Reactions of the Stearoylated Enolic Form of Acetone, Involving Hexadecylketene as the Reactive Intermediate[1]

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Abstract

Enol esters, such as isopropenyl stearate, are useful intermediates capable of forming interesting derivatives of saturated aliphatic fatty acids. Under given conditions, whereas methyl stearate remains unreactive up to 400C, by contrast the isopropenyl stearate ester efficiently liberates hexadecylketene at 170C with the simultaneous expulsion of "isopropenyl alcohol," i.e., acetone. In the presence of even difficulty acylatable OH or NH compounds the liberated aldoketene combines, usually quantitatively, with these hydrogen-bearing compounds to form esters or imides. In this manner such resistant materials as barbituric acids, hydantoins, N-butylstearamide, acetanilide, t-butyl alcohol, and succinimide may be converted to stearoylated derivatives.

In the absence of reactable substrate and with strong dependence on the nature of the reaction medium, liberated hexadecylketene tetramerizes to derivatives of *gamma* pyrone, or forms stearone, or stearoylates the enolic rearrangement product, heneicosane-2,4-dione. The latter compound, in forming, has increased the 18 carbon chain-length to 21 continuous carbon atoms. Di-isopropenyl esters with polyfunctional acetylatable materials, such as bis-N-alkylazelaamide or sucrose, give rise to unusual linear polyimides, three-dimensional network polymers, or oligomers.

Introduction

PROPERTY MODIFICATION of saturated fatty acids, beyond the preparation of the simplest carboxyl group derivatives or of *alpha*-position derivatives, is a more difficult problem than the corresponding operation on unsaturated acids. In looking about for a new approach to the utilization of the long-chain saturated acids, I happened across many interesting properties of enol ester derivatives. These unusually versatile reagents allow access to such diverse compound types as alkylated *beta* lactones, alkylated pyrones, tri- and dihydroxamic acids, and aliphatic imides, to name a few of the products which are obtainable.

For simplicity of presentation, discussion of the enol esters will be limited to the stearoylated enolic form of acetone, viz., to isopropenyl stearate except that, where necessary for polymer generation purposes, a few di-isopropenyl esters of dicarboxylic acids will also be mentioned. The lower homolog, vinyl stearate derived from the enolic form of acetaldehyde will not be considered since, as shown previously (1), the reaction patterns of this homolog are quite different from those of isopropenyl stearate. For example, the former adds carboxylic acid to form ethylidene compounds whereas the latter exchanges acids to form new enol esters; only the isopropenyl ester functions as an acylation agent.

After unpublished studies by co-workers in this laboratory, which parallelled those reported by Jovtscheff (2) on the addition of acyl hypobromites to the double bond of methyl oleate, a possible extension of this reaction was considered. The addition of stearoyl hypobromite to the double bond of isopropenyl acetate should give rise to a molecule with a highly unusual, nonterminal, geminal diester structure. Such compounds, apart from alkylidene (terminal) diesters and cyclic malonate derivatives like "Meldrum's acid" (3), have not yet been reported in the chemical literature. The addition reaction was carried out, and spectral evidence was obtained for the formation of the bromo-geminal diester; but since the bromine atom was difficult to remove without causing destructive changes, a procedural short-cut was tried by avoiding the use of brominated materials. The direct acid-catalyzed addition of stearic acid to isopropenyl acetate was attempted. The expected geminal ester seemed to form but did so within a reversible, dynamic equilibrium so that, in the presence of excess stearic acid, the product isolated was the new compound, isopropenyl stearate (III), rather than the starting material, isopropenyl acetate (I), Equation 1.
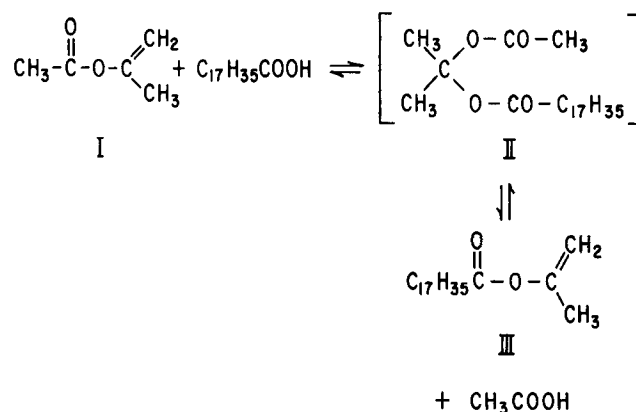
Equation 1

As experiments in studying the properties of the enol ester III became more interesting, the search for the geminal diester II was neglected, although evidence for its transient existence is plainly to be found in the reaction by-product IV, the mixed stearic acetic anhydride (1), the formation of which is indicated in Equation 2.
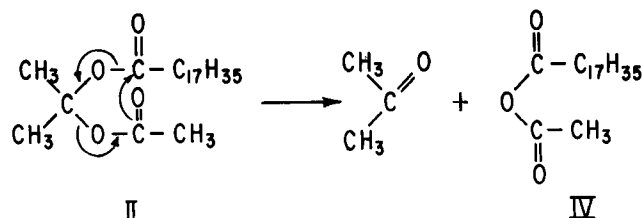
Equation 2

Adelman's results (4) on the analogous vinyl interchange reaction again show differences from the isopropenyl interchange since he reported vinyl ester-

acid interchange to be not catalyzed by acids or bases and similarly noted that even the familiar ester-ester interchange reactions fail under acid or base catalysis conditions when either ester is a vinyl ester. Adelman considered the key intermediate in the vinyl interchange reaction to be "bound" acetylene in complex with mercury salts, thus explaining the specific catalytic function of the mercuric compounds. As work progressed and quantity needs arose, isopropenyl stearate was prepared in better yield by the direct addition of stearic acid to methylacetylene by using mercuric acetate-boron trifluoride catalyst; but both components of the catalyst pair were essential to the reaction (5).

Isopropenyl stearate is a useful reagent for introducing the stearoyl group into a wide variety of compounds. Its advantages include the high reactivity, the favorable yields, which are usually quantitative, and the purity of the crude product uncontaminated (apart from an easily removed trace of acid catalyst) by masses of by-products like stearic acid, pyridine salts, or methanolic sodium methoxide as is the case when the classical reagents like stearic anhydride, stearoyl chloride, or methyl stearate are used.

By the present technique imides such as maleimide, succinimide, and phthalimide produce the N-stearoyl derivatives; amides such as the barbituric acid drugs, e.g., "Veronal," spirohydantoin drugs such as 1,3-diazaspirodecane-2,4-dione, i.e., "pentamethylene spirohydantoin," acetanilide, and N-butyl stearamide react to form N-stearoylated derivatives. Amines and alcohols, even tertiary alcohols, are acylated as easily, but N-unsubstituted amides fail, undergoing dehydration to nitriles (5).

This unusual ability to acylate difficulty acylatable materials such as the amides must be explained by a highly reactive intermediate like hexadecylketene. Isopropenyl stearate, under conditions of trace acid catalysis in the temperature range of 170–220C, expels acetone and liberates the active aldoketene. The ease of this thermolysis is not approximated by saturated alcohol esters like methyl stearate, which are unreactive up to 400C under comparable conditions of brief reaction-time and trace-acid catalysis. The ease of thermolysis may be explained by the cyclic transition state which is possible (Equation 3).
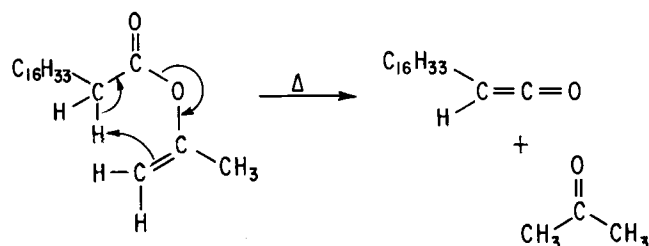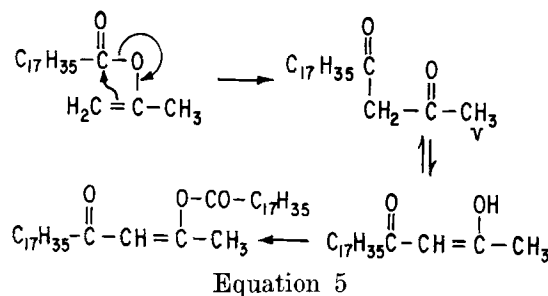
Equation 3

The hexadecylketene monomer cannot itself be isolated. Crystallization from pentane in open vessels, starting with initially anhydride-free material as verified by IR, gives conversion to stearic anhydride (Equation 4).

The fate of the liberated hexadecylketene under anhydrous conditions is dependent to an unusual degree on the solvent in which the elimination reaction is carried out so that the identity of the resulting product may be actually governed by the reaction medium. The use of esteric solvents like methyl stearate or diethyl malonate causes a rearrangement (6) of the enol ester to heneicosane-2, 4-dione (V), the
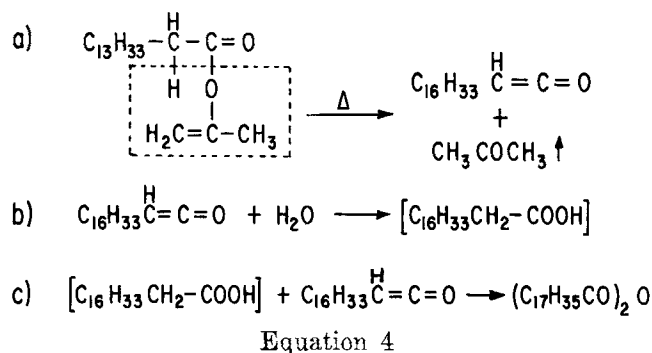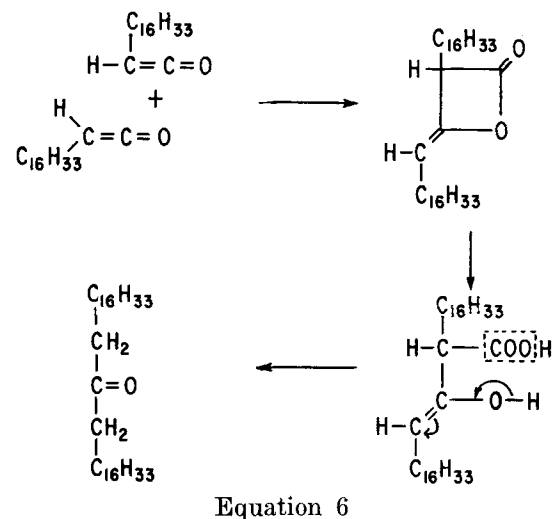
Equation 4

enolic form of which is immediately stearoylated to the enol stearate (VI) by hexadecylketene (Equation 5).

Equation 5

When the thermolysis is carried out in the absence of solvent, the sole product is stearone (8), the formation of which may be rationalized by dimerization of hexadecylketene to a lactone, followed by "hydrolysis" and spontaneous decarboxylation (Equation 6).
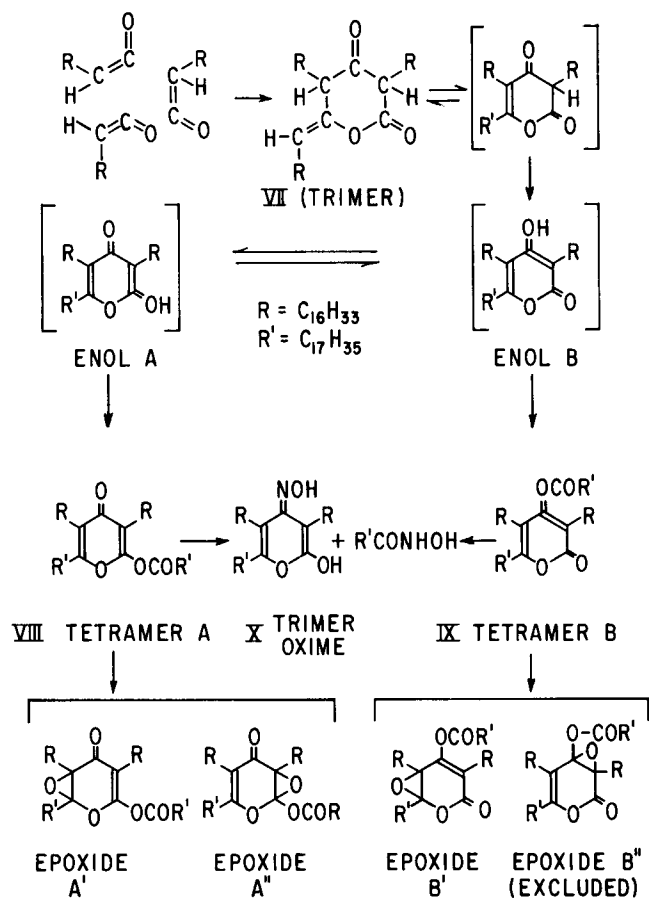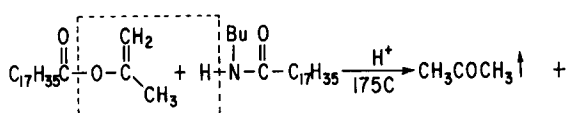
Equation 6

When the thermolysis is carried out in an inert, high-boiling hydrocarbon, the hexadecylketene trimerizes to a ketolactone (VII), the monoenol of which stearoylates through the action of a fourth molecule to form the tetrameric enol ester VIII or its isomer IX (Equation 7). The evidence for the structures of these compounds will be briefly developed in the discussion of results and has not been previously reported.

Mention has been made of the addition of N-butyl stearamide to hexadecylketene to form the aliphatic imide, N-butylstearimide (Equation 8). By extension of the acylation-addition reaction to bifunctional compounds, this previously unreported reaction was used to produce short polymeric chains (Equation 9). In such a way, by heating di-isopropenyl sebacate (8) with N,N'-dimethyl azelaamide, was obtained a short polymer (9), related to the Nylons. It consisted of a
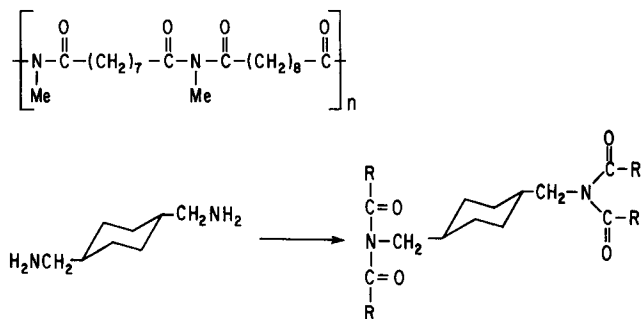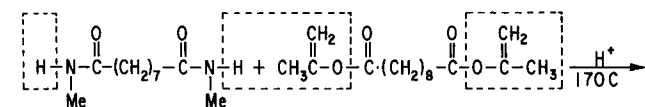
linear N-alkylpolyimide chain rather than of a poly-amide chain.

Ⅶ (TRIMER)

$R = C_{16}H_{33}$
$R' = C_{17}H_{35}$

ENOL A   ENOL B

Ⅷ TETRAMER A   **Ⅹ TRIMER OXIME**   **Ⅸ TETRAMER B**

EPOXIDE A'   EPOXIDE A''   EPOXIDE B'   EPOXIDE B'' (EXCLUDED)

Equation 7

Equation 8

Equation 9

Experimental Procedures and Data

Stearic Acid. The best commercial grade was re-crystallized slowly from acetone three times. Analysis as the methyl ester by GLC indicated 99% purity.

Methylacetylene. This compressed gas, much less hazardous than acetylene, was obtained from Matheson and Company and used as received.

Isopropenyl Stearate. This was prepared by direct addition. A suspension of 44 g of stearic acid in 200 ml of methylene chloride was treated with 4.4 g of mercuric acetate, and the mixture was stirred for an hour. Occasionally homogeneous solutions were formed which redeposited solid matter (mercury soap) on standing or on continued stirring. To the creamy mixture was added, under anhydrous conditions, 0.2 ml of boron trifluoride etherate; methyl acetylene was bubbled through the solution at a slow rate for 20 hrs. The optimum temperature seems to be just below the boiling point of methylene chloride between 35 and 40C.

The boron trifluoride catalyst was neutralized with a slight excess of triethylamine, and the mixture was freed of acidic matter, of metallic mercury droplets in nearly colloidal state, and of salts by passage through a column of Florisil. The percolate was freed of methylene chloride on the steam bath, was diluted with pentane, and, if necessary to remove color, was rechromatographed on a fresh Florisil column. The isopropenyl ester was eluted rapidly. The eluates were cooled to −20C, and the crops of isopropenyl stearate crystals were collected by filtration. The colorless ester, mp 36–37C, obtained in 75% (re-crystallized) yield, was identical with the preparation obtained by the ester-acid interchange procedure pre-viously reported (1).

Freshly prepared materials may contain residual mercury compounds. On standing a few days, air oxidation of these causes turbidity of solutions and yellowness of the solid form. Rechromatography through a short Florisil column by using pentane elution gives a colorless, mercury-free product.
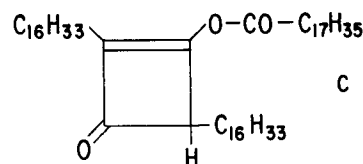
3,5-Dihexadecyl-6-Heptadecyl-2-Stearoyloxy gam-ma-Pyrone ("Hexadecylketene Tetramer"). Isopro-penyl stearate (80 g), Nujol (100 ml), and p-toluene-sulfonic acid (1 g) were placed in a distillation flask,
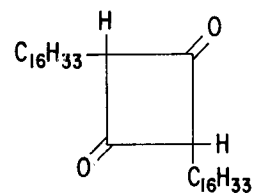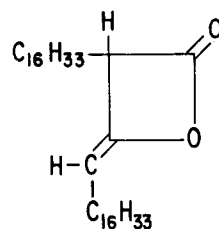
provided with a thermometer submerged in the melt and with a magnetically powered stirring bar. The mixture was rapidly heated and held at 205–220C for 0.5 hr, during which time 12 g (80%) of acetone distillate were collected. On standing at room temperature, the mixture solidified to a semicrystalline solid. On standing longer (over a weekend), tetramerization had largely occurred. The mixture was dissolved in hot heptane, treated with decolorizing carbon, and filtered hot through a 4-cm × 4-cm column of Florisil, which gave a product considerably lightened in color. Crystallization, on cooling, gave 42 g of colorless purified tetramer. The analytical sample, crystallized from hexane, melted from 75.5–

76.4C, $\bar{v}_{max.}^{CS_2}$ 1765, 1720, 1645, 1103^{cm-1}; $\bar{v}_{film}^{crystal}$ 1752, 1715, 1645, and 1579^{cm-1}, $\lambda_{max.}^{MeOH} = 300$ mu, E = 8900, mass spectrum ion peaks at 68–71, 73, 82, 95, 111, 264–267.

Anal. calcd. for $C_{72}H_{136}O_4$: C, 81.13; H, 12.85, mol wt 1066. Found: C, 81.24; H, 12.76; mol wt 999 (thermistor in CCl_4).

3,5-Dihexadecyl-6-Heptadecyl-2-Hydroxy gamma-Pyrone Oxime ("Hexadecylketene Trimer Oxime"). One gram each of tetramer and hydroxylamine hydrochloride and 5 ml each of pyridine and ethanol were refluxed for 2 hrs. Since the mixture was inhomogeneous at the end of this time, another gram of hydroxylamine salt and another 5 ml each of the solvents were added with continued refluxing for another 2 hrs. Solvents were then removed under nitrogen, the product was taken up in hot chloroform, and washed free of salts with water. The product, insoluble in cold chloroform, was recrystallized six times from ether and superheated to 100C in the steam bath in a sealed glass jar which served as a pressure bomb. The product was microcrystalline, mp 95.8–96.0C, $\bar{v}_{max.}^{crystal film}$ 3000–3400 (broad, rounded envelope); 1611, 1540, and 1467 k (prominent), 1166 and 720 k (medium strength), $\lambda_{max.}^{iso-oct}$ 300 mv, E = 6666.

Anal. calcd. for $C_{54}H_{103}O_3N$: C, 79.63; H, 12.75; N, 1.72; mol wt 814. Found: C, 79.70; H, 12.80; N, 1.72; mol wt 826 (thermistor in $CHCl_3$ vs. octadecanol reference); 1130 in CCl_4 (association).

A repeat run at higher dilution also gave N-stearoylhydroxylamine (stearoylhydroxamic acid), mp, after recrystallization from chloroform and from superheated ether, 107–108C (Ref. 10), 106.5–107C, $\bar{v}_{max.}$ 3220, 3015, 1667, 1612, 1480, and 1434 k.

Anal. calcd. for $C_{18}H_{37}NO_2$: C, 72.19; H, 12.45; N, 4.68; mol wt 300 g/m. Found: C, 72.32; H, 12.78; N, 4.44; mol wt 332 (thermistor).

Monoepoxide of Hexadecylketene Tetramer. This preparation was carried out by S. Serota. The tetramer, 6.3 g (0.006 mole) in 100 ml of carbon tetrachloride, was treated with 10 g of m-chloroperbenzoic acid (0.06 mole), and the stirred mixture was let stand for 30 hrs. The mixture was filtered; excess acid and peroxyacid were removed on a Sephadex LH-20 column (30 g) and equilibrated with carbon tetrachloride by using techniques (5) designed to avoid the acyloxyepoxide rearrangement. The first 75 ml of eluate contained the epoxide.

The second 75 ml of eluate contained 0.54 g of a 1:1 mixture of unreacted (!) tetramer and epoxide. Recrystallization from 4:1 pentane/methylene chloride gave the analytical sample mp 59–59.5C, $\lambda_{max.}^{iso-octane}$ 239

m, E = 9600, $\lambda_{max.}$ (in alkaline ethanol) 292 mμ

E = 12,800, $v_{max.}^{CS_2}$ 1738, 1775 k.

Anal. calcd. for $C_{71}H_{134}O_5$: C, 79.86; H, 12.65; mol wt, 1068. Found: C, 80.09; H, 12.62; mol wt 1094.

Polymer from Sucrose and Di-isopropenyl Sebacate. Crystalline sucrose (as the usually supplied, finely granular table sugar), 0.01 mole, and di-isopropenyl sebacate, 0.04 mole, were treated with 10 mg of p-toluenesulfonic acid in a round-bottomed flask, immersed in an oil bath. Electromagnetic stirring was provided since the bumping-stone action of the stirring bar assisted acetone vapor elimination. As the temperature of the oil bath was gradually raised to 125C, homogenization of the mixture occurred despite the widely different polarities of the sugar and fatty ester reactants. As the temperature was gradually increased to 150C, the liquid became more and more viscous, the magnetic bar ceased to rotate, and finally the setting to a translucent, friable gum occurred. The polymer was insoluble in the usual organic solvents. Some care in heating was required to avoid scorching the sugar.

Polymer from 1,4-bis(Aminomethyl)Cyclohexane. A mixture of 0.71 g of the commercially available diamine (a mixture of cis and trans forms), di-isopropenyl sebacate, 2.68 g, and p-toluenesulfonic acid, 10 mg, was heated from 110 to 120C and agitated. At 114° frothing occurred as acetone vapors were expelled; the mixture solidified as polymerization occurred. The reaction required 10 minutes to reach the solidification stage.

Linear Polymer from 1,4-bis(Hydroxymethyl) Cyclohexane and Di-isopropenyl Sebacate. A stirred mixture of commercial 1,4-bis-hydroxymethyl cyclohexane (cis and trans forms), 1.872 g, di-isopropenyl sebacate, 3.675 g, and p-toluenesulfonic acid was placed in a heating bath at 170°. Within three minutes a vigorous expulsion of acetone vapors took place. The mixture quickly became viscid, but heating was continued for an additional 30 minutes. The linear polymer which was prepared under these conditions had a molecular weight of about 2,000 g per mole.

Discussion of Results

The complexity of alkylketene polymerization is well known (11), and Farnum et al. (12) have made some generalizations about the effect of monomer structure and reaction medium in directing the method of the polymerization to determine whether the product will contain the cyclobutane, oxetane, or pyrane nucleus. Evidence for the tetrameric structure of the hexadecylketene polymerization product indicates that a monoepoxide can be formed which absorbs strongly in the ultraviolet at 239 mμ. This single datum immediately rules out dimer structures A and B, also trimer structure C. The proportion of nitrogen in the oxime derivative, coupled with the isolation of stearoylhydroxamic acid, as well as the molecular weights observed for the parent, oxime, and epoxide derivative, all point to a tetrameric formulation. Finally the infrared and ultraviolet maxima (11) agree well with values previously reported for *gamma*-pyrone derivatives. The mass spectrum does not show the principal ion peak since the mass is so large, but the smaller fragments are in harmony with the proposed structure. A series of derivatives with the grignard reagent, not reported fully, can also be interpreted in terms of the tetrameric structure. There

is no wish, at this stage, to choose between the two enol ester derivatives of trimer VII in Equation 7, but tentatively isomer VIII is favored.

Significance

The successful use of isopropenyl esters to generate aldoketene derivatives from long-chain fatty acids uncovers a new potential in fatty acid chemistry. Since it has been demonstrated that these higher-molecular-weight aldoketenes have a great avidity for amino, amido, imino, and hydroxyl groups, immediately suggested is the application to natural and synthetic polymeric fibers as well as to carbohydrates in order to give useful property modification, such as a water-proof quality or modified surface. Preliminary experiments with cotton have not been encouraging, but sucrose reacts with diisopropenyl dioates. Sucrose reacts with isopropenyl stearate to give distearate esters rather than the more useful monoesters desired for detergent purposes, but it is hoped that continued work will solve current experimental difficulties such as co-solubility. The natural polyamide, leather, is rendered waterproof by combination with hexadecyl-ketene, but at lower temperatures the weight gain is small. At higher temperatures the leather under-goes alteration. The lactonic compound IV-a in Equa-tion 6 is already known in the paper-making industry as an excellent sizing material. Isopropenyl stearate, as well as the hexadecylketene tetramers, ought to function in the same manner since the active compound is probably hexadecylketene, liberated by de-polymerization. The isopropenyl ester can probably be prepared more cheaply than lactone IV-a. Similarly polylactic acid stearate for cake mixes and dehydrated potato modifiers, currently prepared by means of stearoyl chloride, may be manufactured more economically by the enol ester procedure.

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