

# Preparation and Etherification Reaction of Fatty Dichlorocyclopropanes<sup>1</sup>

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## Abstract

Dichlorocarbene was added to *cis*-9-octadecene, methyl oleate, methyl elaidate, and methyl linoleate to form the corresponding mono- or bis-dichlorocyclopropanes in yields of 75-88%. The dichlorocyclopropanes underwent ring-opening substitution on heating with alcohols (or water) to form  $\beta$ -chlorallylic ethers (or alcohols). The ethers were obtained in yields of 46 to 84%. Tetraethylene glycol and methyl lactate, as hydroxyl compounds, gave a polyethenoxy ester and an ether-linked diester, respectively.

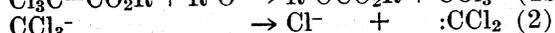
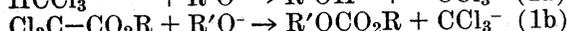
## Introduction

DURING THE 1950's, the fundamental chemistry of dihalocarbenes was elucidated. Proof was given of their existence (1a,2), their electrophilic character (1b,3b,5), and their *cis*-addition to isomeric 2-butenes (3a,4).

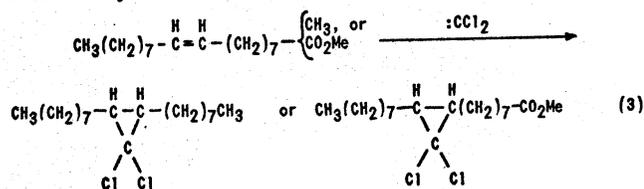
It was desired in the present study to extend the carbene addition reaction, originated with small molecules, to the field of fat chemistry. Dichlorocarbene was chosen as the first carbene to study in this way, and it was added to *cis*-9-octadecene, as a model, and to methyl oleate, methyl elaidate, and methyl linoleate, selected as olefinic fatty esters. These unsaturated compounds were prepared in better than 99% purity by published methods (6,7,8,9).

## Procedures

The generation of dichlorocarbene is usually accomplished by the action of an alkoxide on either chloroform (2) or on ethyl trichloroacetate (10), according to the equations:



As applied to *cis*-9-octadecene and to methyl oleate, the formation of dichlorocyclopropanes is described by the following equation:



To methyl linoleate two moles of the carbene were attached. Since in these substrates, the double bonds are all *cis*, and since the mode of addition is *cis* (3a,4), each resultant cyclopropane ring must also have the *cis* structure. The dichlorocyclopropane from methyl elaidate must similarly be *trans*. In assigning product structures any isomerization of the parent olefin by the alkaline conditions has been neglected.

In initial experiments with *cis*-9-octadecene, the ethyl trichloroacetate method (Equations 1b,2,3) gave better results than the chloroform procedure. Yields,

however, were still much lower with octadecene than in repetitions of Parham's addition of dichlorocarbene to cyclohexene (10). The yield of 1,1-dichloro-2,3-dioctylcyclopropane (I) was improved by several techniques. A high speed stirrer with cruciform impeller improved reaction rate, and the ethyl trichloroacetate was added at rates causing substantial but controllable evolution of heat. The exothermicity was accommodated by the use of n-heptane instead of n-pentane as solvent, by large reaction flasks, and by a cooling bath applied as needed. The procedure developed was also applied in the additions to methyl oleate, methyl elaidate, and methyl linoleate. Two typical preparations are described below, while yield and analytical data for products are listed in Table I.

1,1-Dichloro-2-octyl-3-(7-Carbomethoxyheptyl)-Cyclopropane. (II). Methyl oleate, 15g (0.05 mole), was placed with 30 ml of n-heptane and 15g (0.28 mole) of sodium methoxide in a four-necked, round-bottomed 1-liter flask fitted with a thermometer, a by-pass addition funnel, and a condenser protected with a drying tube. Nitrogen was introduced through the addition funnel. The reaction mixture was cooled to 2C with an ice-salt bath and stirred at high speed while 30 ml (0.22 mole) of ethyl trichloroacetate were added dropwise. Heat of reaction caused refluxing of solvent. Upon completion of the addition (1 hr) the mixture was removed from the cooling bath, stirred for 4 hr, and allowed to stand overnight at room temp. After addition of water, the mixture was extracted by shaking with three 100-ml portions of diethyl ether. The ether layer was washed with five 75-ml portions of water and dried over sodium sulfate. Excess ether was removed under vacuum in a rotating evaporator. The product was purified by column chromatography using a Florisil:sample ratio of 20:1. Fractions eluted with hexane afforded the desired dichlorocyclopropane, 15.1g.

(2,2-Dichloro-3-pentyl)cyclopropyl-(2,2-dichloro-3-(7-carbomethoxyheptyl)-cyclopropyl)-Methane. (IV). In the apparatus described for the previous preparation, 10g (0.034 mole) methyl linoleate, 20 ml n-heptane, and 10g (0.185 mole) of sodium methoxide were stirred at 2C. Within 20 min 20 ml (0.144 mole) of ethyl trichloroacetate was added. The ice bath was removed; the mixture warmed gradually for 1/2 hr, when it refluxed violently for several minutes. Stirring was continued at room temp; the mixture was briefly cooled to 2C (after 2 hr and 5 hr reaction) for two additions of 2g of sodium methoxide and 3.7 ml of ethyl trichloroacetate. Maximum temp reached after these additions were 30 and 60C respectively. After 6 1/2 hr stirring, at room temp except as noted, the mixture was worked up as before, affording 13.6g of compound IV.

*Properties.* The dichlorocyclopropane from *cis*-9-octadecene was stable to distillation, but those from methyl oleate and elaidate were not, and had to be purified by chromatography. The bis-dichlorocyclopropane from methyl linoleate was, in addition, unstable to prolonged contact with Florisil, so that its

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TABLE II  
Ether (or Alcohol) Preparations

Alcohol Etherified, ROH	Product No.	Reaction Temp., C	Reaction Time, Hrs.	Yield, %	25 n <sub>D</sub>	Carbon, %		Hydrogen, %		Chlorine, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
$\text{cis-9-Octadecene product type: } \text{CH}_3(\text{CH}_2)_7\text{CH}=\overset{\text{OR}}{\underset{\text{Cl}}{\text{C}}}-\text{CH}(\text{CH}_2)_7\text{CH}_3$											
Ethanol } Water }	V-B	reflux	24	68	1.4548	73.10	72.55	11.98	11.97	10.28	10.19
	V-A			29		72.00	72.23	11.77	11.71	11.19	10.86
Tetraethylene Glycol	V-D	130	6 <sup>b</sup>	74	1.4650	65.75	65.56	10.83	10.67	7.19	7.52
Methyl Lactate	V-E <sup>a</sup>	80	4 <sup>c</sup>	69		68.54	68.27	10.75	10.97	8.80	8.97
2-Methoxyethanol	V-F	reflux	2	76	1.4578	70.45	70.70	11.56	11.54	9.46	9.58
$\text{Methyl oleate product type: } \text{CH}_3(\text{CH}_2)_7 \left[ \begin{array}{c} \text{---CH=C(Cl)---CH(OR)---} \\ \text{or} \\ \text{---CH(OR)---C(Cl)=CH---} \end{array} \right] (\text{CH}_2)_7\text{CO}_2\text{Me}$											
H <sub>2</sub> O	VI-A	100	8 <sup>f</sup>	33 <sup>e</sup>		66.55	66.58	10.33	10.37	9.82	9.90
Ethanol	VI-B	reflux	9 <sup>c, g</sup>	79 <sup>d</sup>	1.4584	68.54	68.67	10.75	10.73	8.80	8.83
Cetyl Alcohol	VI-C	130	13 <sup>h</sup>	46	1.4622	73.86	74.28	11.88	11.80	6.06	6.18
Tetraethylene Glycol	VI-D	110	6 <sup>h</sup>	84		62.74	62.72	9.96	9.91	6.62	6.53
Methyl Lactate	VI-E	112	6 <sup>b</sup>	69	1.4625	64.46	64.53	9.69	9.81	7.93	7.99
1,4-Butanediol	VI-G	105	6	75	1.4690	66.56	66.76	10.47	10.63	8.19	8.13
$\text{Methyl elaidate product type: } \text{CH}_3(\text{CH}_2)_7 \left[ \begin{array}{c} \text{---CH=C(Cl)---CH(OR)---} \\ \text{or} \\ \text{---CH(OR)---C(Cl)=CH---} \end{array} \right] (\text{CH}_2)_7\text{CO}_2\text{Me}$											
1,4-Butanediol	VII-G	106	4	73	1.4677	66.56	66.85	10.47	10.55	8.19	8.53
$\text{Methyl linoleate product type: } \text{CH}_3(\text{CH}_2)_4 \left[ \begin{array}{c} \text{---CH=C(Cl)CH(OR)---} \\ \text{or} \\ \text{---CH(OR)C(Cl)=CH---} \end{array} \right] \text{CH}_2 \left[ \begin{array}{c} \text{---CH=C(Cl)CH(OR)---} \\ \text{or} \\ \text{---CH(OR)C(Cl)=CH---} \end{array} \right] (\text{CH}_2)_7\text{CO}_2\text{Me}$											
Tetraethylene Glycol	VIII-D	110	6	55		57.28	56.95	8.84	8.66	9.14	8.49

<sup>a</sup> From this product the free acid was later obtained by saponification at 40C with 10% methanolic NaOH, and acidification.

<sup>b</sup> Molecular sieves 4A used to assure anhydrous conditions.

<sup>c</sup> U.V. irradiation for 1 hr.

<sup>d</sup> Ethyl ester.

<sup>e</sup> After allowance for recovered cyclopropane.

<sup>f</sup> U.V. irradiation for 4 hrs.

<sup>g</sup> 10% acetonitrile present

<sup>h</sup> U.V. irradiation for 2 hrs.

<sup>i</sup> As a second product the corresponding butanediol monoester was formed in 20% yield.

ether layer washed with water. After drying with sodium sulfate the solvent was removed in a rotatory vacuum evaporator. The crude substitution product was purified on a chromatography column with 30:1 Florisil to product, using benzene to elute the main product. Evaporation of solvent afforded 3.94 g of the pure tetraethylene glycol monoether (VI-D).

**Modified Procedures.** It was found that even with elevated temp and prolonged reaction times some of the substitution products could be obtained only in low yields. In such cases, irradiation of the reaction flasks with UV light caused silver chloride to be precipitated in a reasonable time, and the products could be obtained in good yield.

In several cases a reduction of reaction time was accomplished by addition of acetonitrile to the reaction system to increase the solubility of silver nitrate in the alcohol.

**Chromatographic Purification.** Reaction mixtures were purified by column chromatography using Florisil adsorbent and hydrocarbon eluants. This removed resinous impurities and provided separation into fractions of different polarities, which were examined by analytical-scale TLC, and IR spectrophotometry. Usually this procedure identified fractions affording

the substitution products in good yield and purity. A few products prepared on micro scale, or more difficult to purify, were also submitted to preparative-scale TLC.

#### Infrared Spectra

Infrared data, obtained with Perkin-Elmer Infracord 137, accorded well with the expected structures of the present compounds. The spectra of the fatty dichlorocyclopropanes resembled that of dichloronorecarane (2) but with less distinct peaks in the 1050-1000 cm<sup>-1</sup> region. Figures 1 and 2 show corresponding sections of the spectra in a methyl oleate and a methyl elaidate series.

The dichlorocyclopropane derivatives of the *cis*-unsaturated ester (or of *cis*-octadecene) showed a doublet at 805 and 780 cm<sup>-1</sup>, attributable to the two chlorine atoms. On etherification the first peak disappeared and only a trace of the second was left. The presence of an ether linkage after reaction with 1,4-butanediol is suggested by strong absorbance at about 1110 cm<sup>-1</sup>. An allylic double bond is reported to have little effect on the C-O-C frequency (12a); similarly β-chloroethers are reported to behave normally in this respect.

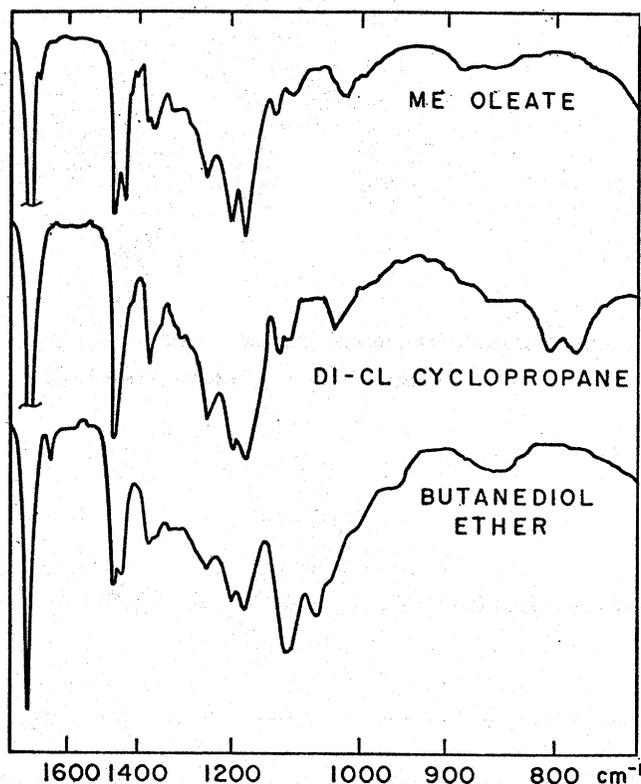


Fig. 1. Section of infrared spectra: methyl oleate, the corresponding dichlorocyclopropane, and the 1,4-butanediol monoether derivative of the latter.

A peak at  $1655\text{ cm}^{-1}$  in the ether suggests a double bond (12b), shifted to lower frequency by halogen. The broad band near  $840\text{ cm}^{-1}$  is further indication of a trisubstituted ethylenic structure in the final product.

In the methyl elaidate series, addition of dichlorocarbene caused disappearance of the *trans* band at  $970\text{ cm}^{-1}$  and appearance of a single strong peak at  $800\text{ cm}^{-1}$ . Etherification with butanediol resulted in a trace band at  $780$  and bands at  $1110, 1655$ , and  $840$  similar to those in the corresponding  $\beta$ -chlorallylic ether from methyl oleate. Indeed, superimposability of spectra suggests possible identity of these two final products.

The spectra of the other compounds were similar, with occasional exceptions. The bis-dichlorocyclopropane from methyl linoleate showed one broad, flat peak from  $805$  to  $780\text{ cm}^{-1}$ , which after etherification with tetraethylene glycol was replaced with a small peak at  $810\text{ cm}^{-1}$ . When the cyclopropanes from octadecene and methyl oleate were reacted with the large tetraethylene glycol molecule, both the  $805$  and  $780\text{ cm}^{-1}$  bands gave way to a new one at  $800\text{ cm}^{-1}$ .

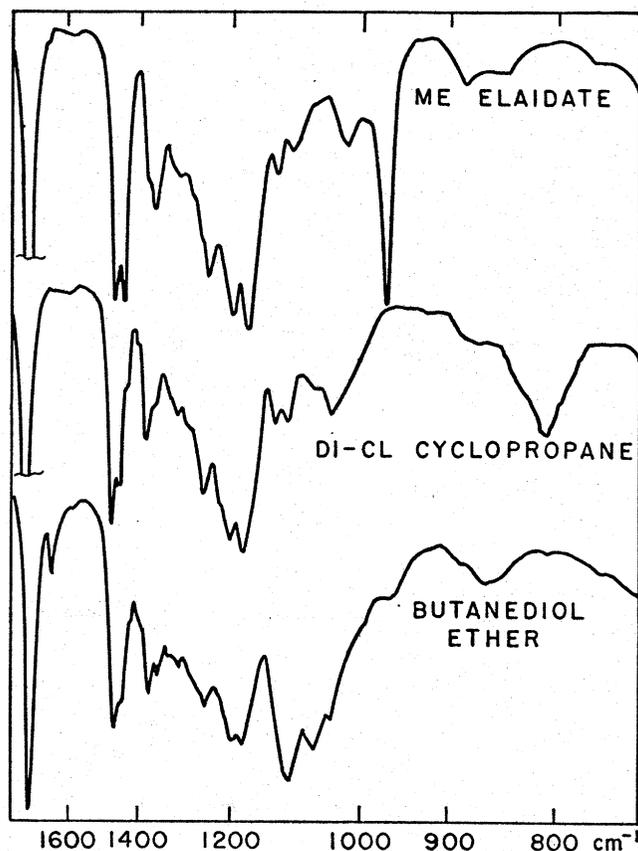


Fig. 2. Section of infrared spectra: methyl elaidate, the corresponding dichlorocyclopropane, and the 1,4-butanediol monoether derivative of the latter.

All alcohols and hydroxyethers prepared showed OH peaks at  $3500$  to  $3600\text{ cm}^{-1}$

#### ACKNOWLEDGMENTS

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