Synthesis and Properties of Mono-, Di- and Trienoic Fatty Esters Containing a 12,13 Double Bond[1]

H. RAKOFF and E.A. EMKEN, Northern Regional Research Center, Agricultural Research Service, USDA, Peoria, IL 61604

ABSTRACT

Methyl *trans*-12-octadecenoate-9,10-d_2 was obtained from methyl *threo*-12,13-dihydroxy-*cis*-9-octadecenoate by a sequence of reactions involving formation of an ethoxydioxolane, catalytic deuteration of the double bond, and conversion of the ethoxydioxolane group to an ethylenic bond. Methyl *cis*- and *trans*-12-octadecenoate-15,15,16,16-d_4 and methyl *cis*- and *trans*-12-octadecenoate-9,10,15,15,16,16-d_6 were obtained from the Wittig coupling of hexyl-3,3,4,4-d_4-triphenylphosphonium bromide with methyl 12-oxododecanoate and methyl 12-oxododecanoate-9,10-d_2, respectively. The four geometrically isomeric methyl 12,15-octadecadienoates-9,10-d_2 were prepared by the Wittig reaction between *cis*- or *trans*-3-hexenyltriphenylphosphonium bromide and methyl 12-oxododecanoate-9,10-d_2 with butyl lithium in ethyl ether. The Wittig reaction between hexyl-3,3,4,4-d_4-triphenylphosphonium bromide and methyl 12-oxo-*cis*- or *trans*-9-dodecenoate was used to prepare the four geometric isomers of methyl 9,12-octadecadienoate-15,15,16,16-d_4, whereas the same reaction between *cis*- or *trans*-3-hexenyltriphenylphosphonium bromide and methyl 12-oxo-*cis*- or *trans*-9-dodecenoate afforded the eight geometrically isomeric methyl 9,12,15-octadecatrienoates. In each case, the stereochemistry of the double bond formed in the Wittig reaction was controlled by choice of reaction conditions. Pairs of isomers formed during each synthesis were separated by partial silver resin chromatography. Physical constants presented include ^{13}C nuclear magnetic resonance chemical shifts, melting points, equivalent chain lengths and percentage *trans* by infrared spectroscopy.

INTRODUCTION

For a number of years, we have been engaged in a study of the metabolism in humans of isomeric fats formed during the hydrogenation of soybean oil (1,2). For this purpose, deuterated analogs of many of these compounds have been synthesized by us (3-12). Various methods for preparing deuterated fatty esters have been reviewed (13). This paper will cover the preparation of deuterium labeled geometrical isomers of methyl 12-octadecenoate, methyl 12,15-octadecadienoate and methyl 9,12-octadecadienoate, since compounds with a double bond in the 12,13 position display especially significant metabolic characteristics (1). Our discussion will then extend to the preparation and properties of the eight geometrically isomeric methyl 9,12,15-octadecatrienoates since the ω-3 fatty esters are also of current metabolic interest.

PREPARATION

Preparation of Deuterated Methyl 12-Octadecenoates

The Wittig reaction was used in the synthesis of all the compounds except methyl *trans*-12-octadecenoate-9,10-d_2. Reagents and products of the Wittig reactions are summarized in Figure 1. Methyl *cis*- and *trans*-12-octadecenoate-15,15,16,16-d_4,3, were obtained (6) from the Wittig coupling of hexyl-3,3,4,4-d_4-triphenylphosphonium bromide, 1, with methyl 12-oxododecanoate, 2, in dimethylformamide solution with sodium methoxide. The mixture of *cis* and *trans* isomers that formed (86% *cis*) was separated by silver resin chromatography.

Larger quantities of *trans* isomer were obtained by isomerizing the *cis* isomer with nitrous acid (14). This gave a product mixture containing 81% *trans* isomer, which was separated by silver resin chromatography.

The reaction of the tetradeuterated phosphonium salt, 1, with a deuterated aldehyde ester, 4, methyl 12-oxododecanoate-9,10-d_2, afforded methyl *cis*- and *trans*-12-octadecenoate-9,10,15,15,16,16-d_6, 5 (6). The isomers were separated on the silver resin column, and larger quantities of *trans* isomer were prepared by nitrous acid isomerization of the *cis* isomer followed by silver resin chromatography.

For the preparation of methyl *trans*-12-octadecenoate-9,10-d_2, a reaction described by Eastwood and coworkers (15,16) and applied to fatty acids by us (7) was used. Methyl *threo*-12,13-dihydroxy-*cis*-9-octadecenoate was treated with triethyl orthoformate and benzoic acid to form methyl 12,13-di-O-(ethoxymethylene)-*cis*-9-octadecenoate as shown in Figure 2 (6). Reduction of this compound with deuterium in the presence of Wilkinson's catalyst, $[(C_6H_5)_3P]_3RhCl$, gave methyl 12,13-di-O-(ethoxymethylene)-octadecanoate-9,10-d_2. Thermal decomposition of the dideutero compound at 210 C gave a mixture (93% *trans*) of methyl *cis*- and *trans*-12-octadecenoate-9,10-d_2 from which the *trans* isomer was separated by silver resin chromatography.

Preparation of Deuterated Methyl 9,12- and 12,15-Octadecadienoates

For the preparation of a methylene-interrupted diene by the Wittig reaction, one of the two reagents, the aldehyde ester or the phosphonium salt, must contain a double bond. Due to the propensity of β, γ-unsaturated aldehyde esters to isomerize to the α, β-unsaturated aldehyde ester, Bergelson and Shemyakin (17) recommended placing the double bond in the phosphonium salt. This recommendation was followed in the preparation of the methyl 12,15-octadecadienoate-9,10-d_2 isomers, 9, (4).

cis- or *trans*-3-hexenyltriphenylphosphonium bromide, 8, (Fig. 1) was coupled with methyl 12-oxododecanoate-9,10-d_2, 4, in ethyl ether in the presence of butyl lithium to give the dienoic ester, 9. With the *cis* phosphonium salt, the product mixture contained ca. 80% 12*c*,15*c* and ca. 20% 12*t*,15*c* isomers. With the *trans* phosphonium salt, the product mixture contained ca. 80% 12*c*,15*t* and ca. 20% 12*t*,15*t* isomers. These binary mixtures were readily separated by partial silver resin chromatography (18).

We required substantial amounts of all the isomers.

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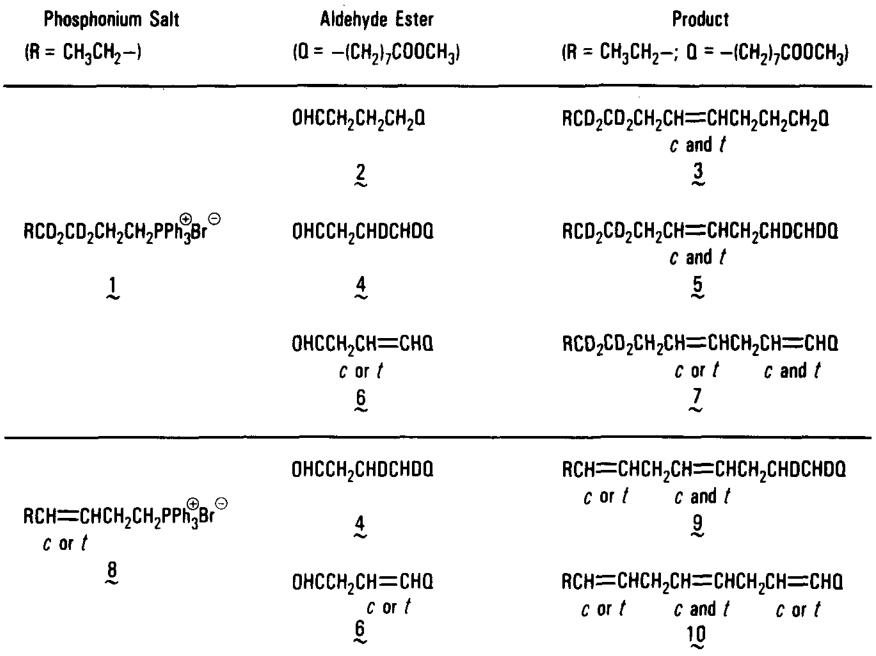
[1] Presented in part at the 73rd AOCS annual meeting, Toronto, 1982.



Phosphonium Salt ($R = CH_3CH_2-$)	Aldehyde Ester ($Q = -(CH_2)_7COOCH_3$)	Product ($R = CH_3CH_2-$; $Q = -(CH_2)_7COOCH_3$)
	$OHCCH_2CH_2CH_2Q$ 2	$RCD_2CD_2CH_2CH{=}CHCH_2CH_2CH_2Q$ c and t 3
$RCD_2CD_2CH_2CH_2\overset{\oplus}{P}Ph_3\overset{\ominus}{Br}$ 1	$OHCCH_2CHDCHDQ$ 4	$RCD_2CD_2CH_2CH{=}CHCH_2CHDCHDQ$ c and t 5
	$OHCCH_2CH{=}CHQ$ c or t 6	$RCD_2CD_2CH_2CH{=}CHCH_2CH{=}CHQ$ c or t c and t 7
$RCH{=}CHCH_2CH_2\overset{\oplus}{P}Ph_3\overset{\ominus}{Br}$ c or t 8	$OHCCH_2CHDCHDQ$ 4	$RCH{=}CHCH_2CH{=}CHCH_2CHDCHDQ$ c or t c and t 9
	$OHCCH_2CH{=}CHQ$ c or t 6	$RCH{=}CHCH_2CH{=}CHCH_2CH{=}CHQ$ c or t c and t c or t 10

FIG. 1. Fatty esters synthesized via Wittig reaction.

Nitrous acid isomerization of either of the reaction mixtures would yield a complex mixture containing all four isomers. This mixture could not be completely separated because it is not possible to separate the components in a *ct/tc* mixture by silver resin chromatography.

Anderson and Henrick (19) have demonstrated a method for increasing the percentage of *trans* bonds formed during the Wittig reaction. Their method involves partial equilibrium of the relatively unstable betaine intermediate at −40 to −70 C in the presence of methanol or ethanol. This procedure was used (4) to obtain 60-65% *trans* geometry in the double bond generated in the Wittig reaction. In this way we were able to prepare synthetically useful amounts of the 12*t*,15*c* and the 12*t*,15*t* isomers.

Adlof and Emken (3) prepared methyl *cis*-9,*cis*-12-octadecadienoate-16,16,17,17-d_4 by the Wittig coupling between methyl 9-oxononanoate (available from the ozonization of methyl oleate) and *cis*-3-nonenyl-7,7,8,8-d_4-triphenylphosphonium bromide. This deuterated phosphonium salt was obtained by a seven-step synthesis from 3-pentynol and involved an acetylenic coupling in liquid ammonia and a Lindlar reduction. As a consequence, the 9*c*,12*c* isomer was accompanied by ca. 10% of the other three isomers. These contaminants were removed by partial silver resin chromatography.

To obtain all four isomers in synthetically useful amounts, we developed a synthesis based on our experience in preparing the 12,15-isomers. Hexyl-3,3,4,4-d_4-triphenylphosphonium bromide, **1**, (Fig. 1) was coupled, in the presence of butyl lithium in tetrahydrofuran, with methyl 12-oxo-*cis*- or *trans*-9-dodecenoate, **6**, to give mixtures containing 9*c*,12*c* and 9*c*,12*t* or 9*t*,12*c* and 9*t*,12*t*-octadecadienoates-15,15,16,16-d_4, **7**. The relative percentages of the isomers in each binary mixture were varied by controlling the temperature of the Wittig reaction as described for the synthesis of the 12,15 isomers. In this way, all four isomers were obtained.

Problems involved in working with the unsaturated aldehyde ester will be discussed later.

Preparation of Methyl 9,12,15-Octadecatrienoates

Intermediates prepared for the synthesis of methyl 9,12- and of methyl 12,15-octadecadienoates can also be used to prepare all eight geometrically isomeric methyl 9,12,15-octadecatrienoates, as shown in Table I.

Each reaction yields a mixture of only two isomers, which can be separated on a 60% Ag/Na silver resin chromatography column (70% Ag/H for the *ttt*,*tct* separation). The preparation of these binary mixtures, **10**, was accomplished (5) by treating *cis*- or *trans*-3-hexenyltriphenylphosphonium bromide, **8**, (Fig. 1) with methyl 12-oxo-*cis*- or *trans*-9-dodecenoate, **6**, with butyl lithium in tetrahydrofuran.

TABLE I

Binary Mixtures from Geometrically Isomeric Reactants

Configurations in:		
Aldehyde ester	Phosphonium salt	Methyl 9,12,15-octadecatrienoate
cis	*cis*	*ccc* and *ctc*
trans	*cis*	*tcc* and *ttc*
cis	*trans*	*cct* and *ctt*
trans	*trans*	*tct* and *ttt*

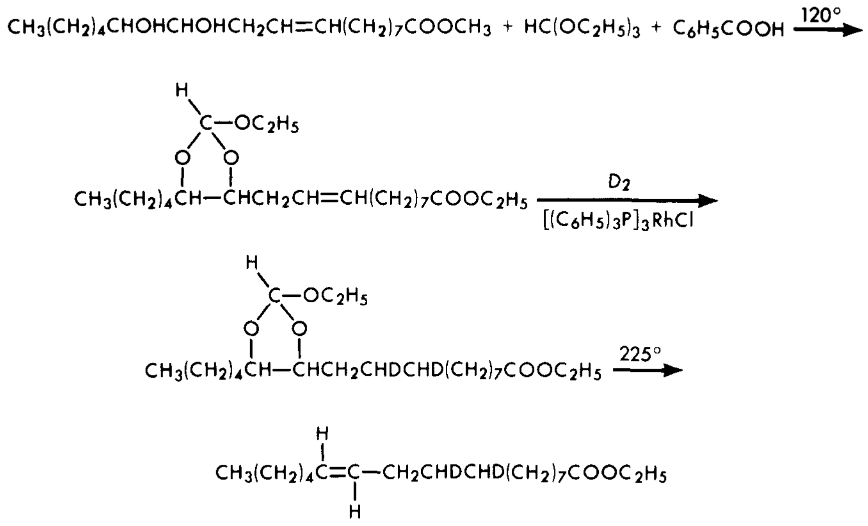


FIG. 2. Synthesis of methyl *trans*-12-octadecenoate-9,10-d_2.

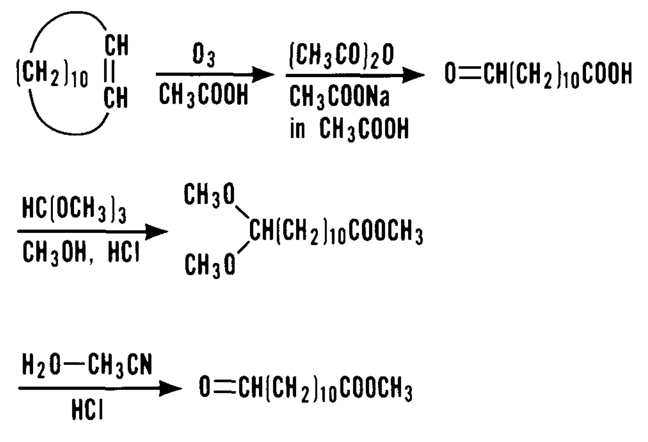


FIG. 3. Synthesis of methyl 12-oxododecanoate.

The relative proportions of the components of each mixture were varied as in the preparation of the isomeric dienes.

Preparation of Aldehyde Esters

Methyl 12-oxododecanoate was obtained from the ozonolysis of cyclododecene (6), (Fig. 3). Cyclododecene was ozonized in glacial acetic acid. Reaction of the viscous mass with acetic anhydride and sodium acetate in glacial acetic acid formed the aldehyde acid, which was converted to the acetal ester on reaction with trimethyl orthoformate. Acid hydrolysis then yielded the aldehyde ester.

Methyl *threo*-12,13-dihydroxy-*cis*-9-octadecenoate (methyl dihydroxyoleate) obtained from *Vernonia anthelmintica* seed oil (6,20) was used as a starting material for the other aldehyde esters required. *Vernonia* oil contains about 79% of glycerides of vernolic acid, 12,13-epoxy-*cis*-9-octadecenoic acid. Acetolysis and saponification of the oil yields a mixture of dihydroxyoleate and nonhydroxy esters. The methyl dihydroxyoleate is separated most conveniently by reverse-phase high performance liquid chromatography (HPLC) on a Waters Associates Prep Pak-500/C18 column with the solvent system acetonitrile/water = 90:10.

Methyl 12-oxododecanoate-9,10-d_2, 4, was obtained (4, 6) from methyl dihydroxyoleate, 11, as shown in Figure 4. Deuterium was added to dihydroxyoleate, 11, in the presence of Wilkinson's catalyst, $[(C_6H_5)_3P]_3RhCl$. Periodic acid cleavage of the dihydroxydideuterostearate, 12, gave the desired aldehyde ester, but this material trimerized in the receiver of the distillation apparatus (6). Numerous attempts to prevent this trimerization were unsuccessful, and this approach was abandoned when it was found that cleavage with lead tetraacetate (generated *in situ* from red

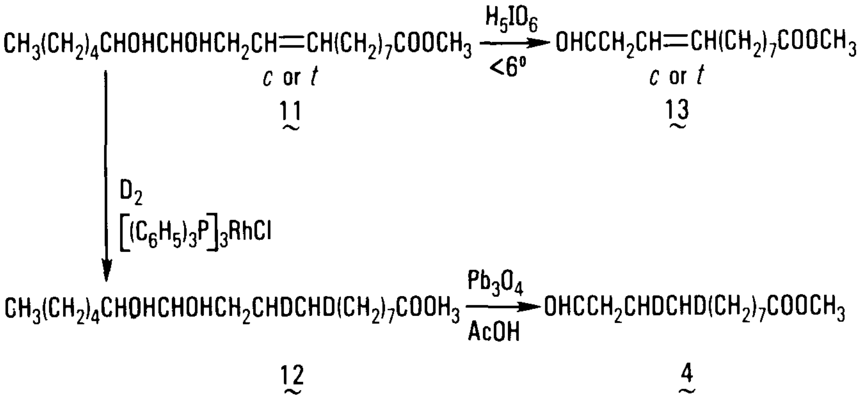


FIG. 4. Preparation of aldehyde esters.

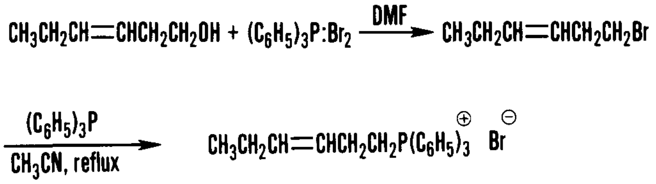


FIG. 5. Synthesis of *cis-* or *trans-*3-hexenyltriphenylphosphonium bromide.

lead and acetic acid) would give the desired aldehyde ester, 4, without trimerization.

Methyl 12-oxo-*cis-* or *trans-*9-dodecenoate, **13**, was obtained by periodic acid oxidation below 6 C (21) of methyl 12,13-dihydroxy-*cis-* or *trans-*9-octadecenoate, 11 (Fig. 4). (The *trans-*dihydroxy ester was obtained by nitrous acid isomerization (20) of the naturally occurring *cis* isomer.)

Oxidation at room temperature yields predominantly the conjugated aldehyde ester, methyl 12-oxo-*trans-*10-dodecenoate. The nonconjugated aldehyde ester isomerizes partially during silica gel chromatography or ordinary distillation. It may be distilled without isomerization in a falling film molecular still (0.05 torr, refluxing xylene). The extent of isomerization cannot be determined by gas liquid chromatography because the aldehyde ester conjugates partially in the gas chromatograph. It can, however, be measured by infrared spectroscopy since, in the nonconjugated aldehyde ester, the two carbonyl bands overlap at ca. 1740 cm^{-1}, whereas in the conjugated aldehyde ester, two bands of equal and large intensity (at 1740 cm^{-1} and 1690 cm^{-1}) are obtained. The presence of 5% conjugated isomer in nonconjugated aldehyde ester can easily be detected.

Preparation of Phosphonium Salts

The *cis-* or *trans-*3-hexenyltriphenylphosphonium bromide, **8**, was obtained from *cis-* or *trans-*3-hexenol (4) as shown in Figure 5. The ethylenic alcohol was converted to the bromide by reaction with triphenylphosphine dibromide in dimethylformamide (22) or, more conveniently, in dichloromethane (3). The phosphonium bromide was obtained by reaction of the unsaturated bromide with triphenylphosphine in acetonitrile. Reaction in xylene gives an unidentified product that does not undergo a Wittig reaction.

3-Hexynol served as the starting material for the preparation of hexyl-3,3,4,4-d_4-triphenylphosphonium bromide, **1**. The acetylenic alcohol was converted to the tetrahydropyranyl ether to obviate exchange with the hydrogen of the hydroxy group during deuteration in the presence of $[(C_6H_5)_3P]_3RhCl$. The hexyl-d_4-tetrahydropyranyl ether thus obtained contained 94% d_4. The saturated THP ether was converted to the iodide by the method of Stone and Shechter (23) or to the bromide as shown in Figure 5. The halide was converted to the phosphonium halide by refluxing with triphenylphosphine in xylene.

PROPERTIES

^{13}C NMR chemical shifts for the four isomeric methyl 12,15-octadecadienoates-9,10-d_2 are presented in Table II and for the eight geometrically isomeric methyl 9,12,15-octadecatrienoates in Table III. The chemical shifts of the isomeric 9,12-18:2 isomers and of the 12-18:1 isomers have already been published by others (24,25).

The chemical shifts for all carbons are what would be calculated using the parameters available in the literature (24,25). Each of the 12,15-18:2-d_2 isomers and each of the 9,12,15-18:3 isomers has unique chemical shifts which

TABLE II

Observed Chemical Shifts[a] for the Isomeric Methyl 12,15-Octadecadienoates-9,10-d_2

Isomer[b]	Carbon number												
	1	2	3	4–10	11	12	13	14	15	16	17	18	OCH_3
12*c*,15*c*-18:2	174.30	34.18	25.02	29.31–29.51	27.17	130.24	128.03	25.61	127.51	131.80	20.60	14.30	51.41
12*t*,15*c*-18:2	174.30	34.12	25.02	29.44	32.43	130.83	128.36	30.35	127.25	132.06	20.47	14.30	51.34
12*c*,15*t*-18:2	174.30	34.18	25.02	29.31–29.57	27.04	130.50	127.84	30.48	127.51	132.38	25.61	13.84	51.41
12*t*,15*t*-18:2	174.30	34.18	25.02	29.31–29.96	32.50	131.15	128.68	35.68	127.77	132.58	25.61	13.91	51.41

[a] ppm Downfield from $(CH_3)_4Si$.

[b] The abbreviation for a given compound in this table follows the pattern pg-N:d where d is the number of double bonds in a fatty acid chain of N carbons while p is the position and g is the geometry (*cis* or *trans*) of the double bond(s).

TABLE III

Observed Chemical Shifts for Selected Carbons of the Isomeric Methyl 9,12,15-Octadecatrienoates

Isomer (9,12,15)	Carbon number										
	8	9	10	11	12	13	14	15	16	17	18
c,c,c	27.25	130.30	127.85	25.70	128.35	128.35	25.60	127.20	132.00	20.60	14.25
c,c,t	27.20	130.25	127.90	25.60	128.60	128.10	30.40	127.20	132.55	25.50	13.75
c,t,c	27.20	130.55	127.75	30.45	128.90	128.95	30.35	127.10	132.25	20.55	14.30
t,c,c	32.50	130.90	128.00	30.45	128.15	128.60	25.50	127.25	131.90	20.55	14.25
t,t,c	32.50	131.10	128.55	35.55	129.15	129.10	30.30	127.05	132.20	20.50	14.25
t,c,t	32.60	130.95	128.30	30.45	128.40	128.40	30.45	127.30	132.55	25.60	13.90
c,t,t	27.15	130.45	127.70	30.45	129.05	129.15	35.55	127.55	132.70	25.55	13.85
t,t,t	32.45	131.15	128.60	35.50	129.40	129.40	35.55	127.55	132.75	25.50	13.75

TABLE IV

Equivalent Chain Lengths of Methyl Monoenoates and Dienoates

	Isomer							
	9,12-18:2		12,15-18:2		12-18:1			
Configuration	d_0^a	d_4	d_0^a	d_2	d_0^a	d_2	d_4	d_6
c					18.75	18.74	18.72	18.70
t					18.54	18.52	18.50	18.48
cc	19.51	19.46	19.81	19.79				
tc	19.40	19.36	19.62	19.59				
ct	19.32	19.27	19.52	19.49				
tt	19.13	19.09	19.32	19.29				

[a]Reference 26.

TABLE V

Properties of Methyl 9,12,15-Octadecatrienoates

Isomer (9,12,15)	*ttt*	*tct*	*ctt*	*ttc*	*cct*	*tcc*	*ctc*	*ccc*
ECL values	19.93	20.12	20.11	20.23	20.20	20.38	20.39	20.52
R_f values	0.52	0.48	0.46	0.46	0.41	0.40	0.35	0.31
% *trans*	258	175	165	165	95	100	78	–
mp	−3.5	−45.5	−43.5	−50.5	−60	−57	−52 β'-54.5	−57

may be used to identify it.

The chemical shifts are the same for the ethylenic carbons of the 12,13-double bond in 9,12,15-18:3 when the configurations of the 9,10 and 15,16 double bonds are the same, reflecting similar magnetic influence on these carbons.

Equivalent Chain Lengths

Equivalent chain lengths for methyl 12-octadecenoates and for the 9,12 and 12,15-octadecadienoates are presented in Table IV. It is apparent from these tables that the deuterated isomers elute more rapidly from the Silar 10C column than do the undeuterated isomers and that the difference in equivalent chain lengths (ECL) is proportional to the number of deuterium atoms; it is ca. 0.01 ECL unit for each deuterium atom. We thus confirm with specifically deuterated pure fatty esters on Silar 10C the observation of Patton and Lowenstein (27) on EGSSX with mixtures of deuterated fats produced by perfused rat livers that relative retention times of deuterated and nondeuterated fatty acids are inversely proportional to the average number of deuterium atoms.

Scholfield (26) has reported ECL values for the isomeric methyl 9,12,15-octadecatrienoates, but since he had complex mixtures and identification was based on relative

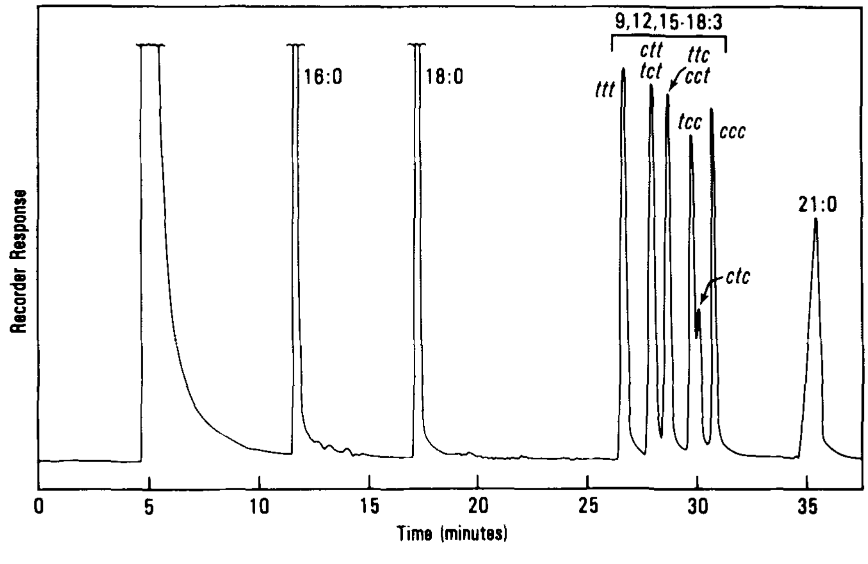


FIG. 6. Gas liquid chromatogram of a mixture of all isomeric methyl 9,12,15-octadecatrienoates on a 50 m × 0.25 mm id Silar 10C Quadrex glass capillary column. Column temperature 170 C.

TABLE VI

Melting Points (C) by DSC of Isomeric Methyl Monoenoates and Dienoates

18:2-d$_4$		18:2-d$_2$		12*t*-18:1	No. of D atoms	12*c*-18:1
9*c*,12*c*	—44.5	12*c*,15*c*	—25.5	15.5	d$_2$	—10.5
9*c*,12*t*[a]	—45.5	12*c*,15*t*	—17	11.5	d$_4$	—3
9*t*,12*c*[b]	—31.5	12*t*,15*c*	—14	13	d$_6$	—3
9*t*,12*t*	—12.5	12*t*,15*t*	—2.5			

[a] Also, —51 C.

[b] Also, —33.5, —39 C.

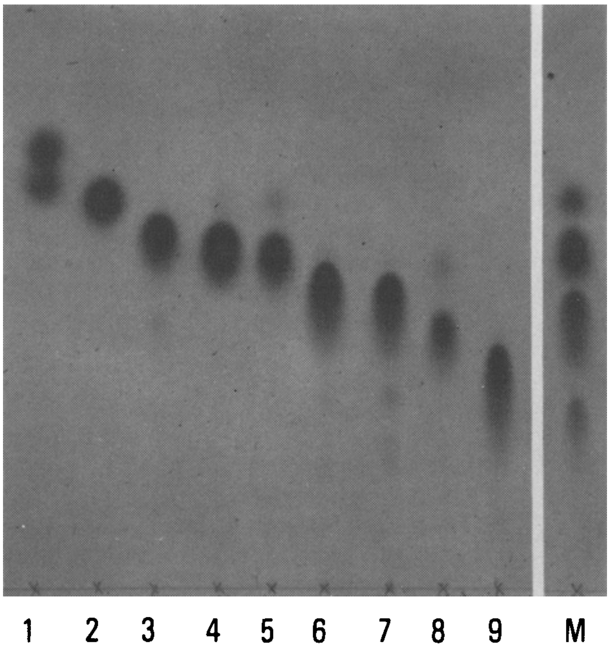


FIG. 7. Thin layer chromatogram of methyl *cis*- and *trans*-9-octadecenoate (lane 1), methyl 9,12,15-octadecatrienoates (lane no., configuration of 9,12,15) 2,*ttt*; 3,*tct*; 4,*ctt*; 5,*tcc*; 6,*cct*; 7,*tcc*; 8,*ctc*; 9,*ccc*, and a mixture of them (M, 10 µL). Silica gel 60 F254 plate impregnated with AgNO$_3$. Solvent system: benzene ethyl ether = 85.15.

position in countercurrent distribution and on comparison with values published by Ackman and Hooper (28) for Silar 5CP, some of the assignments were tentative. Our results agree closely (within 0.01 unit) for four of the isomers and differ for the other four. Our results are presented in Table V.

Figure 6 is a gas liquid chromatogram of a mixture of all the isomers on Silar 10C. The eight isomers give six peaks, two of which are not completely separated. The assignments of the various compounds to the various peaks is based on the ECL of these peaks compared to the ECL in the binary mixtures. It is interesting to note the symmetry in the elution pattern: *ttt, tct, ctt, ttc, cct, tcc, ctc, ccc.* A *trans* on one side of the pattern is matched by a *cis* on the other side. This results in one peak containing both a mono *trans* and a di *trans*. This fact was recognized, but the compounds were not identified by Strocchi and Piretti (29).

Melting Points

Melting points were determined by differential scanning calorimetry and were read to 0.5 C. The results obtained with the monoenoic and dienoic esters are presented in Table VI and those with the trienoic esters in Table V. In all cases, as expected, the all *trans* isomer has the highest melting point.

Percent *trans* by Infrared

Percent *trans* of the various isomers was determined by the method of Allen (30). In this procedure methyl *trans*-9-octadecenoate is assigned the value 100% *trans* and other esters are compared with it. On this basis previous investigators (31) have reported a value of 166% *trans* for a *trans,trans* diene and 85% *trans* for a *cis,trans* diene. Our results for the diene isomers are consistent with these observations. The results for the isomeric trienes are presented in Table V. The value for the *ttt* isomer is ca. 3 X

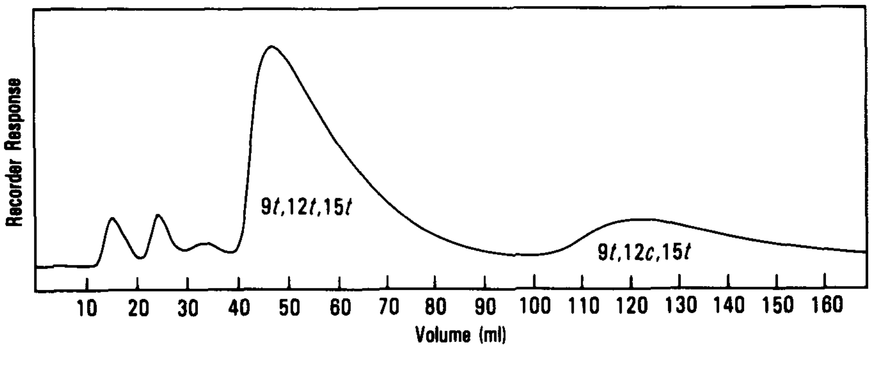


FIG. 8. Separation of 117 mg of 2:1 mixture of methyl *ttt* and *tct*-9,12,15-octadecatrienoates on a 0.67 X 70 cm column of XN1010 (60/80 mesh) 70% Ag/H. Eluent, methanol, 1 mL/min. Jacket temperature 30 C.

85% and that for the di *trans*, mono *cis* isomers is ca. 2 X 85%. The values for the mono *trans*, di *cis* isomers seem to be furthest from what would be predicted.

Thin-Layer Chromatography

Figure 7 is a picture of a thin layer chromatogram of all the isomeric trienes and a mixture of them on $AgNO_3$-impregnated Silica Gel 60F254. The mixture of all eight isomers gives four spots corresponding to the tri *trans*, the di *trans*, the mono *trans* and the all *cis* isomers. The 9*t*,12*t*,15*t* isomer has the same R_f as methyl oleate and its presence could easily be undetected in a sample containing methyl oleate.

The R_f values as well as other properties of methyl 9,12,15-octadecatrienoates are presented in Table V. The order of the equivalent chain lengths, the TLC R_f values and the % *trans* parallel each other, reflecting the fact that all three properties depend on the dipole moments of the molecules.

Silver Resin Chromatography

Binary mixtures of methyl 9,12-octadecadienoate-15,15,16,16-d_4 and binary mixtures of methyl 12,15-octadecadienoate-9,10-d_2 geometric isomers were separated on an XN1010 resin column in which 91% of the sulfonic acid protons had been replaced by silver ions (18). Binary mixtures of methyl 9,12,15-octadecatrienoate isomers were separated on an XN1010 column in which the sulfonic acid protons had first been replaced by sodium ions and then 60% of the sodium ions had been replaced by silver ions (4). For the *ttt,tct* separation, better results were obtained with a 70% partially silvered resin column. This separation is shown in Figure 8.

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