Recombination Products From the Radiolysis of Tricaproin

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ABSTRACT

A low molecular weight triglyceride, tricaproin, has been selected to study the higher molecular weight products produced by irradiation. In a previous publication the identification of the primary radiolytic products in tricaproin was reported. In the present work, 28 compounds considered to have been produced by the combination of free radicals have been identified. Among these are hydrocarbons, ketones, esters, alkanediol diesters and glyceryl ether diesters. Reaction mechanisms for the production of these compounds are discussed.

INTRODUCTION

In a previous publication the effects of gamma radiation on seven simple triglycerides containing C_{12}-C_{18} fatty acids were reported (1). The volatile breakdown products consisted largely of hydrocarbons and certain aldehydes and methyl and ethyl esters. More recently the radiolysis of a low molecular weight triglyceride, i.e., tricaproin, permitted the identification of not only the short chain compounds reported earlier, but also of several higher molecular weight compounds. We have already reported on the products produced from the primary radiolytic cleavage of tricaproin and proposed mechanisms to explain their formation (2). Cleavage at the acyloxy-methylene bond was the most abundant and resulted in the formation of hexanoic acid and propanediol or propenediol dicaproate. The acyl-oxy bond was found to be the second most radio-labile linkage. Its rupture resulted in the formation of hexanal, 2-ethyl cyclobutanone, diglycerides and oxopropanediol diesters. Also abundant was the splitting at the alpha bond of the fatty acid moiety which accounted for the formation of pentane, pentene and formyl dicaproin. Cleavage between the C_1 and C_2 of the glyceryl moiety resulted in the formation of methyl caproate and ethanediol dicaproate. Other cleavages of carbon-carbon bonds along the fatty acid chains occurred to a much smaller extent.

In the present paper, the formation in tricaproin of certain products which are considered to result from the combination of the various radicals is discussed.

EXPERIMENTAL PROCEDURES

Five-gram samples of purified tricaproin were irradiated under vacuum (10^{-2} torr) at 6 megarads and 17 C. The methods used for irradiation of the samples and for the isolation and identification of the radiolytic products were described in detail previously (3). The hydrocarbons were recovered by pre-column distillation and separated by gas chromatography on an alumina column. The remaining compounds were collected by high vacuum coldfinger distillation and analyzed on SE-30. The ketones and esters, however, were trapped from a "DEGS + H_3PO_4" column for rechromatographing on the SE-30 column.

Reference compounds not commercially available were synthesized according to the procedures described below. The spectral properties of certain of these compounds are not available in the literature and hence are discussed here.

Simple Esters

Propyl hexanoate, butyl hexanoate and hexyl hexanoate were synthesized by the reaction of hexanoyl chloride with the appropriate alcohol according to Mattson and Volpenhein (4). The reaction mixtures were washed with a saturated solution of $NaHCO_3$ and the esters were separated by gas chromatography (1/8th in. x 6 ft SE-30 column, programmed from 50-200 C at 4 deg/min) and their structure verified by mass spectrometry under the same operating conditions as described previously (3).

2-Oxoheptyl Hexanoate

This compound was synthesized by reacting the sodium salt of hexanoic acid with 1-chloro-2-heptanone in a manner similar to that described by Hann et al. (5). 1-Chloro-2-heptanone was dissolved in N,N_1 dimethylformamide and an excess of the anhydrous salt added. The reaction was allowed to proceed for 2 hr at 80 C. A few milliliters of a saturated solution of $NaHCO_3$ were then added and chloroform was used to extract the ester from this solution. The ester was later purified by preparative gas chromatography on a 1/2 in. 10% SE-30 column and checked by mass spectrometry and IR spectrophotometry. 1-Chloro-2-heptanone was prepared according to Catch et al. (6). Diazomethane, which was employed in the synthesis of 1-chloro-2-heptanone, was prepared by distillation from a mixture of ether, potassium hydroxide solution and nitrosomethyl urea (7).

The IR spectrum of 2-oxoheptyl hexanoate (Fig. 1, bottom) contains absorption bands at 1750 cm^{-1}, 1168 cm^{-1} and 1108 cm^{-1} corresponding to the ester function while the absorption at 1735 cm^{-1} represents the keto group. In the mass spectrum (Fig. 1, top) a small peak corresponding to the molecular ion can be seen at m/e 228. The peak at m/e 172 $[(M-56)]^+$ represents a McLafferty rearrangement of the keto or the ester portion of the molecule. Both rearrangements could also occur in the same molecule resulting in the ion $[CH_2{=}C(OH)OCH_2C(OH){=}CH_2]^+$ at m/e 116. The ion $[CH_3(CH_2)_4COO + H]^+$ could also contribute to this fragment. The peak at m/e 112 may result from the loss of an acid molecule from the molecule-ion. The base peak (m/e 99) represents the acylium ion and the fragment at m/e 71 the pentyl cation.

6,7-Dodecanedione

6,7-Dodecanedione was prepared by the oxidation of capronoin according to Blomquist and Goldstein (8). Capronoin was mixed with methanol and cupric acetate monohydrate in 30% aqueous acetic acid and heated at 80 C for 15 min. The diketone was extracted from the reaction mixture with ether, dried and examined by combination gas chromatography-mass spectrometry. Capronoin was synthesized according to Hansley (9). Ethyl hexanoate was used for this reaction.

The mass spectral fragmentation of 6,7-dodecadione follows the same pattern observed for 2,3-butanedione (API) and consists essentially of three peaks. The molecular ion is detectable at m/e 198. Cleavage of the carbon-carbon bond between the carbonyl groups gives rise to the base peak at m/e 99, and the fragment m/e 71 occurs by cleavage alpha to the carbonyl groups yielding the pentyl cation.

1- and 2-Pentyl Dicaproin

The synthesis and spectral properties of these two isomers were described previously (10).

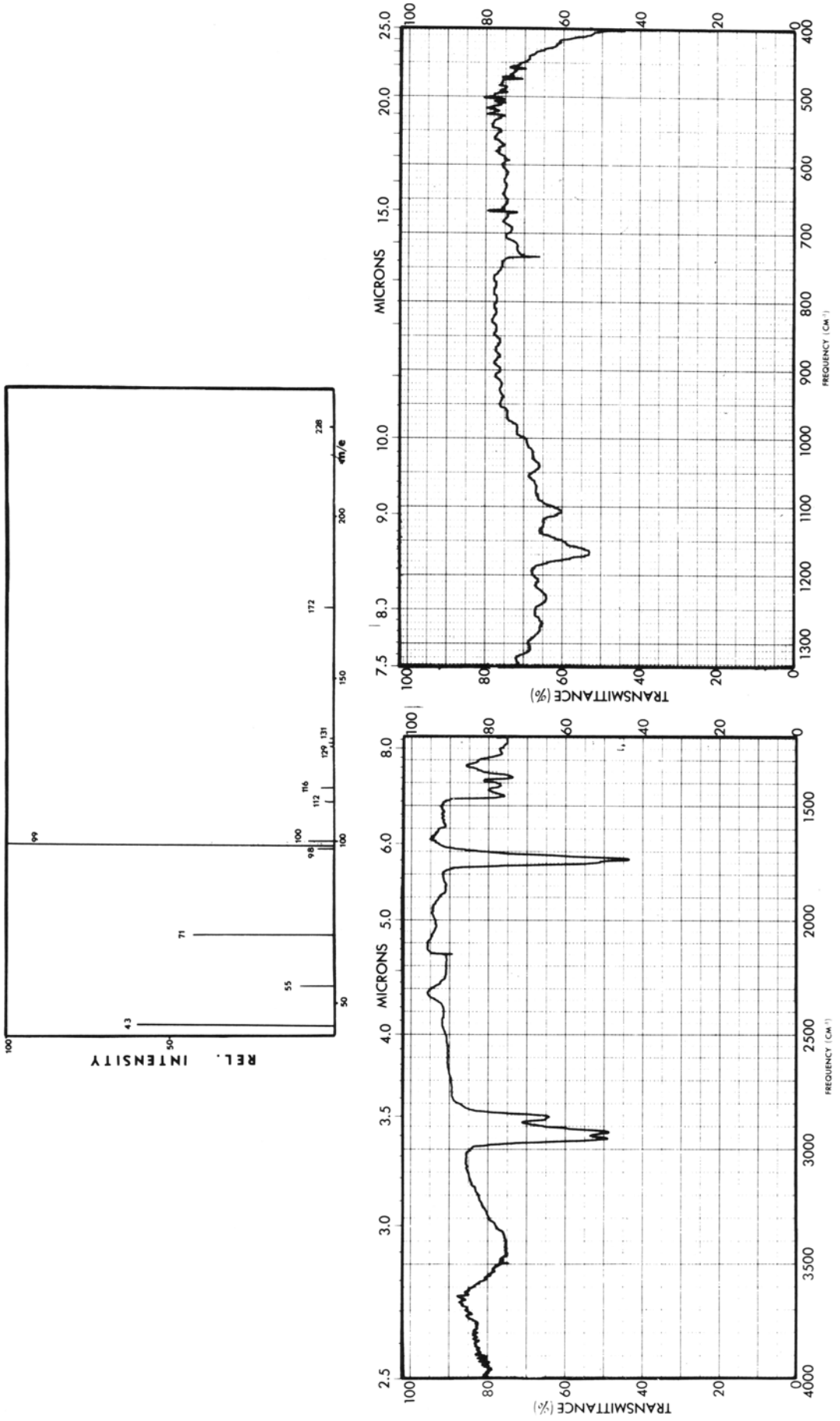


FIG. 1. Mass and IR spectra of 2-oxoheptyl hexanoate.

TABLE I

Recombination Products Recovered From Tricaproin Irradiated at 6 Megarads

Compound	Identification[a]	
	Gas chromatography (GC)	Mass spectrometry (MS)
Hexane	+	*
Heptane	+	*
Octane	+	*
Nonane	+	*
2-Heptanone	++	*
3-Octanone	++	*
Ethyl hexanoate	++	*
Decane	++	*
4-Nonanone	++	*
Propyl hexanoate	++	*
5-Decanone	++	*
Butyl hexanoate	++	*
6-Undecanone	++	*b
Pentyl hexanoate	++	*
6,7-Dodecanedione	++	*
Hexyl Hexanoate	++	*
2-Oxoheptyl hexanoate	++	*b
1,2-Heptanediol dicaproate	+	*
1,2-Octanediol dicaproate	++	*
2-Pentyl-1,3-propanediol dicaproate	+	*
1- and 2-Pentyl dicaproin	+	*b

[a]Symbols: * = mass spectral fragmentation agreed with the authentic compound; + = GC retention agreed with the authentic compound on 1 column; ++ = GC retention agreed with the authentic compound on 2 columns.

[b]Also confirmed by IR spectrophotometry.

1,2-Heptanediol-, 1,2-Octanediol-, 2-Butyl-1,3-propanediol- and 2-Pentyl-1,3-propanediol Dicaproate

The two alkanediol diesters were prepared by the acylation of 1,2-octanediol and 1,2-heptanediol with hexanoyl chloride at room temperature as was previously mentioned. 1,2-Octanediol and 1,2-heptanediol were synthesized by reacting osmic acid with 1-octene and 1-heptene, respectively, according to McCloskey and McClelland (11).

The initial step in the synthesis of 2-butyl- and 2-pentyl-1,3-propanediol dicaproate was the alkylation of diethyl malonate according to Adams and Kamm (12). Diethyl malonate was reacted with n-butyl bromide and n-pentyl bromide in the presence of sodium ethoxide to form ethyl n-butylmalonate and ethyl n-pentylmalonate, respectively. These compounds were partially purified by distillation. The two diesters were then reduced to diols in a manner similar to Moffett (13). The ethyl n-alkylmalonates were refluxed with excess lithium aluminum hydride in anhydrous ether for 30 min. Ethyl acetate was then added to use up any unreacted lithium aluminum hydride. The reaction mixture was then filtered, washed with water and dried. The resulting 2-alkyl-1,3-propanediol compounds were acylated at room temperature with hexanoyl chloride. The ether solution was then washed with a saturated solution of sodium bicarbonate and water and dried.

The mass spectra of these compounds, along with the mass spectrum of 2-butyl-1,3-propanediol dicaproate, are shown in Figure 2. The compound 2-butyl-1,3-propanediol dicaproate was not identified as a recombination product, but it was synthesized in an attempt to aid in the search for it and also in order to assist in the interpretation of and differentiation between the mass spectra of these isomers. Molecular ions are absent in all of the spectra. Generally three types of fragments can be observed: (a) Ions present in all four diol diesters: these fragments are as follows: $[M-56]^+$ resulting from the McLafferty rearrangement of a hexanoate ester; $[M-RCOO]^+$; $[M-RCOOCH_2]^+$; $[M-(RCOOH + 43)]^+$, the loss of 43 resulting from 3,4-cleavage of a hexanoate ester; $[M-(RCOOH + 56)]^+$; $[M-RCO]^+$; $[M-RCOO]^+$, $[M-(RCOOH + RCOO)]^+$; M-2

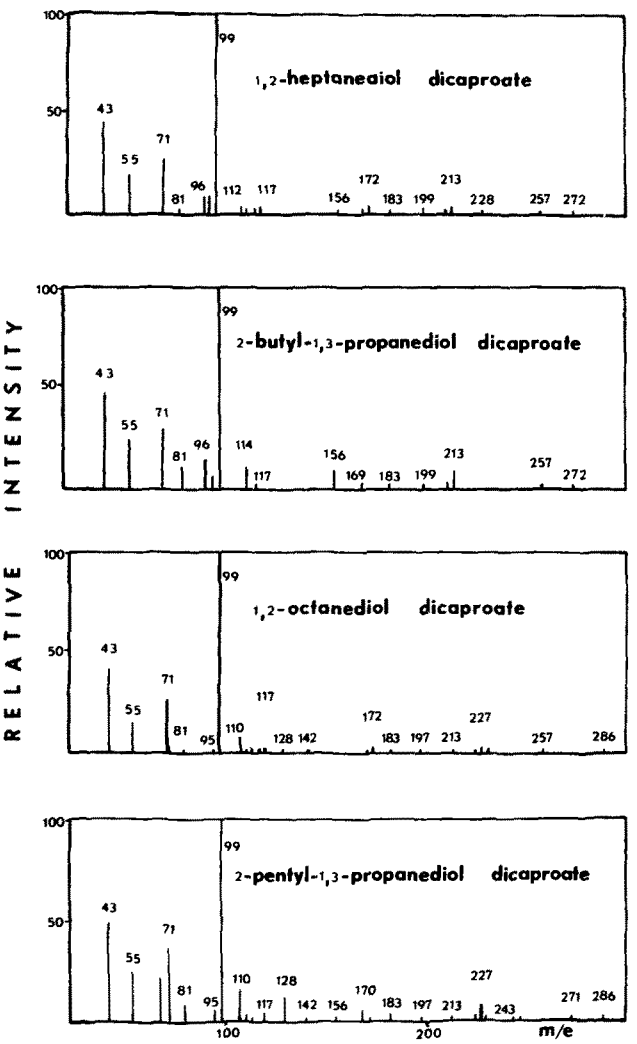


FIG. 2. Mass spectra of 1,2-alkanediol diesters and their isomeric 2-alkyl-1, 3-propanediol diesters.

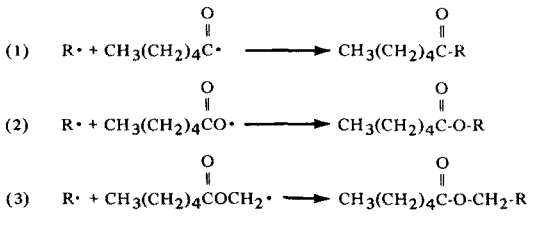
$RCOOH^+$. (b) Ions typical of 1,2-diol diesters: the peak at m/e 288 results from an aldehyde-expulsion type of rearrangement (14). Other ions, apparently including this expulsion (exp.) are those at m/e 172 [M-(56 + exp.)]$^+$; m/e 116 [M-(2 x 56 + exp.)]$^+$; and m/e 112 [M-(RCOOH + exp.)]$^+$. The mass spectra of the 1,2-diol dicaproates also contain an ion at m/e 257 which may result by the loss of an alkyl group from the alcohol moiety of the molecule-ion. The mass spectrum of 2-butyl-1,3-propanediol dicaproate also has a fragment at m/e 257, but this may arise by the loss of a pentyl radical from the acid moiety of the parent-ion, which in this case happens to coincide with the previously discussed mode of fragmentation. (c) The ion at m/e 156 appears to be characteristic in the spectra of the 2-alkyl-1,3-propanediol dicaproates. It may originate by the loss of the alkyl side chain and an acyloxy group from the molecule ion. The small peak at m/e 156 in the spectrum of 1,2-heptanediol dicaproate is that expected from the ion [M-RCOOH + 56]$^+$. The prominence of such fragments as m/e 114 and 128 in the 2-alkyl-propanediol diesters, in contrast to their isomers, is noteworthy.

RESULTS AND DISCUSSION

The compounds identified as recombination products in irradiated tricaproin are listed in Table I together with the criteria used in their identification. In addition, six compounds (ethane, propane, butane, pentane, methyl hexanoate and 1,2-ethanediol dicaproate) identified previously as primary radiolytic products (2) may also be formed, as will be discussed below, via recombination of free radicals.

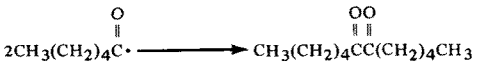
In our previous work on tricaproin it was concluded that the major points of cleavage were those at the acyloxymethylene bond, the acyl-oxy bond and between C_1 and C_2 of the fatty acid moiety. Minor points of cleavage were between the remaining C-C bonds of the fatty acid chains and between C_1 and C_2 of the glycerol moiety. These cleavages (major and minor) result in the formation of a pool of radicals which are available for recombination with one another. The hydrocarbons in Table I, for example, would be expected to be formed by the recombination of the alkyl radicals. The concentrations of the hydrocarbons isolated were as follows: 1,2,1,0.5 and 8 μM/100 g for hexane, heptane, octane, nonane and decane respectively. Decane is the hydrocarbon formed in the largest quantity. This would be expected since the pentyl radical is the most abundant alkyl free radical (2). The hydrocarbons ethane, propane, butane and pentane have previously been classified as primary radiolytic products but it is obvious that a small fraction of these would have originated by recombination.

The simple ketones and most of the simple esters would be expected to be formed as follows:

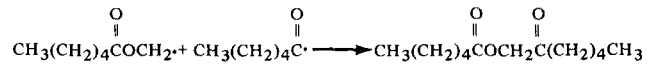


where R· represents the alkyl radicals resulting from cleavage of C-C bonds of the fatty acid chains. 6-Undecanone was found to be the ketone produced in the largest quantity. This is expected since the pentyl radical should be involved in its formation. Reaction 3 appears to be the preferred pathway (over reaction 2) for the formation of the esters since hexyl hexanoate and not pentyl hexanoate was present in a much larger quantity than all other esters (except for methyl hexanoate). The acyloxy radical must be very unstable and must react quickly by either abstracting a hydrogen atom or dissociating into CO_2 and a pentyl radical. Methyl hexanoate is present in a much larger amount than the other esters. But, since the methyl radical should be present only in a small amount, and since it appears that the acyloxy radical does not take part to any great extent in recombination reactions, it is suggested that the major source of this ester is from a primary radiolytic process (2).

The formation of 6,7-dodecanedione can be easily explained by the dimerization of the acyl radical:

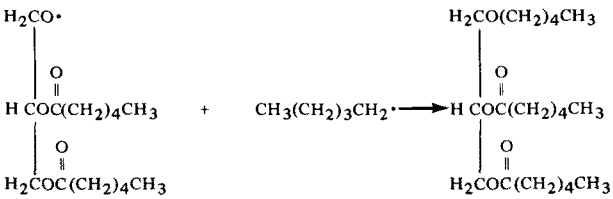


The acyl radical could also react with the acyloxymethylene radical to yield 2-oxoheptyl hexanoate:



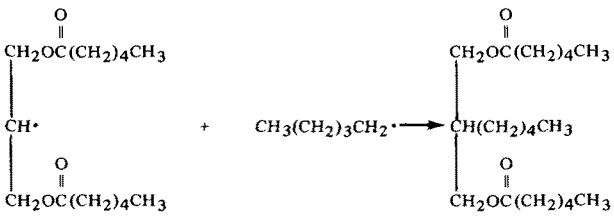
while dimerization of the acyloxymethylene radical would give 1,2-ethanediol dicaproate.

The formation of the higher molecular weight recombination products can be explained in the same manner. Therefore, 1-pentyl dicaproin may be formed as follows:

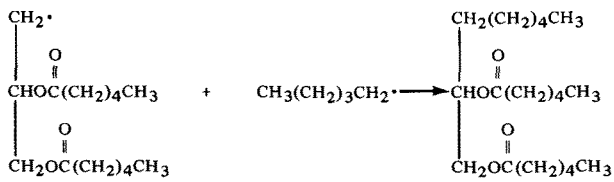


2-Pentyl dicaproin would similarly result from the interaction of the 1,3-dihexanoyloxypropoxy free radicals with the pentyl free radical.

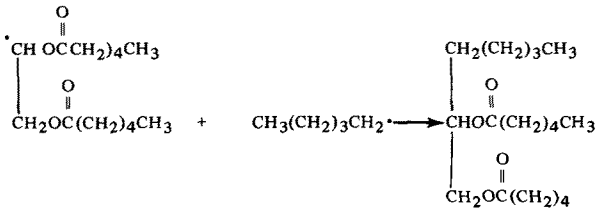
The pentyl radical could also recombine with the 1,3-dihexanoyloxypropyl free radicals to give 2-pentyl-1,3-propanediol dicaproate:



or with the 2,3-dihexanoyloxypropyl free radical to give 1,2-octanediol dicaproate:



1,2-Heptanediol dicaproate may result from the reaction of the pentyl radical with the dihexanoyloxyethyl free radical:



and also by the recombination of a butyl radical with the 2,3-dihexanoyloxypropyl free radical.

Considering all possible recombinations of the lower molecular weight free radicals (i.e., alkyl, acyl, acyloxy and acyloxy methylene free radicals), 26 products would be expected. Of these, 23 have been characterized. The remaining three unidentified compounds (an anhydride, a diacyl peroxide and a 1,1-methanediol diester) are considered to be chemically unstable and, if formed, they would probably readily break down on handling.

It is obvious that products resulting from all of the possible recombinations involving the higher molecular weight radicals (i.e., residual glyceride radicals) have not been identified. While some of these may be chemically unstable and thus decompose before identification, most would be of too high a molecular weight or present in too low a concentration, or both, to be recovered by the methods employed. As compared to the primary radiolytic products reported earlier (2), the compounds identified here correspond to very small gas chromatographic peaks. It is thus believed that the amount of recombination resulting from the irradiation of tricaproin at 6 megarads represents a very small percentage of the total radiolytic process.

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REFERENCES

1. Dubravcic, M.F., and W.W. Nawar, JAOCS 45:656 (1968).
2. LeTellier, P.R., and W.W. Nawar, J. Agr. Food Chem., in press.
3. Nawar, W.W., J. Champagne, M. Dubravcic and P. LeTellier, Ibid. 17:645 (1969).
4. Mattson, F.H., and R.A. Volpenhein, J. Lipid Res. 3:281 (1962).
5. Hann, R.M., E.E. Reid and G.S. Jamieson, J. Amer. Chem. Soc. 52:818 (1930).
6. Catch, J.R., D.F. Elliott, D.H. Hey and E.R.H. Jones, J. Chem. Soc. 278 (1948).
7. Schlenk, H., and J.L. Gellerman, Anal. Chem. 32:1412 (1960).
8. Blomquist, A.T., and A. Goldstein, Org. Syn. 4:838 (1963).
9. Hansley, V.L., J. Amer. Chem. Soc. 57:2303 (1935).
10. LeTellier, P.R., and W.W. Nawar, J. Agr. Food Chem. 19:196 (1971).
11. McCloskey, J.A., and M.J. McClelland, J. Amer. Chem. Soc. 87:5090 (1965).
12. Adams, R., and R.M. Kamm, Org. Syn. 4:250 (1941).
13. Moffett, R.B., Ibid. 4:834 (1963).
14. Sasaki, S., H. Abe, Y. Itazaki and K. Nakanishi, Tetrahedron Letters 2357 (1967).

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