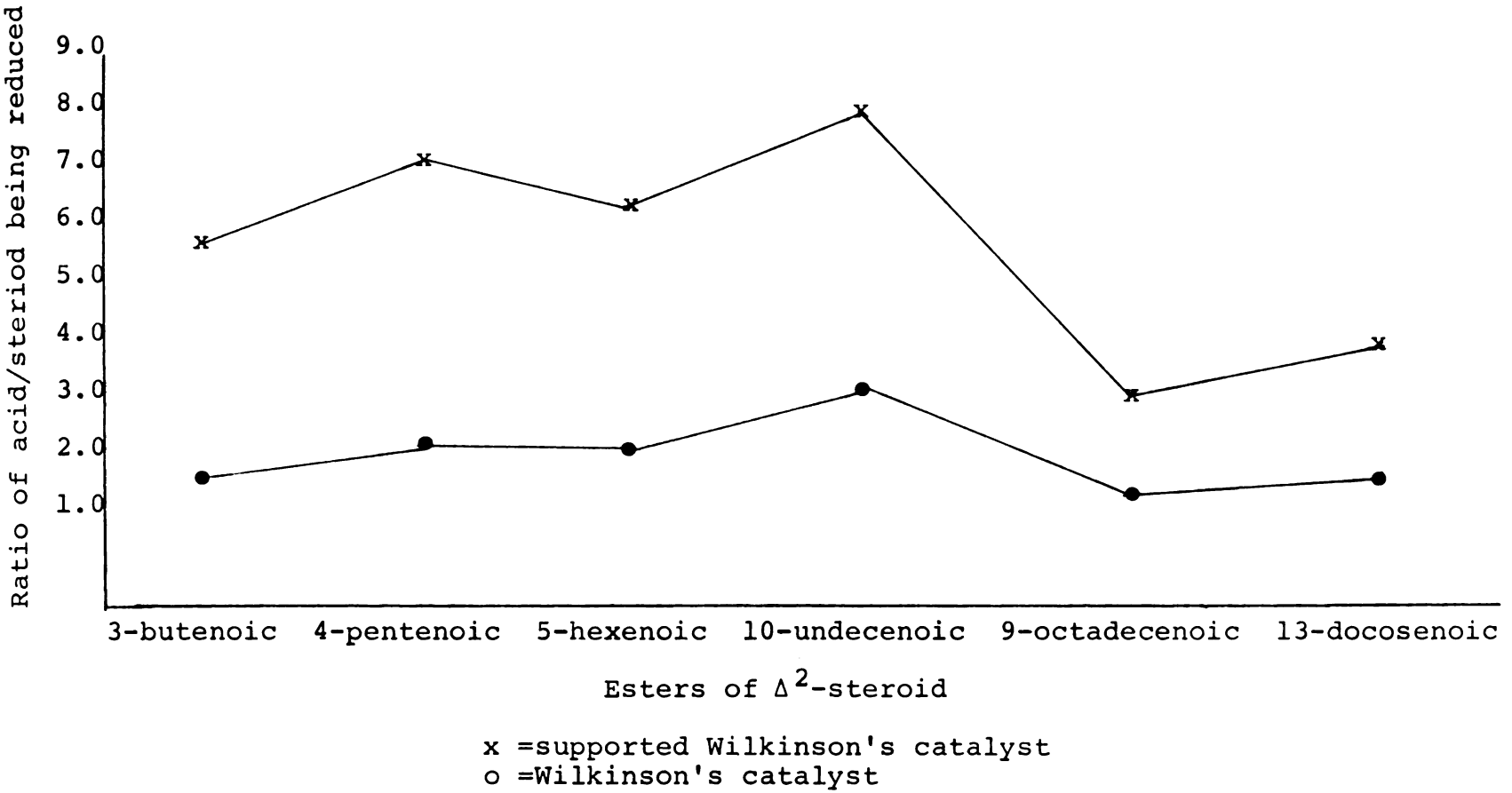


Figure 2. Comparative ratio of acid/steroid being reduced for supported Wilkinson's catalyst vs Wilkinson's catalyst

supported catalyst is about 4-5 folds higher than the homogeneous catalyst while the internal olefin is about one fold higher. The comparison of these results (Figure 2) seems to suggest the possibility that this supported catalyst could be used for a selective reduction of one of two or more double bonds with different sizes.

The effect of the solvent polarity on the selectivity of the supported catalyst

An increase in the polarity of the solvent decreases the pore size of the polymer[9] and increases the size restriction on the substrate for diffusion into the polymer.[6a] Consequently, the reductions were carried out using the esters (4-pentenoic acid and 10-undecenoic acid) as the substrates and an equal mixture of benzene and ethanol as a solvent. The results in Table 2 indicate a small decrease in the selectivity for the short chained ester (4-pentenoic acid), compared to the results in Table 1, whereas the selectivity for the longer chained ester (10-undecenoic acid) increased.

These results suggest that, when the polarity of the solvent was increased, the length of the side chain instead of the steric effect of the catalyst itself becomes an important factor in determining the selectivity of this catalyst. The ester (10-undecenoic acid) with a fairly long side chain should be able to diffuse into the polymer more easily than the shorter one (4-pentenoic acid).

The selectivity for the ester (4-pentenoic acid) is due only to the steric effect of the supported catalyst as mentioned before.

Table 2.--The Percentage of Acids and Steroid Being Reduced with Supported Wilkinson's Catalyst in 1:1 Benzene and Ethanol.

Esters	Beads	
	% fatty acid	% steroid
4-pentenoic acid[a]	83	17
10-undecenoic acid[b]	>95	<5

(a) The percentage ± 5% of the numbers given
(b) The NMR spectrum show no olefenic peak for the acid and the steroid was not reduced

Another reduction was carried out. In this reduction, the beads were thoroughly ground and used in the reduction of the ester (10-undecenoic acid) in benzene solution. The rate of reduction in this reaction increased about ten times over the non-ground rate since the diffusion effects of the polymer are reduced. The NMR spectrum showed 86%[18] of the fatty acid and 13%[18] of the steroid had been reduced. These numbers are closed to the numbers of the products being reduced before the beads were ground. Since the Wilkinson's catalyst was still attached to the polymer after it was ground, the steric effect would still exist in the system, which seem to confirm that

this effect is the factor that determines the selectivity of the supported catalyst.

Hydrogenation with homogeneous Wilkinson's catalyst and the polymer beads

Since the supported catalyst had been shown to have a unique selectivity on the reduction of the ester (10-undecenoic acid) when using the equal mixture of benzene and ethanol as a solvent. This particular substrate and solvent system were chosen in an attempt to selectively reduce the double bond in the steroid nucleus without affecting the double bond in the side chain. In this reduction, the polymer beads alone were stirred with 0.23 g (0.52 mmol) of the ester (10-undecenoic acid) in a small amount (3 ml) of 1:1 benzene and ethanol in order to absorb the side chain into the polymer. The homogeneous Wilkinson's catalyst in 2 ml of 1:1 benzene and ethanol was then injected into the system and the same reduction procedure was used.

The resulting products show 67%[18] of the acid and 34%[18] of the steroid were reduced. These are closed to the results when using homogeneous Wilkinson's catalyst (see Table 1). The lack of success in this attempt is probably due to the solvent system used in this reduction not being polar enough to hold the side chain in the polymer and leave the steroid outside. Another factor might be that the homogeneous catalyst itself could

possibly diffuse into the polymer and reduce the side chain together with the steroid nucleus outside the polymer.

Conclusion

The results outlined above indicate that the size of the olefin and the polarity of the solvent are the factors that determine the selectivity of the supported Wilkinson's catalyst. If the pore size of the polymer can be calibrated (by % cross-linking) and the appropriate solvent is used, there is the possibility of using this catalyst to selectively reduce different size olefins in the same molecule without affecting the others. These same selectivity factors could also be useful in the design and use of other polymer attached reagents and this new type of selectivity could be very useful in the synthetic chemistry.

EXPERIMENTAL

Introduction

All NMR spectra were run on a Varian T-60 Spectrometer in deuteriochloroform solution using TMS as an internal standard. Melting points were determined with a Thomas-Hoover melting point apparatus. Mass spectra were run by Mrs. L. Guile. Microanalyses were done by Spang Microanalytical Laboratory. Column chromatography was done with Woelm chromatographic grade alumina.

Solvents were reagent grade which were dried, deoxygenated and purified by distillation under nitrogen from sodium-benzophenone. Pyridine was distilled from calcium hydride and ethanol was distilled from sodium ethoxide and diethyl phthalate under nitrogen. Solvents were stored under nitrogen. All reactions were carried out under nitrogen or argon atmosphere, otherwise were noted.

Preparation of 5α-Androst-2-ene, 17β-ol (V)

5α-Androstan-17β-ol, 3-one, 17β-acetate (II)

A solution containing 10 g (30.3 mmol) of testosterone acetate in 250 ml of ether was added dropwise with stirring to the flask containing a solution of 2.1 g (0.303 g-atom) of lithium metal in 500 ml of liquid ammonia fitted in a dry-ice and acetone bath over a period of 30 min. Another 75 mg of lithium was added to maintain the blue color. After an additional stirring for 35 min, ammonium chloride was added slowly until the solution became white and 150 ml of water was added slowly to dissolve the inorganic salts. The ammonia was allowed to evaporate overnight in the hood.

The residue was extracted several times with methylene chloride and the combined organic extracts were washed with water, dried over anhydrous magnesium sulfate, and evaporated to dryness under reduced pressure. The resulting precipitate was acetylated[15] by stirring with 20 ml of freshly distilled acetic anhydride in 40 ml of pyridine overnight at room temperature. After dilution with water, the mixture was extracted with methylene chloride, washed several times with dilute hydrochloric acid, water and 10% sodium bicarbonate solution, dried with anhydrous magnesium sulfate and evaporated under reduced pressure. The oily residue was chromatographed on

alumina. Elution with ether gave 6.4 g (64%) of II. Recrystallization from ethyl acetate-hexane gave mp 155-157°C, reported[11] 154-156°C.

5α-Androstan-17β-ol, 3-one, 2α-bromo, 17β-acetate (III)

To a solution of 6 g (18.0 mmol) of II in 60 ml of tetrahydrofuran was added 6.9 g (18.0 mmol) of phenyltrimethyl ammonium tribromide (PTAB)[12] with stirring. The mixture was stirred for one hour and water was added to dissolve the white precipitate. The solution was extracted several times with ether, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to give 6.0 g (80%) of III, (recrystallized from methanol-hexane) mp 176-177°C.

5α-Androst-2-ene, 3-diethylphosphate, 17β-acetate (IV)

A solution of 5 g (12.1 mmol) of (III) and 50 ml of freshly distilled triethyl phosphite was refluxed at 160°C for 4 hr and distilled under reduced pressure to remove ethyl bromide and excess triethyl phosphite. The residual crystallized while standing in the refrigerator overnight. The precipitates were filtered, washed with pentane, and vacuum dried at room temperature to give 4.1 g (72%) of IV mp 86-91°C (reported[10] 90-91°C) which was used for reduction without further purification.

5α-Androst-2-ene, 17β-ol (V)

A solution of 3.5 g (7.5 mmol) of IV in 25 ml of tetrahydrofuran and 25 ml of tert-butyl alcohol was added dropwise with stirring to a flask containing 2.5 g (0.361 g-atom) of lithium and 100 ml of liquid ammonia which was cooled in a dry-ice acetone bath. Stirring was continued for 3-4 hr and methanol was added dropwise until decoloration appeared. The ammonia was allowed to evaporate overnight and the residue was extracted several times with ether, washed with saturated sodium bicarbonate solution, water and saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure. The white precipitate was recrystallized from methanol gave 1.3 g of 5α-androst-2-ene, 17β-ol (V) mp 161-163°C, reported[10] 163-164°C.

The mass spectrum has a parent peak at m/e=274 (calculated molecular weight of V is 274.4)

The NMR spectrum in $CDCl_3$ down field from TMS

5.4 - 5.6 δ 2H at double bond
3.4 - 3.7 δ H at C-17
0.7 - 0.8 δ 6H at Me 18 and 19.

Preparation of acid chlorides

A solution of 20 mmol of the unsaturated fatty acid in 10 ml of benzene was added dropwise with stirring 5 ml (42 mmol) of thionyl chloride.[16] The mixture was warmed to 40-50°C to initiate the reaction and stirring was continued for 1-2 hr at 30-35°C. Benzene and excess

thionyl chloride were removed by distillation.[17] Another 2 ml of benzene was added and distilled off to remove the last traces of thionyl chloride. The pressure was reduced and the acid chloride was distilled and used immediately in the preparation of the ester. Some high boiling acid chlorides were used without distillation.

Preparation of 5α-androst-2-ene, 17β-ol, esters

In each case 2.0 g (7.3 mmol) of Δ^2-steroid (V) was dissolved in 30 ml of benzene and 1 ml (12.7 mmol) of pyridine. The solution was cooled to 0-5°C and 10 mmol of the acid chloride was added dropwise with stirring. After stirring for 24-30 hr at room temperature, the mixture was poured into the mixture of 20 g of ice and 5 ml of hydrochloric acid. The organic layer was extracted with benzene, washed with water, 10% sodium bicarbonate and water several times, finally with saturated sodium chloride, dried over magnesium sulfate and evaporated under reduced pressure. The solid (some were oily) residue was chromatographed on alumina. The impurities were removed in hexane eluates, elution was continued with 20% benzene-hexane to remove the ester (see Table 3).

Hydrogenations

Two series of hydrogenations of Δ^2-steroid esters were carried out using either insoluble polymer-supported Wilkinson's catalyst or soluble Wilkinson's catalyst. The

Table 3.--The Esters of Δ^2-Steroid.

Acylating Group	Structure of acids	Yield %	mp°C
3-butenoic acid	$CH_2=CH-CH_2-\overset{O}{\overset{\|}{C}}-OH$	40	80-81
4-pentenoic acid	$CH_2=CH-(CH_2)_2-\overset{O}{\overset{\|}{C}}-OH$	65	65-66
5-hexenoic acid	$CH_2=CH-(CH_2)_3-\overset{O}{\overset{\|}{C}}-OH$	45	60-61
10-undecenoic acid[a]	$CH_2=CH-(CH_2)_8-\overset{O}{\overset{\|}{C}}-OH$	66	oil
9-octadecenoic acid[b] (trans)	$CH_3-(CH_2)_7-CH=CH-(CH_2)_7-\overset{O}{\overset{\|}{C}}-OH$	56	oil
13-docosenoic acid[c] (cis)	$CH_3-(CH_2)_7-CH=CH-(CH_2)_{11}-\overset{O}{\overset{\|}{C}}-OH$	51	oil

Analysis:	% Carbon		%Hydrogen	
	Calc.	Found	Calc.	Found
(a)	81.82	82.29	10.91	10.89
(b)	82.47	82.76	11.60	11.88
(c)	82.83	82.81	11.86	11.95

atmospheric pressure hydrogenation apparatus was used and the temperature was controlled between 24.5-25.5°C throughout the reductions by the water flowed from a thermostat bath. A 50 ml gas burette was used for volume measurement.

The polymer-supported Wilkinson's catalyst (microanalysis shows 2.24% of Rh/gram of beads, or 0.22 mmol of Rh/gram of beads) and Wilkinson's catalyst [$RhCl(P\phi_3)_3$] were prepared by Edward M. Sweet.

Hydrogenations with polymer-supported Wilkinson's catalyst

One gram of the beads and a magnet stirring bar was put into 250 ml round bottom flask with a sidearm, the flask was then connected to the hydrogenation apparatus. The reactor was evacuated and filled with hydrogen. This cycle was repeated 3-4 times. Benzene (12 ml) was injected with a syringe through the sidearm of the flask and the beads were equilibrated by stirring for an hour in the hydrogen at atmospheric pressure.

One or two mmol of the Δ^2-steroid ester to be reduced was dissolved in 3 ml of benzene and injected into the reaction flask. After standing for 2-3 min, stirring was continued and the hydrogen volume was measured at 15-30 min intervals until the equimolar amount of hydrogen was consumed.

The solution was removed with a syringe after the reduction was stopped, the beads were rinsed 3-4 times

with 10 ml portions of benzene and dried in the vacuum. The combined benzene solution was evaporated and the hydrogenated ester was hydrolyzed. The steroid and fatty acid were recovered for analysis.

Two additional hydrogenations were carried out using 1 mmol of the ester (4-pentenoic acid and 10-undecenoic acid respectively) and 15 ml of 1:1 benzene and ethanol mixture as a solvent. Finally the beads were thoroughly ground and the same reduction procedure was used in the reduction of the ester (10-undecenoic acid) in benzene.

The reduction times and the volume of hydrogen uptake per min for each esters are shown in Table 4.

Hydrogenations with homogeneous Wilkinson's catalyst

In this series, 10 mg (0.012 mmol) of Wilkinson's catalyst was used for each reduction. The catalyst and a magnet stirring bar were put into a 250 ml round bottom flask with a sidearm and connected to the hydrogenation apparatus. After 3-4 times of vacuum-hydrogen cycles were introduced, the catalyst was equilibrated with hydrogen in benzene in the same procedure as the supported catalyst. The ester to be reduced was injected into the flask and the volume of hydrogen was measured at 5-10 min intervals until the equimolar amount of hydrogen was consumed. The volume of hydrogen uptake per min and the reduction times for each esters are shown in Table 5.

Table 4.--Supported Wilkinson's Catalyst Reduction Rates for the Δ^2-Steroid Esters.

Esters	Volume of H_2[a] (ml)	Reduction Time (min)	Rate of Reduction (ml per min)
3-butenoic acid[b]	44.80	812	0.055
4-pentenoic acid	22.40	478	0.047
5-hexenoic acid	22.40	417	0.054
10-undecenoic acid	22.40	580	0.039
9-octadecenoic acid (trans)	22.40	768	0.029
13-docosenoic acid (cis)	22.40	636	0.035
4-pentenoic acid[c]	22.40	214	0.105
10-undecenoic acid[c]	22.40	197	0.114
10-undecenoic acid[d]	22.40	165	0.135

(a) $\pm$ 0.05 ml of hydrogen.

(b) 2 mmol of the ester was used, others used 1 mmol.

(c) solvent was 15 ml of 1:1 benzene and ethanol mixture.

(d) the beads were thoroughly ground before using in the reduction.

Table 5.--Homogeneous Wilkinson's Catalyst Reduction Rates for the Δ^2-Steroid Esters.

Esters	Volume of H_2[a] (ml)	Reduction Time (min)	Rate of Reduction (ml per min)
3-butenoic acid[b]	44.80	126	0.36
4-pentenoic acid	22.40	58	0.39
5-hexenoic acid	22.40	61	0.37
10-undecenoic acid	22.40	68	0.33
9-octadecenoic acid (trans)	22.40	112	0.20
13-docosenoic acid (cis)	22.40	95	0.24

(a) $\pm$ 0.05 ml of hydrogen.

(b) 2 mmol of the ester was used, others used 1 mmol.

The entire solution was chromatographed with benzene on alumina. The catalyst stayed at the top of the column. After benzene was evaporated, the hydrogenated ester was hydrolyzed, the steroid and fatty acid were recovered for analysis.

Hydrogenation with Wilkinson's catalyst and 2% divinylbenzene-styrene copolymer beads

In this reduction 2 g of the beads and 0.23 g (0.52 mmol) of the ester (10-undecenoic acid) were put into a 100 ml round bottom flask with a sidearm with a magnet stirring bar and attached to the hydrogenation apparatus. After air was flushed out of the system, 3 ml of 1:1 benzene and ethanol mixture was injected into the reaction flask. The mixture was stirred for 30 min and 5.5 mg (0.007 mmol) of Wilkinson's catalyst was dissolved in 2 ml of 1:1 benzene and ethanol mixture and injected into the reaction flask. Stirring was continued under hydrogen atmosphere. The volume of hydrogen was measured at 5-10 min intervals until 11.70 $\pm$ 0.05 ml (0.52 mmol) of hydrogen was consumed. The reduction rate was 0.27 ml of hydrogen per min. The entire sample after reduction was chromatographed on alumina, the ester was eluted with benzene, and evaporation gave the ester which was hydrolyzed for analysis.

Hydrolysis of the hydrogenated esters

The entire sample of the hydrogenated ester was dissolved in 5 ml of methanol, the solution was cooled to 10-15^{o}C and was added dropwise with stirring 10 ml of dilute sodium hydroxide solution (5% of NaOH in 15 ml of water and 85 ml of MeOH). The mixture was stirred for 5-6 hr at room temperature and the methanol was distilled off under reduced pressure. Water (15 ml) was added and the organic layer was extracted several times with methylene chloride. The combined organic extracts were dried with magnesium sulfate and evaporated. The recovered steroid (see Table 6) was analyzed for the amounts of saturated and unsaturated by comparing the integration ratio of the NMR spectra.

The aqueous solution was acidified with 10% hydrochloric acid until the solution was acid to litmus paper, another 1 ml of HCl was added and stirring was continued for 20-30 min. The aqueous solution was extracted 3-4 times with methylene chloride. The extracts were dried with magnesium sulfate and evaporated. The fatty acids (see Table 6) were analyzed for the amounts of saturated and unsaturated in the same manner as steroid.

The results of the analyses are shown in Table 1.

Table 6.--The Yields of Recovered Acids and Steroid After Hydrolysis.

Esters	Weight of esters (g)	Recovered	
		acid (g)	steroid (g)
3-butenoic acid	0.6841	0.1595	0.5199
4-pentenoic acid	0.3560	0.0873	0.2504
5-hexenoic acid	0.3702	0.0996	0.2481
10-undecenoic acid	0.4403	0.1782	0.2691
9-octadecenoic acid	0.5381	0.2658	0.2583
13-docosenoic acid	0.5940	0.3159	0.2418

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BIBLIOGRAPHY

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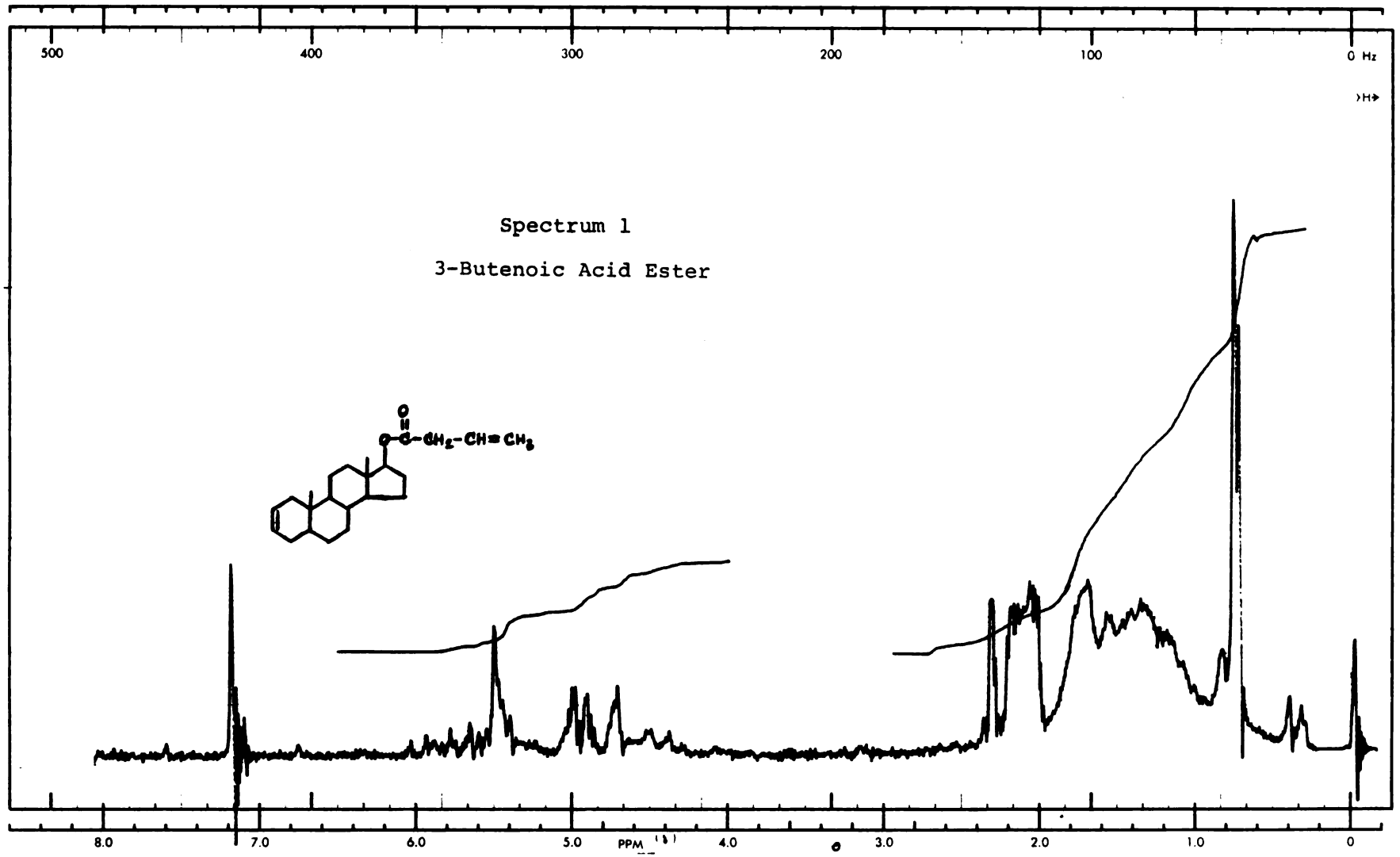
15. As partial de-acetylation occurred during reduction.

16. Thionyl chloride was purified by the method of Friedman, L., and Wetter, W. P. "Reagent for Organic Synthesis," Fieser and Fieser, John Wiley & Sons, Inc., Vol. 1, 1158 (1968).

17. For high boiling acids, benzene and excess thionyl chloride were distilled off under reduced pressure.

18. The error is $\pm$ 5% of the numbers given.

SPECTRA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400
300
200
100
0 Hz
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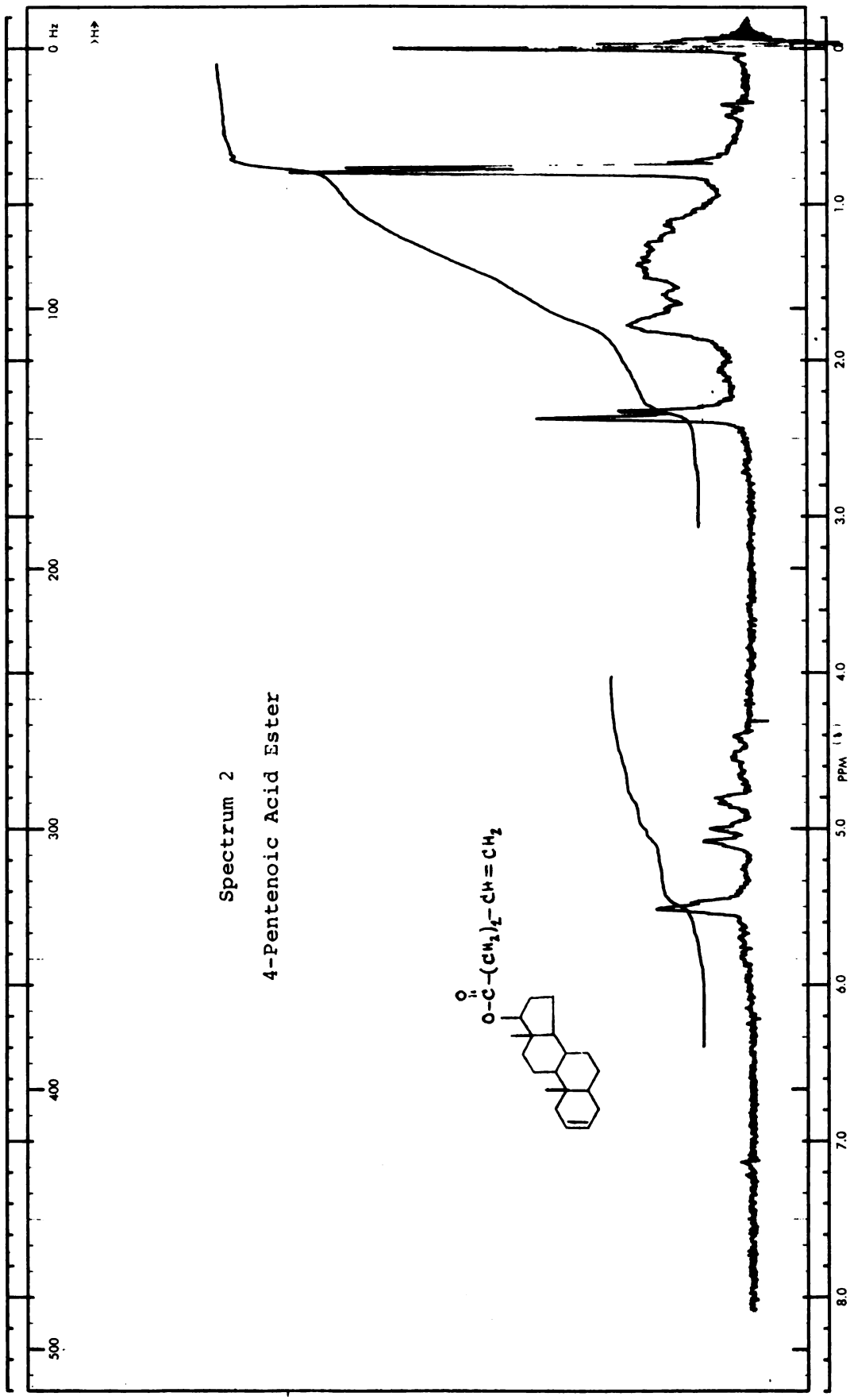
6.0
5.0
PPM
4.0
3.0
2.0
1.0
0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4-Pentenoic Acid Ester
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200
300
400
500
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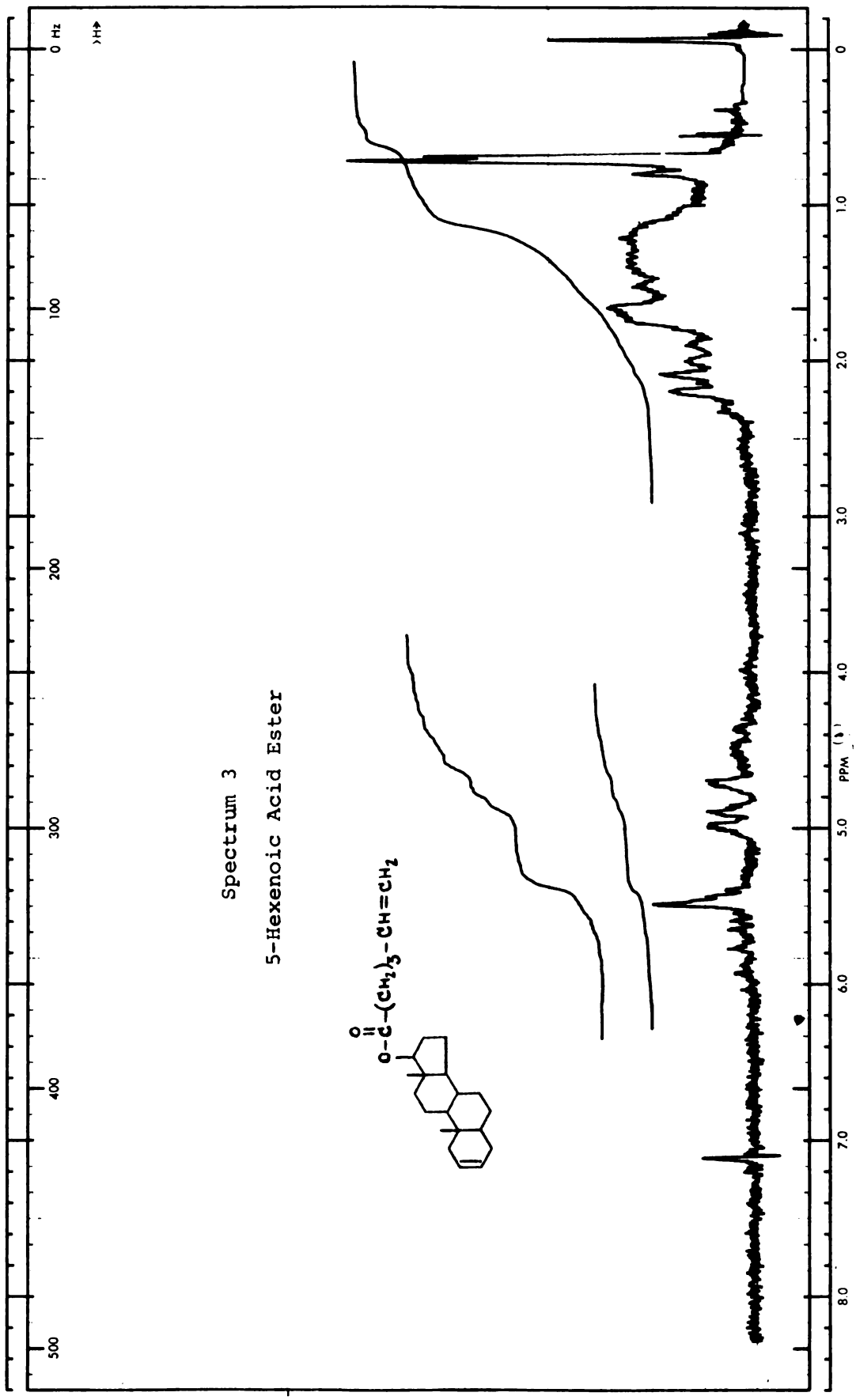
3.0
4.0
5.0
6.0
7.0
8.0
PPM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5-Hexenoic Acid Ester
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100
200
300
400
500
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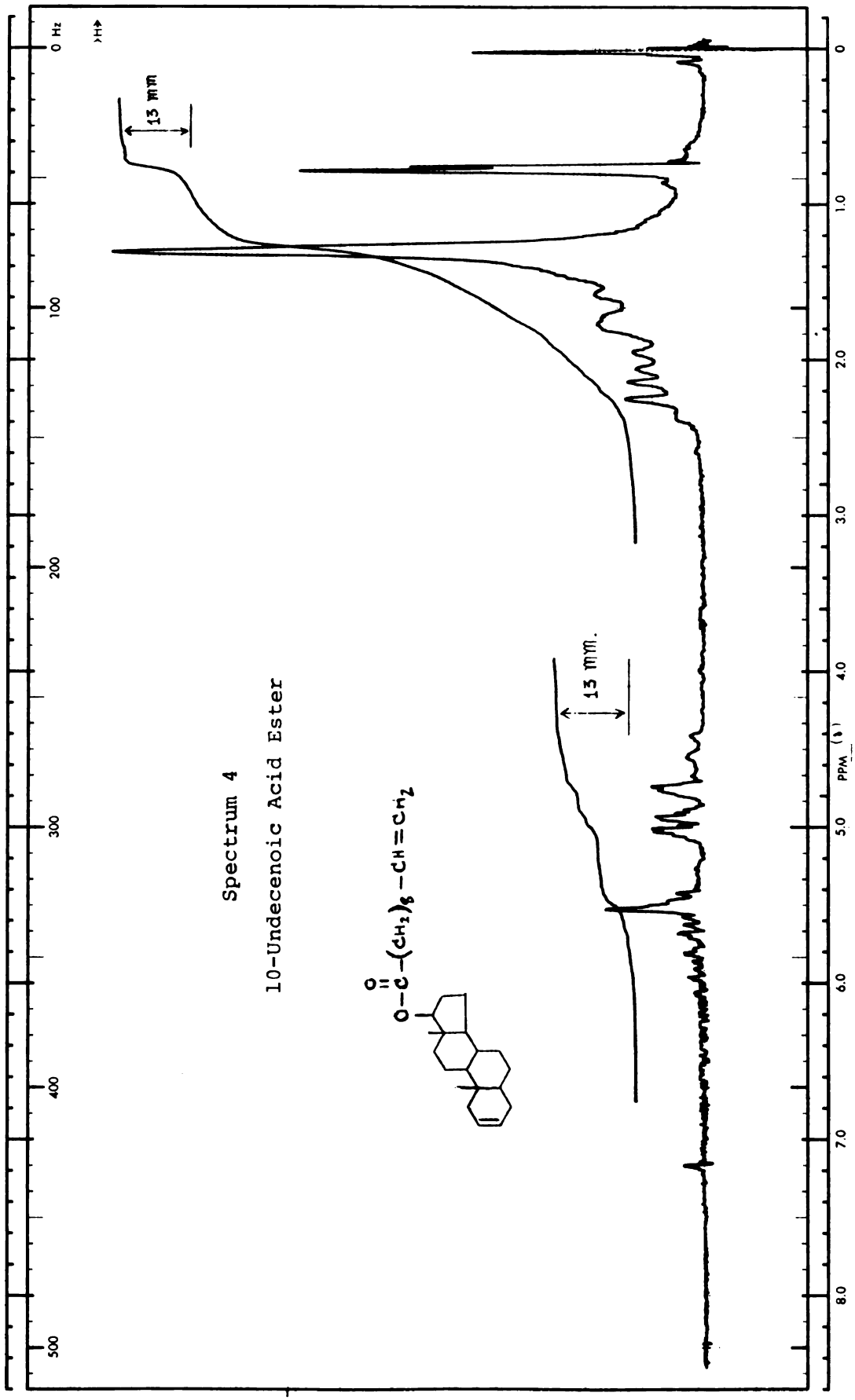
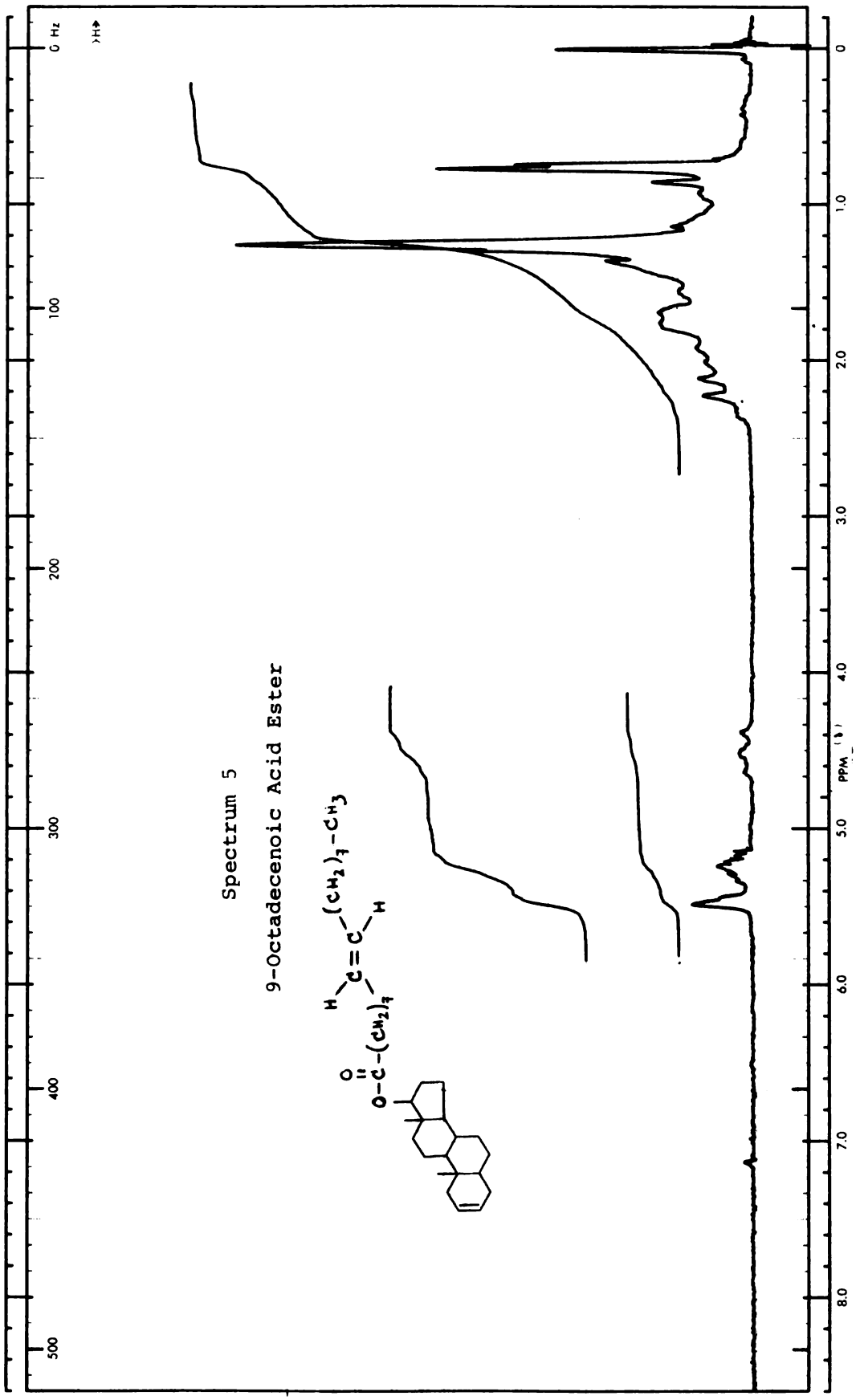
2.0
3.0
4.0
5.0
6.0
7.0
8.0
PPM (δ)
0



Spectrum 4

10-Undecenoic Acid Ester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9-Octadecenoic Acid Ester
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H
C=C
H
(CH2)7-CH3
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400
300
200
100
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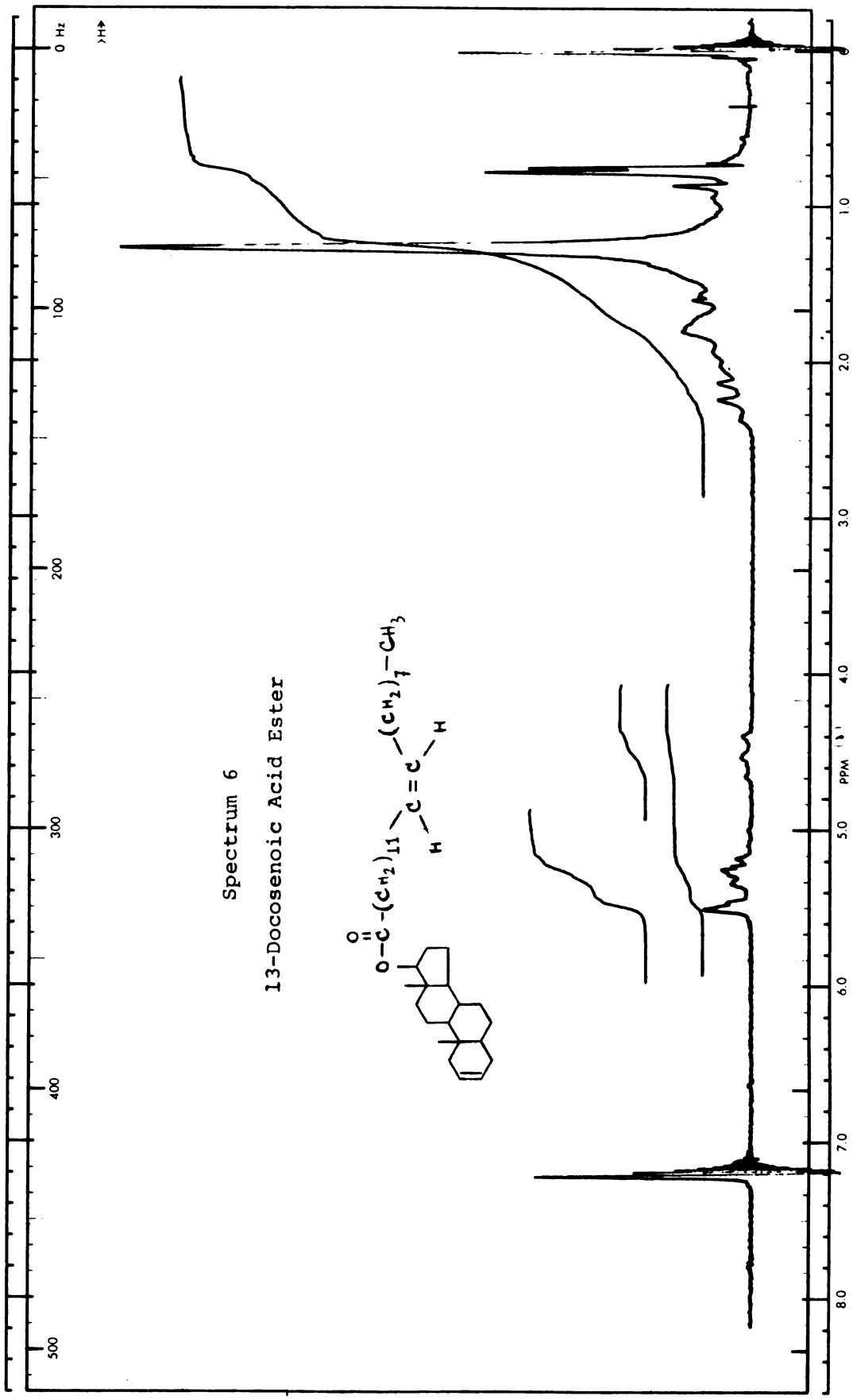
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
PPM (δ)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200
300
400
500
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2.0
3.0
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5.0
6.0
7.0
8.0
PPM
Spectrum 6
13-Docosenoic Acid Ester