



3 SEP 1966

3 NOV 1966

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SOME STUDIES IN FATTY ACID SERIES

A THESIS SUBMITTED TO
THE UNIVERSITY OF POONA
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY



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TH-762

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(1965)

3 NOV 1966

C O N T E N T S

PART ONE

STERCULIC ACID

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PART ONE
STERCULIC ACID

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C O N T E N T S

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SYNTHESIS OF
STERCULIC ACID

SYNTHESIS OF STERCULIC ACID

This Chapter describes the successful synthesis of sterculic acid [ω -(2-n-octylcycloprop-1-enyl)-octanoic acid] (I), the structure of which had been a point of controversy during the last few years and drew the attention of several workers. It appears appropriate, in connection with this synthesis to survey briefly the background literature on sterculic acid.

STERCULIC ACID

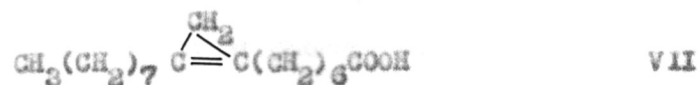
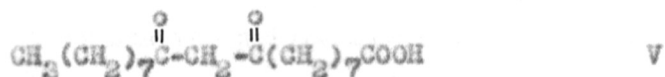
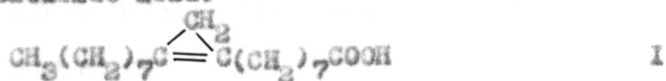
Sterculic acid forms the major component (more than 70%) of the total fatty acids of the seed fat of Sterculia foetida (Jungli Badam in Hindi; also known as Java Olive or Java almond) belonging to the natural order sterculiaceae and was first isolated from this source. Its occurrence has also been reported in various other seed fats: sterculiaceae (Sterculia parviflora¹, Brachychiton acerifolium², Brachychiton populneum²); Malvaceae (several malvaceous plants^{2,3} Malva parviflora², Malva verticillata², Gossypium hirsutum², various Gossypium species⁴, Hibiscus moschontos^{5,6}, Hibiscus syriacus^{5,7,8}, Lavatera trimestris^{5,7,8}; Bombacaceae (Bombax oleagineum⁹, Coiba acuminata¹⁰); possibly in baobab oils derived from several species of Adansonia¹¹, Basiloxylon brasiliensis¹¹ Uilaceae^{12,13} and cotton seed and kapok seed oils^{12,13,14,15}.

Structure

Hilditch and coworkers¹⁶ were the first to examine the structure of sterculic acid. They established its molecular formula ($C_{19}H_{34}O_2$) and, based on degradative experiments, suggested that the acid may be formulated as 12-methyl octadeca-9,11-dienoic acid (II). However, these authors noted that the acid does not exhibit any characteristic conjugated diene absorption in the ultra violet.

The acid was later reinvestigated by Mann¹⁷ who succeeded, for the first time, in preparing pure sterculic acid (m.p. 18.2 - 18.9°). The acid showed no absorption maximum in the ultra violet. On hydrogenation over palladised calcium carbonate in methanol gave a dihydro derivative which did not give colour with tetranitromethane. Further hydrogenation of the material over Adam's platinum oxide catalyst resulted in the uptake of one more mole of hydrogen to give a product which was considered to be a mixture of n-nonadecanoic acid and two methyl substituted octadecanoic acids. Potassium permanganate oxidation furnished pelargonic (III) and azelaic (IV) acids. The same products were obtained when sterculic acid was ozonised and the ozonide oxidatively cleaved with hydrogen peroxide in acetic acid. However, when the ozonide was reductively cleaved (Pd-C and H_2) a $C_{19}H_{34}O_4$ acid (m.p. 57.5-58.3°) could be obtained as a major product; this material on oxidation with hydrogenperoxide and acetic

acid gave same mixture of pelargonic and azelaic acids and hence was formulated as α -ketone acid (V). Based on these considerations Munn proposed structure (I) for sterculic acid. It may also be pointed out that Munn examined the IR spectrum of dihydro sterculic acid which showed the absorption at 9.8μ assignable to a cyclopropane ring, in analogy with the work of Hofmann and Lucas¹⁸ on lactobacillic acid.



Though the above structure for sterculic acid is well supported by reported experimental evidence Varma *et al.*¹⁹, chiefly on the basis of some infrared studies,

suggested that sterculic acid may in fact be ω -(2-n-hexyl-cyclopropyl)-dec-9-enoic acid (VI).

As can be seen the diketone acid, which can arise only from the structure (I), constitutes a decisive degradation product. This lead three different sets of workers²⁰⁻²² to undertake its synthesis when in each case the synthetic product was shown to be identical with degradation product obtained by Mann. Thus the structure (I) uniquely represents sterculic acid.

The nuclear magnetic resonance (NMR) spectrum of sterculic acid has been studied by two groups of workers^{23,24} who concluded that the spectrum is consistent with structure (I) and structure (VI) can be definitely ruled out. Another NMR study of this acid has recently appeared²⁵.

Sterculic acid undergoes rapid polymerisation at room temperature and its polymerisation has been studied by Reinhart *et al.*²⁶

Detection and estimation

The most characteristic colour reaction of sterculic acid is the development of cherry-red colour when a small amount of acid is heated with carbon disulphide, sulphur and amyl alcohol (Halphen-Test)²⁷. This reaction is considered specific for cyclopropenes²⁸ and can be used for determination of this structure in oils, just detectable in 100 PPM²⁹. The reaction

has been investigated by many workers^{12-15, 30-42}. Based on IR spectral changes during the Halphen reaction, Faure³⁵ using freshly prepared sterculic acid and *sterculia foetida* oil, proposed a tentative reaction mechanism and stated that strong absorption band at 4.88μ was due to the double bond in the grouping $-S-C=S$, which is first formed by the reaction between the carbon disulphide and cyclopropene ring and subsequent polymerisation across the $C=S$ double bond. Addition of sulphur and amyl alcohol does not appear to be essential³⁵ for the Halphen-test.

The reaction has also been used for the quantitative estimation of sterculic acid using both the visible^{28,42,43} and IR^{8,44,45} spectrophotometry.

Several other methods for the estimation of sterculic acid have been proposed^{7,8,46-51}.

Acids related to sterculic acid

Besides sterculic acid the only other naturally occurring fatty acid with a cyclopropene ring is malvalic acid (VII) a constituent of seed fats of: Sterculiaceae (*Sterculia foetida*^{5,10}; *Brachychiton acerifolium*²; *Brachychiton populneum*²); Malvaceae: (lipid fraction from leaves and seeds of *Malva parviflora*²; *Malva verticillata*²; *Gossypium hirsutum*²; some other *Gossypium* species⁴²; *Hibiscus moscheutos*^{5,6}; *Hibiscus syriacus*^{5,7}; *Lavatera trimestris*⁷; and Bombacaceae (*Bombax oleaginum*⁹,

Kopak seed oil¹⁵). Its structure has been recently established as (VII)^{29,52,53}.

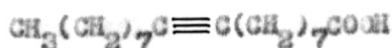
SYNTHESIS OF STERCULIC ACID

The unique structure of sterculic acid as cyclopropene derivative, and announcement of a general method for cyclopropene synthesis by Doering and Mole⁵⁴ prompted us to undertake its synthesis⁵⁴ employing the method of Doering et al.

Doering et al. showed that butyne-2 (IX) on treatment with diazomethane and simultaneous irradiation with ultra violet light furnished us 1,2-dimethyl cyclopropene (X) in 17% yield of theory based on *N*-nitrosomethyl urea. In principle methyl stearolate (XI) under these conditions could give methyl sterculate (XII), and this Chapter describes the results of this investigation.

*While this work was in progress, Griffin⁵⁵ reported a synthesis of sterculic acid by the addition of carbene to stearolic acid (VIII). Though our scheme envisaged the same essential features, this author employed methylene iodide zinc-copper couple for the generation of carbene, (or its equivalent). Sterculic acid could thus be synthesized from stearolic acid in a yield of 4%. However, no details of this work have appeared so far.

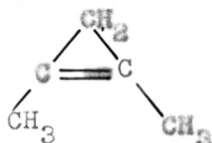
*Varma et al.¹⁹ claimed to have synthesized sterculic acid by the reaction of CH_2N_2 on stearolic acid. This work has been adversely criticised by Brook and Smith⁵⁶ who by a repetition of their¹⁹ procedure failed to detect (Halphen-test) the presence of any sterculic acid.



VIII



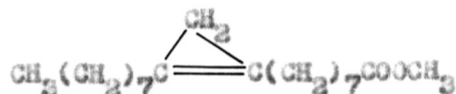
IX



X



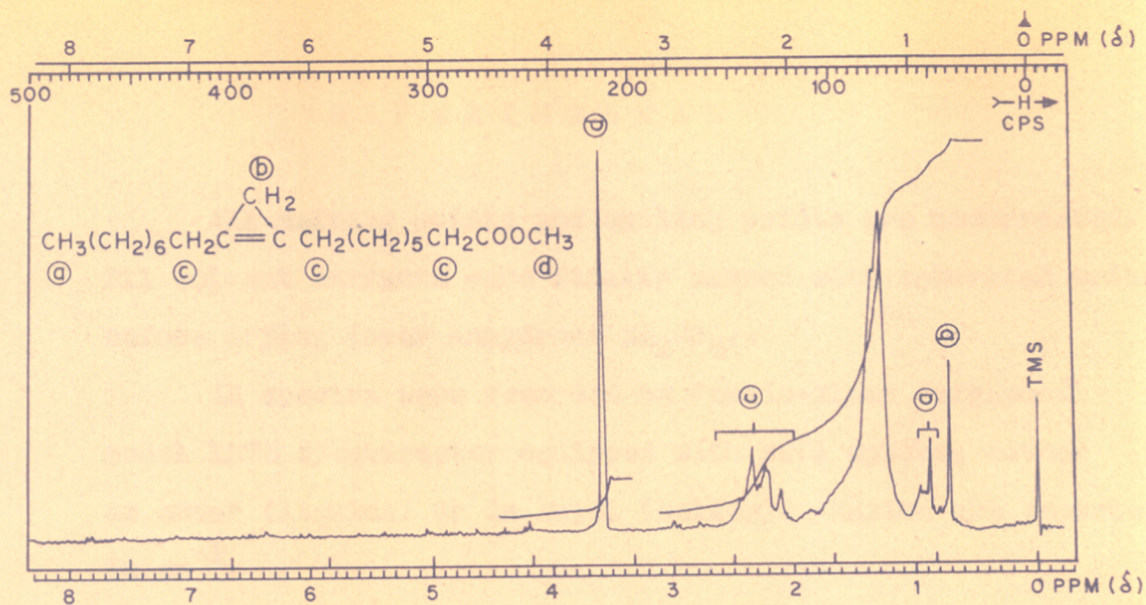
XI



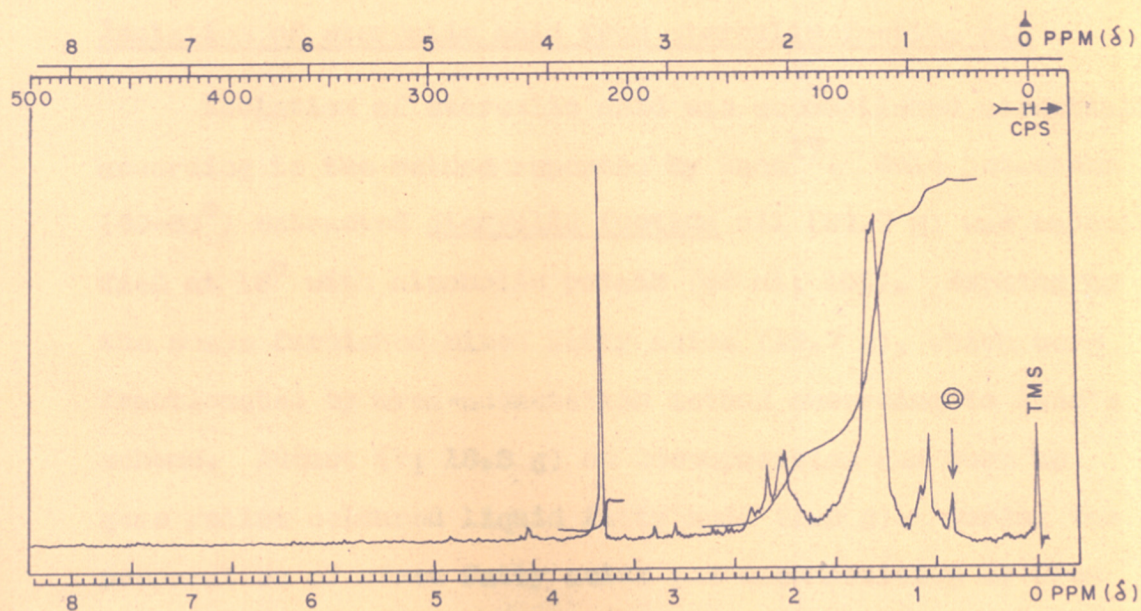
XII

When methyl stearolate (XI) was irradiated and simultaneously treated with ethereal solution of diazomethane at reflux, the product failed to show (Halphen-test) any trace of the required compound. The experiment was modified by avoiding the use of ether, and employing only diazomethane dissolved in excess of methyl stearolate and irradiating it. However, again no success could be achieved. These experiments were repeated by the addition of small quantities of copper powder, but without no avail. Ultimately success was achieved by carrying out the reaction at $\sim -5^\circ$ in a set-up as described in the experimental. The product readily gave Halphens' test. The material was segregated by urea-adductation

(compare isolation of stercularic acid by Dunn) into seven fractions, and the one giving the strongest Halphen-test selected for its NMR spectrum. Fig.1 shows the NMR spectrum of pure methyl sterculate and that of the material corresponding to the above fraction. As can be seen the product shows the characteristic signal for the cyclopropene methylene at 43.5 cps. Integration of the cyclopropene methylene signal in this fraction leads to a value of $\sim 25\%$ of methyl sterculate in the product. Based on this an overall yield of approximately 5% can be computed (on stearolic acid).



PMR SPECTRUM OF METHYL STERULATE.



PMR SPECTRUM OF THE FRACTION No. 4 OF THE PRODUCT OF CH_2N_2 -UV IRRADIATION OF METHYL STEAROLATE.

EXPERIMENTAL

All melting points and boiling points are uncorrected. All solvent extracts were finally washed with saturated brine before drying (over anhydrous Na_2SO_4).

IR spectra were recorded on Perkin-Elmer Infracord model 137E spectrometer equipped with NaCl optics, either as smear (liquids) or in Nujol (solids). Maxima are reported in cm^{-1} .

PMR spectra were taken in a 20% solution in CCl_4 with tetramethylsilane as internal standard, on a Varian Associates A-60 spectrometer; peaks are reported in cps.

Isolation of sterculic acid from Sterculia foetida oil

Isolation of sterculic acid was accomplished essentially according to the method reported by Munn¹⁷. Cold pet. ether (40-60°) extracted Sterculia foetida oil (21.7 g) was saponified at 16° with alcoholic potash (65 ml; 10%). Working up the soaps furnished mixed fatty acids (19.7 g), which were fractionated by urea-adductation method according to Munn's scheme. Adduct (V; 18.3 g) on decomposition and work up gave yellow coloured liquid fatty acid (1.3 g). During the preparation of mixed fatty acids and decomposition of urea adduct, at no stage the product was either allowed to come into contact with atmospheric oxygen or the temperature raised beyond 10-12°. Crystallisation (thrice) of the acid fraction

from acetone (3,2,2 ml) at -50° , and reverse filtration afforded sterculic acid (1.1 g). Halphen-test (acid 160 mg; CS_2 -S solution 2 ml; amyl alcohol 2 ml: heating at $45-50^{\circ}$ for 45 minutes gradually raising to 110° and further heating for 1 hr) gave deep cherry-red colour. IR spectrum: COOH 2680, 1708; CH_2 of the cyclopropene ring 1010 cm^{-1} .

Methyl sterculate

Sterculic acid (0.9 g) was reacted with excess of ethereal solution of diazomethane in cold. Working up the reaction product furnished methyl sterculate (0.94 g). Halphen-test with the ester (165 mg) in the usual fashion gave deep cherry-red colour. IR spectrum: COOCH_3 1765; CH_2 of the cyclopropene ring, 1010 cm^{-1} (Fig.2). PMR spectrum: $-\text{OCH}_3$ (3H) 216.2; 2, $-\text{CH}_2-\overset{!}{\text{C}}=(4\text{H})$, $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{O}-$ (2H) 138.2; CH_3-CH_2- (3H), 53.2; $-\text{CH}_2-$ of cyclopropene (2H), 43.5 cps (Fig.1).

Stearolic acid

Stearolic acid was prepared essentially according to the method reported by Khan *et al.*⁵⁷

9,10-dibromostearic acid: Oleic acid^{*} (112 g) was brominated in dry ether (450 ml) at 2° in the usual fashion.

^{*}Oleic acid (BDH, CP grade) was purified by converting it to methyl ester and fractional distillation. Fraction distilling at $151-153^{\circ}/1\text{ mm}$ was hydrolysed and refractionated before use.

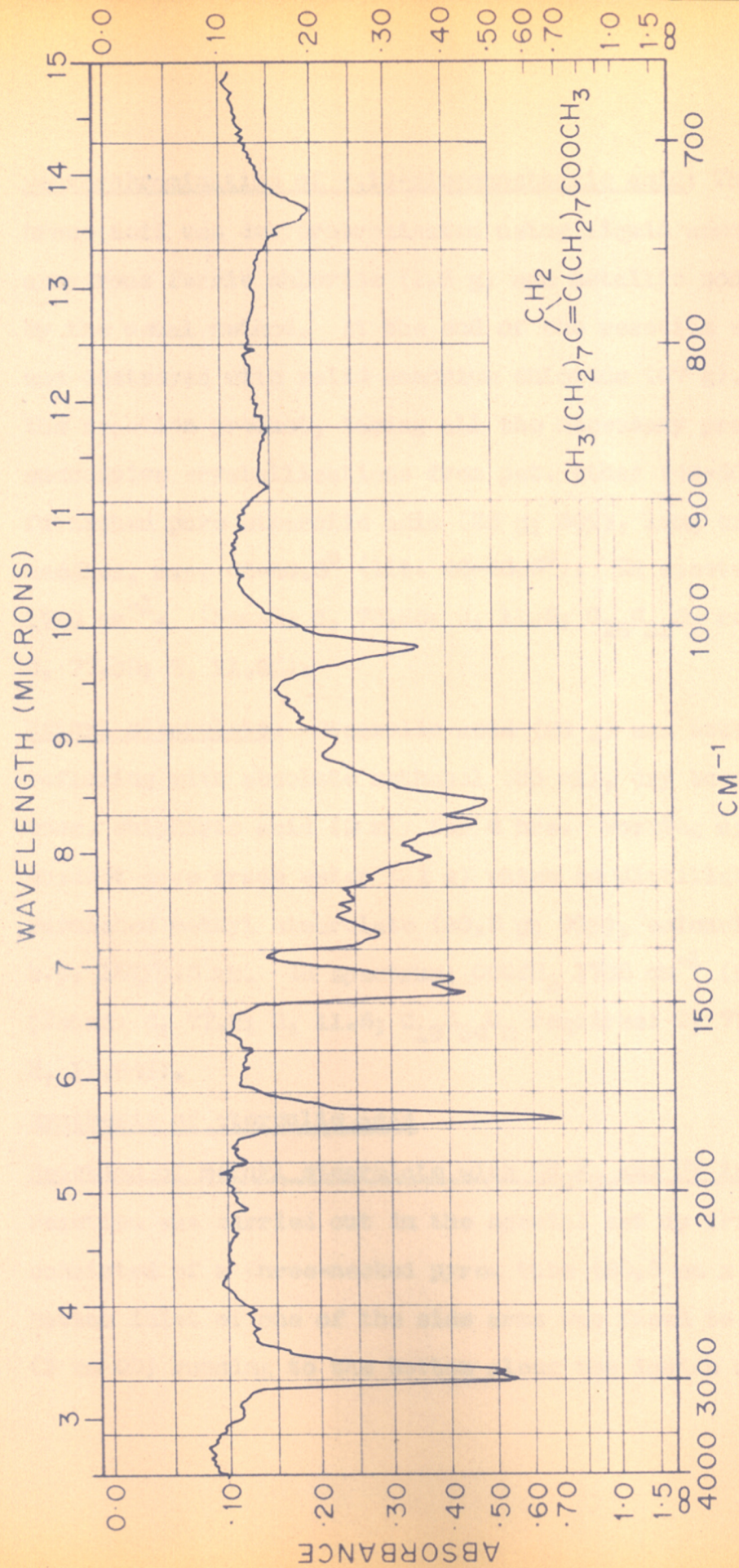


FIG. 2. IR SPECTRUM OF METHYL STERCULATE.

Dehydrobromination of 9,10-dibromostearic acid: The above bromo acid was dehydrobrominated using liquid ammonia (2 lit), anhydrous ferric chloride (1.8 g) and metallic sodium (48 g) by the usual method. At the end of the reaction excess sodamide was destroyed with solid ammonium chloride (67 g). Working up the reaction product, taking all the necessary precautions, and successive crystallisations from pet. ether (40-60°) in cold, furnished pure stearolic acid (55 g; 50%), long crystalline needles, m.p. 46-46.5° (lit. 46-46.5°). IR spectrum: COOH 2680, 1710 cm^{-1} . (Found: C, 76.85; H, 11.5; $\text{C}_{18}\text{H}_{32}\text{O}_2$ requires: C, 77.09; H, 11.5%).

Methyl stearolate: Stearolic acid (20 g) was esterified by refluxing with absolute methanol (60 ml), dry benzene (60 ml), conc. sulphuric acid (3 ml) for 4 hrs. Working up the reaction product gave crude ester (21 g) which on distillation in vacuo furnished methyl stearolate (20.5 g; 98%), colourless liquid, b.p. 157/0.5 mm. IR spectrum: COOCH₃ 1765 cm^{-1} (Fig.3). (Found: C, 77.3; H, 11.5; $\text{C}_{19}\text{H}_{34}\text{O}_2$ requires: C, 77.49; H, 11.64%).

Synthesis of sterculic acid

Reaction of methyl stearolate with CH_2N_2 and UV irradiation: The reaction was carried out in the special set up (Fig.4) which consisted of a three-necked pyrex tube (35.5 cm x 5.2 cm OD). Bottom inlet of one of the side arms was fused to a thin tube (3 mm OD) running to the bottom along the inside wall of the

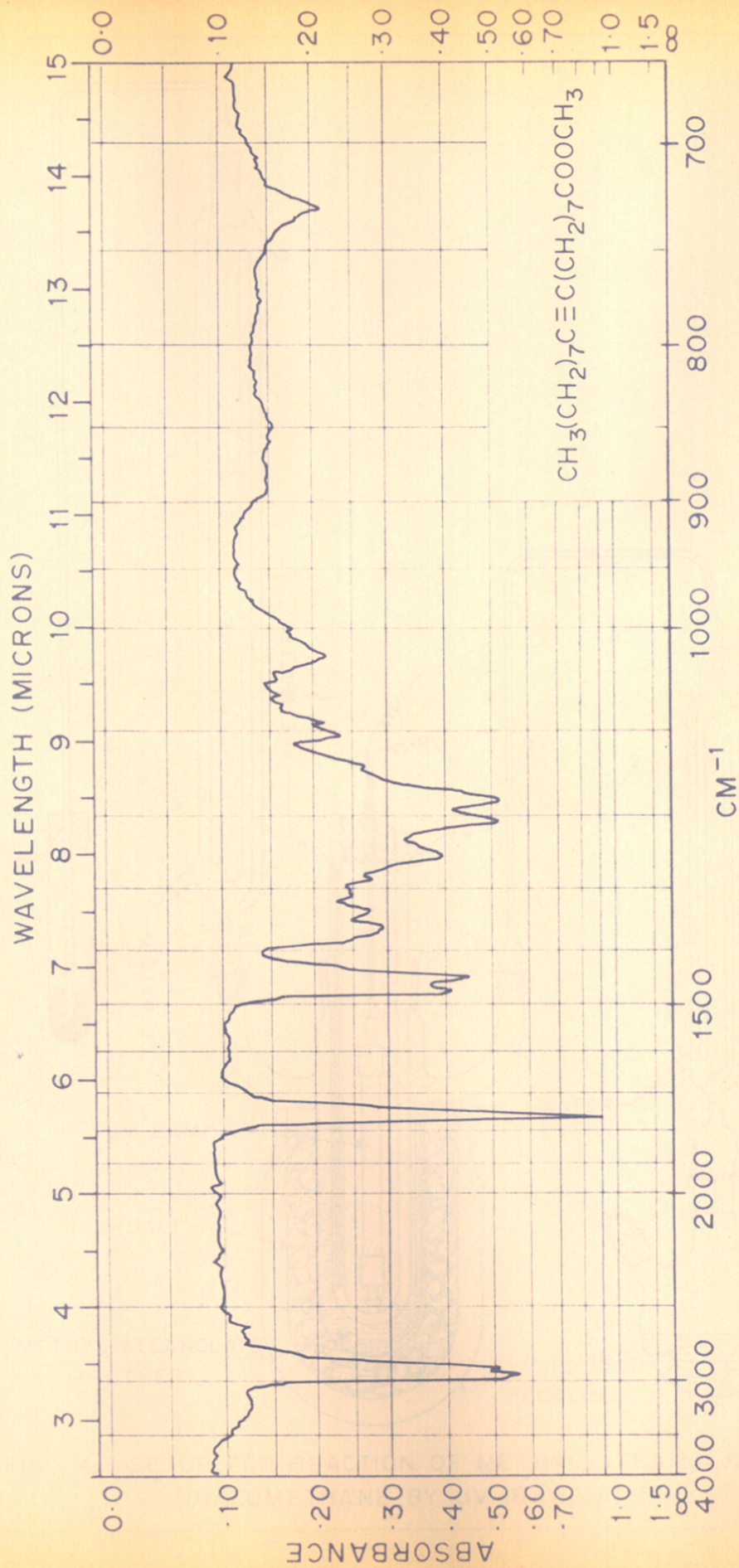


FIG. 3. IR SPECTRUM OF METHYL STEAROLATE.

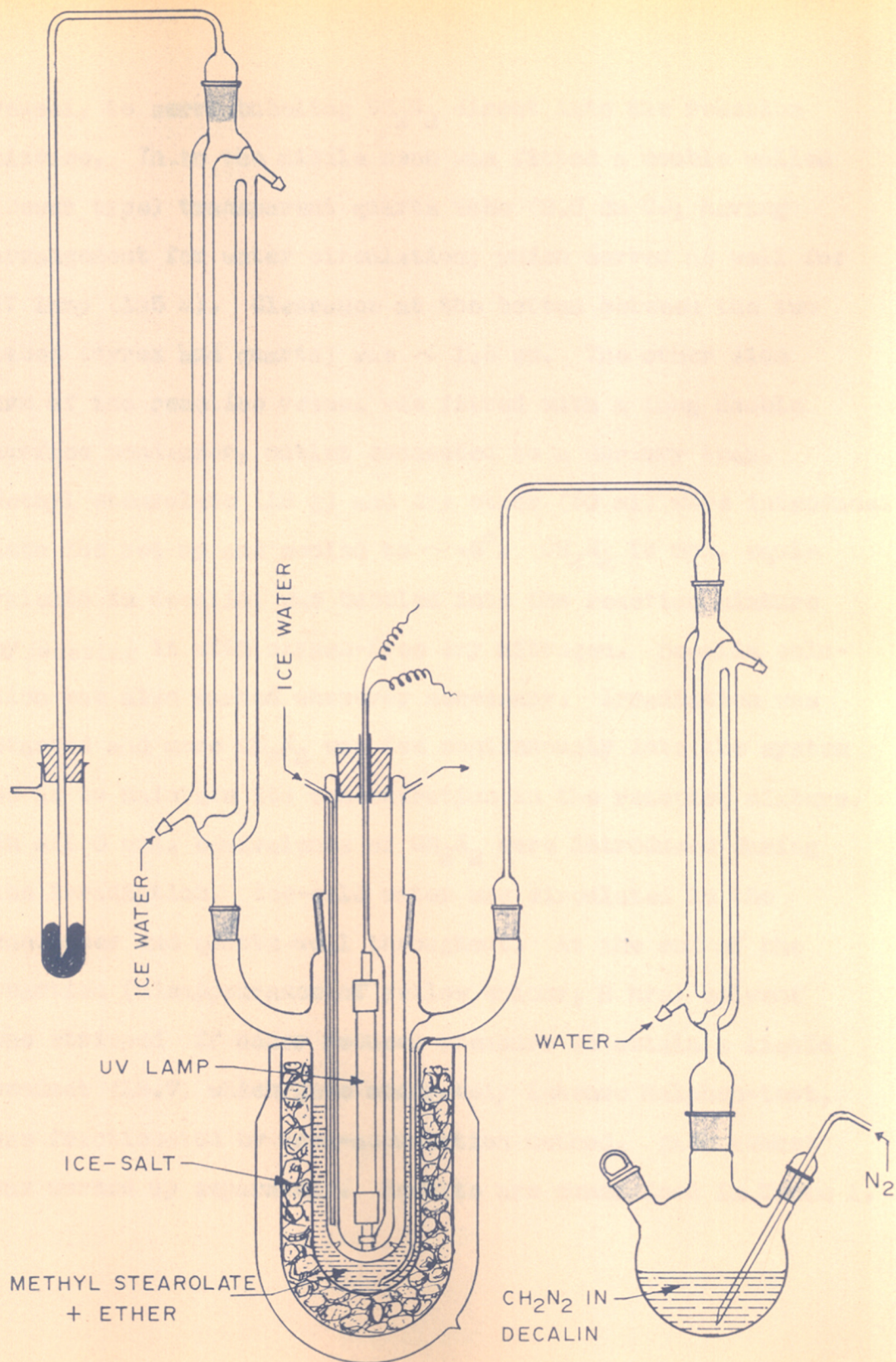


FIG. 4. SETUP FOR REACTION OF METHYL STEAROLATE WITH DIAZOMETHANE BY UV IRRADIATION.

vessel, to serve bubbling CH_2N_2 direct into the reaction mixture. In to the middle neck was fitted a double walled (Dewar type) transparent quartz tube (3.6 cm OD; having arrangement for water circulation) which served as well for UV lamp (125 W). Clearance at the bottom between the two tubes (Pyrex and quartz) was ~ 1.5 cm. The other side arm of the reaction vessel was fitted with a long double surface condenser, outlet connected to a mercury trap. Methyl stearolate (18 g) and dry ether (50 ml) were introduced into the set-up and cooled to $\sim -5^\circ$. CH_2N_2 (2 mol. equivalents in decalin) was bubbled into the reaction mixture by sweeping it with oxygen-free dry nitrogen. Decalin solution was also warmed whenever necessary. Irradiation was started and more CH_2N_2 was fed continuously into the system so as to maintain its concentration in the reaction mixture. In all 6 mol. equivalents of CH_2N_2 were introduced during the irradiation. Ice-cold water was circulated in the condenser and quartz-well throughout. At the end of the reaction (disappearance of yellow colour; 8 hrs) solvent was stripped off under reduced pressure to obtain a liquid product (18.7) which gave moderately intense Halphen-test, was fractionated by urea-adductation method. Each adduct was worked up separately. Results are summarised in Table 1.

TABLE 1 - FRACTIONATION OF REACTION PRODUCT (CH_2N_2 - UV
IRRADIATION) BY UREA-ADDUCTATION

Total product: 18.7 g

Absolute methanol: 56 ml

S.No.	Amount of urea (g)	Adduct (complex) g	No.	Ester obtained on decomposi- tion of the adduct. (g)	Halphen- test.
1	18.7	13.8	1	7.5	Positive
2	9.4	15.1	2	4.7	"
3	4.7	6.8	3	2.7	"
4	9.4	9.3	4	1.9	Intense
5	12.6	15.6	5	0.27	Positive
6	Filtrate concd. to 1/3 volume	3.4	6	0.45	"
7	Filtrate concd. to 1/2 volume	3.1	7	1.0	"

Soon after work up, IR spectra of all the fractions were recorded. IR spectra of fractions 1,2,3 were similar to that of the spectrum obtained for methyl stearolate. Spectra of fractions 4,5,6 exhibited bands for the cyclopropene group in the range of $1005\text{-}1010\text{ cm}^{-1}$ but it was distinctly perceptible in the spectrum for fraction No.4 (Fig.5). PMR spectrum for this fraction exhibited signal for the methylene in the

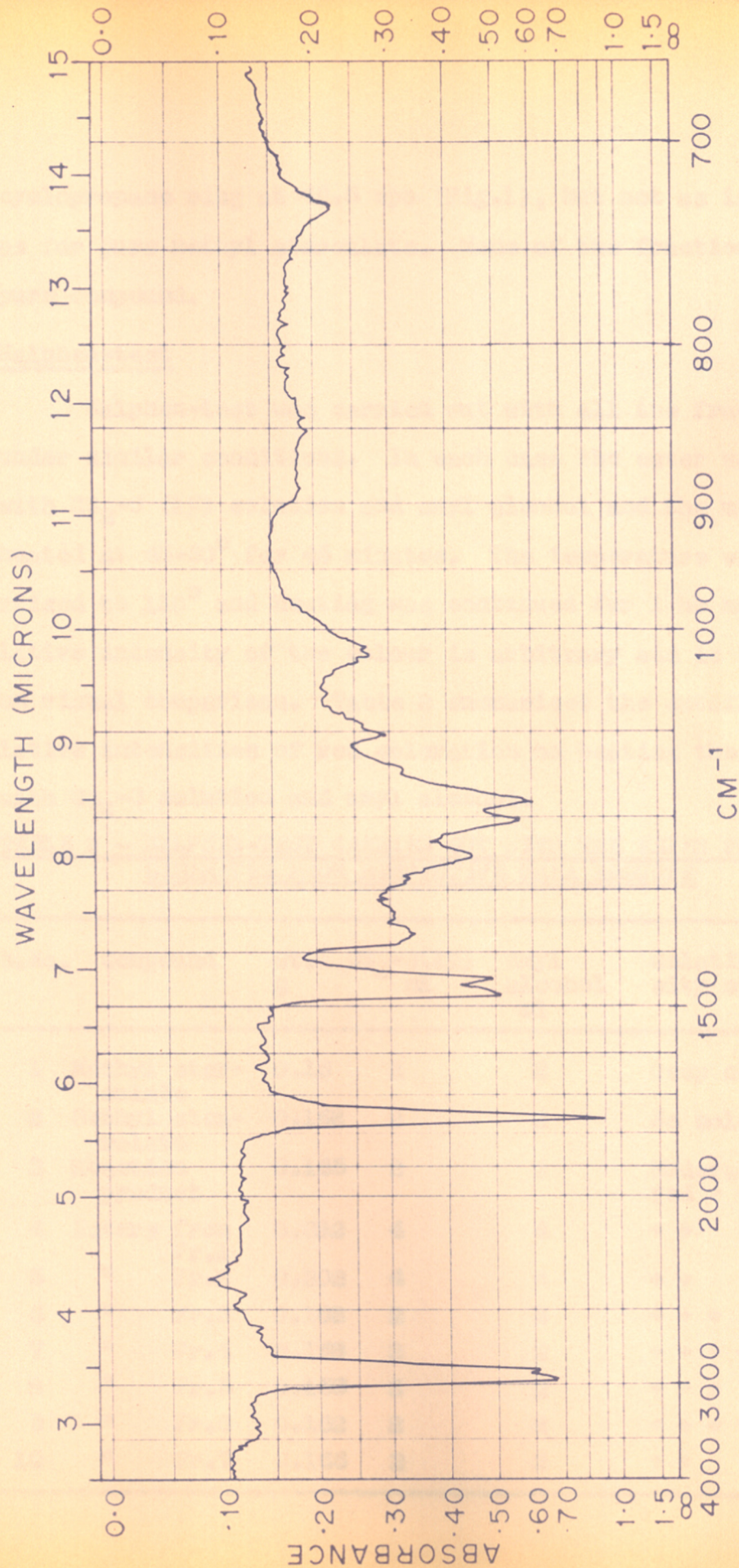


FIG. 5. IR SPECTRUM OF THE FRACTION No. 4 OF THE PRODUCT OF
 CH_2N_2 -UV IRRADIATION OF METHYL STEAROLATE.

cyclopropane ring at 43.5 cps (Fig.1), but not as intense as for pure methyl sterulate. None of the fractions was a pure compound.

Halphen-test

Halphen-test was carried out with all the fractions under similar conditions. In each case the ester was mixed with CS_2 -3 (1%) solution and amyl alcohol and the mixture was heated at 45-50° for 45 minutes. The temperature was gradually raised to 110° and heating was continued for 1 hr more. Relative intensity of the colour is arbitrary and is based purely on visual comparison. Table 2 summarises the details and relative intensities of red coloration on heating the product with CS_2 -3 solution and amyl alcohol.

TABLE 2 - HALPHEN-TEST CARRIED OUT WITH THE ESTER FRACTIONS
LIBERATED FROM RESPECTIVE UREA ADDUCTS

S.No.	Compound	Wt. g	CS_2 -3(1%) ml	Amyl alcohol ml	Relative inten- sity of colouration.
1	Methyl ster- culate	0.16	2	2	Deep cherry-red
2	Methyl stea- rolate	0.168	2	2	No colouration.
3	Reaction product	0.165	2	2	Moderately intense red + + + +
4	Esters from Fr.1	0.382	4	4	+ +
5	" Fr.2	0.302	4	4	+ +
6	" Fr.3	0.168	2	2	+ + +
7	" Fr.4	0.169	2	2	+ + + + +
8	" Fr.5	0.159	2	2	+ + +
9	" Fr.6	0.162	2	2	+ + + +
10	" Fr.7	0.166	2	2	+ +

SUMMARY

A synthesis of methyl sterulate involving the photochemical addition of diazomethane to methyl stearolate has been described. The relevant literature on sterculic acid has been reviewed.

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SOME STUDIES IN
FATTY ACID SERIES

PART TWO
 ω -OLEFINIC FATTY ACIDS

NATIONAL CHEMICAL LABORATORY,
POONA-8.
(1965)

C O N T E N T S

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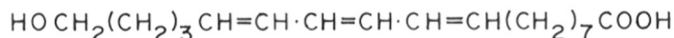
CHAPTER I

INTRODUCTION

ω-OLEFINIC FATTY ACIDS

INTRODUCTION

The work described in this Part deals with the development of general method for the preparation of long chain ω-olefinic fatty acids. ω-Olefinic acids offer an unique opportunity for degrading the molecule from one end in bits of one or more carbon atoms at a time. This work was of interest in connection with the possible utilization of kamulonic acid:

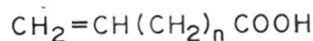


the major component of the oil from the seeds of Mallotus philippinensis.

It appears relevant, in connection with this work, to describe very briefly the state of our knowledge with regard to ω-olefinic acids. Unlike the other saturated and unsaturated acids, terminally unsaturated fatty acids are not at all wide spread in nature, though 9-decenoic acid has either been detected, isolated or identified in human milk fat¹, in butter and milk fats of various animals²⁻⁶, and in sperm head oil⁹.

METHODS OF SYNTHESIS

Table 1 summarises the properties of the known ω-olefinic acids.

TABLE 1 : PROPERTIES OF α -OLEFINIC FATTY ACIDS

No.	n	m.p. °C	b.p. °C	Pr. mm	d_4^{20}	n_D^{20}	Ref.
1	0	[12.3	141.9		1.0621 ¹⁶	1.4224 ²⁰	10,12
		[	65	30	-	-	12
		[13.5			1.045 ²⁵	1.485 ²⁵	13
2	1	[-29	163		1.013 ¹⁵	1.4257 ¹⁵	10,14
		[	72-72.5	14	-	-	16
3	2	[<-18	189		0.9843 ¹⁸	1.4341 ^{7.5}	10,11,14
		[	186-87	745	0.9987 ⁰		11
		[	187-89		0.98416 ¹⁵	-	15
4	3	[	203		0.9610 ²⁰	1.4343 ²⁰	10,11
		[+1	107	16	0.9610 ²⁰	1.4385 ²⁰	17
5	4	[-6.5	225		0.952 ¹⁷	1.4425 ²⁰	10
		[	225-27				18
		[-6.5	125	15	0.9515 ^{14.9}	1.4404 ^{14.9}	19,11
6	5	(Ethyl ester 210-12)	-	-	-	-	20,11
7	6	5	116-18	1	0.9146 ^{15.8}	1.4492 ¹⁵	19
8	7	[	143-48	15	0.9238 ¹⁵	1.4488 ²⁰	10,11
		[-0.5	155-60	14	-	1.4462 ²⁰	4
		[	142	4	-	-	2
9	8	[24.5	275		0.9075 ²⁵	1.4464 ²⁰	10
		[24-25	165	15	-	-	11
		[22-23	131	1	0.9072 ²⁴	-	19

....contd.

TABLE 1 (Contd.)

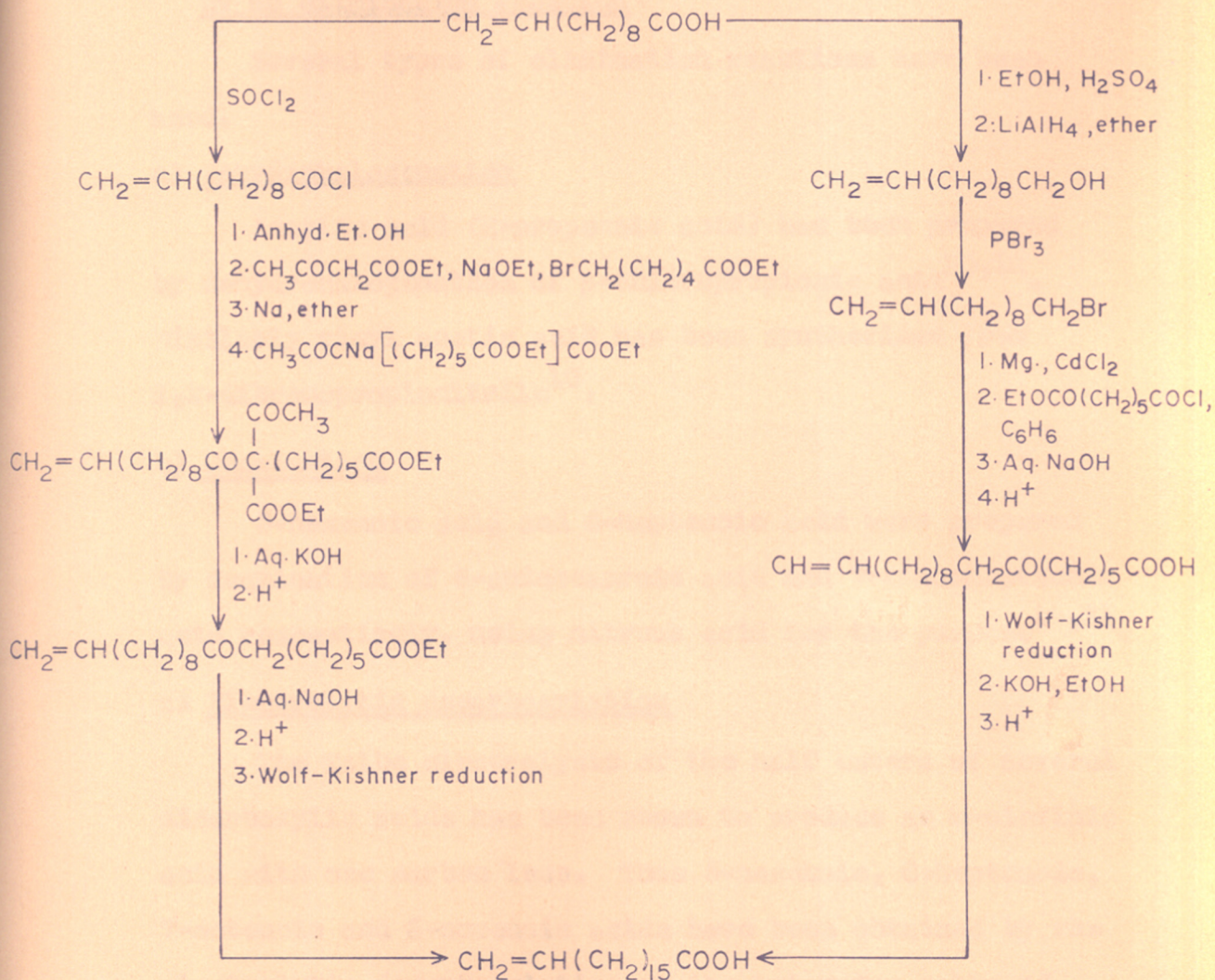
No.	n _D	m.p. °C	b.p. °C	Pr. mm	d ₄ ²⁰	n _D ²⁰	Ref.
10	9	[	143-44	3	0.9030 ²⁰	1.4510 ²⁰	10,11,21
		[F.P.19	171-72	13	0.907 ²⁰	-	22
11	10	[38	192	25	-	-	10
		[38-39	192	20	-	-	21
		[162	8	-	-	-	22,11
		[38-38.2	185	15	-	-	
12	11	Not reported					
13	12	[	198	8	-	-	10
		[49.8-	195	8	-	-	22
		[50					
14	13	Not reported					
15	14	Not reported					
16	15	[55-55.5	-	-	-	-	23,25
		[55.5-					24
		[56.1					

Several methods have been used for the preparation of these compounds, and these may be broadly divided into three groups.

- A. Methods utilising components in which the α -olefinic group is already present.
- B. Methods in which the α -olefinic group is produced by an elimination reaction.
- C. Other methods.

A. Methods utilising components in which the
 α -olefinic group is already present.

A number of compounds have been synthesized by chain extension of a suitable starting material by several of the available methods (Grignard reaction, exchange with cyanide, malonic acid synthesis etc.). Starting from vinyl magnesium and allyl magnesium halides, acrylic and vinyl acetic acids have been prepared respectively^{10,13}. From allyl bromide, vinyl acetic acid¹⁰ and allyl acetic acid^{10,11} have been synthesized. Vinyl ethyl bromide has been used to prepare 5-hexenoic acid^{17,19}, vinyl propyl bromide was used to prepare 6-heptenoic acid²⁶, which in turn, was elaborated to 8-nonenoic acid, which was, next, used as a starting material for 10-undecenoic acid synthesis²⁶. The ready availability of 10-undecenoic acid from castor oil cracking^{10,11,30} made possible its further elaboration into 11-dodecenoic acid²¹, 12-tridecenoic acid^{21,22}, and 14-pentadecenoic acid²². 17-octadecenoic acid has been prepared from 10-undecenoic acid by the following two routes^{23,24}.



B. Methods in which the α -olefinic group is produced by an elimination reaction

Several types of elimination reactions have been used.

a) Dehydrohalogenation

Acrylic acid (2-propenoic acid) has been prepared by dehydrohalogenation of β -chloropropionic acid^{10,12}. Similarly vinyl acetic acid has been synthesized from 1,2-dibromopropionitrile¹⁰.

b) Deamination

5-hexenoic acid and 6-heptenoic acid were prepared by deamination of 6-aminocaproic acid and 7-aminoheptanoic acid respectively, using nitrous acid for the purpose^{10,11}.

c) Electrolytic decarboxylation

The Kolbe electrolysis of the half esters of several dicarboxylic acids has been shown to produce an α -olefinic acid with one carbon less. Thus 5-hexenoic, 6-heptenoic, 7-octenoic and 8-nonenic acids have been obtained by the electrolytic decarboxylation of the potassium salts of the half esters from pimelic¹⁰, suberic^{10,11}, azelaic^{10,11} and sebacic acids¹¹ respectively.

d) Pyrolysis of polyesters

Acrylic acid is being prepared commercially by the pyrolysis of polyesters obtainable from the polymerization of β -propiolactone¹³.

e) Pyrolysis of 8-hydroxy olefinic acid

10-Undecenoic acid is commercially prepared by the pyrolysis of castor oil. The mechanism of this reaction has been investigated by Arnold and Smolinsky, who have profitably exploited this reaction for a variety of purposes³¹⁻³³.

C. Other methods.

Some specific methods are available for the synthesis of certain ω -olefinic acids. Thus, for example, acrylic acid is being manufactured commercially by "carbonyl reaction" for which basic raw materials are acetylene, carbon monoxide (supplied as such or in the form of nickel carbonyl) and water¹³. This acid has also been prepared by decarboxylation of maleic acid¹³ and catalytic "hydrolysis" of maleic anhydride^{10,12}.

Vinyl acetic acid has been synthesized from 3-butyneic acid by converting it to allenic acid followed by reduction with lithium aluminium hydride¹⁴.

Allyl acetic acid was prepared by the reduction of methyl 4-pentynoate with sodium and alcohol²⁷.

5-Hexenoic acid was obtained by decarboxylation of $\Delta\beta$ -butenyl malonic acid²⁸. It has also been prepared from cyclohexanone through formation of 5-hexenal by ring-rupture

and conversion of the aldehyde to hydroxamic acid
followed by treatment with sulphuric acid^{10,11}.

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CHAPTER II

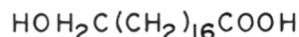
PYROLYSIS OF MANY-MEMBERED LACTONES: A GENERAL METHOD FOR THE SYNTHESIS OF **ω -OLEFINIC FATTY ACIDS**

PYROLYSIS OF MANY-MEMBERED LACTONES: A GENERAL
METHOD FOR THE SYNTHESIS OF α -OLEFINIC FATTY ACIDS

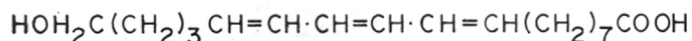
The purpose of the present work was to evolve a simple procedure for the preparation of 17-octadecenoic acid (I) from 18-hydroxy stearic acid (II), a compound readily available by the hydrogenation of the naturally occurring kamolenic acid (III), the main fatty acid component of Kamala seed oil obtained from Kamala seeds (Mallotus philippinensis). This Chapter describes the successful conclusion of this phase of work, while the next Chapter deals with the methods adopted for the further chain shortening of the 17-octadecenoic acid.



I



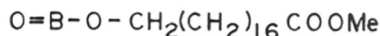
II



III

PRELIMINARY INVESTIGATIONS*

Of the various methods available for the dehydration of primary alcohols the method of pyrolytic cis-eliminations² appeared promising. For this purpose, pyrolysis of the metaborate ester of methyl-18-hydroxy stearate (IV), was investigated in the first instance.

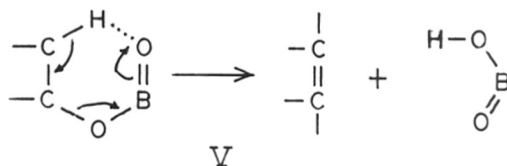


IV

Pyrolysis of borate esters derived from a variety of alcohols has been investigated by several workers³⁻⁵, and good yields of the olefins have been obtained. O'Connor and Nace⁴ suggested that this reaction proceeds via the

*Gupta¹ in a preliminary communication reported the preparation of 17-octadecenoic acid (I) from 18-hydroxy stearic acid (II). The hydroxy acid was converted to the corresponding ω -chlorostearic acid by treatment with thionyl chloride, which was then dehydrohalogenated by heating with alcoholic potassium hydroxide solution (25%). The product which was obtained in an unspecified yield was shown to have the melting point of 17-octadecenoic acid (55-55.5°C), and was further characterized by its oxidation to 1,17-heptadecadiolic acid and to stearic acid by catalytic hydrogenation of the unsaturated acid. Details of this work have not been published so far.

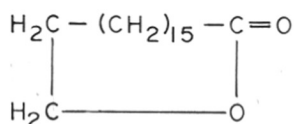
unstable metaborate ester which undergoes cis-elimination to yield an olefin and, in analogy with the well-accepted mechanism of pyrolytic cis-eliminations, the borate pyrolysis was assumed to proceed as in V:



However, it has been pointed out by De Puy² that the pyrolysis of borate esters may not, in fact, be a cis-elimination reaction as the metaborate esters are linear and are consequently unfavourable for a cyclic elimination.

Methyl-18-hydroxy stearate, and boric acid were refluxed in toluene with continuous removal of water when the corresponding borate (IV) was readily obtained. This on pyrolysis at elevated temperature (free flame), and pressures of 0.5 to 0.6 mm gave only a poor yield of pyrolysate and a lot of polymeric material was obtained as a residue. Further modification in the design of the distillation flask (vide experimental), did not make any difference in the yields of the pyrolysate. The pyrolysate was found to be a mixture containing a liquid

compound which analysed for $C_{18}H_{34}O_2$. This did not give any colour with tetranitromethane and in the infrared (Fig.1) displayed its $\nu^{C=O}$ at 1738 cm^{-1} and did not exhibit any strong band around 910 or 990 cm^{-1} , where terminal vinyl group displays its characteristic out-of-plane CH deformations⁶; the absence of hydroxyl group is also clear from the IR spectrum. On hydrolysis it yielded 18-hydroxy stearic acid (II). On the basis of these data the compound is formulated as the lactone (VI).



VI

This was confirmed by its comparison (IR) with an authentic sample of the lactone (VI) prepared according to the method described by Gupta et al.⁹

The pyrolysis of the borate was, next, investigated in a column reactor (Fig.2) so as to minimise the period of stay of the product in the pyrolysis zone. However, in this case also none of the expected α -olefinic acid was obtained and the only identifiable products were the lactone (VI) and the dilactone (VII) (m.p. $110-112^\circ$), identified by comparison (IR, mixed m.p.) with an authentic

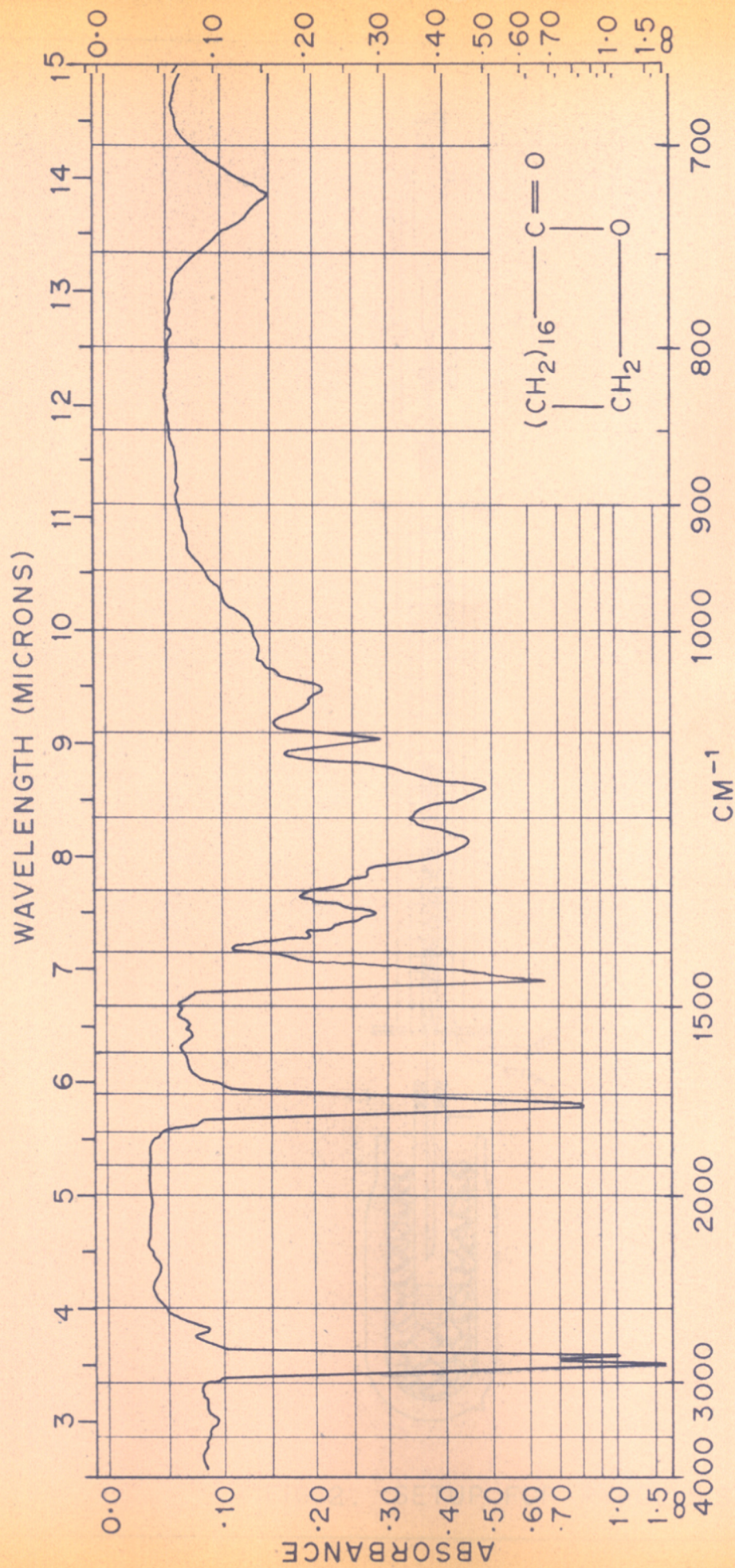


FIG. 1. IR SPECTRUM OF NEUTRAL FRACTION (1,18-OCTADECANOLIDE) FROM PYROLYSIS OF
 METABORATE ESTER OF METHYL 18-HYDROXYSTEARATE.

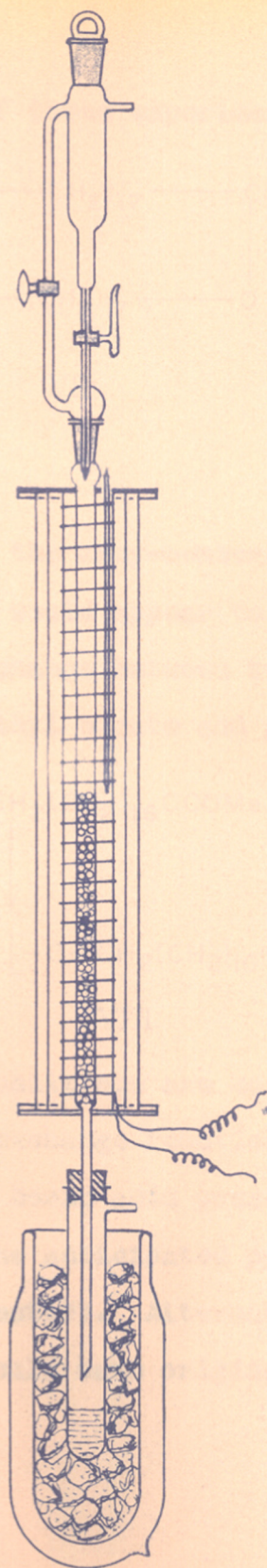
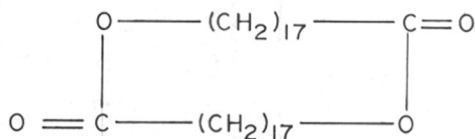


FIG. 2. SETUP FOR PYROLYSIS.

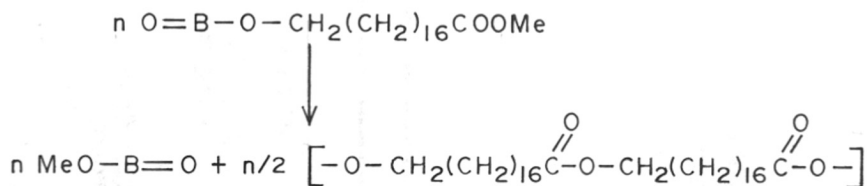
sample⁹. The results of these experiments are



VII

summarised in Table 1.

The formation of the many-membered lactone (VI) during borate pyrolysis would appear to be due to the possibility of ester exchange between two moles of the borate ester to give methyl borate and polyesters (VIII):

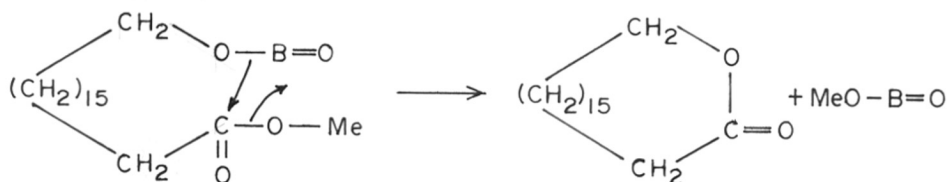


VIII

which under pyrolytic conditions are known to yield lactones¹⁰. The ester exchange reaction could have been initiated by a trace of boric acid present in the starting material or formed in the anticipated pyrolytic elimination (to give olefinic ester). Alternatively it is possible that the lactone (VI) could have originated directly by the pyrolytic cleavage:

TABLE 1 - PYROLYSIS OF THE BORATE OF METHYL 12-HYDROXY STEARATE (IV)

No.	Methods and conditions of pyrolysis				Re- marks
	0.5" x 18" ver- tical reactor Filled with glass beads. Temp. 350°C Pressure 0.5-0.6 mm Time of melt drop- ping 1 hr. Subsequent heating 1/2 hr.	0.5" x 18" ver- tical reactor. Filled with glass beads. Temp. 350°C Pressure 0.5-0.6 mm Time of melt drop- ping 1/2 hr. Subsequent heating 1/2 hr.	0.5" x 18" ver- tical re- actor. Filled with glass beads. Temp. 400°C. Pressure 0.5-0.6 mm. Time of melt dropping 15 min. Subsequent heating 4 min.	0.5" x 18"	
1	Borate ester wt. g	5.0121	5.0123	4.5977	
2	Pyrolysate wt. g	2.5168	2.4133	2.7863	
3	Solids after tritu- ration and crystal- lisation. wt. g	0.0526	0.0530	0.0530	Essentially polymeric lactones (VII).
4	M.p. of solids °C	110-112	110-112	110-112	
5	Liquid compound. wt. g	0.4362	1.3212	0.7134	
6	B.p. of liquid compd. °C/mm	142/0.4	141-42/0.4	137-38/ 0.25-0.3	Essentially lactone (VI).
7	Yield of liquid compd. %	8.7	26.36	15.51	

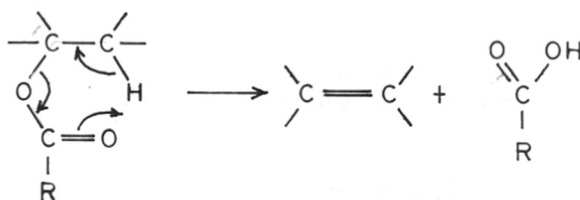


VI

In this connection it may be mentioned that when the acetate $[\text{CH}_3\text{C}(=\text{O})\text{O}-\text{CH}_2(\text{CH}_2)_{16}\text{COOMe}]$ was subjected to the same conditions of continuous pyrolysis as the borate ester (IV), the acetate was recovered unchanged.

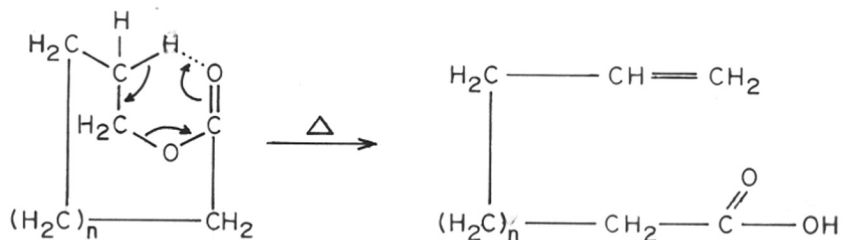
PYROLYSIS OF MANY-MEMBERED LACTONES

As mentioned earlier it is well recognised now that pyrolysis of esters to yield olefins proceeds through a cyclic transition state:



It was argued that if instead of an ester a lactone be subjected to these conditions one should end up with α -olefinic fatty acids, provided the lactone ring-size is such as to allow the attainment of planarity of the

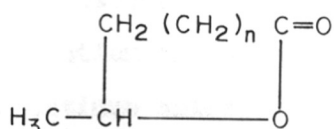
concerned atoms in the transition state:



The method appeared all the more attractive because isomerisation of olefinic linkages under these pyrolytic conditions normally does not take place².

A preliminary experiment³ with the lactone (VI)

³After this preliminary work had been completed, a review article on *cis*-eliminations was published by De Puy et al. [*Chem. Rev.* 60, 431 (1960)] wherein it is mentioned that Bird and Bailey [Abstracts of papers presented before the Division of Organic Chemistry, at the 131st Meeting of the American Chemical Society, Miami, Florida, April 1957, p.44-0], studied the pyrolysis of some lactone of the type:



$n = 1$ and 3

Details of this work have not appeared so far.

described earlier, showed great potentialities for the reaction. It was decided to prepare a series of lactones of varying ring-sizes and study their pyrolysis. For this purpose a series of ω -hydroxy acids had to be synthesized and the following two sections describe the preparation of various ω -hydroxy acids and the lactones derived from them.

PREPARATION OF ω -HYDROXY FATTY ACIDS

[$\text{HO}-(\text{CH}_2)_n\text{COOH}$; $n = 17, 15, 14, 12, 11, 10$ and 9]

The ω -hydroxy fatty acids, required for our investigation, have all been described in the literature. Several methods are available for the preparation of ω -hydroxy acids^{11,12}. Special mention must be made of the procedures developed by Chuit *et al.*¹³ in which use has been made of the half esters of dicarboxylic acids which by Bouveault-Blanc reduction yielded the hydroxy acids. These authors also utilized several α,ω -bromohydrins for synthesizing ω -hydroxy acids. Lycan and Adams¹⁴ synthesized several ω -hydroxy acids by the ozonolysis of suitable olefinic fatty acids followed by reduction of the resulting aldehydic acids with hydrogen, and platinum oxide, using minute quantities of ferrous sulphate as catalyst activator; Diaper *et al.*¹⁵ and Benton *et al.*¹⁶ have recently used sodium borohydride for the direct reduction of the ozonides to give ω -hydroxy

acids. The Russian group of workers¹⁷⁻¹⁹ have developed the Kolbe's electrolytic reaction for the syntheses of these hydroxy acids. Another important route to the synthesis of ω -hydroxy acids involves the reaction of carbontetrachloride and ethylene (Telomerization)²⁰. The telomers or the tetrachloroalkanes $[\text{Cl}(\text{CH}_2\text{CH}_2)_n\text{CCl}_3]$ have been hydrolyzed to give a variety of ω -hydroxy acids^{21,22}.

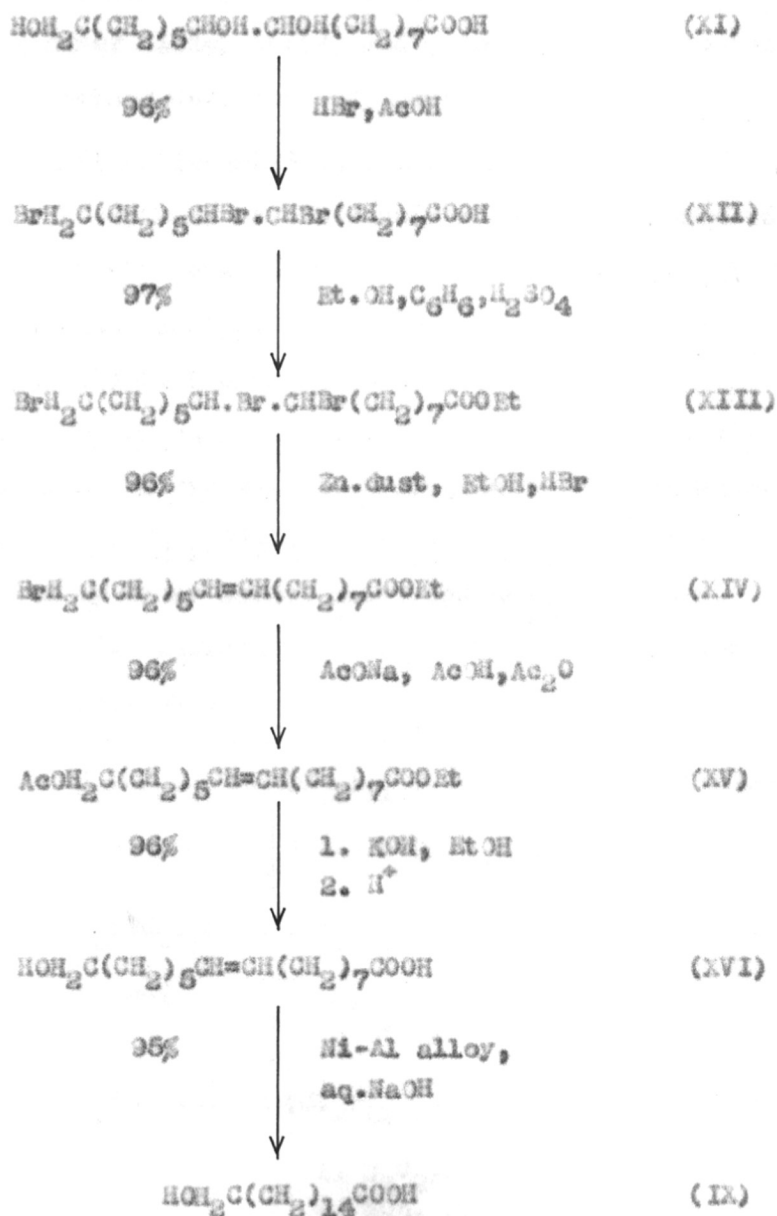
For the purpose of the present work, 18-hydroxy stearic (II), 16-hydroxy palmitic (IX), and 15-hydroxy-pentadecanoic (X) acids were prepared essentially according to the procedures described in the literature, with suitable modifications wherever necessary. For the preparation of the remaining acids [$n = 12, 11, 10$ and 9] new and more convenient procedures have been worked out.

1. 18-Hydroxy stearic acid (II)^{9,13,23}

18-Hydroxy stearic acid (II) could be prepared in excellent yields by the catalytic hydrogenation of kamolenic acid (III) over Raney Nickel in alcohol⁹.

2. 16-Hydroxy palmitic acid (IX)¹¹

16-Hydroxy palmitic acid, also known as juniperic acid, was prepared starting from aleuretic acid (XI) (obtained by hydrolysis of shellac) according to the procedure described by Mathur *et al.*²⁴

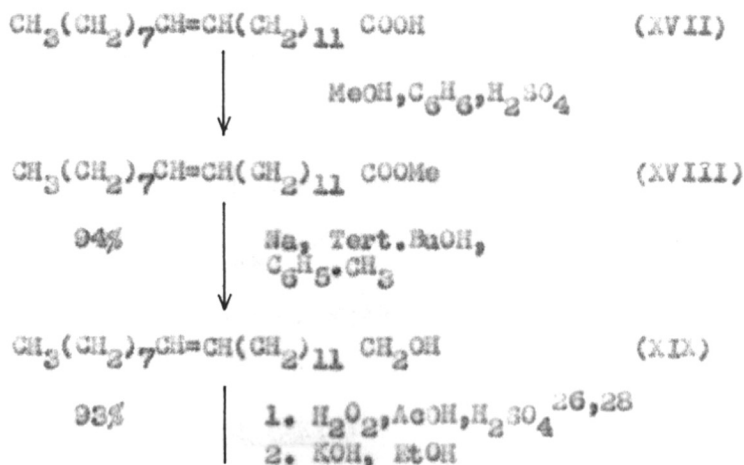


The modification introduced in this synthesis is the

hydrogenation of 16-hydroxy hexadec-9-enoic acid (XVI) using Raney Nickel alloy, and aqueous alkali according to the method described by Schwenk *et al.*²⁵

3. 15-Hydroxypentadecanoic acid (X)¹¹

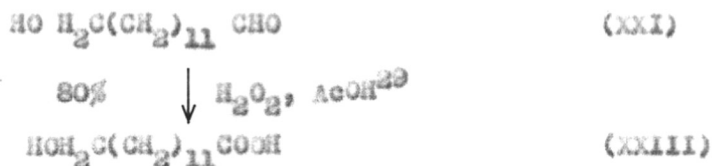
15-Hydroxy pentadecanoic acid was prepared essentially by the method described by Bhattacharyya *et al.*²⁶ with slight modifications. Thus, reduction of erucic acid (XVII) to the corresponding alcohol was carried out profitably by Hansley's modification²⁷ of Bouveault-Blanc reduction. Likewise, the hydrogenation of the unsaturated acid $\text{HOCH}_2\text{C}(\text{CH}_2)_{11}\text{CH}=\text{CH}\text{COOH}$ (XVII) was conveniently accomplished by Raney Nickel alloy and aqueous alkali. Erucic acid (XVII) required for this synthesis was isolated from mustard seed oil.





4. 13-Hydroxy tridecanoic acid (XXIII)

13-Hydroxy tridecanoic acid could be conveniently made by the peracid oxidation of the aldehydic alcohol (XXI), an intermediate in the synthesis of 15-hydroxy pentadecanoic acid (X), described earlier.

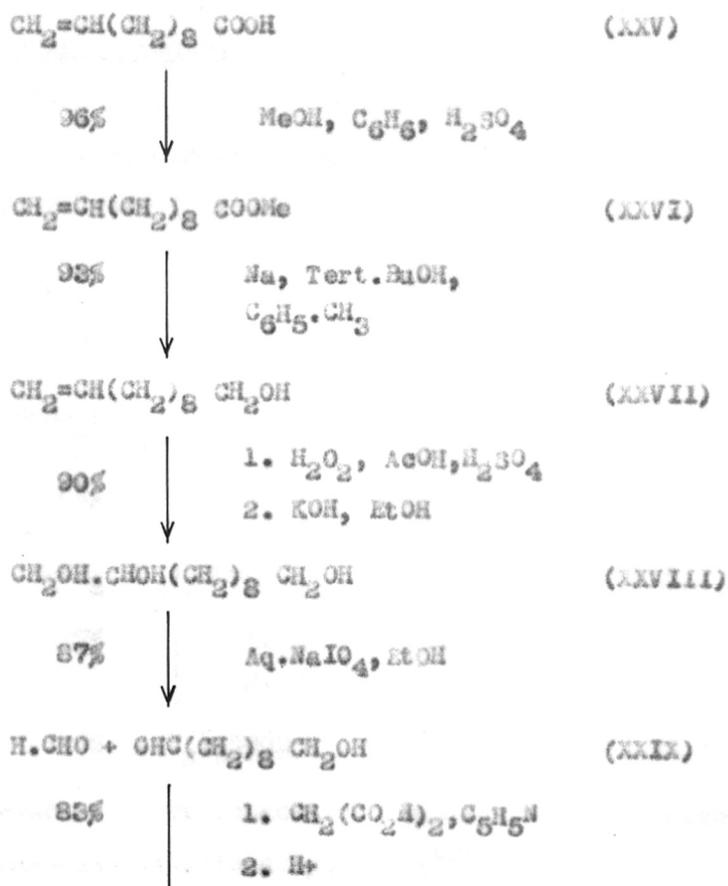


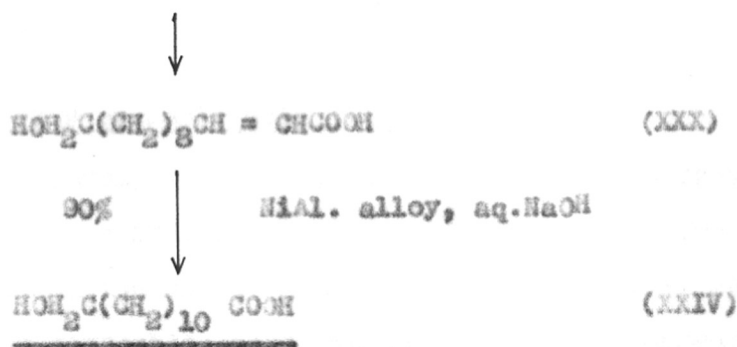
This acid has been prepared previously by different methods^{13,14}.

5. 12-Hydroxy lauric acid (XXIV)

A new method for the synthesis of 12-hydroxy lauric

acid (XXIV), also known as sabinic acid was worked out. The scheme followed for the preparation of this acid is shown below. The route was preferred as the intermediate aldehydic alcohol (XXIX) could also be utilized for the synthesis of 10-hydroxydecanoic acid (XXXIV). The starting material 10-undecenoic acid (XXV) was readily available as a product of pyrolysis of castor oil.

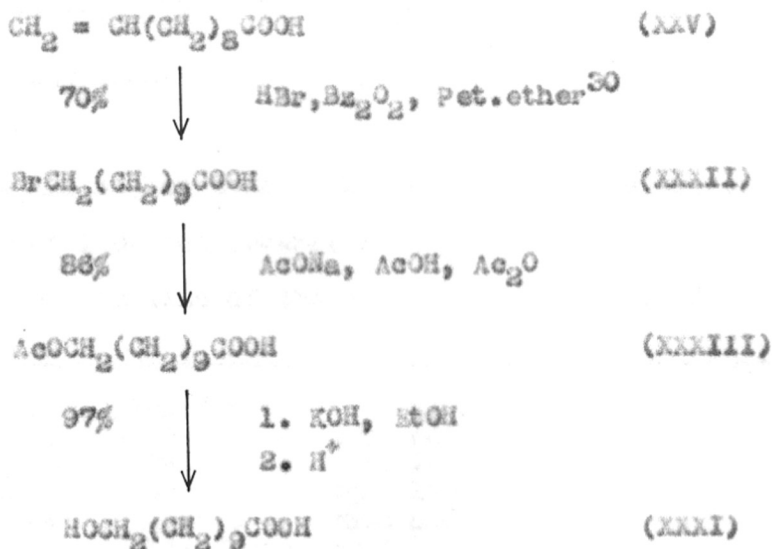




12-hydroxy lauric acid has been prepared previously by several workers¹³⁻¹⁵, but by different methods.

6. 11-Hydroxy undecanoic acid (XXXI)

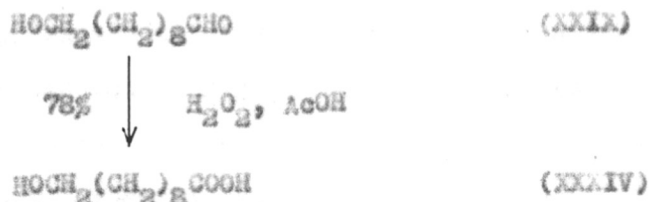
11-Hydroxy undecanoic acid (XXXI) could readily be made by the procedure shown below, starting with 10-undecenoic acid (XXV).



The procedure is more convenient than the various methods of its synthesis described by others¹²⁻¹⁴.

7. 10-Hydroxy decanoic acid (XXXIV)

10-Hydroxy decanoic acid (XXXIV), or 10-hydroxy capric acid, as indicated previously was made by the peracid oxidation of the aldehydic alcohol (XXIX), obtained earlier in connection with the synthesis of 12-hydroxy lauric acid (XXIV).



The preparation of 10-hydroxy decanoic acid by other methods has been described¹³⁻¹⁶.

PREPARATION OF LACTONES

The lactones required for the purposes of our study are all higher than δ -lactones. For the preparation of such lactones several methods are available, depending on the size of the ring^{*}. In the following pages

^{*}The classification of the ring compounds into small rings (3- and 4-membered), common rings (5-, 6- and 7-membered), medium rings (8- to 12-membered), and large rings (13-membered or larger) has been suggested by Brown and Prelog [*J. Am. Chem. Soc.* **73**, 215 (1951); footnote 21]. For our purposes this nomenclature will be used, the oxygen atom of the ring being counted as one of the members of the cycle.

a brief introductory survey of the available methods is given followed by a discussion of the methods used for the present work.

Available methods of synthesis

Basically the various methods of synthesis may be divided into two groups.

- A. Ring expansion of a cyclic ketone to a lactone.
- B. Methods which involve cyclization of acids or esters through a suitably placed functional group (hydroxyl, halogen, ester).

A. Ring expansion of a cyclic ketone to a lactone

The Baeyer-Villiger^{31,32} oxidation of cyclanones to lactones by interaction with a peracid is especially useful for the preparation of common (6-, 7-membered^{31,33-38}) and medium ring^{33,37,38} lactones. The method has also been used for the preparation of large membered lactones, for example exaltolide (1,15-pentadecanolide)³⁹. The method has been discussed in a review article⁴⁰. The chief limitation of this method for the preparation of higher-membered lactones is the availability of the required cyclic ketones which, in any case, have to be prepared from longchain α,ω -dicarboxylic acids.

- B. Methods which involve cyclization of acids or esters through a suitably placed functional group (hydroxyl, halogen, ester). The intramolecular cyclization of

hydroxy acids to lactones constitutes an important and flexible method. Stoll and Rouve⁴¹ studied the cyclization of hydroxy acids $[\text{HO}(\text{CH}_2)_n\text{COOH}; n = 3 \text{ to } 17 \text{ and } 22]$ under special conditions of high dilution and obtained lactones in yields of 40 to 75% for large-membered (14 to 19) lactones and 2 to 15% for the medium-ring (10 to 13) lactones. Others^{9,42} have also reported the preparation of various lactones through high dilution technique. The ω -hydroxy acids (as formates) have been cyclized in vapour phase over titanium-dioxide at about 300°C ⁴³.

Stoll⁴⁴ and Hunsdieker and coworkers⁴⁵ effected ring-closure of ω -bromo-, and ω -iodo fatty acids in the presence of potassium carbonate in methyl ethyl ketone, and have reported excellent yields for several lactones (10 to 18-membered). Allen *et al.*⁴⁶ reported a modified dilution head for the purpose.

Carothers and coworkers¹⁰ discovered that polyesters of hydroxy fatty acids can be slowly depolymerized in high vacuum at $\sim 270^\circ\text{C}$ using magnesium chloride as a catalyst, to furnish lactones in good yields. The method has the advantage of speed and simplicity over the high dilution method, and is suited for large scale preparations. Several catalysts for the depolymerization step have been described and modifications of the original procedure have

been reported^{47,48}.

A number of monocyclic lactones of different ring sizes have also been prepared from telomers⁴⁹.

Present work

For the present work cyclization of ω -hydroxy fatty acids in the presence of an acid catalyst was selected. The chief drawback of the high-dilution technique (use of large volumes of solvents) has been offset by use of the special apparatus (Fig.3), in which advantage has been taken of the refluxing solvent to dilute the hydroxy acid. The apparatus has been adopted from the^{one} described by Cope and Herrick⁵⁰ for effecting reactions under high dilution. Since in the lactonization reaction the equilibrium is forced in favour of the lactone by continuous removal of the water formed in the reaction, it was necessary to modify the apparatus of Cope and Herrick⁵⁰, so that the water formed in the reaction is constantly removed during the recycling of the solvent; incorporation of a tube filled with activated silica gel in the path of returning solvent, [Fig.(3)], effectively answered the purpose.

By using this method, several ω -hydroxy acids [$\text{HOCH}_2\text{C}(\text{CH}_2)_n\text{COOH}$; $n = 16, 14, 13, 10, 9$ and 8] have been cyclized and Table 2 summarizes these results. The last

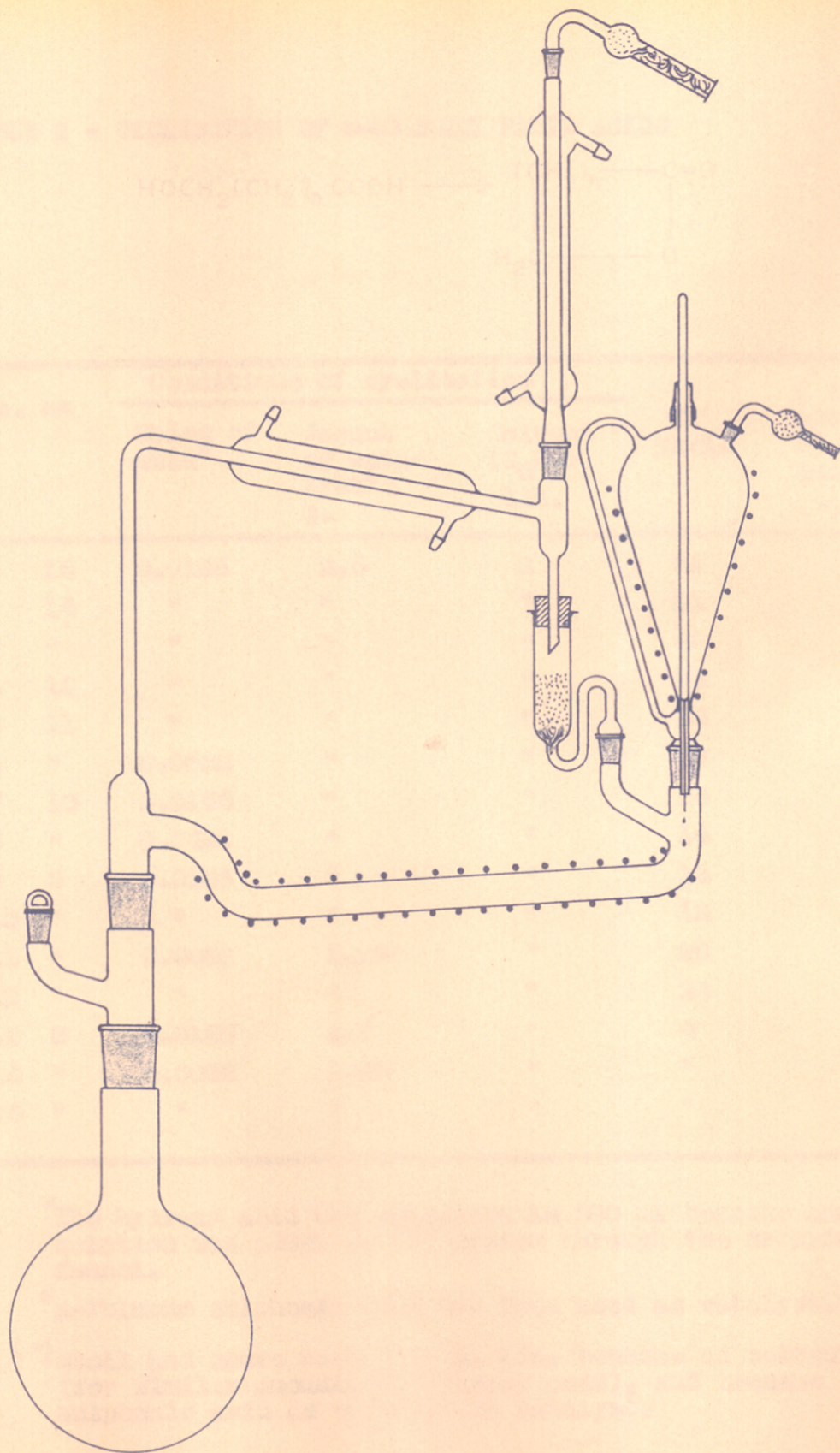
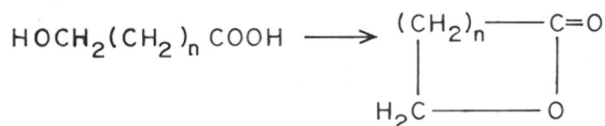


FIG. 3. SETUP FOR CYCLISATION.

TABLE 2 - CYCLISATION OF ω -HYDROXY FATTY ACIDS

No.	n ^a	Conditions of cyclisation			% yield	% yield obtained by Stoll and Rouve ⁴¹ (*)
		Moles of acid ^a	Amount of catalyst ⁺ g.	Solvent (C ₆ H ₆) lit.		
1	16	0.0166	2.5	2	81	76
2	14	"	"	"	81	67
3	"	"	"	"	80	-
4	13	"	"	"	79	23-76
5	11	"	"	"	65	41
6	"	0.0332	"	"	59	-
7	10	0.0166	"	"	24	16
8	"	0.0498	"	"	14	-
9	9	0.0166	"	"	18	11
10	"	"	"	"	18	-
11	"	0.0083	1.25	"	20	-
12	"	"	"	"	22	-
13	8	0.0166	2.5	"	4	1.4
14	"	0.0083	1.25	"	"	-
15	"	"	"	"	"	-

^aThe hydroxy acid was dissolved in 500 ml benzene and the solution was added to the system through the dropping funnel.

⁺p-Toluene sulphonic acid has been used as catalyst.

(*) Stoll and Rouve used 5 to 10 lit. benzene as solvent (for similar amounts of hydroxy acid), and benzene sulphonic acid as cyclization catalyst.

entry in the Table shows the yields of the lactones as obtained by the usual high-dilution technique, for purposes of comparison; Fig.(4) gives a graphical representation of this comparison, and as can be seen from these, the yields of the lactones have not been sacrificed by the use of this new apparatus, which avoids the use of large bulks of solvent and has the further advantage of simplicity of operation. The sudden decrease in the yields of the lactones as we enter the zone of medium ring-size, is as expected and has been discussed by several workers.

Table 3 records the properties of various lactones obtained by this procedure in the present work.

The literature does not record the carbonyl stretching frequencies data for many lactones larger than seven-membered, except for exaltolide (C_{15} lactone), for which a value of 1738 cm^{-1} has been reported⁴⁶. The values obtained in the present work are those expected for an unstrained lactone. A point of special interest is that the medium ring lactones show a double carbonyl stretching frequency (Fig.5), which could possibly be attributed to the presence of two distinct conformers.

The PMR spectra of these lactones are characterized by three sets of signals $\sim 80, 130$ and 240 cps

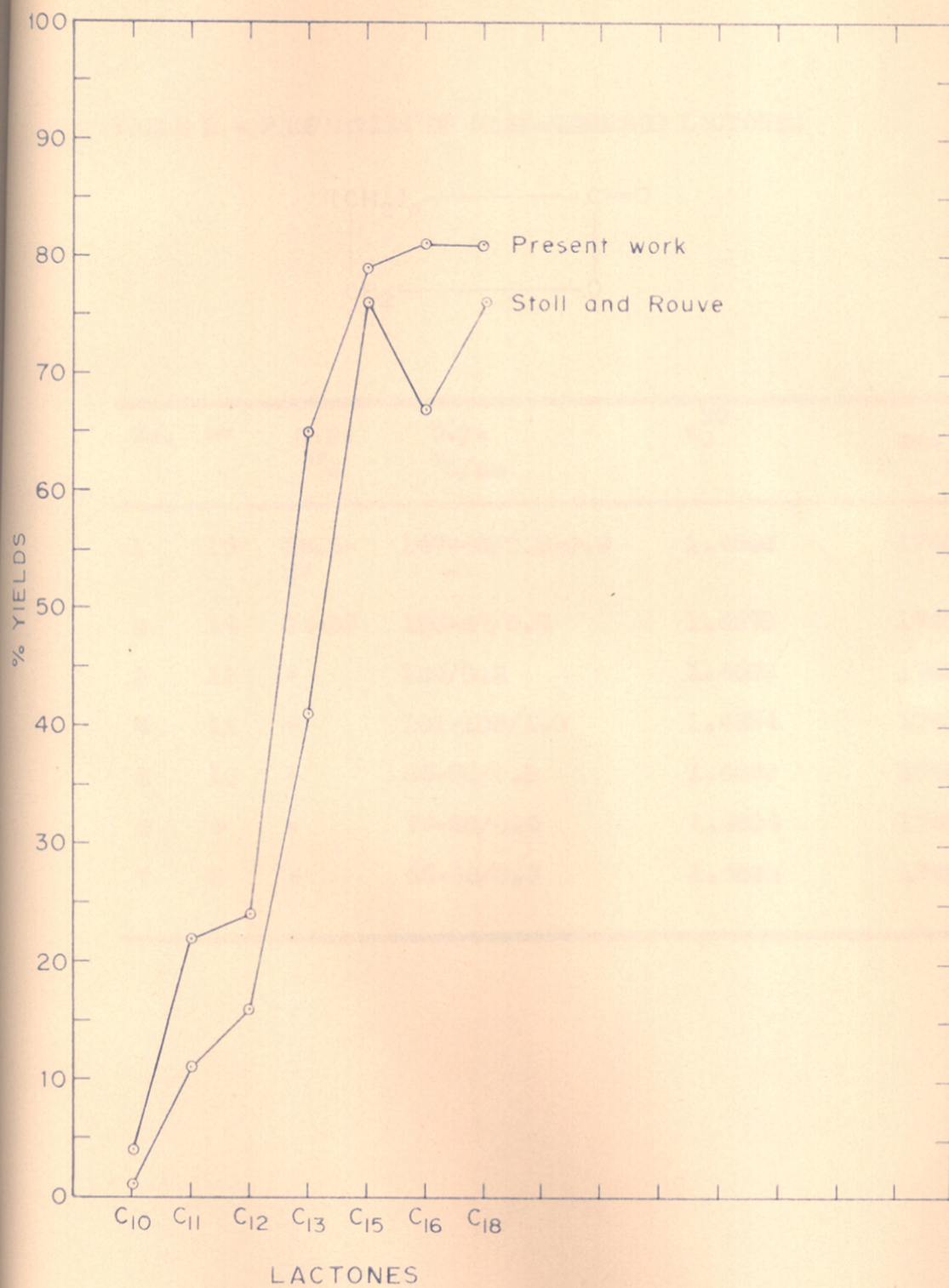
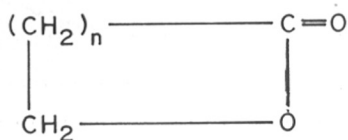


FIG. 4. % YIELDS OF MANY-MEMBERED LACTONES.

TABLE 3 - PROPERTIES OF MANY-MEMBERED LACTONES



No.	n=	m.p. °C	b.p. °C/mm	n_D^{20}	$\nu_{\text{C=O}}$ cm ⁻¹
1	16	36.5-37	147-48/0.2-0.3	1.4666	1740
2	14	34-35	126-27/0.6	1.4678	1740
3	13	-	120/0.3	1.4692	1748
4	11	-	101-102/1.0	1.4684	1748
5	10	-	85-86/0.3	1.4690	1740, 1750
6	9	-	73-80/0.4	1.4694	1740, 1750
7	8	-	65-66/0.3	1.4663	1748, 1752

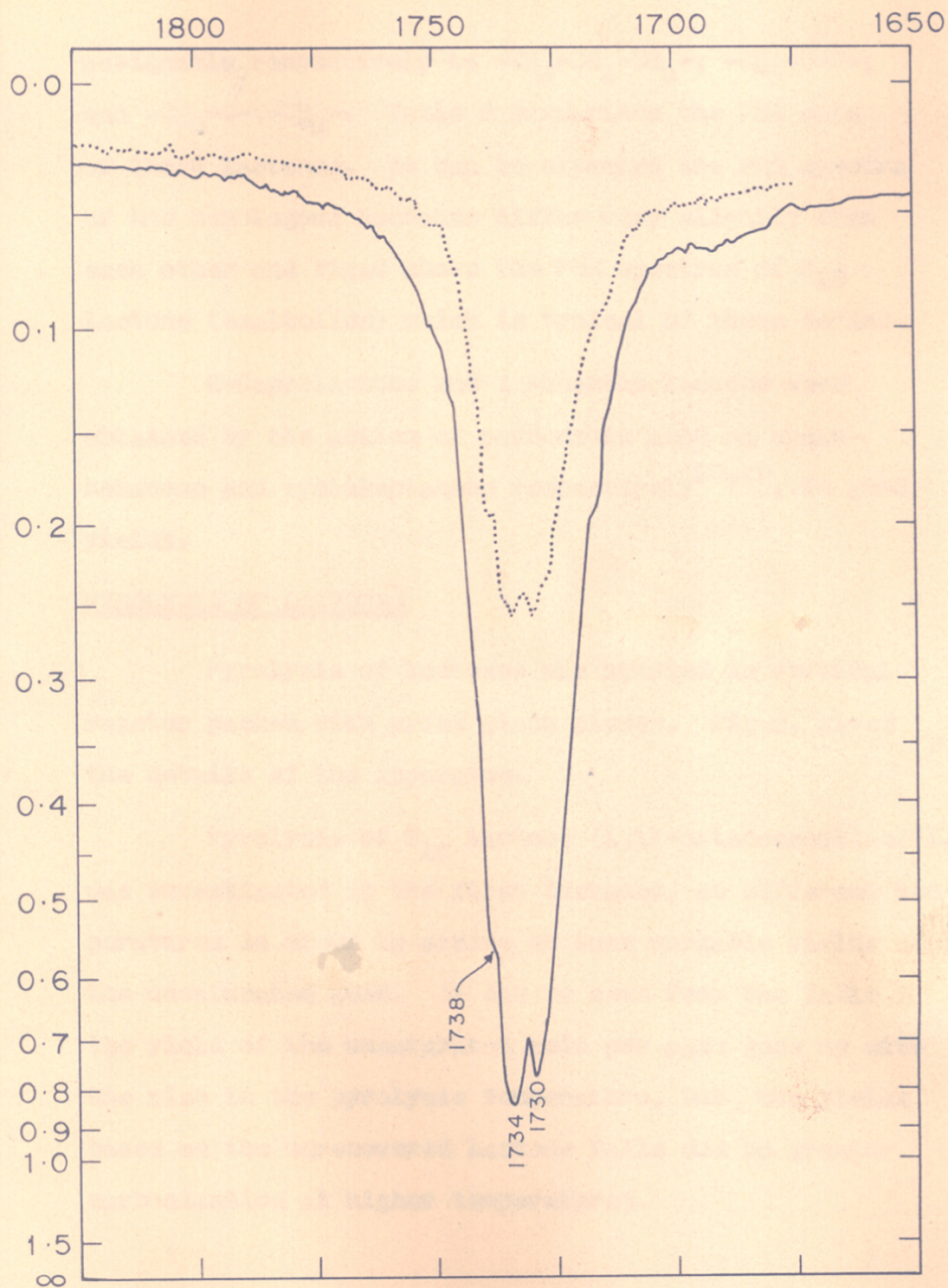


FIG. 5. IR SPECTRA (CARBONYL STRETCHING) OF 1,11-UNDECANOLIDE.

assignable respectively to $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$; $-\text{CH}_2-\overset{\text{O}}{\parallel}\text{C}-\text{O}-$; and $-\text{CH}_2-\overset{\text{O}}{\parallel}\text{C}-\text{O}-\text{CH}_2-$. Table 4 summarizes the PMR data of these lactones. As can be expected the PMR spectra of the homologous lactones differ very slightly from each other and Fig.6 shows the PMR spectrum of C_{15} lactone (exaltolide) which is typical of these series.

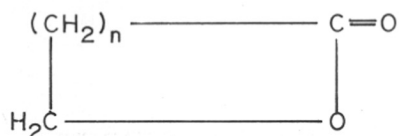
ϵ -Caprolactone and ξ -enantho lactone were obtained by the action of perbenzoic acid on cyclohexanone and cycloheptanone respectively^{35,37}, in good yields.

PIROLYSIS OF LACTONES

Pyrolysis of lactones was studied in vertical reactor packed with pyrex glass pieces. Fig.2, gives the details of the apparatus.

Pyrolysis of C_{18} lactone (1,18-octadecanolide)VI, was investigated in the first instance, at different temperatures in order to arrive at some workable yields of the unsaturated acid. As can be seen from the Table 5 the yield of the unsaturated acid per pass goes up with the rise in the pyrolysis temperature, but the yields based on the unrecovered lactone falls due to greater carbonization at higher temperatures.

TABLE 4 - PMR DATA OF MANY-MEMBERED LACTONES



No.	n	$-\text{CH}_2-\text{CH}_2-\text{CH}_2-$		$-\text{CH}_2-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{O}-$		$-\text{CH}_2-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{O}-\text{CH}_2-$	
		cps	Multi- plicity	cps	Multi- plicity	cps	Multi- plicity
1	16	79.5	Singlet	133.5	Essential- ly doublet	241.2	Essential- ly triplet
2	14	79.6	"	133.5	"	241.6	"
3	13	79	"	133.7	"	242.2	"
4	11	81	"	136.3	"	242.7	"
5	10	81.9	"	134.1	" triplet	244.1	"
6	9	81.7	"	136.2	" quartet	245.2	"
7	8	82.1	"	135.0	" "	246.2	"

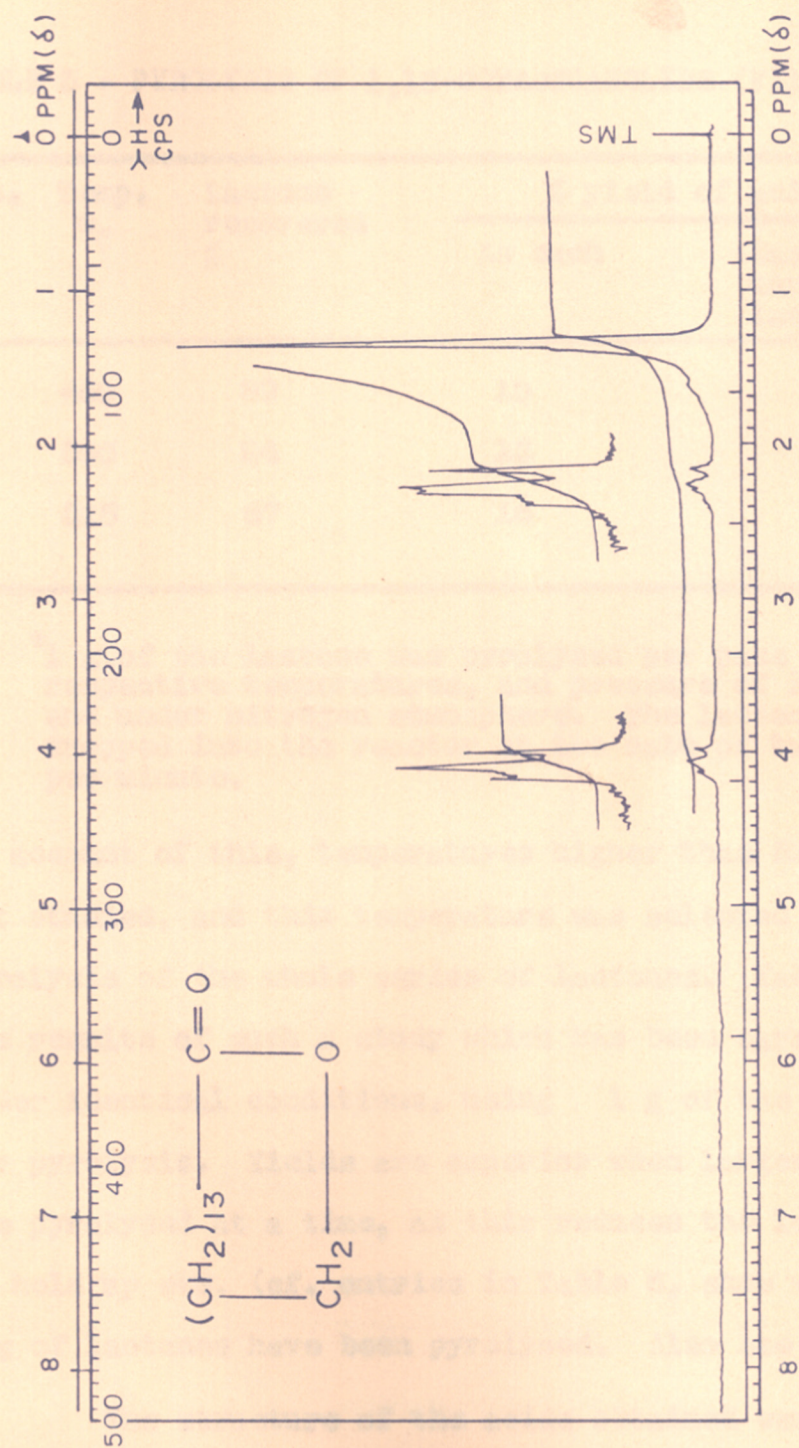


FIG. 6. PMR SPECTRUM OF 1,15-PENTADECANOLIDE (EXALTOLIDE).

TABLE 5 - PYROLYSIS OF 1,18-OCTADECANOLIDE (VI)*

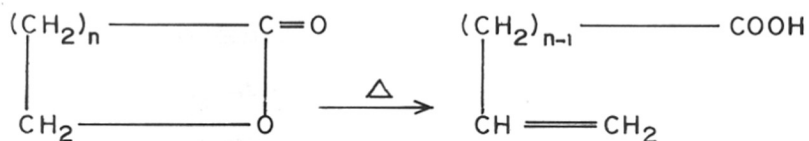
No.	Temp. °C	Lactone recovered %	% yield of acid	
			As such	Based on unrecovered lactone.
1	450	89	10	84
2	500	84	13	87
3	525	67	16	50

* 1 g of the lactone was pyrolyzed per pass at the respective temperatures, and pressure of 150 mm and under nitrogen atmosphere. The lactone was dropped into the reactor at the rate of two drops per minute.

On account of this, temperatures higher than 525°C were not studied, and this temperature was selected for the pyrolysis of the whole series of lactones. Table 6 gives the results of such a study which has been carried out under identical conditions, using 1 g of the lactone for pyrolysis. Yields are superior when larger amounts are pyrolysed at a time, as this reduces the losses due to hold up etc. (cf. entries in Table 6, show where 2 and 5 g of lactones have been pyrolysed. Also see Chapter III).

The structure of the acids obtained were established as the corresponding α -olefinic acid by a study of the infrared and NMR spectra of the methyl esters derived from

TABLE 6 - PYROLYSIS OF MANY-MEMBERED LACTONES



No.	n=	Yield of the pyrolysate	Yield of the acid based on unrecovered lactone.
		%	%
1	16	83	50
2	"	89	79 *
3	14	93	69
4	"	92	67
5	13	90	73
6	"	96	85 +
7	11	98	89
8	10	98	83
9	9	91	70
10	5	74	55

*5 g of the lactone was pyrolyzed.

+2 g. of the lactone was pyrolyzed.

these acids.

As expected, the methyl esters displayed absorption bands due to out-of-plane deformations of vinylic CH_2 at $\sim 910 \text{ cm}^{-1}$. Table 7 records the carbonyl stretching frequency and the olefinic proton deformation frequency of the various esters and acids obtained in this work.

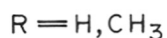
Figs.7 and 8 show the infrared spectra of 15-pentadecenoic acid and its methyl ester respectively and these spectra are typical of these series; while Fig.9 shows the infrared spectrum of the neutral fraction obtained from the pyrolysis of C_{13} lactone which is typical of the spectra of the neutral fractions in the series.

The PMR spectra of the esters is characterized by four sets of protons occurring ~ 75 , 125, 215 and 285-360 cps regions, and assignable respectively to $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$, $-\text{CH}_2-\overset{\text{O}}{\underset{\text{||}}{\text{C}}}-\text{OCH}_3$, $-\text{CH}_2-\overset{\text{O}}{\underset{\text{||}}{\text{C}}}-\text{OCH}_3$ and $\text{CH}_2=\text{CH}-$. Table 8 summarizes the PMR data of these esters, while Fig.10 shows a typical spectrum of the series.

DISCUSSION

The work described above was carried out with the twin purpose of evolving a method for the preparation of α -olefinic fatty acids and to determine the ring size of the lactone which would permit the attainment of

planarity of the concerned atoms for the pyrolytic cis-elimination step. As has been demonstrated the C₇ cyclic lactone (eight-membered) is capable of undergoing this elimination reaction. When the ϵ -caprolactone (seven-membered) was subjected to the same reaction, none of the α -olefinic acid was formed and the only product isolated after the work up was the corresponding hydroxy acid (δ -hydroxy caproic acid). Thus the steric requirements of this reaction can be met in the eight-membered lactone cycle which represents the lowest limit of the lactones capable of undergoing this reaction.

TABLE 7 - INFRARED SPECTRAL DATA OF α -OLEFINIC ACIDS AND THEIR ESTERS

No.	n=	$\nu_{\text{C=O}}$		$\nu_{\text{C=C}}$		$\delta_{\text{-CH=CH}_2}$		$\delta_{\text{-CH=CH}_2}$	
		Acid	Ester	Acid	Ester	Acid	Ester	Acid	Ester
1	15	1700-1715	1750	1650	1650	917	913	995	995
2	13	1705-1710	1750	1647	1650	919	913	993	995
3	12	1695-1710	1750	1643	1645	917	913	995	996
4	10	1725	1750	1645	1645	915	915	995	995
5	9	1705	1750	1643	1645	910	913	995	995
6	8	1717	1750	1639	1645	912	913	990	995
7	4	1709	1745	1639	1642	915	920	1000-1020	971

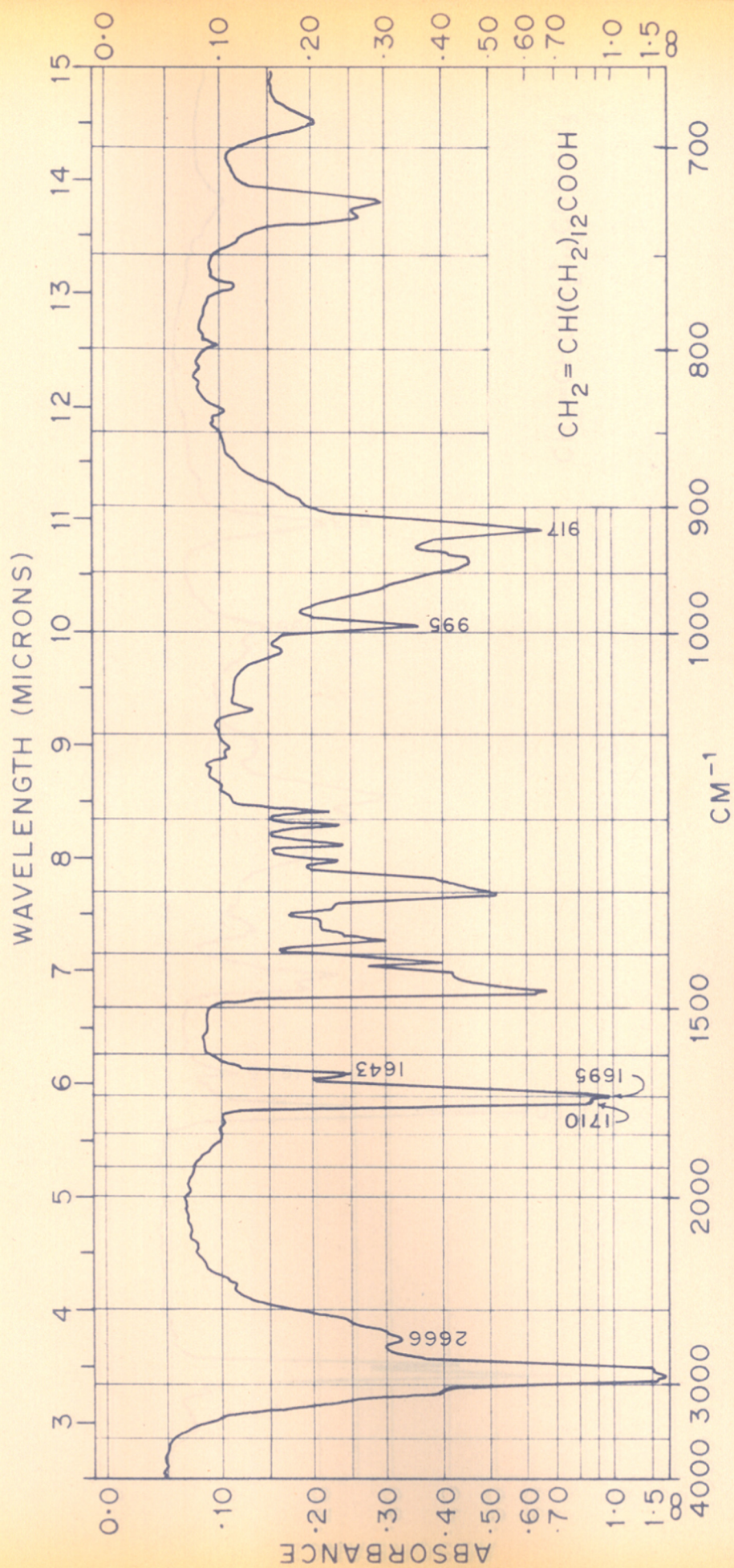


FIG. 7. IR SPECTRUM OF 15-PENTADECENOIC ACID.

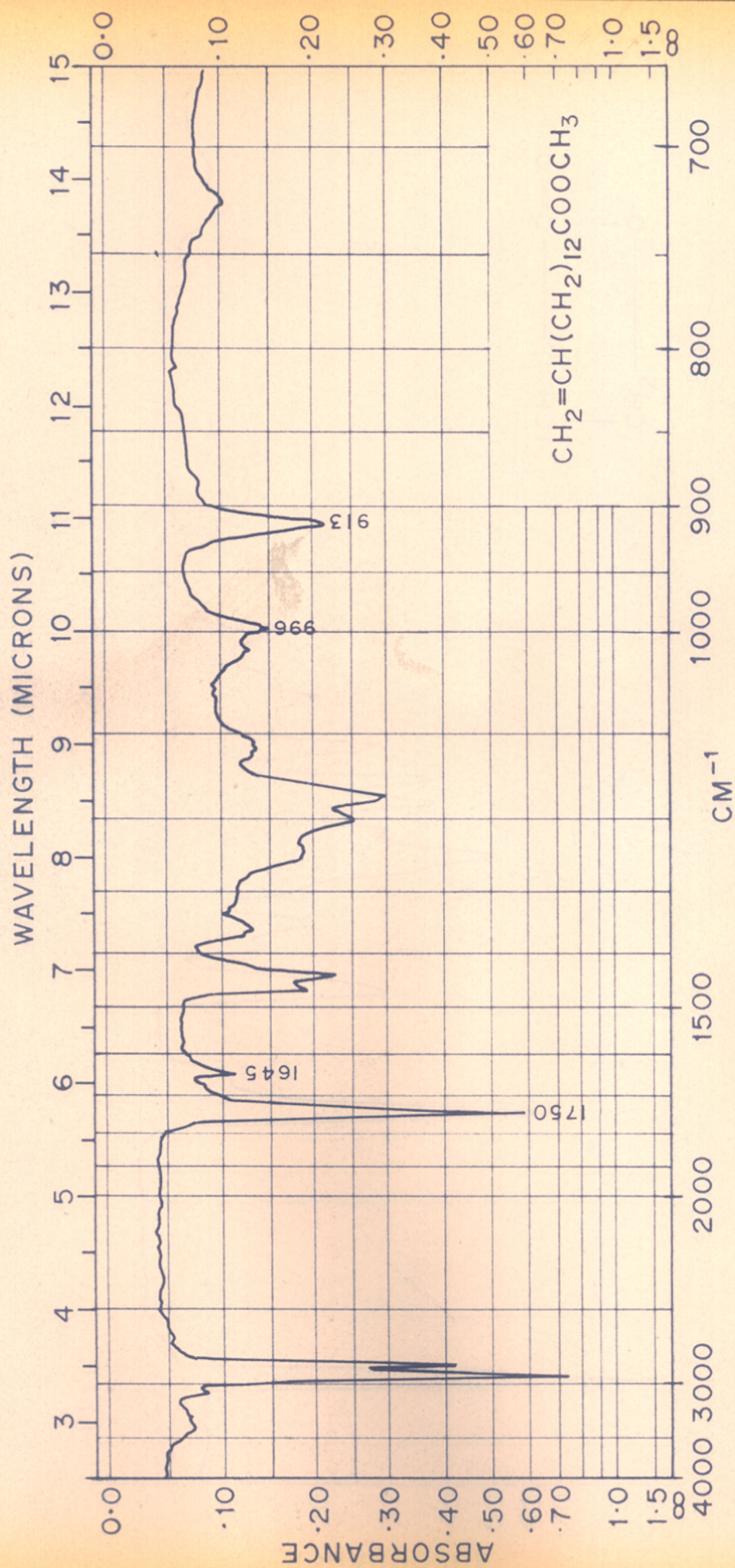


FIG. 8. IR SPECTRUM OF METHYL 15-PENTADECENOATE.

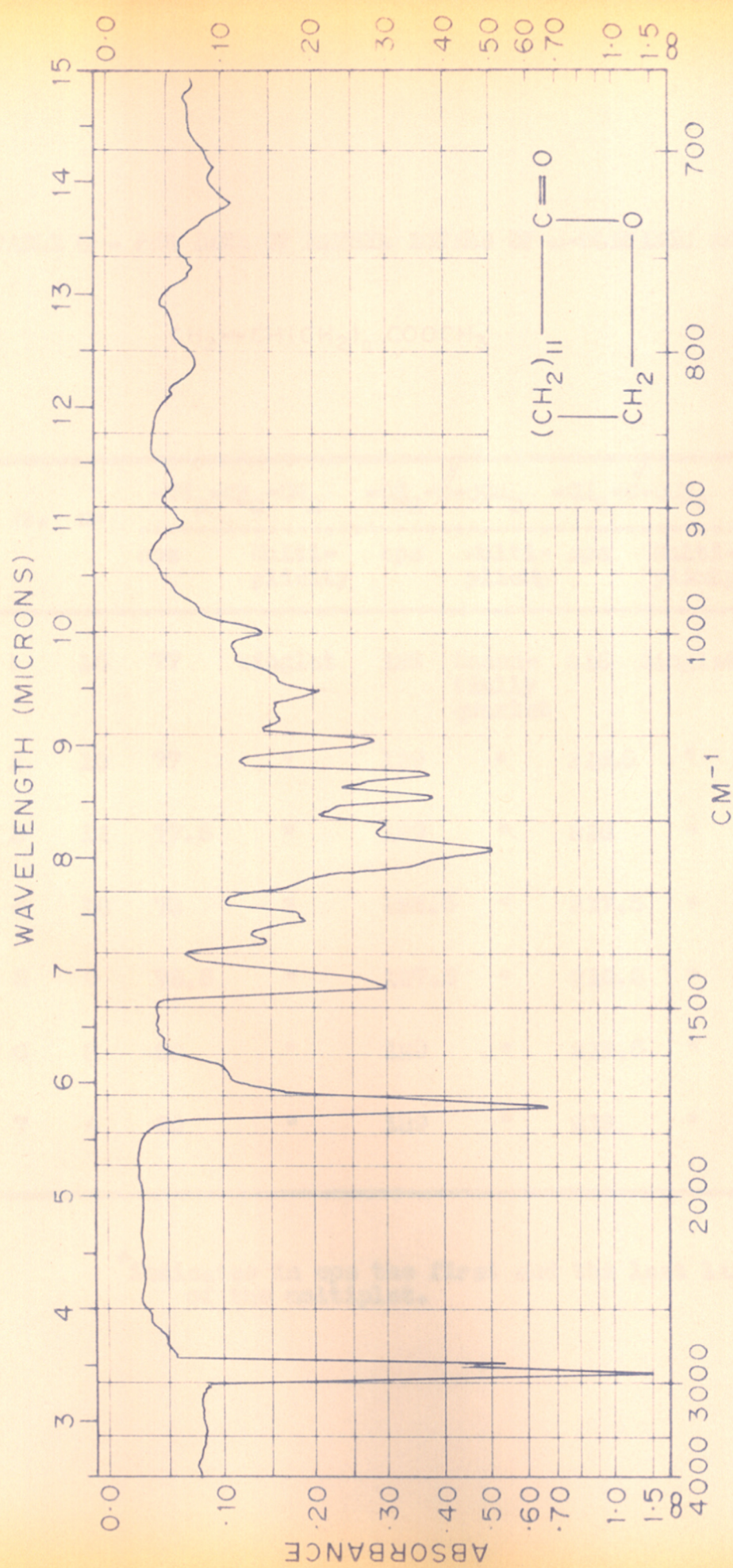
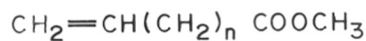


FIG. 9. IR SPECTRUM OF NEUTRAL FRACTION FROM PYROLYSIS OF 1,13-TRIDECANOLIDE.

TABLE 8 - PMR DATA OF METHYL ESTERS OF ω -OLEFINIC ACIDS

No.	n=	$-\overset{\text{O}}{\text{CH}_2}-\overset{\text{O}}{\text{CH}_2}-\overset{\text{O}}{\text{CH}_2}$		$-\overset{\text{O}}{\text{CH}_2}-\overset{\text{O}}{\text{C}}-\overset{\text{O}}{\text{OCH}_3}$		$-\overset{\text{O}}{\text{CH}_2}-\overset{\text{O}}{\text{C}}-\overset{\text{O}}{\text{OCH}_3}$		$\text{CH}_2=\overset{\text{O}}{\text{CH}}-$	
		cps	Multi- plicity	cps	Multi- plicity	cps	Multi- plicity	cps	Multi- plicity
1	15	77	Singlet	128	Essen- tially quartet	216	Singlet	285- 358	Multi- plet
2	13	77	"	129	"	216.5	"	286- 349	"
3	12	77.5	"	129	"	216	"	287- 359	"
4	10	78	"	128.5	"	217.5	"	287- 363	"
5	9	78.5	"	127.5	"	216.5	"	285- 365	"
6	8	80	"	129	"	218.5	"	288.5- 368.5	"
7	4	80	"	129	"	219	"	288- 368	"

* indicates in cps the first and the last lines of the multiplet.

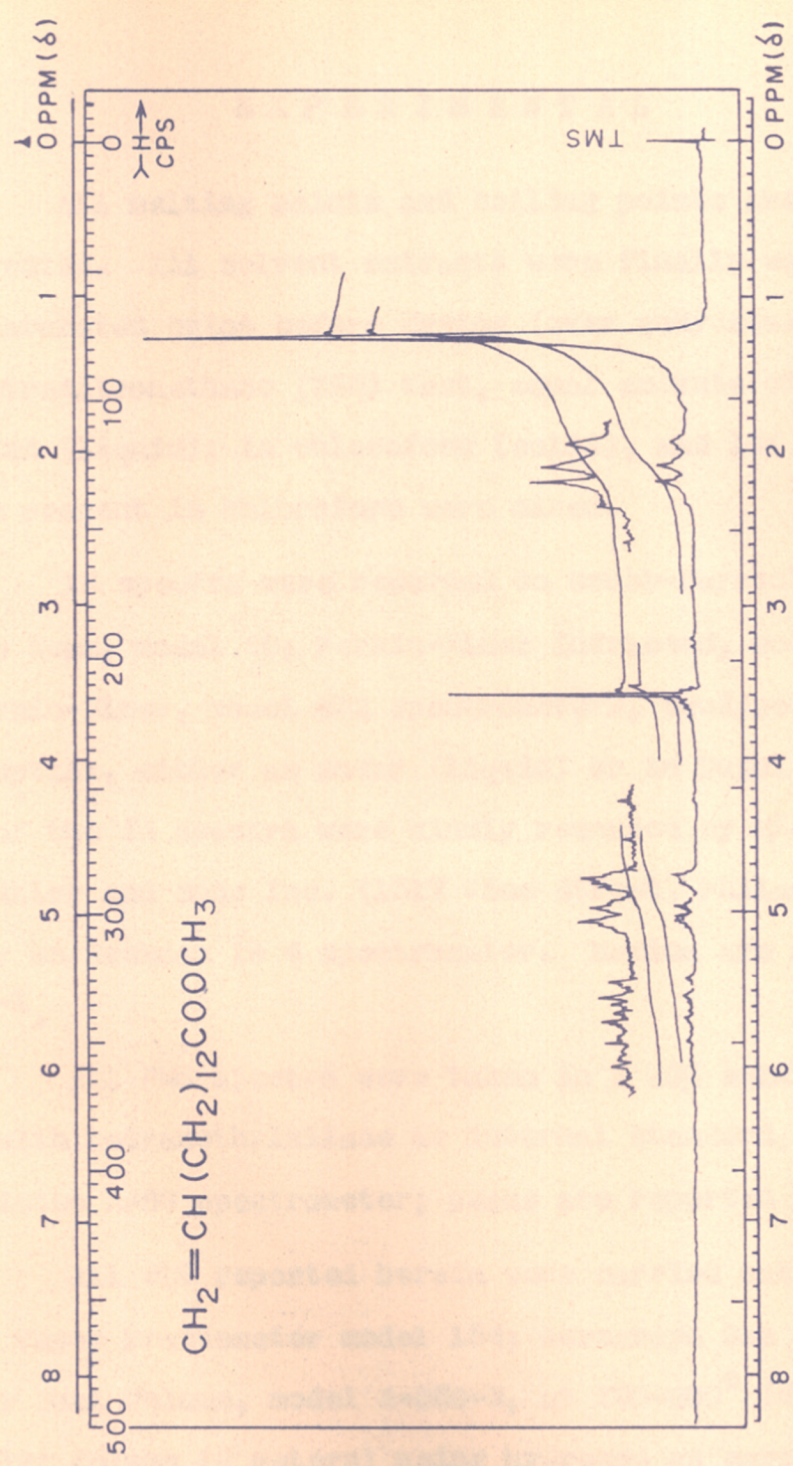


FIG. 10. PMR SPECTRUM OF METHYL 15-PENTADECENOATE.

E X P E R I M E N T A L

All melting points and boiling points are uncorrected. All solvent extracts were finally washed with saturated brine before drying (over anhydrous Na_2SO_4). For tetranitromethane (TNM) test, equal amounts of undiluted compound (liquid); in chloroform (solid), and 10% solution of the reagent in chloroform were mixed.

IR spectra were recorded on Grubb-Parson's double beam, model S3; Perkin-Elmer Infracord, model 137E or Perkin-Elmer, model 221 spectrometers, equipped with NaCl optics, either as smear (liquid) or in Nujol (solids). Some of the IR spectra were kindly recorded by M/s. Samuel P. Sadtler and Sons Inc. (1517 Vine Street, Philadelphia) in KBr on Beckman IR 4 spectrometer. Maxima are reported in cm^{-1} .

All PMR spectra were taken in a 20% solution in CCl_4 with tetramethylsilane as internal standard, on a Varian Associates A-60 spectrometer; peaks are reported in cps.

All GLC reported herein were carried out on Perkin-Elmer Vapor Fractometer model 154; Aerograph Gas Chromatography Dual Column, model A-350-B, at $160-200^\circ$ (column temp.) over 'P' Column (2 meters) using hydrogen as carrier gas.

Kamala seed oil

Fresh Kamala seeds* (4530 g) were soaked in dilute NaOH solution (0.5%; 7.5 lit) for 45 minutes with occasional stirring⁵¹. The resultant dark coloured thick syrupy liquid (pH 7.65)⁺ was drained off and collected separately. Treated seeds on washing free of alkali, resinous and fibrous material and sun drying weighed 3583 g. (21% loss in weight).

Solvent Extraction: Cleaned seeds (3583 g) were crushed gently through a roller mill and the seed meal was extracted thrice with benzene (6, 3, 3 lit) at room temperature. The solvent extract after filtration and flashing off the solvent gave a clear light yellowish orange viscous oil (1300 g, 30%).

*Supplied by The Chief Forest Utilisation Officer, Govt. of Bihar, Mino, Bihar State, India.

⁺The alkali wash on extraction with ether-pet. ether (40-60°) mixture (1:1) yielded a fatty product (~ 1.5% on volume) which was further separated into the neutral (32%) and acid (68%) components by the usual methods. The acid fraction on analysis (isolation, saponification equivalent and identification by IR and VPC of the methyl esters against authentic samples) was found to be rich in palmitic, oleic and linoleic acids. The neutral fraction b.p. 160-205°/0.6 to 0.1 mm giving pleasant smell (IR 2895, 2670, 2360, 1827, 1748, 1725, 1461, 1422, 1377, 1354, 1268, 1237, 1163, 1117, 1090, 1028, 970, 810 and 724 cm⁻¹ by smear) was not investigated further. Solvent extracted alkali wash, on acidification, filtration, washing and drying yielded Kamala dye.

Kamlolenic acid III

Total fatty acids

Kamala seed oil (1200 g) was heated under reflux (N_2) with ethanolic KOH (2.5 lit; 12%) for 3 hrs. After concentration in vacuo at reduced temperature (75-80% of the alcohol by volume used was distilled), the soap was dissolved in water (3 lit) and the fatty acids were liberated by the addition of phosphoric acid to the soap solution, taking care not to allow the liberated acids coming into contact with atmospheric oxygen, by maintaining a layer of nitrogen in the system. The total fatty acids were taken in benzene (2 lit.) washed free from mineral acid, then with brine and dried.

Estimation of Kamlolenic acid

Methyl esters were prepared by reacting above fatty acids (2.5 g) with CH_3I in ether and working up. Crude methyl esters (2 g) were chromatographed over activated alumina grade III (60 g). The column (0.25 x 51 cm; alumina column height 20 cm) was eluted successively with pet. ether (40-60°), ether, ether-methanol mixture (1,10 and 25% methanol) and methanol. In all fifty fractions of 20 ml each were collected, and after preliminary studies, were combined to form three main fractions as shown in Table 3.

TABLE 9 - CHROMATOGRAPHY OF METHYL ESTERS OF TOTAL ACIDS FROM KAMALA SEED OIL

No.	Eluent	Frac-tions	Weight g	Final frac-tions g.	Appearance
1.	Pet. ether (40-60°)	8 x 20 ml	0.5369	0.5369 I	Liquid.
2.	Ether	12 x 20	1.0614	1.1270 II	Semisolid.
3.	Ether + MeOH (1%)	6 x 20	0.0656		"
	"	4 x 20	0.0306	0.1881 III	Solid.
4.	Ether + MeOH (10%)	6 x 20	0.0861		"
5.	Ether + MeOH (25%)	8 x 20	0.0404		"
6.	MeOH	4 x 20	0.0310		"

Fraction I (Pet. ether soluble). The product was distilled to yield clear liquid (0.52 g; b.p. 85-155°/1 mm). IR spectrum; COOMe 1745, 1205, 1176, 1124; C=C 1650; peak for hydroxyl group completely absent. Analysis by GLC (Perkin-Elmer Vapor Fractometer, model 154; 200°C, Column 'P'; flow rate 70 cc/mt H₂; attenuation 1; Chart speed 15 in/hr; and ester injected 1 μ l), showed peaks and retention time for methyl esters of lauric, myristic, palmitic, oleic, linoleic and stearic acids, in which lauric and myristic

acids were found to be in minute quantities. The peaks were further confirmed by injecting separately, authentic samples of methyl esters of the respective fatty acids along with the mixture of total esters.

Fraction II (ether soluble). The fraction was distilled in vacuo to yield very pale lemon coloured liquid (1.1 g) b.p. $186^{\circ}/1$ mm, which became slightly waxy at room temp. m.p. $25-26^{\circ}$. IR spectrum: OH 3333, 1055; COOMe 1751, 1205, 1178, 1119; C=C 1645; cis-, trans- C=C 991, 971, 930 cm^{-1} . The spectrum was superimposable with that of methyl eleostearate except for the peak for hydroxyl group which is absent in the latter one. PMR signals: $-\text{CH}_2\text{O}$ 211.5 (t); $-\text{OCH}_3$ 216 (s); 6 vinylic H 336-373 (m); two $\text{CH}_2\text{CH=}$ and one $-\text{CH}_2-\text{C=O}$ 128-140 (6-H, m) $-\text{CH}_2-$ 71-110 (14H; m). (Found: C, 73.76; H, 10.4; $\text{C}_{19}\text{H}_{32}\text{O}_3$ requires: C, 73.98; H, 10.46%).

Fraction III. The product was crystallized from acetonitrile to yield white crystalline product (0.16 g) m.p. $31-31.5^{\circ}\text{C}$. IR spectrum: OH 3344, 1064; COOMe 1745, 1203, 1176, 1124; C=C 1650, 995, 984, 929 cm^{-1} . Higher m.p. indicates the presence of β -isomer in sufficient quantity.

Trials for the analysis of fractions II and III either by Perkin-Elmer Vapor Fractometer, or by Aerograph Gas Chromatography Dual Column at 200, 225 and 250°C , Column 'P'; flow rate 70 cc/min H_2 , attenuation 1, Chart speed $15^{\circ}/\text{hr}$;

and ester (in acetone) injected 2:1, 1:1 gave broad and irregular peaks, exhibiting the possibility of decomposition or polymerisation of the highly unsaturated compound. Hence the content of Kamlolenic acid in Kamala seed oil was 65.8%.

Isolation of Kamlolenic acid*

Benzene extract of the total kamala fatty acids was kept at 16° overnight. The crystallized material was filtered and washed with cold benzene (2 x 150 ml) to yield shining light cream coloured crystalline acid (550 g) m.p. 74-75°. Recrystallisation from benzene (1 lit) afforded Kamlolenic acid m.p. 75-76°.

18-hydroxy stearic acid II

Kamlolenic acid (550 g) m.p. 75-76° dissolved in alcohol (2 lit) was hydrogenated in presence of Raney nickel (5.5 g) initially at 90° and finally at 100-110°/600 lbs/sq.in. during 12 hrs when no more hydrogen gas was further absorbed. The filtered solution was cooled and white

*This is modified and improved method for the isolation of kamlolenic acid over other methods reported previously. Gupta *et al.*²³ reported the isolation of the acid by precipitation (twice) with addition of pet. ether (40-60°) to the ether solution of the total fatty acids, followed by crystallisation from benzene and ethyl acetate respectively, while Gremble *et al.*⁵² obtained the acid by chilling ether solution at 0°, in low yields. In the present modified method solvent losses are low and yield of acid was high.

crystalline 18-hydroxy stearic acid (450 g) m.p. 96.5 - 97.5° was filtered off. Recrystallisation from alcohol gave acid m.p. 97-98°. Mother liquors on concentration, crystallisation and recrystallisation furnished second crop of acid (90g), total yield (96%). IR spectrum (in KBr): OH 3281, 1059; COOH 2618, 1715 cm^{-1} . (Found: C, 71.8; H, 11.94; $\text{C}_{18}\text{H}_{36}\text{O}_2$ requires: C, 71.95; H, 12.08%).

Methyl-18-hydroxy stearate

18-Hydroxy stearic acid (50 g), anhydrous methanol (250 ml), dry benzene (250 ml), and sulphuric acid C.P. sp. gr. 1.84 (5 ml) were heated under reflux for 4 hrs. After distilling off the solvent mixture (75% by volume) the reaction product was poured into water (200 ml) and was taken into ether (250 ml). Ether solution was extracted with sodium carbonate solution (3 x 50 ml; 7%), washed free of alkali and dried. Flashing off the solvent afforded white shining crystalline product (52 g, 99%) m.p. 61-62°. The ester on crystallisation from ether-pet.ether (40-60°) mixture (1:1) furnished white shining flakes (47.6 g) m.p. 62-62.5°. Concentration of the mother liquor furnished a second crop of the ester (3.1 g) m.p. 61.5 - 62°. (Reported Aggarwal *et al.*²³ 62°; Beilstein 61.5 - 62°). IR spectrum: (in KBr): OH 3356, 1057; COOCH₃ 1742, 1214, 1198, 1176 cm^{-1} . (Found: C, 72.42; H, 12.1; $\text{C}_{19}\text{H}_{38}\text{O}_2$ requires: C, 72.56; H, 12.18%).

Metaborate ester of methyl 18-hydroxy stearate (IV)

Methyl 18-hydroxy stearate (11.8 g), boric acid (2.4 g slight excess over the molar proportion) and dry xylene (50 ml) heated to reflux in a system fitted with modified moisture trap. Four hours heating gave out water of reaction (1.35 ml). Xylene (20 ml) was drawn from the trap. Removal of rest of solvent and traces under reduced pressure yielded light cream coloured brittle metaborate ester (12.7 g) m.p. 76-150°C. IR spectrum: COOMe 1732, 1216, 1197, 1182 cm^{-1} . Several lots of the borate ester were prepared as and when required.

Methyl-18-acetoxy stearate

To a chilled solution of methyl 18-hydroxy stearate (20 g) in dry benzene-ether mixture (60 ml), pyridine (20 ml) was added with stirring. This was followed by the addition of acetyl chloride (20 ml) in five lots. The reactants were mixed thoroughly and allowed to remain in ice bath for 15 minutes. After slowly bringing to room temperature, the reaction was kept overnight. Excess acetyl chloride was decomposed in cold with ice-cold water and the reaction product was taken in ether (100 ml), washed free from acid and dried. Removal of solvent and traces under suction gave white shining material (21.6 g; 95%) m.p. 50-52°C, which on crystallisation from benzene-pet. ether mixture (50 ml) in cold yielded white pearly

shining crystalline product (19.4 g) m.p. 51-52°.

IR spectrum: (in KBr): ester groups, 1748, 1250, 1212, 1196, 1168 cm^{-1} . (Found: C, 70.6; H, 11.19; $\text{C}_{21}\text{H}_{40}\text{O}_4$ requires: C, 70.74; H, 11.31%).

Pyrolysis of metaborate ester IV

Metaborate ester (5.02 g) was pyrolyzed in a flask fitted with a short distillation head, using free flame. Pyrolyzed product b.p. 150-180°/0.5-0.8 mm (1.97 g; 39.25%) was obtained while rest of the ester gelled in the flask. Pyrolysate was taken in hexane (25 ml), extracted with sodium carbonate solution (3 x 5 ml; 5%), washed free of alkali and dried. Removal of solvent gave waxy product (1.6 g). The product was triturated with pet. ether successively (3 x 10 ml) and solids separated by filtration. Solid product was crystallized from benzene to yield white crystalline material (0.21 g) m.p. 111-112°. Liquid fraction on distillation gave water white liquid (0.51 g; 10.12%) b.p. 139-143°/0.5-0.4 mm, n_D^{25} 1.4615 which did not give TMM test. The product solidified at room temperature. IR spectrum: $\text{C}=\text{O}$ 1738 cm^{-1} (Found: C, 76.62; H, 12.09; $\text{C}_{18}\text{H}_{34}\text{O}_2$ requires: C, 76.54; H, 12.13%).

Pyrolysis of metaborate in a modified flask

Metaborate ester (5.01 g) was pyrolysed in a modified flask with the side arm fused at the bottom the flask neck, using free flame. Pyrolysed product (1.85 g; 36.94%) b.p.

150-185°/0.4-1 mm was obtained while rest of the ester gelled in the flask. Pyrolysate on working in the usual fashion afforded solid (0.025 g) m.p. 110-112°, and liquid fraction (0.61 g; 12.13%) b.p. 138-141°/0.4-0.5 mm, n_D^{25} 1.4619; also did not give TMM test. IR spectrum: $\nu_{C=O}$ 1738 cm^{-1} . (Found: C, 76.58; H, 11.98; $\text{C}_{18}\text{H}_{34}\text{O}_2$ requires: C, 76.54; H, 12.13%). Several experiments were carried out with similar results.

Pyrolysis of metaborate ester through reactor

(i) Metaborate ester (5.01 g) was pyrolyzed through an electrically heated vertical furnace as shown in Fig.2 at 350°/0.5-0.6 mm. Borate ester melt was dropped in 1 hr followed by further heating for 0.5 hr, and pyrolysate (2.52 g; 50.2%) was obtained which on working up in the usual manner gave solid crystalline material (0.053 g) m.p. 110-112° and clear liquid component (0.44 g; 8.7%) b.p. 142°/0.4 mm, n_D^{25} 1.4591, did not give TMM test and solidified at room temperature. IR spectrum: $\nu_{C=O}$ 1736 cm^{-1} . (Found: C, 76.42; H, 11.9; $\text{C}_{18}\text{H}_{34}\text{O}_2$ requires: C, 76.54; H, 12.13%).

(ii) Pyrolysis of metaborate ester (5.01 g) was carried out through the furnace at 350°/0.5-0.6 mm by dropping the ester melt in 0.5 hr (to minimise the time of contact) followed by subsequent heating for 0.5 hr. This run furnished

semi-liquid pyrolysate (2.41 g; 48.11%), which on processing by the usual method gave solid crystallized product (0.053 g) m.p. 110-112° and a colourless mobile liquid (1.32 g; 26.36%) b.p. 140-141°/0.3-0.4 mm. n_D^{25} 1.4660. Did not give TMM test. IR spectrum: $\nu_{C=O}$ 1740 cm^{-1} .

(iii) Metaborate ester (4.6 g) was pyrolysed through the furnace at 400°/0.5 mm by adding the ester melt in 15 minutes and subsequent heating for 5 minutes to obtain semi-liquid pyrolysate (2.79 g; 60.6%), which on working up in the usual fashion furnished white crystalline solid (0.053 g) m.p. 110-112° and a liquid fraction (0.71 g; 15.81%) b.p. 136-138°/0.25 - 0.3 mm. n_D^{25} 1.4649, also did not give TMM test. IR spectrum: $\nu_{C=O}$ 1740 cm^{-1} .

Without exception the liquid fractions obtained from all the pyrolyses gave faint pleasant odour characteristic of large ring lactones. Several experiments were carried out in each case with similar results.

Lactonisation of 18-hydroxystearic acid (VI)^{9*}

Dry benzene (3 lit.) and benzene sulphonic acid (2.5 g)

*This method adopted by Gupta *et al.*⁹ is a modification of Stoll and Rouves' method⁴¹ and was first reported by Toyama and Hirai⁴² for lactonising juniperic acid (16-hydroxy palmitic acid).

were placed in a flask (5 lit. cap.) and the solution was refluxed on a waterbath. A 0.15% solution of 18-hydroxy stearic acid (10 g) in benzene (6.33 lit) was added dropwise at a rate of 100 ml per 30 min. During this treatment a portion of benzene in the flask was distilled off so as to keep the volume of the benzene in the flask at about 3 lit. After the completion of the addition (12 hrs) of 18-hydroxy stearic acid solution, the contents were refluxed for another 30 min. The solution was then washed with water in order to remove benzene sulphonic acid and dried. Benzene was distilled off and the residue (9.26 g; 48.42%) was dissolved in hot hexane (100 ml). On cooling the hexane solution the crystalline solid was separated by filtration and the filtrate was concentrated, chilled and filtered. The filtrate was diluted to 100 ml with hexane and was washed with dilute sodium carbonate solution (2%, 25 ml x 5), washed free from alkali and dried. After removal of solvent the product was distilled to furnish monolactone (1,18-octadecanolide, 7.59 g 81%) b.p. 140-43°/4 mm, n_D^{30} 1.4662, single peak (GLC), having faint pleasant odour and which solidified at room temperature m.p. 37°. IR spectrum; $\nu_{C=O}$ 1740 cm^{-1} (Found: C, 76.52; H, 12.19; $\text{C}_{18}\text{H}_{34}\text{O}_2$ requires: C, 76.54; H, 12.13%). Total solids on crystallisation from benzene furnished dilactone (1.64 g) m.p. 112-113° (reported 113° and 114°⁴¹). IR spectrum;

$\nu_{\text{C=O}}$ 1745 cm^{-1} , mix. m.p. with dilactone (VII) obtained from pyrolyses 111-112°. IR spectrum of dilactones from pyrolyses, $\nu_{\text{C=O}}$ 1745 cm^{-1} .

Hydrolysis of lactone

Lactone (VI) (1 g) from the pyrolyses was refluxed with alcoholic potassium hydroxide solution (10%; 15 ml) on a waterbath for 4 hrs. The soap solution on acidification (after removal of solvent) with dilute hydrochloric acid, liberated white powdery solid, which was then washed free from acid, dried and crystallised from benzene to furnish white solid m.p. 97-98°, mix. m.p. (with authentic sample of 18-hydroxystearic acid) 97-98°. IR spectrum: OH 3300, COOH 2618, 1715 cm^{-1} .

Pyrolysis of methyl-18-acetoxy stearate

Methyl-18-acetoxy stearate (5 g) was pyrolyzed at 400°/0.5 mm through the column reactor (Fig.2) by dropping the ester melt in 30 min. The pyrolysate on working up in the usual fashion did not furnish any liquid fraction. The crude product, m.p. 49-51° on crystallisation from benzene-pet. ether mixture, furnished white pearly shining crystalline product (4.5 g) m.p. 51-52°, mix. m.p. (with authentic sample of methyl-18-acetoxy stearate) 51-52°. IR spectrum: was identical with that of the authentic sample of the acetoxy ester.

PREPARATION OF ω -HYDROXY FATTY ACIDS

16-Hydroxy palmitic acid (IX)

Aleuritic acid (XI)

Dewaxed blonde shellac (1000 g) was saponified by boiling for 4 hrs with aqueous caustic soda solution (20%; 1 lit.). The mixture was diluted with common salt solution (20%; 2 lit.) and kept at room temperature for 48 hrs, when sodium aleuritate separated in granular form. It was filtered off, washed with salt solution (2 lit.) and decomposed with dilute hydrochloric acid to liberate aleuritic acid, which was ^{de}colourised in alcoholic solution with activated charcoal and crystallised from alcohol. The first crop of aleuritic acid was again decolourised and recrystallised to yield sharp melting acid (159 g) m.p. 100-101°. From the mother liquors, a second crop was obtained (16 g) m.p. 97.5-99°; total yield 17%. IR spectrum: OH 3310, COOH 1715, 1656, ⁵⁸ C=O 1116, 1058 and 1024 cm⁻¹. ⁵⁹ (Found: C, 63.35; H, 10.4; C₁₆H₃₂O₅ requires: C, 63.12; H, 10.6%).

3,10,16-tribromo-hexadecanoic acid (XII)

Aleuritic acid (100 g) was heated with a solution of hydrogen bromide in glacial acetic acid (15% w/v; 1.5 lit.) on a waterbath for 8 hrs under anhydrous conditions. Hydrobromic acid solution was recovered by distillation under

reduced pressure. The product obtained as residue was dissolved in ether and washed free from acid, dried and decolourised with activated carbon. Ether was distilled to obtain the crude 9,10,16-tribromo hexadecanoic acid (156 g; 96%). (Found: C, 40.2; H, 5.9; Br, 46.9; $C_{16}H_{29}Br_3O_2$ requires: C, 39.0; H, 5.9; Br, 48.6%).

Ethyl-9,10,16-tribromo-hexadecanoate (XIII)

The crude tribromo acid XII was esterified azeotropically by refluxing with absolute alcohol (100 ml) and benzene (400 ml) containing sulphuric acid (1 ml, sp.gr.1.84), until water separation ceased (20 hrs). Solvent was distilled off under reduced pressure and the product poured in ice-cold water, extracted with ether and washed with sodium carbonate solution (5%; 3 x 50 ml) to remove free acid. The ether solution was washed free of alkali, dried and ether flashed off to obtain crude ethyl-9,10,16-tribromo-hexadecanoate (160 g; 97%), $n_D^{25.0}$ 1.5030. (Found: C, 42.8; H, 6.6; Br, 44.5. $C_{18}H_{33}Br_3O_2$ requires: C, 41.5; H, 6.4; Br, 46.0%).

Ethyl-16-bromo-hexadec-9-enoate (XIV)

Zinc dust (105 g) was suspended by mechanical stirring in absolute alcohol (1.2 lit.) containing hydrobromic acid solution (3 ml), and the mixture boiled for 20 min. The reactants were cooled (ca. 50°) and to the warm suspension of zinc dust, the tribromo ester XIII (160 g) was gradually

added in 30 min. The mixture was refluxed with stirring for 1 hr to complete the reaction. Zinc dust was filtered off, and from the filtrate alcohol was recovered under reduced pressure. The residue was dissolved in ether, washed and processed as described earlier to obtain the crude ω -bromo ester (106 g; 96%), which was distilled to yield pure ethyl-16-bromo-hexadec-9-enoate (94 g) b.p. $152-153^{\circ}/0.1$ mm; $n_D^{25.0}$ 1.4679. IR spectrum: COOC_2H_5 1724, 1285, trans- $\text{CH}=\text{CH}$ 966 cm^{-1} . (Found: C, 60.1; H, 9.8; Br, 31.8; $\text{C}_{18}\text{H}_{33}\text{BrO}_2$ requires: C, 59.8; H, 9.2; Br, 22.1%).

Ethyl-16-acetoxy-hexadec-9-enoate (XV)

Ethyl-16-bromo-hexadec-9-enoate (92 g) was refluxed under stirring with glacial acetic acid (184 ml) acetic anhydride (10 ml) and fused sodium acetate (92 g) for 12 hrs. Acetic acid was recovered by distillation under reduced pressure and the product was poured in cold water, extracted with n-hexane (250 ml) and washed free from acid and dried. The solvent was recovered and the residue was distilled to obtain ethyl-16-acetoxy-hexadec-9-enoate (82.8 g; 96%). b.p. $140^{\circ}/0.016$ mm; n_D^{27} 1.4565 (Found: C, 70.6; H, 10.8; $\text{C}_{20}\text{H}_{36}\text{O}_4$ requires: C, 70.5; H, 10.7%).

16-hydroxy-hexadec-9-enoic acid (XVI)

The acetoxy ester (XV) (82 g) was saponified by refluxing with alcoholic potash (10%; 600 ml) for 4 hrs.

Excess alcohol was distilled off (75% by volume), residue was dissolved in water (500 ml) and acidified with dilute hydrochloric acid to liberate the hydroxy acid, filtered, washed free from mineral acid and dried. The crude hydroxy acid on crystallisation from benzene furnished pure 16-hydroxy hexadec-9-enoic acid (62.5 g; 96%), m.p. 70.5-71.5°. IR spectrum: OH 3210; COOH 2645, 1930, 1680; C=C 1617, 996, 978, 963 cm^{-1} . (Found: C, 71.2; H, 11.3; $\text{C}_{16}\text{H}_{30}\text{O}_2$ requires: C, 71.1; H, 11.2%).

16-Hydroxypalmitic acid (IX)

16-Hydroxy hexadec-9-enoic acid (10 g) was dissolved in aqueous NaOH solution (10%; 300 ml) and heated to 90° with stirring. To it was added Raney-Nickel alloy (30 g) in small lots taking care that the succeeding lot was added only when the evolution of gas from the previous addition of alloy stopped. Addition was completed in ~ 1 hr. The reaction mixture was stirred for an additional hour, the temperature being maintained at 90°. The original volume was maintained by the addition of water as and when needed. The hot solution was filtered and the residue was washed thoroughly with warm water. Filtrate was cooled and acidified by pouring into hydrochloric acid with stirring. The liberated hydroxy acid was filtered, washed and dried. Crystallisation from alcohol afforded pure 16-hydroxy palmitic acid [Synonym: Juniperic acid (9.6 g; 95%)] m.p. 94.5-95.0°. IR spectrum;

OH 3226; COOH 2604, 1938, 1695 cm^{-1} . (Found: C, 70.45; H, 12.0; $\text{C}_{16}\text{H}_{32}\text{O}_3$ requires: C, 70.5; H, 11.8%). Several lots of this hydroxy acid have been prepared with similar results.

15-Hydroxy pentadecanoic acid (X)

Methyl erucate (XVIII)*

Mustard seed oil (952 g), methanol (250 g) and anhydrous potassium carbonate (95 g) were refluxed over waterbath for 6 hrs when the whole reaction mixture formed a single layer. After cooling to room temperature, it was poured into water (2 lit.) and the resultant turbid mixture was extracted with ether (4 x 500 ml) combined ether extracts were further extracted with potassium carbonate solution (7%; 3 x 150 ml), washed free of alkali and dried. Recovery of solvent and removal of traces under reduced pressure afforded crude mixed fatty esters (428 g).

Alkaline aqueous layer was acidified with dilute hydrochloric acid and the liberated fatty acids were taken in ether (4 x 250 ml), washed free from acid and dried. The solvent was distilled to obtain mixed fatty acids (450 g)⁺,

*Methanolysis of mustard seed oil was accomplished according to the procedure reported by Hartman⁵⁸ on fat, coconut and linseed oils.

⁺Excessive formation of soap is due to free fatty acids present in the starting unrefined mustard oil. Experiments with refined oil gave high yield of methyl esters.

which were further refluxed with dry methanol (200 ml), benzene (800 ml) and conc. sulphuric acid (15 ml, sp. gr. 1.84) for 6 hrs. Excess solvent mixture was distilled (75% by volume) and the reaction product was poured into water (1.5 lit.). Methyl esters were taken in ether (4 x 250 ml) and the solvent extract was washed with sodium carbonate solution (7%; 3 x 150 ml), washed free from alkali and dried. Solvent was flashed off to obtain a second lot of crude methyl esters of the mixed fatty acids (473 g). The total methyl esters (900 g) on straight distillation yielded pale lemon coloured mixture of methyl esters (851 g) b.p. 115-205°/0.3-1 mm. The distilled methyl esters were carefully fractionated through Todd's Precise Fractionation Assembly, model 'A', and in all 19 fractions were collected (738 g total). Fractions 10 to 16, b.p. 170-175°/0.9-1 mm after testing their purity by GLC were combined (389 g) and refractionated to obtain methyl erucate (375 g; 44%), b.p. 170-172°/1 mm, TMM, GLC tested, n_D^{30} 1.4518. IR spectrum: COOCH_3 1750; $\text{C}=\text{C}$ 1670, 972 cm^{-1} . (Found: C, 78.12; H, 12.4; $\text{C}_{23}\text{H}_{44}\text{O}_2$ requires: C, 78.34; H, 12.58%).

Erucyl alcohol (XIX)

Shining sodium metal (75 g; 3.25 g atom) was finely pulverized in dry toluene (150 ml) at reflux temp. using efficient Hershberg stirrer in a three-necked flask. Methyl erucate (228 g; 0.65 M) dissolved in anhydrous tert-butyl

alcohol (144 g; 1.95M) and toluene (500 ml) was then let in during 45 minutes with stirring. During the exothermic reaction the bath temperature was maintained at $120^{\circ} \pm 5^{\circ}$. After the addition, it was stirred and heated for another 30 minutes, cooled, finally in ice-water and carefully treated with small quantities of ice-water with swirling. When 800 ml of water had thus been added, the toluene layer was separated and washed with water (4 x 250 ml). The alkaline washings and previous aqueous portions were combined and extracted with ether (3 x 300 ml). The combined toluene and ether extracts were washed once with dilute acetic acid (5%) and finally with brine. After drying, the solvents were fractionated off and obtained crude erucyl alcohol (202 g; 96.77%). The product was fractionated under vacuum to yield pure erucyl alcohol (197 g; 94%), b.p. $215-217^{\circ}/1.6$ mm, m.p. 34° ; (positive TMM test and GLC, single peak). IR spectrum: $\text{OH } 3350$; $\text{C}=\text{C } 1660$, 728 cm^{-1} . (Found: C, 81.2; H, 13.6; $\text{C}_{22}\text{H}_{44}\text{O}$ requires: C, 81.41; H, 13.66%).

13,14-dihydroxy behenyl alcohol (XX)

Erucyl alcohol (284 g. 0.88M), glacial acetic acid (1200 ml) and conc. sulphuric acid (11 ml) were taken in a three necked flask and cooled to 20° . Hydrogenperoxide (100 volumes; 150 g; 1.1M + 20% excess) was let in quickly while stirring the reactants. After stirring for 10 minutes

the temperature was brought to room temperature and slowly raised to 40° and the reaction was allowed to proceed overnight. At the completion of the reaction contents were poured into water (3 lit.) at 20°C and the acetoxy-hydroxy derivative was washed free from acid. The derivative was refluxed with ethanolic potassium hydroxide solution (900 ml; 10%) for 4 hrs and worked it up in the usual fashion. Solid 13,14-dihydrobehenyl alcohol was washed and dried (yield 311 g; 99%). The crude glycol so obtained was crystallised from alcohol and 13,14-dihydroxybehenyl alcohol resulted in a white crystalline form (290 g) m.p. $91.5 - 92^{\circ}$ (reported 92°). IR spectrum: OH 3413, 1344, 1263, 1134, 1070, 1035 cm^{-1} . (Found: C, 73.9; H, 12.8; $\text{C}_{22}\text{H}_{46}\text{O}_3$ requires: C, 73.68; H, 12.93%).

Oxidation of 13,14-dihydrobehenyl alcohol.

13,14-dihydroxy behenyl alcohol (54 g; 0.15M) was taken in absolute alcohol (750 ml) and was treated with 10% aqueous sodium meta periodate* solution (375 ml) by letting in the meta periodate solution during 30 minutes with efficient stirring at 35° . Stirring was continued for

*Prepared in the laboratory according to the method reported by H.H. Willard [Inorg. Syntheses Vol.I, p.168 (1939)].

1 hour more during which period the temperature was raised to 37° . At the end of the reaction the contents were tested for excess of sodium meta periodate with potassium iodide solution (10%). Reaction mixture was filtered through No.4 sintered funnel and the sodium iodate residue was washed with alcohol (3 x 50 ml). Filtrate was poured into water (5 lit.) and the turbid solution was extracted with ether (4 x 500 ml). Ether extract was washed, dried and flashed off the solvent. The crude product (53 g) m.p. $56-58^{\circ}$ was fractionated under reduced pressure, to give pelargonic aldehyde (20 g), b.p. $70^{\circ}/10$ mm, n_D^{27} 1.4207, and 13-hydroxy tridecanal XXI (21.0 g; 96%) b.p. $153-155^{\circ}/0.9$ mm, m.p. 74° . IR spectrum: OH 3320; CHO 2690, 1730, 964 cm^{-1} . (Found: C, 72.7; H, 12.1; $\text{C}_{13}\text{H}_{26}\text{O}_2$ requires: C, 72.84; H, 12.23%). 13-hydroxy tridecanal has also been prepared with 100 g. lot of 13,14-dihydroxy behenyl alcohol with similar yields.

15-Hydroxy penta dec-2-enoic acid (XXII)

13-hydroxy tridecanal (30 g) dissolved in pyridine (25 g) was added to a cooled solution of malonic acid (23 g) in pyridine (70 g) by means of a dropper in about 10 minutes while the reaction mixture was kept swirling. The contents were mixed thoroughly at the completion of addition of aldehyde solution and kept at room temperature for 36 hrs, then heated over a waterbath for 3 hrs. After removal of

pyridine in vacuo the light reddish liquid residue was extracted with ether (3 x 40 ml); the extract was washed with dilute hydrochloric acid, water and aqueous sodium carbonate solution (7%; 4 x 25 ml). The carbonate extract was acidified with phosphoric acid. Solid acid was filtered and washed free of mineral acid and dried in vacuo to give 15-hydroxy pentadec-2-enoic acid (32 g) m.p. 77-79° which on crystallisation from alcohol afforded white crystalline unsaturated acid (29 g) m.p. 80°.

IR spectrum: OH 3380; COOH 2645, 1438, -C=C-COOH; 1690 C=C 1675, 1019, 994, 959 cm^{-1} . (Found: C, 70.1; H, 10.9; $\text{C}_{15}\text{H}_{28}\text{O}_3$ requires: C, 70.27; H, 11.01%).

15-Hydroxy pentadecanoic acid (X)

In a three necked flask fitted with Herschberg stirrer (slip sleeve), 15-hydroxypentadec-2-enoic acid (20 g) was dissolved in aqueous sodium hydroxide solution (10%; 600 ml) and the solution was heated to 90° and stirred for 15-20 minutes when clear soap solution resulted. Heating was stopped and Raney Nickel-aluminium alloy (60 g) was added to the hot solution in very small lots taking care that the next lot was added only when the evolution of gas from the previous addition of alloy stopped completely. Addition was accomplished in ~ 2 hrs. When the frothing stopped, finally the contents were heated at 85-95° for 5 hrs with vigorous stirring. The

reaction mixture was diluted with water to filterable consistency, and filtered through cotton padded Büchner funnel. Washed the catalyst several times with small portions of warm water. The filtrate was chilled and poured into concentrated hydrochloric acid with stirring. White precipitate was filtered and washed free from acid and dried in vacuo. Crude hydroxy acid (20 g) m.p. 82-84°, was crystallised from ethyl acetate to yield white 15-hydroxy pentadecanoic acid (19 g, 95%) m.p. 84.5-85°. IR spectrum: OH 3333, COOH 2604, 1709. (Found: C, 70.0; H, 11.8; $C_{15}H_{30}O_3$ requires: C, 69.7; H, 11.7%).

13-Hydroxy tridecanoic acid (XXIII)

To 13-hydroxy tridecanal XXI (20 g) was added peracetic acid (132 ml, prepared by mixing 100 ml glacial acetic acid and 32 ml hydrogen peroxide, 100 volumes) and the contents were heated at 85°C for 15 minutes. The resulting clear solution was cooled to 40° and kept overnight at that temperature with stirring. At the completion of reaction the solution was cooled to room temperature and poured into cold water (1500 ml). The white precipitate was filtered and washed free from acid. The crude acid (21.0 g) was refluxed with alcoholic potassium hydroxide solution (10%; 75 ml) for 3 hrs and after removal of excess alcohol and working up in the usual fashion afforded white crystalline hydroxy acid (17 g) which on crystallisation

from benzene yielded 13-hydroxy tridecanoic acid (16 g) m.p. 78.0-78.5°. IR spectrum: OH 3344, COOH 2632, 1706 cm^{-1} . (Found: C, 67.73; H, 11.36; $\text{C}_{13}\text{H}_{26}\text{O}_3$ requires: C, 67.73; H, 11.38%).

Oxidation of 13-hydroxy tridecanal with alkali H_2O_2

13-hydroxy tridecanal (1 g) was kept in a three necked flask and to it was added aqueous sodium hydroxide solution (5%; 26.5 ml) and hydrogen peroxide (3%; 40 ml prepared by diluting 6 ml H_2O_2 100 volumes to 50 ml with distilled water). Initially the hydroxy aldehyde floated on the surface of the reaction mixture. Reactants were slowly heated to 65-75° in 15 minutes and maintained for another 15 minutes with stirring. The aldehyde gradually disappeared and a turbid soapy solution resulted. The solution was filtered through a sintered funnel (No.2), cooled and acidified with dilute sulfuric acid. The white precipitate was filtered, washed free from acid and dried in vacuo. The crude product (1 g) m.p. 55-57° was saponified with alcoholic potassium hydroxide solution (10%; 5 ml) and was worked up in the usual fashion and dried. Resultant acid (0.6 g) m.p. 75-77°C was crystallised from benzene to afford 13-hydroxy tridecanoic acid (0.4 g) m.p. 78.0-78.5. mix. m.p. with the previous sample of 13-hydroxy tridecanoic acid 78.0-78.5°.

12-Hydroxy lauric acid (XXIV)10-Undecenoic acid (XXV)

10-Undecenoic acid prepared in this Laboratory by castor oil cracking⁵⁴ has been used for the preparation of C_{12} , C_{11} and C_{10} ω -hydroxy fatty acids. 10-Undecenoic acid was purified by careful fractionation and the purity was tested by VPC and analysis, b.p. 131-132°/1 mm, m.p. 31°, n_D^{29} 1.4489. Positive TMM test. IR spectrum: COOH 2600, 1716; C=C 1635, 990, 916 cm^{-1} . (Found: C, 71.8; H, 11.2; $C_{11}H_{20}O_2$ requires: C, 71.69; H, 10.94%).

Methyl 10-undecenoate (XXVI)

10-Undecenoic acid (500 g), anhydrous methanol (1000 ml); dry benzene (1000 ml) and concentrated sulphuric acid (10 ml) were refluxed for 6 hrs, and excess solvent mixture was distilled under reduced pressure. The reaction product was poured into water (2 lit.). Esters were taken in ether (3 x 400 ml), washed free from acid, extracted with sodium carbonate solution (7%; 3 x 50 ml), washed free from alkali and dried. Solvent was recovered and the traces were removed under reduced pressure and crude methyl 10-undecenoate (520 g; 99%) was obtained. The crude ester was distilled carefully to give water white pure methyl ester (500 g), b.p. 104-105°/0.7 mm (TMM and GLC tested); n_D^{28} 1.4383. IR spectrum: COOCH₃ 1748, C=C 1645, 994, 919 cm^{-1} . (Found: C, 72.5; H, 11.3; $C_{12}H_{22}O_2$ requires: C, 72.68; H, 11.18%).

10-Undecenol (XXVII)

Bright sodium (76 g; 3.25 g atom; 25% excess) was placed in a dry three-necked flask fitted with a Herschberg stirrer (slipseal), an efficient reflux condenser and a dropping funnel. Sodium was immediately covered with anhydrous toluene (150 ml) and heated on an oil bath at 120° and stirred to somewhat disperse the sodium. A mixture of methyl ester (126 g, 0.65M), anhydrous tert.butyl alcohol (144 g; 1.95M) and toluene (500 ml) was added in 45 minutes with stirring. During the exothermic reaction the bath temperature was maintained at $120^{\circ} \pm 5^{\circ}$. After the addition, the reactants were heated with stirring for another 30 minutes, cooled, finally in ice-water, and carefully treated with small quantity of ice-water with swirling while maintaining nitrogen atmosphere in the flask. When 500 ml of water had been added, the toluene layer was separated and washed with water (4 x 150 ml). The alkaline washings and previous aqueous portions were combined and extracted with ether (3 x 300 ml). The combined toluene and ether extracts were washed once with dilute acetic acid (5%) and finally with brine and dried. The solvents were distilled off and crude 10-undecenol (109 g; 98.5%) was obtained. On careful fractionation it afforded pure 10-undecenol (102 g; 93%); b.p. $125^{\circ}/3$ mm (TMM and GLC

tested). n_D^{20} 1.4520; IR spectrum: OH 3350, 1055; C=C 3095, 1820, 1640, 991, 912 cm^{-1} . (Found: C, 77.46; H, 12.9; $\text{C}_{11}\text{H}_{22}\text{O}$ requires: C, 77.58; H, 13.02%). Few more batches of 10-undecenol were prepared with similar yields.

10,11-Dihydroxy undecanol (XVII)

10-Undecenol (190 g; 1.11M); glacial acetic acid (1200 ml) and sulphuric acid (11.5 ml, sp. gr. 1.84) were taken in a three-necked flask and chilled to 20° . Hydrogen peroxide (195 g; 100 volumes) was quickly added to the reactants while stirring and the reaction was continued at 20° for 5 minutes. The contents were slowly brought to room temperature and gradually raised to 40° and kept overnight. Reaction mixture was poured into water (3 lit.) at 20° and extracted with ether (4 x 200 ml), washed free from acid, dried and distilled off the solvent. The acetoxy-hydroxy-derivative was refluxed with 10% ethanolic potassium hydroxide solution (1000 ml) for 4 hrs. Excess alcohol was flashed off and the product was worked up in the usual manner to afford crude 10,11-dihydroxy undecanol (225 g; 98.77%) which was crystallised from alcohol to yield a first crop of the glycol (156 g; 70.3%) m.p. $73-74^\circ$. Mother liquors on concentration, crystallisation and recrystallisation from alcohol afforded a second crop of 10,11-dihydroxy undecanol (44 g; 20%) m.p. $73-73.5^\circ$. IR

spectrum: OH 3333, 1350, 1130, 1059 cm^{-1} . (Found: C, 64.74; H, 11.77; $\text{C}_{11}\text{H}_{24}\text{O}_3$ requires: C, 64.66; H, 11.84%).

10-Hydroxy decanal (XIX)

In a three necked flask fitted with efficient stirrer (slipseal) condenser and dropping funnel, 10,11-dihydroxy undecanol (2 g) was dissolved in absolute alcohol (25 ml) and treated with freshly prepared 10% aqueous sodium meta periodate (25 ml) during ~ 45 minutes at 35° . Stirring was continued for another one hour and after testing the reactants for excess of metaperiodate, the reaction mixture was filtered through a sintered funnel (No.4), washed the residue with alcohol (3 x 5 ml) and the filtrate was poured into cold water (250 ml). The liberated compound was extracted with ethyl acetate, washed, dried and solvent was distilled off under reduced pressure. Crude 10-hydroxydecanal (1.76 g; theoretical) m.p. $68-70^\circ$ was crystallised from alcohol to afford first crop of the pure compound (1.26 g; 74.6%) m.p. $76-77^\circ$. Mother liquors on concentration, and crystallisation afforded a second crop of 10-hydroxy decanal (0.21 g; 13%) m.p. $75-76^\circ$. IR spectrum: OH 3460; CHO 1724 cm^{-1} . (Found: C, 69.4; H, 11.5; $\text{C}_{10}\text{H}_{20}\text{O}_2$ requires: C, 69.72; H, 11.7%). The 2,4-dinitrophenyl hydrazone prepared in alcohol and acid, crystallised from

dilute alcohol had a m.p. 98-99°. IR spectrum: OH 3460, 1059; CHO 2885, 1724, 1458, 980, 964 cm^{-1} . (Found: C, 54.7; H, 6.6; N, 15.7; $\text{C}_{16}\text{H}_{24}\text{N}_4\text{O}_5$ requires: C, 54.53; H, 6.87; N, 15.9%). The semicarbazone prepared in pyridine and crystallised from methyl alcohol had a m.p. 106.5°. More quantity of 10-hydroxydecanal was prepared in 10 g lots also with similar results.

12-Hydroxy dodec-2-enoic acid (XXX)

To a cooled solution of malonic acid (8.20 g) in dry pyridine (30 ml), 10-hydroxydecanal (10 g) in pyridine (15 ml) was added drop by drop in ~ 15 minutes with shaking. The reactants were kept at room temperature for 36 hrs, then heated on a waterbath for 3 hrs. Pyridine was removed under reduced pressure and the residue was extracted with ether (2 x 50 ml), the extract was washed with dilute hydrochloric acid, water and aqueous sodium carbonate (7%, 5 x 25 ml). The combined carbonate extracts on acidification with dilute hydrochloric acid gave 12-hydroxy dodec-2-enoic acid (12.2 g; 66.6%) which crystallised from alcohol yielded the acid (8 g) m.p. 67-67.5°. Mother liquors on concentration and recrystallisation afforded a second crop (2 g, 16.7%) m.p. 66.5-67°. IR spectrum: OH 3348, 1053; COOH 2620, 1440; C=C-COOH 1705, 1680 cm^{-1} . (Found: C, 67.26; H, 10.47; $\text{C}_{12}\text{H}_{22}\text{O}_3$ requires: C, 67.25; H, 10.35%). More quantity of

the acid was prepared in batches with similar results.

12-Hydroxy lauric acid (XXIV)

(i) 12-Hydroxy dodec-2-enoic acid (0.5 g) dissolved in glacial acetic acid (15 ml, E. Merck) was hydrogenated in the presence of palladium-carbon (10%; 0.052 g) at room temperature. The compound absorbed hydrogen gas (65 ml) in the first hour of reaction and no further perceptible absorption of gas was observed even after stirring for 3 hrs. The catalyst was separated by filtration, washed with acetic acid (3 x 2 ml) and the acetic acid was removed from the filtrate under reduced pressure. The residue on saponification and hydrolysis afforded crude 12-hydroxy lauric acid (0.5 g) m.p. 82°C , which on crystallisation from benzene gave pure acid (0.48 g) m.p. $83-84^{\circ}$. IR spectrum: OH 3333, 1054; COOH 2571, 1923, 1684, 1316 cm^{-1} . (Found: C, 66.4; H, 11.1; $\text{C}_{12}\text{H}_{24}\text{O}_3$ requires: C, 66.63; H, 11.18%).

(ii) 12-Hydroxy dodec-2-enoic acid (13.3 g) was dissolved in aqueous NaOH solution (10%; 400 ml) and heated to 90° . Raney-nickel alloy (40 g) was added to the hot solution in small lots taking all care as described previously. Addition was accomplished in ~ one and half hour and the reaction mixture was heated for another hour at 90°C with stirring. Insoluble material was filtered off

and the filtrate was worked up in the usual manner to obtain crude 12-hydroxy lauric acid (13.2 g) m.p. $79-81^{\circ}$, which on crystallisation from ethyl acetate afforded pure acid (12 g; 90%) m.p. $83-84^{\circ}$. There was no depression in melting point with 12-hydroxy lauric acid from the previous batch. IR spectrum: OH 3333, COOH 2571, 1923, 1684 cm^{-1} . Sufficient quantity of the hydroxy acid was prepared in batches with similar yields.

11-Hydroxy undecanoic acid (XXXI)

11-bromoundecanoic acid (XXXII)

10-Undecenoic acid (50 g) was dissolved in pet. ether ($40-60^{\circ}$, sulphuric acid washed, distilled, 350 ml) in a three necked flask fitted with thermometer, wide bored inlet tube and calcium chloride guard tube. After adding freshly crystallised benzoyl peroxide (1 g) to the solution, cooled to 0° and hydrogen bromide (evolved by dropping 53 ml of bromine into 51 g of tetralin) was rapidly passed into the solution. Solids started appearing after 5 minutes and as solids separated the flask was shaken and process was continued till all the hydrogen bromide passed into the reaction mixture ($\sim 25-30$ minutes). The temperature was maintained at 0° throughout. The contents were shaken for a further 20 minutes. The pink precipitate was chilled to -12° and filtered off and transferred to a porous plate and dried. When dry it was colourless and

shining (57 g; 72%) m.p. 47-49°. The crude product was crystallised from pet. ether (40-60°; 100 ml) twice at -15°. Filtered and dried in vacuo to obtain 11-bromo undecanoic acid (54 g) m.p. 50.5-51°C, white shining flaky crystalline material.

11-Acetoxy undecanoic acid (XXXIII)

11-bromo undecanoic acid (50 g), freshly fused sodium acetate (55 g), glacial acetic acid (100 ml), and acetic anhydride were refluxed over a controlled hot oil bath for 12 hrs. The reaction mixture was cooled and poured into water (250 ml) and the contents were extracted with ether (4 x 50 ml). The combined ether extracts were washed free from acid, finally with brine and dried. Recovery of the solvent gave crude 11-acetoxy undecanoic acid (42.4 g; 96%) which was distilled fractionally to obtain pure acetoxy derivative (35.5 g) b.p. 176-177°/0.7 mm. About 2 g forerun of the distillate was collected separately. IR spectrum: COOH 2660, 1718, 1636; CH₃COO-; 1234 cm⁻¹. (Found: C, 63.7; H, 9.8; C₁₃H₂₄O₄ requires: C, 63.90; H, 9.9%).

11-Hydroxy undecanoic acid (XXXI)

11-acetoxy undecanoic acid (34 g) was refluxed with alcoholic potassium hydroxide solution (10%; 150 ml) for 6 hrs. Excess alcohol was distilled off and the residue after dissolving in water (200 ml) was acidified with dilute

hydrochloric acid. The precipitated acid on filtration, washing and drying afforded crude 11-hydroxy undecanoic acid (28 g; theoretical); m.p. 65-67°, which was crystallised from ethyl acetate gave pure acid (27 g; 97%) m.p. 67-67.5°. IR spectrum: OH 3320; COOH 2625, 1711 cm^{-1} . (Found: C, 65.1; H, 10.9; $\text{C}_{11}\text{H}_{22}\text{O}_3$ requires: C, 65.31; H, 10.96%).

10-Hydroxy decanoic acid (XXXIV)

10-Hydroxy decanal (XXIX) (10 g) and peracetic acid (67 ml, prepared by mixing 51 ml glacial acetic acid and 16 ml hydrogen peroxide, 100 volumes) were heated on a waterbath at 85° for 15 minutes and left overnight. The reaction mixture was filtered, poured into water and extracted with ethyl acetate (3 x 50 ml). Solvent extract was washed free from acid, dried, and flashed off the solvent to obtain a slimy product was refluxed with alcoholic potassium hydroxide solution (10%; 50 ml) for 4 hrs. Alcohol was distilled off and the product was worked up in the usual manner to obtain crude 10-hydroxy decanoic acid (10.9 g) m.p. 68-70°. Crystallisation from benzene-ethyl acetate afforded pure hydroxy acid (8.5 g; 78%), m.p. 75.5-76.0°. IR spectrum: OH 3333, 1050; COOH 2646, 1923, 1698 cm^{-1} . (Found: C, 63.9; H, 10.81; $\text{C}_{10}\text{H}_{20}\text{O}_3$ requires: C, 63.79; H, 10.71%).

CYCLIZATION OF ω -HYDROXY FATTY ACIDS1.18-Octadecanolide

Thiophene free dry benzene (2 lit.) and p-toluene sulphonic acid (2.5 g) were taken in the flask shown in the set up (Fig.2) heated to gentle distillation and allowed the distilled solvent to circulate through the system for one hour. 18-Hydroxy stearic acid (5 g; 0.0166 M) dissolved in dry benzene (500 ml; 0.0083 M/l) was dropped into the set up, through the dropping funnel in 32 hrs. Rate of addition of the hydroxy acid solution was controlled by adjusting the tungsten wire tipped plunger fitted in the capillary tube fused at the bottom of the dropping funnel and efficient dilution was ensured through steady distillation of solvent and recirculation. Solvent was stripped of water of reaction while passing through the drying tube filled with activated indicating silica gel which was changed as and when needed. Hydroxy acid was kept dissolved in the dropping funnel and the horizontal tube where dilution was accomplished, with the help of a heating tape. At the completion of addition, the reaction mixture was refluxed for another one hour, cooled to room temperature, washed free from acid, followed by washing with aqueous sodium carbonate solution (7%; 3 x 100 ml), washed free from alkali and dried. Benzene was recovered under reduced pressure, and the residue was

dissolved in n-hexane (50 ml), chilled. Solids were separated by filtration. Filtrate was concentrated and cooled. The process was continued till no solids separated. Hexane was recovered and the product on distillation afforded colourless 1,18-octadecanolide (3.46 g; 81.1%) b.p. 147.5-148/0.8-0.9 mm; m.p. 36.5-37°, n_D^{30} 1.4666; (GLC single peak). IR spectrum: $\nu_{C=O}$ 1740; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ 79.5 (s), $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{O}-$ 133.5 (d), $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{O}-\text{CH}_2-$ 241.2 (t). (Found: C, 76.52; H, 12.19; $\text{C}_{18}\text{H}_{34}\text{O}_2$ requires: C, 76.54; H, 12.13%). Dilactone m.p. 111-112°.

1,16-Hexadecanolide

16-Hydroxy palmitic acid (4.53 g; 0.0116 M) dissolved in dry benzene (500 ml; 0.0083 M/l) was cyclised in the same manner as described previously, by adding the hydroxy acid solution to the reaction mixture (benzene 2 lit, p-toluene sulphonic acid 2.5 g) in 36 hrs. On working up in the usual fashion and distillation it afforded colourless 1,16-hexadecanolide (synonym: dihydro ambrettolide) (3.42 g; 80.9%); b.p. 126-127°/0.6 mm; m.p. 34-35°, n_D^{30} 1.4678 (GLC tested). IR spectrum: $\nu_{C=O}$ 1740; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ 79.6 (s); $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{O}-$ 133.5 (d); $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{O}-\text{CH}_2-$ 241.6 (t) cps. (Found: C, 75.71; H, 11.85; $\text{C}_{16}\text{H}_{30}\text{O}_2$ requires: C, 75.53; H, 11.89%).

1,15-pentadecanolide

15-Hydroxy pentadecanoic acid (4.28 g; 0.0166 M)

dissolved in benzene (500 ml; 0.0083 M/l) was lactonised in the usual manner. Addition of the hydroxy solution to the reaction mixture (benzene 2 lit., p-toluene sulphonic acid 2.5 g) was completed in 32.5 hrs. Working up of the reaction product and distillation gave colourless pleasant smelling 1,15-pentadecanolide (synonym: exaltolide) (2.73 g; 78.9%) b.p. $120^{\circ}/0.3$ mm; n_D^{30} 1.4692; (GLC single peak). IR spectrum: $\nu_{C=O}$ 1748; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ 79(s), $\text{CH}_2-\overset{\text{O}}{\underset{\text{||}}{\text{C}}}-\text{O}-$ 133.7 (d); $-\text{CH}_2-\overset{\text{O}}{\underset{\text{||}}{\text{C}}}-\text{O}-\text{CH}_2-$ 242.2 (t) cps. (Found: C, 75.21; H, 11.8; $\text{C}_{15}\text{H}_{28}\text{O}_2$ requires: C, 74.95; H, 11.74%).

1,13-Tridecanolide

13-Hydroxy tridecanoic acid (3.82 g; 0.0166 M) dissolved in benzene (500 ml; 0.0083 M/l) was cyclised accordingly. Addition of the hydroxy acid solution to the reaction mixture (benzene 2 lit.; p-toluene sulphonic acid 2.5 g) was accomplished in 33.5 hrs. The product was worked up as described previously and distilled to obtain colourless pleasant smelling 1,13-tridecanolide (2.3 g; 65.4%); b.p. $101-102^{\circ}/1.0$ mm; n_D^{30} 1.4684; (GLC tested); IR spectrum: $\nu_{C=O}$ 1748; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ 81(s); $-\text{CH}_2-\overset{\text{O}}{\underset{\text{||}}{\text{C}}}-\text{O}-$ 136.3 (d); $-\text{CH}_2-\overset{\text{O}}{\underset{\text{||}}{\text{C}}}-\text{O}-\text{CH}_2-$ 242.7 (t) cps. (Found: C, 73.39; H, 11.53; $\text{C}_{13}\text{H}_{24}\text{O}_2$ requires: C, 73.53; H, 11.39%).

1,12-dodecanolide

12-Hydroxy lauric acid (3.59 g; 0.0166 M) dissolved

in benzene (500 ml; 0.0083 M/l) was lactonised in the usual manner. Addition of the hydroxy acid solution to the reaction medium (benzene 2 lit., p-toluene sulphonic acid 2.5 g) was carried out in 33 hrs. The reaction product was processed in the same fashion as described previously, distilled and redistilled to afford colourless strong smelling 1,12-dodecanolide (0.78 g; 23.7%) b.p. 85-86°/0.2 mm; n_D^{30} 1.4690; (GLC single peak). IR spectrum: $\nu_{C=O}$ 1740, 1750; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ 81.9(s); $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-$ 134.1(d); $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{CH}_2-$ 244.1(t) cps. (Found: C, 72.54; H, 11.1; $\text{C}_{12}\text{H}_{22}\text{O}_2$ requires: C, 72.68; H, 11.18%).

1,11-Undecanolide

11-Hydroxy undecanoic acid (3.35 g; 0.0166 M) dissolved in benzene (500 ml; 0.0083 M/l) was cyclised by adding to benzene (2 lit.), p-toluene sulphonic acid (2.5 g) in the usual manner in 33 hrs. The reaction product on working up according to the usual method and distillation yielded colourless strong smelling 1,11-undecanolide (0.56 g; 18.33%); b.p. 79-80°/0.4 mm; n_D^{30} 1.4694; (GLC tested); IR spectrum: $\nu_{C=O}$ 1740, 1750; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ 81.7(s); $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-$, 136.2(d); $-\text{CH}_2-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{CH}_2-$, 245.2 (t) cps. (Found: C, 72.0; H, 11.04; $\text{C}_{11}\text{H}_{20}\text{O}_2$ requires: C, 71.69; H, 10.94%).

1,10-decanolide

10-Hydroxy decanoic acid (3.12 g; 0.0166 M) dissolved

in benzene (500 ml; 0.0083 M/l) was lactonised by letting it into the reaction medium (benzene 2 lit., p-toluene sulphonic acid 2.5 g) in the same manner as described previously in 32 hrs. The reaction product was worked up in the usual fashion and distilled to give 1,10-decanolide (0.114 g; 4.03%); b.p. 65-66°/0.3 mm, n_D^{30} 1.4663; (GLC tested). IR spectrum: C=O 1748, 1752; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ 82.1 (s); $-\text{CH}_2-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-$ 135.0 (d); $-\text{CH}_2-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{CH}_2-$ 246.2 (t) cps. (Found: C, 70.9; H, 10.8; $\text{C}_{10}\text{H}_{18}\text{O}_2$ requires: C, 70.54; H, 10.66%).

1,7-Heptanolide (ξ -enantholactone):cycloheptanone⁵⁵: In a three-necked flask fitted with efficient stirrer, dropping funnel and thermometer, cyclohexanone (45 g; b.p. 154-156°), methyl alcohol (35 g; acetone free) and dry analar potassium carbonate (catalytic amount) were cooled to 20° with stirring and the agitation was continued for 10 minutes. Nitroso-methylurethane (56 g; prepared in the laboratory,⁵⁶ was slowly added to the reactants through the dropping funnel at such a rate that temperature of the reaction mixture did not rise above 20°. After completion of addition, reactants were stirred for another 30 minutes, brought to room temperature and kept overnight. The product after filtration was carefully fractionated and compound distilling at 179-181° was collected and refractionated to afford cycloheptanone (31 g; 60%) b.p. 179.5 - 180.5°; n_D^{31} 1.4566; IR spectrum:

$\nu_{\text{C=O}}$ 1701 cm^{-1} .

Preparation of lactone: Cycloheptanone (5.6 g) and perbenzoic acid (8.3 g; ca. 250 ml chloroform, prepared according to the procedure of Braun⁵⁷) were mixed thoroughly by shaking in a flask covered with black paper and kept in dark, at room temperature. Same volume of perbenzoic acid solution in chloroform was also kept side by side in a separate flask as a control. Aliquots of the reaction mixture and blank solution (5 ml each) were removed at intervals of 48 hrs and titrated iodometrically in the normal manner⁵⁷. After 17 days (408 hrs) the ketone consumed perbenzoic acid (6.5 g). Reaction mixture was extracted several times with sodium bicarbonate solution (3%), washed free from alkali and dried. After removal of solvent at reduced pressure the product (5.4 g; 84.37%) was fractionally distilled in vacuo, keeping the receiver in ice-salt mixture to yield 1,7-heptanolide (3.7 g; 60%) b.p. 81-83°/1 mm, n_D^{26} 1.4662. IR spectrum; $\nu_{\text{C=O}}$ 1742, 1786 cm^{-1} .

ε-Caprolactone

A mixture of cyclohexanone (7 g; b.p. 154-156°) and perbenzoic acid (12 g; ca. 190 ml chloroform) solution; was mixed thoroughly and kept at room temperature for 8 hrs with occasional swirling. The reaction mixture was processed as described already, dried and solvent was removed under reduced

pressure. The product was carefully distilled to give ϵ -caprolactone (5.5 g; 68%) b.p. 80-81°/1.2 mm, n_D^{26} 1.4665. IR spectrum; $\nu_{C=O}$ 1735 cm^{-1} .

PYROLYSIS OF LACTONES

17-Octadecenoic acid (I) ($\text{CH}_2=\text{CH}(\text{CH}_2)_{15}\text{COOH}$)

1,18-Octadecanolide (1 g) was pyrolysed in a vertical reactor shown in Fig.2. The reactor consists of an inner tube (1.4 O.D. x 30 cm) fused at the bottom with another tube (8 mm O.D. x 21 cm). Rest three outer tubes form the electrically heated furnace. The reactor tube was filled with pyrex glass pieces (1.5 to 2 mm cubes approx.) to a height of 15 cm. Furnace was heated to 450° and after fitting the micro dropping funnel containing lactone to the reactor tube, the system was flushed several times with oxygen-free dry nitrogen, by means of a nitrogen system, at 150 mm pressure. Temperature was gradually raised to 525°, and when it stabilised, lactone was dropped on the hot bed of glass pieces (one drop every half minute) maintaining the pressure at 150 mm. Pyrolysis was completed in one hour. Reactor was heated for another 15 minutes and the system was brought to room temperature. Pyrolysate (0.82 g, 83%) was dissolved in ether (20 ml) and ether solution was extracted with aqueous sodium carbonate solution (5%; 6 x 5 ml). The combined alkali extracts was further extracted with ether (2 x 15 ml). Ethereal solution was

washed free from alkali, dried and recovered the solvent to afford neutral fraction (0.67 g), which on distillation afforded colourless liquid (0.6 g) b.p. $140-141^{\circ}/6$ mm. IR spectrum: $\nu_{C=O}$ 1740 cm^{-1} , and similar to the IR curve of the starting lactone (1,18-octadecanolid). Alkali extracts were combined and acidified with dilute hydrochloric acid. Liberated acid was taken in ether (3 x 20 ml), washed free from acid, dried and recovered the solvent to afford 17-octadecenoic acid (0.162 g; 50% based on the unrecovered lactone) m.p. $52-54^{\circ}$ which on crystallisation from acetonitrile afforded white shining crystalline unsaturated acid (0.155 g) m.p. $54.5-55^{\circ}$, gave TMM test. IR spectrum: $\nu_{C=O}$, $1700-1715$; $\nu_{C=C}$ 1650 ; δ -CH=CH₂ 917 ; δ -CH=CH₂ 995 . (Found: C, 76.76; H, 12.27; C₁₈H₃₄O₂ requires: C, 76.64; H, 12.13%).

Methyl-17-octadecenoate ($\text{CH}_2=\text{CH}(\text{CH}_2)_{15}\text{COOCH}_3$): 17-octadecenoic acid (85 mg) was esterified by reacting with diazomethane in ether, worked up and distilled (in bulb) in vacuo to yield methyl, 17-octadecenoate, b.p. $143-44^{\circ}$ (bath)/ $0.2-0.3$ mm, n_D^{20} 1.4469 (gave TMM test and single peak GLC); IR spectrum: COOCH_3 1750 ; $\nu_{C=C}$ 1650 ; δ -CH=CH₂ 913 ; δ -CH=CH₂ 995 ; PMR signals: -CH₂-CH₂-CH₂ 77 (s); -CH₂-C(=O)-OCH₃ 129 (q); -CH₂-C(=O)-CH₃ 216 (s); -CH₂=CH- $285-288$ (m). (Found:

C, 76.63; H, 12.33; $C_{19}H_{36}O_2$ requires: C, 76.97; H, 12.34%. More of 17-octadecenoic acid was prepared by pyrolyzing 5 g lots of 1,18-octadecanolide.

Hydrogenation of 17-octadecenoic acid: Methyl, 17-octadecenoate (0.5 g) was hydrogenated in alcohol (10 ml) in the presence of Pd on calcium carbonate catalyst (0.25 g; 10%) at room temperature. Reaction was continued for 6 hrs. When no absorption of hydrogen gas was observed, the catalyst was filtered and washed with alcohol (3 x 3 ml). Solvent was removed from the filtrate at room temperature under suction. Residue was heated with alcoholic potassium hydroxide (10%; 10 ml) under reflux, removed solvent and soap was hydrolysed with dilute hydrochloric acid. Liberated solid acid was filtered, washed free from acid, dried to afford stearic acid (0.48 g; 100%); m.p. 68-69°. Crystallised from acetonitrile, and obtained pure shining stearic acid (0.45 g; 96%) m.p. 69-69.5°; mix. m.p. with authentic sample of stearic acid 69-69.5°. IR spectrum: COOH 2632, 1698 cm^{-1} .

15-Hexadecenoic acid ($CH_2=CH(CH_2)_{13}COOH$)

1,16-Hexadecanolide (1 g) was pyrolyzed at 525°/150 mm in one hour. Pyrolysate (0.93 g; 93%) was separated into neutral and acid fractions in the usual

fashion. Neutral product (0.67 g). IR spectrum: $\nu_{\text{C=O}}$ 1740 cm^{-1} , was very similar to the starting lactone. Acid fraction (0.23 g; 69% based on the unrecovered lactone) m.p. 45-47° was crystallised from acetonitrile to afford pure 16-hexadecenoic acid (0.2 g) m.p. 48-48.5°. gave TMM test. IR spectrum: $\nu_{\text{C=O}}$ 1705-1710; $\nu_{\text{C=C}}$ 1647; $\delta_{\text{CH=CH}_2}$ 919; $\delta_{-\text{CH}-\text{CH}_2}$ 993; (Found: C, 75.61; H, 11.74; $\text{C}_{16}\text{H}_{30}\text{O}_2$ requires: C, 75.53; H, 11.89%).

Methyl-16-hexadecenoate ($\text{CH}_2=\text{CH}(\text{CH}_2)_{13}\text{COOCH}_3$): 16-hexadecenoic acid (90 mg) was esterified by reacting with diazomethane in ether. Methyl ether, after working up, distilled (bulb) in vacuo to give pure methyl 17-hexadecenoate b.p. 140-145° (bath)/0.6 mm; n_D^{30} 1.4445 (positive TMM test, single peak GLC). IR spectrum: $\nu_{\text{C=O}}$ 1750; $\nu_{\text{C=C}}$ 1650; $\delta_{-\text{CH=CH}_2}$ 913; $\delta_{-\text{CH}-\text{CH}_2}$ 995; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2$ 77(s); $-\text{CH}_2-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{OCH}_3$ 129 (q); $-\text{CH}_2-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{OCH}_3$ 216.5(s); $\text{CH}_2=\text{CH}$ - 286-349(m) cps. (Found: C, 76.21; H, 12.09; $\text{C}_{17}\text{H}_{32}\text{O}_2$ requires: C, 76.06; H, 12.02%).

14-Pentadecenoic acid ($\text{CH}_2=\text{CH}(\text{CH}_2)_{12}\text{COOH}$)

1,15-Pentadecanolide (1 g) was pyrolysed at 525°/150 mm in one hour and pyrolysate (0.903 g; 90%) was as usual separated into neutral (0.65 g), IR spectrum of which was similar to that of the starting lactone, and acid fraction (0.26 g; 73%, based on unrecovered lactone) m.p. 45-47°, crystallised from acetonitrile gave crystalline 15-pentadecenoic

acid (0.19 g) m.p. 50-50.5°; (positive TMM test).

IR spectrum: $\nu_{\text{C=O}}$ 1695-1710; $\nu_{\text{C=C}}$ 1643; $\delta_{\text{-CH=CH}_2}$ 917;
 $\delta_{\text{-CH=CH}_2}$ 995. cm^{-1} . (Found: C, 75.06; H, 11.85;
 $\text{C}_{15}\text{H}_{28}\text{O}_2$ requires: C, 74.95; H, 11.74%).

Methyl-14-pentadecenoate ($\text{CH}_2=\text{CH}(\text{CH}_2)_{12}\text{COOCH}_3$): 15-penta-
 decenoic acid (100 mg) esterified with diazomethane in
 ether and after processing distilled (bulb) gave methyl
 15-pentadecenoate, b.p. 120-125°(bath)/0.4-0.5 mm;
 n_D^{20} 1.4426, gave TMM test. GLC tested. IR spectrum:
 $\nu_{\text{C=O}}$ 1750; $\nu_{\text{C=C}}$ 1645; $\delta_{\text{-CH=CH}_2}$ 913; $\delta_{\text{-CH=CH}_2}$ 996;
 PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2$ 77.5(s); $-\text{CH}_2-\overset{\text{O}}{\parallel}\text{C}-\text{OCH}_3$ 129(q);
 $-\text{CH}_2-\overset{\text{O}}{\parallel}\text{C}-\text{OCH}_3$ 216(s); $\text{CH}_2=\text{CH}-$ 287-359(m) cps. (Found: C, 75.68;
 H, 11.85; $\text{C}_{16}\text{H}_{30}\text{O}_2$ requires: C, 75.53; H, 11.89%).

12-tridecenoic acid, $\text{CH}_2=\text{CH}(\text{CH}_2)_{10}\text{COOH}$: 1,13-tridecanolide
 (1 g) was pyrolysed at 525°/150 mm in one hour. Pyrolysate
 (0.96 g; 98%) on working up by usual procedure afforded
 neutral fraction (0.68 g), IR spectrum of which was very
 similar to the one obtained for the starting lactone; and
 acid fraction (0.29 g; 89% based on unrecovered lactone);
 m.p. (double capillary) 36-37°, which on crystallisation from
 acetonitrile in cold afforded first crop of 13-tridecenoic
 acid (62 mg), m.p. 38°. Mother liquor on concentration
 and chilling gave a second crop, recrystallised from aceto-
 nitrile to give unsaturated acid (46 mg), m.p. 38° (positive

TNM test), single peak (GLC). Rest of the product after removal of solvent was distilled (bulb), b.p. 135-140°(bath)/1 mm; m.p. 27.5-28°; IR spectrum: ν C=O 1725; ν C=C 1645; δ -CH=CH₂ 915; δ -CH=CH₂ 995; (Found: C, 73.1; H, 11.58; C₁₃H₂₄O₂ requires: C, 73.53; H, 11.39%).

Methyl-13-tridecenoate (CH₂=CH(CH₂)₁₀COOCH₃): 13-tridecenoic acid (30 mg) esterified with diazomethane in ether, processed and distilled (bulb) to give methyl 13-tridecenoate, b.p. 120-125°(bath)/1 mm, n_D^{30} 1.4395; gave TNM test, GLC tested. IR spectrum: ν C=O 1750; ν C=C 1645; δ -CH=CH₂ 915; δ -CH=CH₂ 995; PMR signals: -CH₂-CH₂-CH₂ 78(s); -CH₂-C(=O)-OCH₃ 128.5(q); -CH₂-C(=O)-OCH₃ 217.5(s); CH₂=CH- 287-263 (m) cps. (Found: C, 74.61; H, 11.67; C₁₄H₂₆O₂ requires: C, 74.28; H, 11.58%).

11-Dodecenoic acid (CH₂=CH(CH₂)₉COOH):

1,12-dodecanolide (1 g) was pyrolysed at 525°/150 mm in 1 hr. Pyrolysate (0.98 g; 38%) was separated into neutral component (0.73 g), IR spectrum of which was observed to be very similar to the spectrum of 1,12-dodecanolide and acid fraction (0.23 g; 83% based on unrecovered lactone), by usual method, which on distillation (bulb) gave 12-dodecenoic acid, b.p. 125-130°(bath)/0.8 mm, n_D^{30} 1.4398. Positive TNM test, single peak (GLC). IR spectrum: ν C=O 1705;

$\nu_{\text{C}=\text{C}}$ 1643; δ -CH=CH₂ 910; δ -CH=CH₂ 995. (Found: C, 72.49; H, 11.27; C₁₂H₂₂O₂ requires: C, 72.68; H, 11.18%).

Methyl-11-dodecenoate (CH₂=CH(CH₂)₉COOCH₃): 12-dodecenoic acid (91 mg) was esterified with diazomethane in ether, processed and distilled to afford methyl 12-dodecenoate, b.p. 80-85°(bath)/0.6 mm; n_D^{30} 1.4362, positive TMM test (GLC tested). IR spectrum: $\nu_{\text{C}=\text{O}}$ 1750; $\nu_{\text{C}=\text{C}}$ 1645; δ -CH=CH₂ 913; δ -CH=CH₂ 995; PMR signals: -CH₂-CH₂-CH₂- 78.5(s); -CH₂-C(=O)OCH₃ 127.5(q); -CH₂-C(=O)OCH₃ 216.5(s); CH₂=CH- 285-365(m) cps. (Found: C, 73.93; H, 11.42; C₁₃H₂₄O₂ requires: C, 73.53; H, 11.39%).

10-Undecenoic acid (CH₂=CH(CH₂)₈COOH)

1,11-Undecanolide (0.75 g) was pyrolysed at 525°/150 mm in 45 minutes and pyrolysate (0.68 g; 91%) was processed to give neutral fraction (0.51 g) and acid component (0.17 g; 70% based on unrecovered lactone). Neutral portion, IR spectrum of which was similar to the one obtained for starting lactone, on distillation (bulb) afforded 1,11-undecanolide b.p. 115-125°(bath)/2 mm. IR spectrum: $\nu_{\text{C}=\text{O}}$ 1740, 1750, superimposable on the IR spectrum of authentic sample of lactone. (Found: C, 71.73; H, 10.96; C₁₁H₂₀O₂ requires: C, 71.69; H, 10.94). Acid fraction was distilled (bulb) to obtain 11-undecenoic acid, b.p. 130-135(bath)/1 mm; n_D^{30} 1.4462; positive TMM test, GLC tested.

IR spectrum: $\nu_{\text{C=O}}$ 1717; $\nu_{\text{C=C}}$ 1639; $\delta\text{-CH=CH}_2$ 912;
 $\delta\text{-CH=CH}_2$ 990 cm^{-1} . (Found: C, 71.73; H, 11.0; $\text{C}_{11}\text{H}_{20}\text{O}_2$
 requires: C, 71.69; H, 10.94%).

Methyl-10-undecenoate ($\text{CH}_2=\text{CH}(\text{CH}_2)_9\text{COOCH}_3$): 11-Undecenoic
 acid (93 mg) esterified with diazomethane in ether, was
 distilled (bulb) to afford methyl 11-undecenoate, b.p.
 90-95°(bath)/0.5 mm; n_D^{30} 1.4360; gave positive TMM test,
 GLC single peak. IR spectrum: $\nu_{\text{C=O}}$ 1750; $\nu_{\text{C=C}}$ 1645;
 $\delta\text{-CH=CH}_2$ 913; $\delta\text{-CH=CH}_2$ 995; PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$
 80(s); $-\text{CH}_2-\overset{\text{O}}{\parallel}\text{C}-\text{OCH}_3$ 129(q); $-\text{CH}_2-\overset{\text{O}}{\parallel}\text{C}-\text{OCH}_3$, 218.5(s);
 $\text{CH}_2=\text{CH}-$ 288.5-368.5(m) cps. (Found: C, 72.44; H, 11.24;
 $\text{C}_{12}\text{H}_{22}\text{O}_2$ requires: C, 72.68; H, 11.18%).

6-Heptenoic acid ($\text{CH}_2=\text{CH}(\text{CH}_2)_4\text{COOH}$)

1,7-heptanolide (0.9 g) was pyrolysed at 525°/150 mm
 in 45-50 min. Pyrolysate (0.67 g; 74%) when processed gave
 neutral component (0.35 g), IR spectrum of which was
 similar to that of 1,7-heptanolide, and acid fraction
 (0.3 g; 55% based on the unrecovered lactone). On dis-
 tillation (bulb) this afforded 7-heptenoic acid, b.p.
 110-115°(bath)/6 mm; gave TMM test. IR spectrum: $\nu_{\text{C=O}}$ 1709;
 $\nu_{\text{C=C}}$ 1639; $\delta\text{-CH=CH}_2$ 915; $\delta\text{-CH=CH}_2$ 1000-1020 cm^{-1} .

Methyl 6-heptenoate ($\text{CH}_2=\text{CH}(\text{CH}_2)_4\text{COOCH}_3$): 6-heptenoic acid
 (95 mg) was esterified with diazomethane in ether in cold,

processed under cold conditions, distilled quickly to obtain methyl 6-heptenoate b.p. 100-110(bath)/9 mm; positive TMM test. IR spectrum: ν C=O 1745; ν C=C 1642; δ -OH-CH₂ 920; δ -CH=CH₂ 971. PMR signals: -CH₂-CH₂-CH₂-80(s); -CH₂-C(=O)-OCH₃ 129(q); -CH₂-C(=O)-OCH₃ 219 (s); -CH₂=CH-288-368 cps.

Pyrolysis of ϵ -caprolactone

ϵ -Caprolactone (1 g) was pyrolysed at 525°/150 mm in 1 hr. Pyrolysate (0.9 g; 90%) on working up in cold yielded a liquid neutral fraction (0.13 g), IR spectrum: ν C=O 1724 cm⁻¹; similar to that of starting lactone in every respect; and an acid component (0.69 g; 80% based on the unrecovered lactone which did not give positive TMM test). IR spectrum: OH 3344, COOH 2632, 1695 cm⁻¹ and any peak for vinylic unsaturation in the region of 910-920 was completely absent, and it did not give TMM test.

Esterification of acid fraction: Above acid fraction (0.68 g) was esterified with diazomethane in ether, in cold, processed and fractionated. Fraction I (0.37 g) b.p. 87-89°/10 mm. IR spectrum: OH 3430; COOCH₃ 1740; and Fraction II (.16 g) b.p. 110-115°/8 mm. IR spectrum: OH 3410; COOCH₃ 1738 cm⁻¹.

Fractionation by VPC: Methyl esters (0.68 g) prepared from the acid fraction obtained from a second pyrolysis of ϵ -caprolactone were fractionated through Perkin-Elmer Vapor

Fractometer, model 154 (Column 'P', length 6'; temp. 160°; pressure (hydrogen gas) 15 lbs; attenuation 4; material injected 20ml/injection, total number of injections 28).

Two distinct fractions were collected, first being in minute quantity and the second forming the major fraction.

Fraction I distilled (bulb), b.p. 80-85°(bath)/8 mm,

IR spectrum: OH 3420; COOCH₃ 1740 cm⁻¹.

Fraction II distilled (bulb), b.p. 110-115°/8 mm.

IR spectrum: OH, 3420; COOCH₃ 1745 cm⁻¹. (Found: C, 58.02; H, 9.45; C₇H₁₄O₃ requires: C, 57.51; H, 9.65%); PMR signals: -CH₂-CH₂-CH₂-(OH) 74-114(m); -CH₂-C(=O) (2H) 135.5(t); OH(1H) 180(s); CH₃-O (2H) 210.5 (t); COOCH₃ (3H) 217 (s) cps.

Several pyrolyses were carried out with similar results.

Hydrolysis of ε-caprolactone: ε-Caprolactone (0.37 g)

was refluxed with alcoholic potassium hydroxide solution (10%; 15 ml) for 3 hr. Alcohol was removed, soaps dissolved in water (25 ml), and carefully acidified in cold with dilute hydrochloric acid, maintaining a layer of nitrogen in the flask. Liberated acids were taken in ether (3 x 15 ml)(after saturating the aqueous layer with ammonium sulphate), washed with brine, dried, solvent was flashed off and the product after drying under reduced pressure was immediately esterified with diazomethane in ether. Methyl esters, on careful distillation afforded

two fractions.

Fraction I, b.p. 80-85°(bath)/8 mm. IR spectrum: OH 3400; COOCH_3 1740 cm^{-1} ; superimposable on the spectrum obtained for the first fraction from VPC.

Fraction II, b.p. 110-115°(bath)/8 mm. IR spectrum: OH 3420; COOCH_3 1745 cm^{-1} ; superimposable on the spectrum obtained for the second fraction from VPC. PMR signals: $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ (6H) 73.5-114.5(m); $\text{CH}_2-\text{C}=\text{O}$ (2H) 135.5(t); OH(H) 182(s); $\text{CH}_2-\text{O}-$ (2H) 210.5(t); COOCH_3 (3H) 217(s) cps.

SUMMARY

A general procedure for the synthesis of ω -olefinic fatty acids involving pyrolytic cis-elimination of lactones having eight or more members in the ring is described.

The method which gives high overall yields has been applied for the synthesis of (C_{18} , C_{16} , C_{15} , C_{13} , C_{12} , C_{11} and C_7) ω -olefinic acids.

In connection with the above work new procedures for the synthesis of the following ω -hydroxy fatty acids have been worked out (C_{15} , C_{13} , C_{12} , C_{11} and C_{10}).

A simplified procedure for the lactonization of ω -hydroxy acids to give large-membered lactones is described.

Spectral data (IR, NMR) of many-membered lactones ω -olefinic acids and their methyl esters have been presented and discussed.

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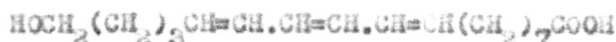
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CHAPTER III

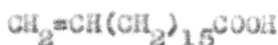
SYSTEMATIC CHAIN-SHORTENING OF
 ω -OLEFINIC FATTY ACIDS

SYSTEMATIC CHAIN-SHORTENING OF α -OLEFINIC FATTY ACIDS

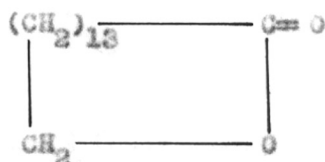
The previous Chapter describes the development of a general method for the preparation of α -olefinic fatty acids from the corresponding α -hydroxy acids by the pyrolysis of their lactones. As indicated earlier, this work was undertaken to explore the utilisation of 18-hydroxy stearic acid, readily accessible from Kamolenic acid (I). In the present Chapter we report on the systematic chain-shortening of 17-octadecenoic acid (II) by one, two or three carbons at a stretch. This work has lead to a simple preparation of 15-hydroxy pentadecanoic acid, a necessary intermediate for the preparation of exaltolide (III)¹⁻¹⁹, a valuable perfumery chemical²⁰⁻³³.



I



II

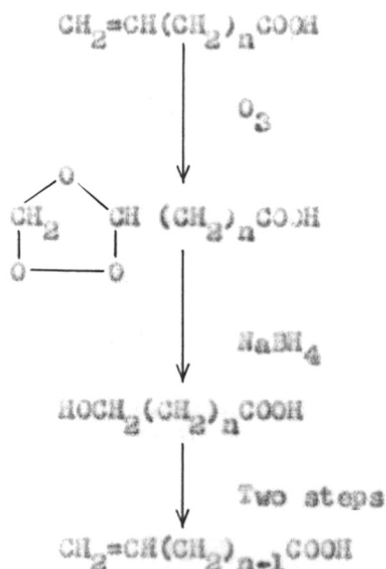


III

Obviously the chain-shortening methods described in this Chapter can be applied to any other ω -olefinic fatty acid, and by the application of these methods in combination with the work described in the previous Chapter, it should be possible, in principle, to convert 17-octadecenoic acid (II) to lower ω -olefinic fatty acids including the C_{10} chain-length.

CHAIN-SHORTENING BY ONE CARBON

Chain-shortening of an ω -olefinic fatty acid by one carbon atom is evidently a straightforward procedure. Of the various possibilities available the method of sodium-borohydride reduction of an ozonide³⁴⁻³⁷ was selected as the resulting product would be an ω -hydroxy acid (ester), which can be lactonised and pyrolysed to yield the next lower ω -olefinic fatty acid.



Ozonolysis of 17-octadecenoic acid (II) was best carried out in methanolic solution and the resulting solution containing the ozonide was straightaway treated with NaBH_4 and worked up to furnish 17-hydroxy heptadecanoic acid in an overall yield of 95%. Its IR spectrum is shown in Fig.1.

CHAIN-SHORTENING BY TWO CARBONS

The scheme successfully developed for chain-shortening by two carbons is shown in Fig.2.



Fig.2

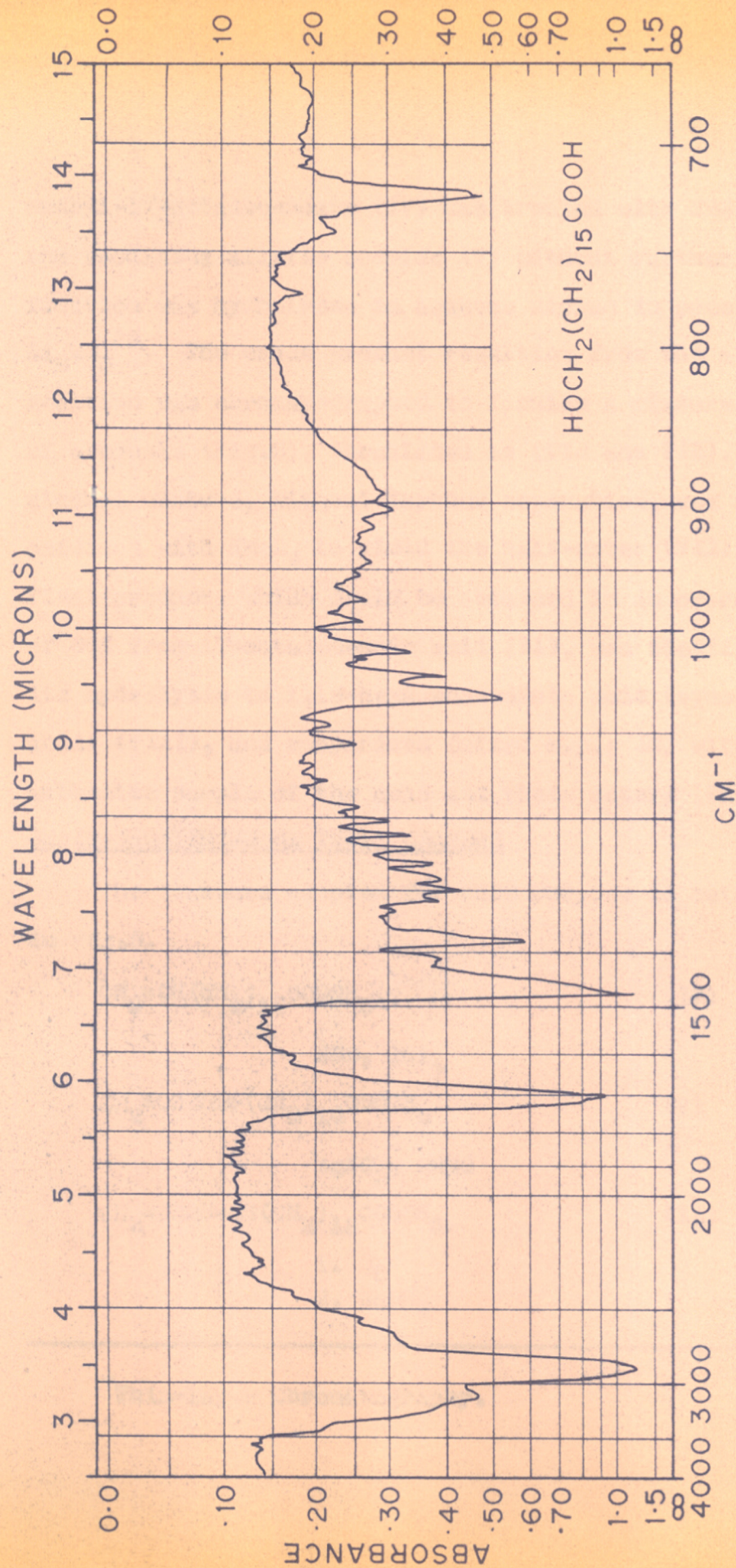
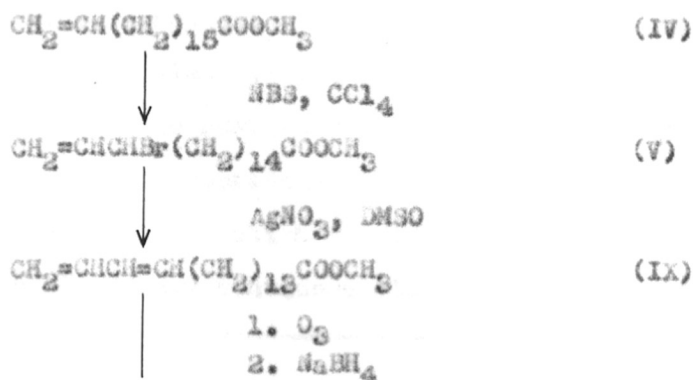


FIG. 1. IR SPECTRUM OF 17-HYDROXY HEPTADECANOIC ACID.

Methyl-17-octadecenoate (IV) was treated with NBS and the resulting allylic bromide (V) without further purification was hydrolysed in aqueous dioxan in presence of Li_2CO_3 ³⁸. The crude product resulting from the above reaction was chromatographed to furnish a mixture (TLC)* of alcohols (Fig.3), formulated as (VIa and VIb). The alcohol mixture, without further separation, was smoothly oxidised with KMnO_4 to yield the half-ester (VII). The final product, which could be obtained in an overall yield of 66% from 17-octadecenoic acid (II), was identified by its hydrolysis to 1,16-hexadecanedioic acid (synonym thapsic acid) (VIII), and comparison (mixed m.p.; IR) with an authentic sample of the acid and their esters (Fig.4).

CHAIN-SHORTENING BY THREE CARBONS

The sequence adopted for this purpose is outlined in Fig.5.



*Thin-layer Chromatography.

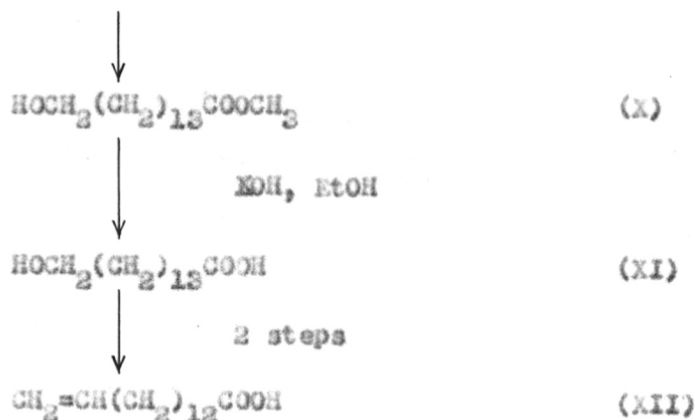


Fig.5

This reaction sequence is an adaptation of modified Barbier-Wieland degradation first introduced by Wettstein^{39,40}. The debromination step is normally carried out by heating with quinoline⁴¹ or a pyridine base⁴². When this debromination sequence was used on the allylic bromide (V) only poor yields of the diene (IX) resulted. This difficulty was successfully overcome by the use of AgNO_3 and dimethylsulphoxide, a reagent recently developed* in our laboratory. The resulting diene (IX) (λ_{max} 222.5 m μ , ϵ = 9300) was ozonised and the resulting ozonide reduced with NaBH_4 , essentially as described earlier, to yield methyl-15-hydroxy pentadecanoate (X) which was identified by its hydrolysis to the 15-hydroxy pentadecanoic acid (XI) obtained in an

*Work by G. Mehta, S.A. Patwardhan and K.C. Srivastava.

overall yield of 70%, and its comparison (mixed m.p.; IR) with an authentic sample of the acid (Fig.6).

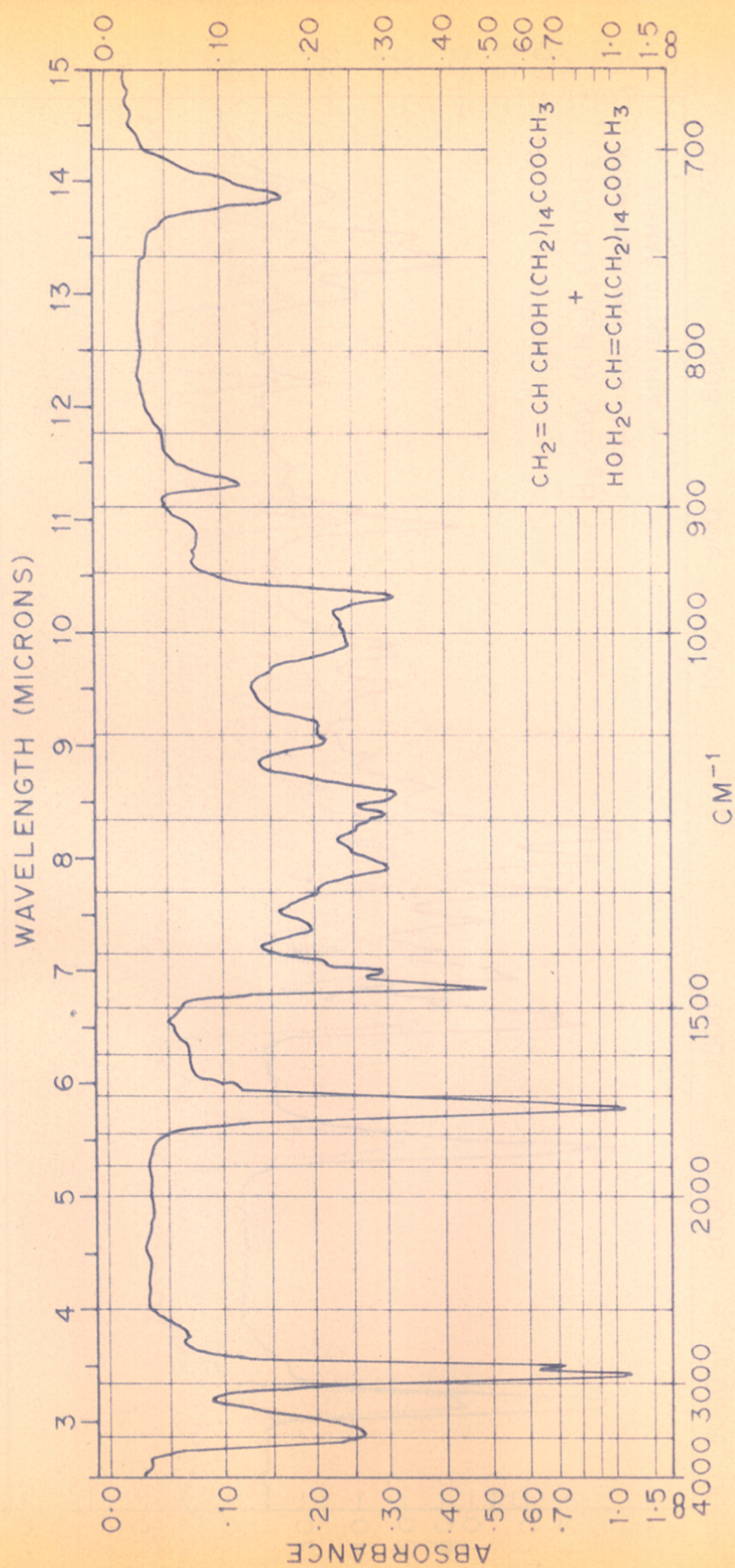


FIG. 3. IR SPECTRUM OF THE HYDROLYSIS PRODUCT OF THE BROMIDE.

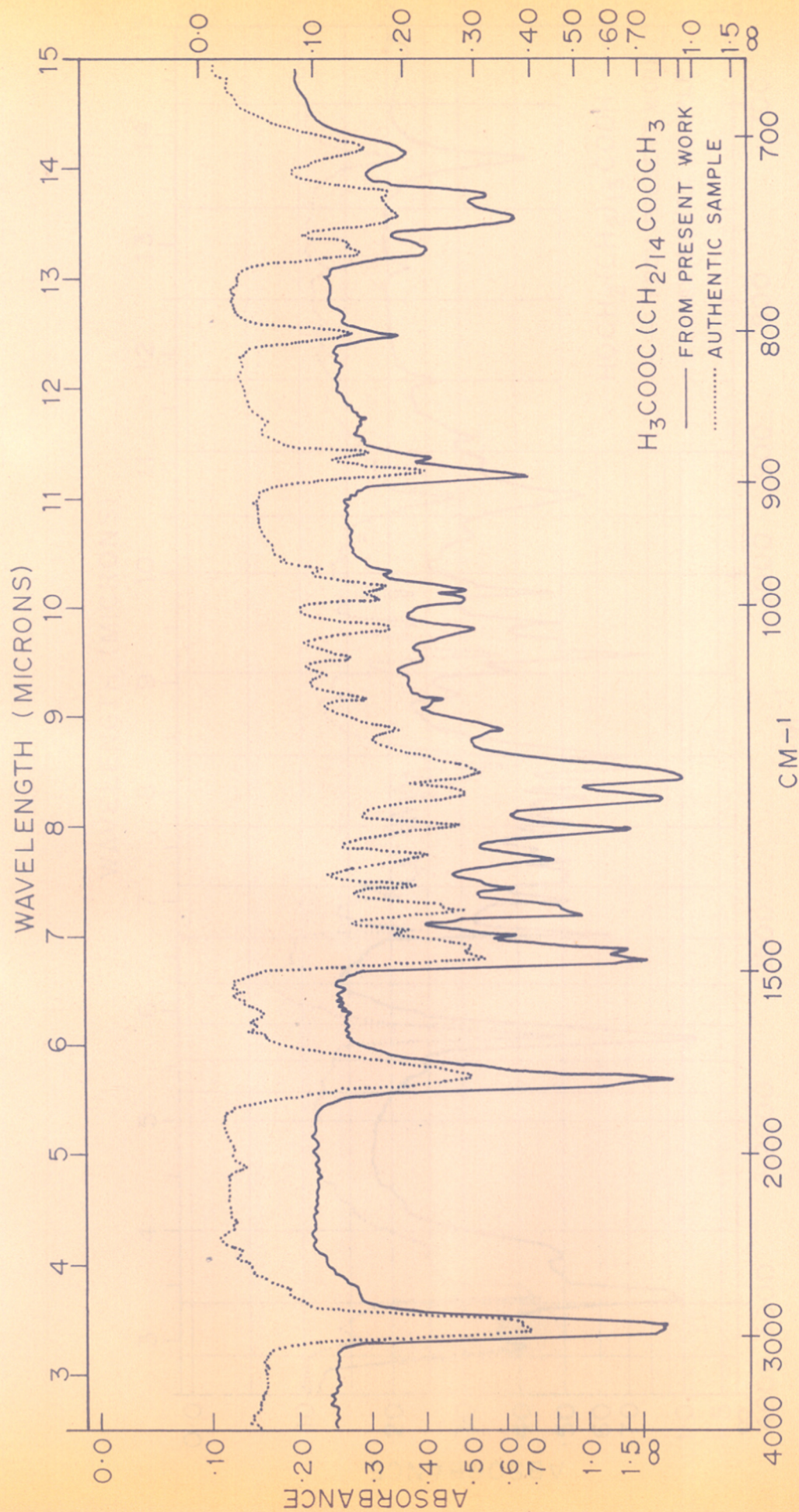


FIG. 4. IR SPECTRA OF METHYL 1,16-HEXADECANEDIOATES.

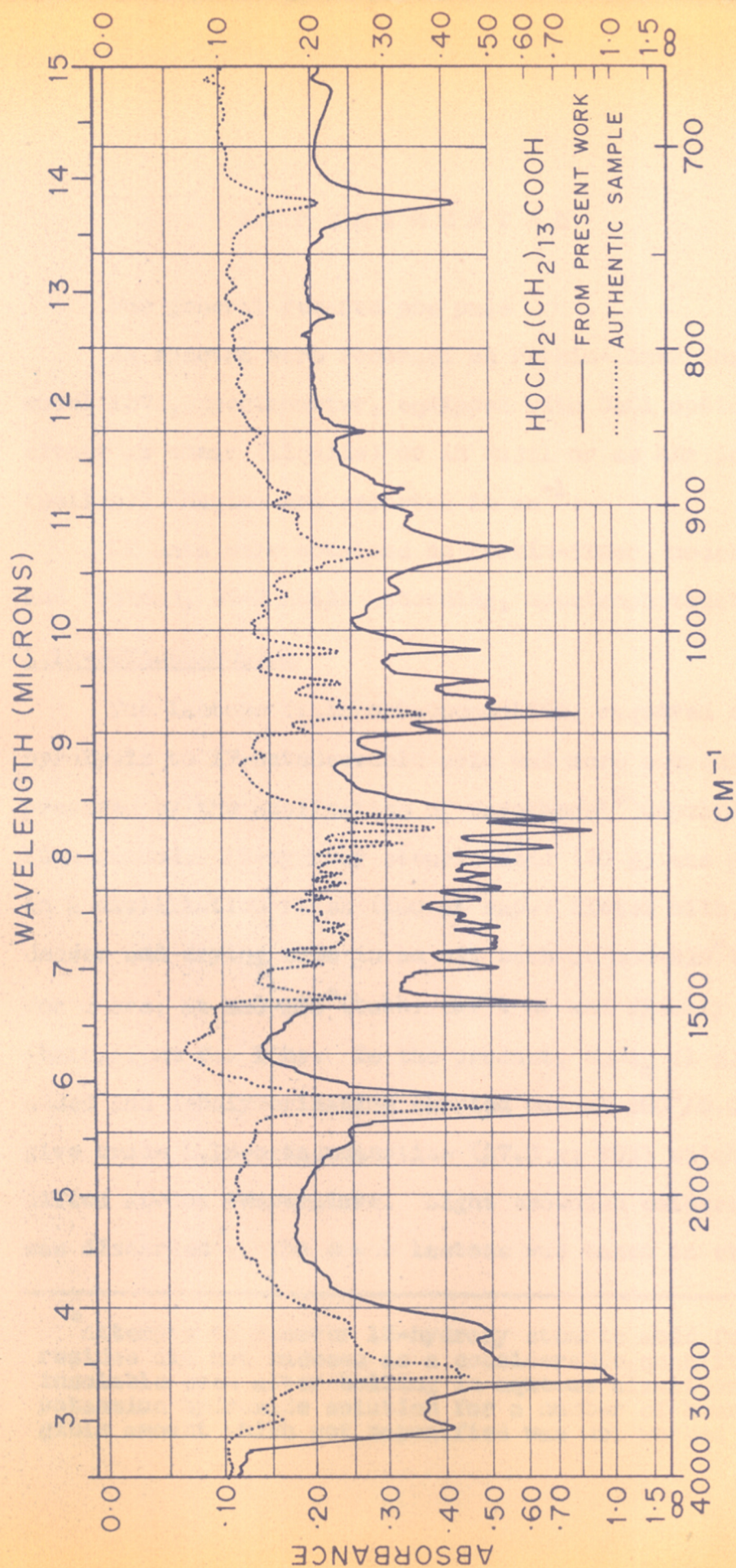


FIG. 6. IR SPECTRA (IN KBr) OF 15-HYDROXY PENTADECANOIC ACIDS.

E X P E R I M E N T A L

For general remarks see page 75 .

IR spectra were recorded on Perkin-Elmer Infracord model 137E, Spectrometer, equipped with NaCl optics, either as smear (liquids) or in Nujol or as KBr pellets (solids). Maxima are reported in cm^{-1} .

UV data were obtained on Perkin-Elmer, model 350, and Beckman, DK-2 Ratio Recording, Spectrophotometer.

1,18-OCTADECANOLIDE

The lactone (1,18-octadecanolide) required for its pyrolysis to 17-octadecenoic acid was more conveniently prepared by the application of Carothers'³ depolymerisation method. 18-hydroxy stearic acid (50 g) was heated in a distillation flask (100 ml cap.) fitted with air condenser and drying tube in an oil bath at $200-210^{\circ}$ (bath) for 2 hrs; at $220-230^{\circ}$ (bath) for 1 hr and finally at $230-240^{\circ}$ (bath)/1 mm for 1 hr. To the product, MgCl_2 (1 g) was added and depolymerisation carried out at $280^{\circ}/0.01$ mm, to give crude 1,18-octadecanolide (37.2 g; 80%) which solidified at room temperature. Light brownish coloured residue was discarded*. The crude lactone was taken in ether (300 ml)

* Attempts to recover 18-hydroxy stearic acid from the residue did not succeed as a considerable quantity remained insoluble even after boiling in aqueous alkali or alcoholic potassium hydroxide solution for a number of hours. Negligible amount which got saponified was not worked up.

extracted with aqueous sodium carbonate solution (3%; 3 x 50 ml), washed free from alkali, and dried. After removing the solvent completely, the product was dissolved in n-hexane (300 ml), chilled and filtered to give white precipitate (0.62 g) m.p. 110-112° (dilactone). Filtrate was next concentrated to ~ 150 ml; no precipitate separated on chilling, indicating the absence of dilactone. After recovering the solvent, crude mono-lactone was fractionally distilled to afford 1,18-octadecanolide (34.1 g; 72.4%), colourless liquid, b.p. 147-148°/0.8-0.9 mm. m.p. 36°. n_D^{30} 1.4659; IR spectrum: $\nu_{\text{C=O}}$ 1740 cm^{-1} . (Found: C, 76.4; H, 12.20; $\text{C}_{18}\text{H}_{34}\text{O}_2$ requires: C, 76.52; H, 12.13%).

17-Octadecenoic acid (II)

Pyrolysis of 1,18-octadecanolide

The lactone (1,18-octadecanolide) was pyrolysed as described in Chapter II. 5 g were passed through a bed maintained at 525° at reduced pressure (150 mm) during 5 hrs. Resultant pyrolysate (4.5 g; 90%) on working up*

*Alkali extraction has to be carried out carefully without much shaking in the initial stages, otherwise a thick emulsion results, and large volume of solvent becomes necessary for working up the product. Starting with dilute alkali solution and gradually increasing the concentration was found convenient.

in the usual fashion to furnish neutral fraction (1.2 g ; IR spectrum: $\nu_{\text{C=O}}$ 1738 and very similar to that of starting lactone) and a solid acid (3.1 g; 79% based on the unrecovered lactone), m.p. 52-54°; mixed m.p. with authentic sample of 17-octadecenoic acid, 52.5-54.5°. IR spectrum: COOH 1700; $\nu_{\text{CH=CH}_2}$ 1650, 916, 996 cm^{-1} .

In a second experiment, when 10 g of the lactone were passed through the reactor in 10 hrs, the pyrolysate (8.2 g; 82%) on processing gave neutral fraction (0.81 g)⁺ and unsaturated acid (6.3 g; 70% based on the unrecovered lactone) m.p. 51.5-53.5°.

The combined crude acid (9 g) on crystallisation from acetonitrile afforded shining crystalline 17-octadecenoic acid (6.2 g), m.p. 55-55.5°; mixed m.p. with an authentic sample of the acid 55-55.5°. Intense yellow colour with THM. Mother liquors were concentrated and crystallized to obtain a second crop of the acid (1.5 g) m.p. 55°.

Methyl 17-octadecenoate (IV)

17-Octadecenoic acid II (3 g) was esterified by reacting with diazomethane in ether, processed and fractionally distilled to give colourless methyl 17-octadecenoate

⁺Low yield of neutral fraction might be due to carbonisation and decomposition on the pyrolysis bed in the reactor in view of long duration.

1.3 g; 95%), b.p. $149-150^{\circ}/4$ mm.

CHAIN-SHORTENING BY ONE CARBON

17-Hydroxy heptadecanoic acid from 17-octadecenoic acid

Ozonolysis: 17-Octadecenoic acid (2 g) dissolved in absolute methyl alcohol (10 ml) was treated with ozonized oxygen at 0° till ozone passed freely (tested with acidified aqueous potassium iodide solution).

NaBH_4 reduction of the ozonide: Methanolic solution of the ozonide was then added dropwise to an ice-cold solution of sodium hydroxide (0.5 g) and sodiumborohydride (0.6 g) in 50% aqueous ethyl alcohol (10 ml), kept stirred magnetically. A gentle evolution of hydrogen resulted. The reaction mixture was slowly brought to room temperature and stirring was continued overnight. Solvent was removed under reduced pressure at room temperature and the residue after diluting with water (15 ml) was then added dropwise to an excess of ice-cold dilute hydrochloric acid (50 ml) under inert atmosphere with stirring. Precipitated acid was filtered, washed free from mineral acid with ice-cold water and dried under reduced pressure to furnish crude hydroxy acid (1.82 g; 96%), m.p. $81-83^{\circ}$. Crystallisation (twice) from benzene afforded pure white 17-hydroxy-heptadecanoic acid (1.7 g; 90%) m.p. $87.5-88^{\circ}$ (Lit. m.p. $87.5-88^{\circ}$),^{2,43}. Combined mother liquors on concentration and crystallisation furnished second crop of the hydroxy

acid (0.095 g; 5%), m.p. 87-88°. IR spectrum: OH 3226; COOH 2604, 1698 cm^{-1} . (Found: C, 71.1; H, 11.84; $\text{C}_{17}\text{H}_{34}\text{O}_3$ requires: C, 71.28; H, 11.96%).

CHAIN-SHORTENING BY TWO CARBONS

1,16-hexadecanedioic acid (Thapsic acid) (VIII) from 17-octadecenoic acid

Allylic bromination of methyl 17-octadecenoate and hydrolysis:

Methyl 17-octadecenoate (1 g) freshly crystallised NBS (0.66 g; 1:1.1 molar ratio) CCl_4 (40 ml), and benzoylperoxide (in catalytic amount) were refluxed over waterbath till succinimide floated on the surface (~30 minutes) (guard tube). Solid succinimide was filtered off and the filtrate was washed with 5% sodium carbonate solution (25 ml x 3), brine and dried. The solvent was then flashed off, when viscous liquid bromide (V) (1.28 g) was obtained. IR spectrum: $-\text{CH}=\text{CH}_2$ 917, 969; C-Br 699 cm^{-1} .

The crude bromo compound (1.2 g) was stirred with dioxan (33 ml), water (11 ml) and Li_2CO_3 (200 mg) over a waterbath for 5 hrs. The product was filtered and the filtrate concentrated (suction/warm waterbath) to ~15 ml, diluted with water (20 ml) extracted with ether (25 x 3) and washed with brine and dried. The solvent was flashed off when a viscous liquid (1.1 g) was obtained. IR spectrum: OH 3390 cm^{-1} . Preliminary test (TLC) showed the product to be a mixture and hence was fractionated chromatographically

over an alumina column.

CHROMATOGRAM

Alumina grade III : 30 g

Height of the bed : 19 cm x 1.6 cm

Wt. of the product: 1 g.

No.	Eluent	Fractions ml	Wt. (g)	Final Frn.	Appearance
1	Pet. ether (40-60°)	9 x 20	0.2261	I	Liquid
2	Ether	14 x 20	0.7601	II	Thick vis- cous liquid.
3	Ether + MeOH (5%)	8 x 20	0.0068	III	Semisolid.

After preliminary investigations (TLC; Silicagel-AgNO₃ 15%; solvent system: benzene: ethyl acetate, 9:1)⁴⁴ the fractions were combined accordingly to form three main fractions.

Fraction I: IR spectrum: bands for hydroxyl group were absent.

Fraction II: Yellow colouration by TMM. In TLC (conditions same as described earlier) the compound gave two spots partially overlapping. IR spectrum: OH 3448; COOCH₃ 1739; C=C 970 cm⁻¹. Formulated as mixture of VIa + VIb (Fig.3).

KMnO₄ oxidation of Fraction II to 1,16-hexadecanedioic acid (VIII).

The above mixture of hydroxy esters (0.48 g) was dissolved in distilled dry acetone (10 ml) and to it, finely powdered KMnO₄ was added in small lots, with stirring till

pink colour persisted in the reaction mixture. Stirring was continued for 4 hrs. Excess permanganate was decomposed with addition of aqueous solution of sodium bisulphite (5 ml), followed by dropwise addition of dilute sulphuric acid till the black precipitate dissolved and the mixture was acidic to Congo red. The liberated half ester was taken in ethyl acetate, washed free from acid and dried. Flashing off the solvent furnished crude half ester (0.42 g) which was refluxed with alcoholic solution of potassium hydroxide (5 ml; 10%) for 3 hrs. Soap solution on acidification, working up and drying in vacuo gave a solid acid (0.4 g; 91% on the basis of hydroxy esters and 66% on the starting methyl-17-octadecenoate) m.p. 118-121°. Crystallisation from acetone afforded white crystals of 1,16-hexadecanedioic acid (VIII) (0.39 g) m.p. 123-124°, mixed m.p. with an authentic sample (m.p. 124.5-125°; Lit.¹²⁴/125, 125.1°)⁴⁶⁻⁴⁸ 123.5-124.5°. IR spectrum: COOH 2710, 1708 cm^{-1} ; superimposable on the spectrum obtained for the authentic sample (Found: C, 66.78; H, 10.42; $\text{C}_{16}\text{H}_{30}\text{O}_4$ requires: C, 67.09; H, 10.56%).

The dicarboxylic acid (62 mg) was esterified by reacting with CH_3NH_2 in ether, worked up and distilled (bulb) b.p. 160-165°/0.2 mm m.p. 51-51.5°, mixed m.p. with authentic ester (m.p. 51.5; Lit. 51.6°) 51.5°. IR spectrum: COOCH_3 , 1755 cm^{-1} . (Fig.4).

CHAIN-SHORTENING BY THREE CARBONS15-hydroxy pentadecanoic acid (XI) from 17-octadecenoic acidAllylic bromination of methyl-17-octadecenoate

Allylic bromination was carried out by reacting methyl-17-octadecenoate (0.5 g), freshly crystallised NBS (0.32 g), CCl_4 (20 ml) and benzoyl peroxide (catalytic amount), according to the method described previously and on working up the reaction mixture furnished bromo compound (V) (0.64 g).

Dehydrobromination of bromo ester (V)

To a solution of silvernitrate (0.34 g) in dimethylsulphoxide (1 ml) (dissolved by warming), the above bromo ester dissolved in DM30 (2 ml) was added dropwise at 15° , when light yellow precipitate separated immediately. The reactants were mixed thoroughly by shaking and kept in dark at 15° for 1 hr with occasional shaking. The precipitate was separated by filtration and washed with benzene (5 ml). Filtrate was poured into cold water (25 ml), followed by extraction with chloroform (5 ml x 3). The solvent extract washed with water, brine and dried. Removal of the solvent in cold at reduced pressure furnished the liquid diene ester (IX) (0.5 g). UV spectrum: λ_{max} 222.5 m μ ϵ = 9300.

15-hydroxy pentadecanoic acid (XI)

The above diene ester (0.48 g), dissolved in absolute

methanol (5 ml), was ozonised in the usual fashion at 0°.

The ozonide was reduced by adding its methanolic solution (dropwise) to a solution of sodium hydroxide (0.4 g), NaBH_4 (0.45 g) in 50% aqueous ethanol (5 ml) at 0°. After stirring the reaction mixture overnight at room temperature, the product was processed according to the procedure described previously, and the resultant hydroxy ester on hydrolysis in the usual way afforded solid acid (0.42 g) m.p. 77-81°. Repeated crystallisation from acetone-acetonitrile furnished white crystalline 15-hydroxypentadecanoic acid (XI) (0.3 g; 70%) m.p. 83-84°; mixed m.p. with authentic sample (m.p. 84.5-85°; Lit. 84.5-85°) 84-85°. IR spectrum: (in KBr): OH 3400; COOH 2675, 1726 cm^{-1} , superimposable on the spectrum obtained for the authentic sample (Fig.6). (Found: C, 69.3; H, 11.9; $\text{C}_{15}\text{H}_{30}\text{O}_2$ requires: C, 69.7; H, 11.7%).

SUMMARY

Conversion of 17-octadecenoic acid into, 17-hydroxy-heptadecanoic, 1,16-hexadecanedioic acid and 16-hydroxy pentadecanoic acid by methods enabling the cleavage of one carbon, two carbons and three carbons at a time, respectively has been described. The methods are obviously general in character.

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ACKNOWLEDGEMENT

It is my privilege to express my unstinted debt of gratitude to Dr. SUKH DEV, Ph.D, D.Sc., for the inspiring and patient guidance I received and for his endearing disposition towards me throughout these investigations.

My sincerest thanks are due to many colleagues:

Shri V.S.Pansare and colleagues for microanalyses; Kum. L.V. Shirole, Dr.C.I.Jose, Sarvashri H. Gopinath, T.K.K.Srinivasan, R.G. Bhandari and Kum. P. Gokhale for IR spectra; Sarvashri V.K.Bhalerao, K.G. Deshpande and Mrs H.V.Kamath for UV spectra; Shri I.S. Mulla for PMR spectra; and Drs.V.G.Naik and T.C.Jain for GLC data.

I am particularly thankful to Shri Miranjan Singh Gyani and colleagues for the construction of special apparatus and all glass-blowing work.

In an acknowledgement of this kind, it is virtually impossible to mention all my friends, colleagues and well-wishers, on whose forbearance and patience I laid claim from time to time in connection with this work. I am deeply indebted to them all and may I be forgiven for not giving them due credit individually.

Finally, I am grateful to the Director, National Chemical Laboratory, Poona, for kindly permitting me to submit this thesis.

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30th December 1965