The oxime was obtained after two recrystallizations from 95% ethanol as colorless needles, m. p. 188–189° (cor.).

*Anal.* Calcd. for $C_{22}H_{20}O_2N_2$: C, 76.7; H, 5.8; N, 8.1. Found: C, 76.7; H, 6.0; N, 8.0.

A solution of 0.4 g. of α-benzamido-β-phenyl-propiophenone in 30 ml. of 6 N hydrochloric acid and 10 ml. of ethanol was refluxed for three hours, the solvents removed, the residue extracted with ether, and dissolved in 10 ml. of ethanol. The addition of 25 ml. of ether gave the hydrochloride of α-amino-β-phenylpropiophenone, lustrous needles, m. p. > 200° with decomposition.

*Anal.* Calcd. for $C_{15}H_{16}ONCl$: C, 68.8; H, 6.2; N, 5.4; Cl, 13.6. Found: C, 68.6; H, 6.4; N, 5.2; Cl, 13.8.

(B) A mixture of 2.7 g. (0.01 mole) of N-benzoyl-DL-phenylalanine, 5.9 g. (0.075 mole) of pyridine and 11.3 g. (0.05 mole) of benzoic anhydride heated at 135–140° for two hours with stirring when treated as described above gave 1.2 g. (36%) of α-benzamido-β-phenylpropiophenone, colorless needles, m. p. 146–147° (cor.).

(C) When 2 g. (0.012 mole) of DL-phenylalanine, 7.9 g. (0.1 mole) of pyridine, and 17 g. (0.12 mole) of benzoyl chloride was heated for one hour at 135–140°, 39–42% of the anticipated quantity of carbon dioxide was evolved but on working up the dark tarry reaction product only 0.36 g. (9%) of α-benzamido-β-phenyl-propiophenone, m. p. 146–147° (cor.), was obtained.

(D) A mixture of 2 g. (0.012 mole) of DL-phenylalanine, 7.9 g. (0.1 mole) of pyridine and 12.5 g. (0.1 mole) of benzoyl fluoride[15] was heated for two hours at 135–140° with stirring and from the reaction mixture there was obtained 1.55 g. (39%) of α-benzamido-β-phenylpropiophenone, m. p. 146–147° (cor.).

(15) Meslans and Girardet, *Bull. soc. chim.*, [3] **15**, 877 (1896).

**Studies Based upon Evolution of Carbon Dioxide.**—A mechanically stirred mixture of 0.7 g. (0.0044 mole) of DL-alanylalanine, 3.6 g. (0.045 mole) of pyridine, and 4.6 g. (0.045 mole) of acetic anhydride heated for two hours at 110–115° gave 0.004 mole of carbon dioxide. In a second experiment heating for one and one-half hours at 115° gave 92% of the anticipated amount of carbon dioxide (one equivalent) and when the reaction mixture was refluxed with 6 N hydrochloric acid no more carbon dioxide was obtained.

A mixture of 0.44 g. (0.004 mole) dimethyldiketopiperazine, 2 g. (0.025 mole) of pyridine and 3.6 g. (0.035 mole) of acetic anhydride was heated with stirring at 120° for two hours. No carbon dioxide was evolved during this period nor after refluxing with 6 N hydrochloric acid.

### Summary

The Dakin–West reaction has been shown to be applicable to the synthesis of α-acylamidoalkyl aryl ketones as well as to the synthesis of α-acylamidoalkyl alkyl ketones other than methyl ketones. It has been found that acetate ion may be used in lieu of pyridine as a condensing agent and that the acid anhydride may be replaced by the corresponding acyl fluoride. The nature of the base catalyzed reaction involving a dipeptide and an acid anhydride has been considered in a preliminary manner.
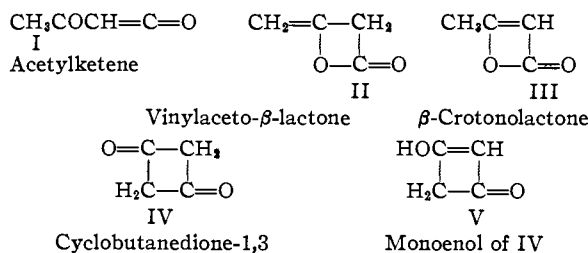
RECEIVED AUGUST 31, 1948

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE LABORATORY FOR NUCLEAR SCIENCE AND ENGINEERING, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

# The Use of Carbon-14 in the Determination of the Structures of Aldoketene Dimers[1,2]

BY JOHN D. ROBERTS, ROSE ARMSTRONG, R. F. TRIMBLE, JR., AND MARION BURG

The structures of aldoketene dimers prepared by the dehydrohalogenation of acyl halides have not been conclusively established. Recent infrared spectroscopic studies by Miller and Koch[3] indicate that the parent compound, diketene, is probably an equilibrium mixture of compounds having structures II and III although IV could not be excluded as a component of the mixture by the infrared data.

CH₃COCH=C=O          CH₂=C—CH₂          CH₃C=CH
I                              |        |              |        |
Acetylketene                O—C=O          O—C=O
                                        II                        III
Vinylaceto-β-lactone          β-Crotonolactone

O=C—CH₂                        HOC=CH
|        |                              |        |
H₂C—C=O                        H₂C—C=O
IV                                        V
Cyclobutanedione-1,3          Monoenol of IV

It was considered that I and V were unlikely because of the absence of absorption at the characteristic hydroxyl and C=C=O frequencies.

(1) Assisted by the joint program of the Office of Naval Research and the Atomic Energy Commission.

(2) Presented at the St. Louis Meeting of the American Chemical Society, September 7, 1948.

(3) Miller and Koch, THIS JOURNAL, **70**, 1890 (1948).

The higher aldoketene dimers prepared from acyl halides by the Wedekind procedure[4,5,6,7] have chemical and physical properties which are generally similar to those of diketene and presumably present a similar structural problem.[8] It is apparently agreed that the dimers of dialkyl-substituted ketenes (ketoketene dimers) have tetra-alkylcyclobutanedione-1,3 structures.[6]

In the present investigation the isotopic tracer

(4) Wedekind, *Ber.*, **34**, 2070 (1901); *Ann.*, **323**, 246 (1902); **378**, 261 (1910); Wedekind and Haeussermann, *Ber.*, **41**, 2297 (1908).

(5) Hill, Ph.D. Thesis, Cornell University, 1941.

(6) Hanford and Sauer, "Organic Reactions," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1947, pp. 127 ff.
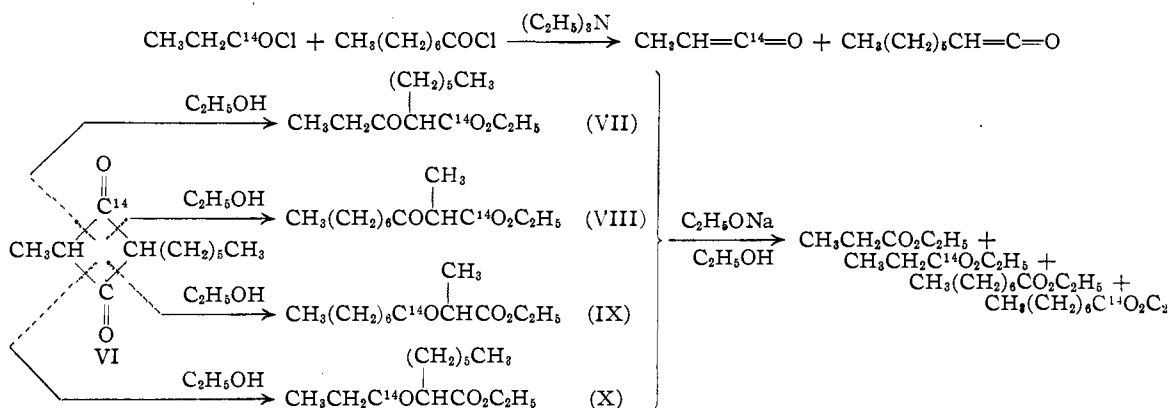
(7) Sauer, U. S. Patent 2,369,919; THIS JOURNAL, **69**, 2444 (1947).

(8) Two seemingly isomeric forms have been reported for methylketene dimer. A liquid, b. p. 50–52° (9 mm.), has been prepared from the dehydrohalogenation of propionyl chloride[5,7] having properties similar to those of diketene and a solid form, m. p. 140°, has been obtained from the polymerization of methylketene prepared from the debromination of α-bromopropionyl bromide with zinc by Staudinger and Klever, *Ber.*, **41**, 906 (1908); Staudinger, *ibid.*, **44**, 533 (1911). The solid compound has also been synthesized by Schroeter, *ibid.*, **49**, 2697 (1916); **53**, 1917 (1920); **59**, 977 (1926), from diethyl α,α'-dimethylacetonedicarboxylate. The structure, 1,3-dimethylcyclobutene-2-ol-4-one was assigned to the solid compound by Staudinger on the basis of its pronounced enolic properties. However, this assignment can only be regarded as tentative in the absence of a molecular weight determination.

technique was used to show that a mixed dimer of methyl- and hexylketenes which was convertible to alkylacetoacetic esters with alcohol probably does not have a structure similar to IV or V. The method utilized the mixed dimer[7] prepared by the Wedekind reaction from $C^{14}$ carbonyl-labeled propionyl and unlabeled caprylyl chlorides and was based on the fact that IV is unique among the five structures proposed for ketene dimers in having two equivalent carbonyl groups. If any of the mixed dimer had the cyclobutanedione-1,3 structure (VI), treatment of this material with alcohol would be expected to give a mixture of four different substituted acetoacetic esters, VII, VIII, IX, and X.
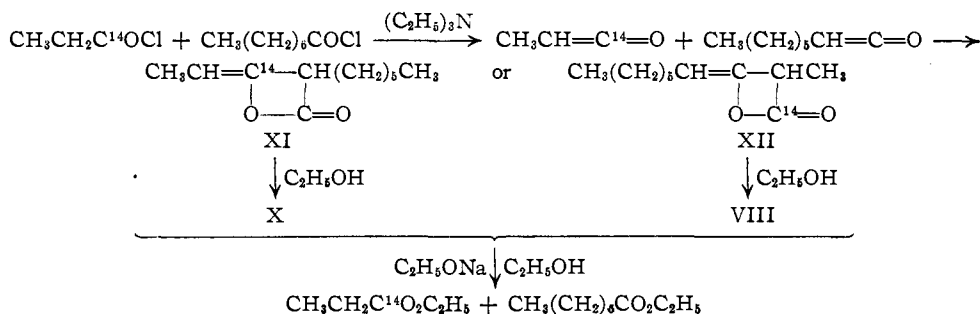
the structure VI then the radioactive carbon atoms would be expected to be distributed equally between the ethyl propionate and ethyl caprylate fractions. Similar results should be obtained from a structure like V since this form should be formed from VI and possess for an instant, at least, the symmetry of VI.

If the mixed dimer had a structure related to I, II or III it could exist in two forms depending on which ketene furnished the C=C=O group of a structure like I, or the carbonyl groups of the lactonic structures similar to II or III. Regardless of the mixture of dimers, degradation through the substituted acetoacetic esters should give only *non-radioactive* caprylic acid derivatives. These

$$CH_3CH_2C^{14}OCl + CH_3(CH_2)_6COCl \xrightarrow{(C_2H_5)_3N} CH_3CH=C^{14}=O + CH_3(CH_2)_5CH=C=O$$

$$\xrightarrow{C_2H_5OH} CH_3CH_2CO\overset{\underset{\displaystyle |}{(CH_2)_5CH_3}}{C}HC^{14}O_2C_2H_5 \quad (VII)$$

$$\xrightarrow{C_2H_5OH} CH_3(CH_2)_6CO\overset{\underset{\displaystyle |}{CH_3}}{C}HC^{14}O_2C_2H_5 \quad (VIII)$$

$$\xrightarrow{C_2H_5OH} CH_3(CH_2)_6C^{14}O\overset{\underset{\displaystyle |}{CH_3}}{C}HCO_2C_2H_5 \quad (IX)$$

$$\xrightarrow{C_2H_5OH} CH_3CH_2C^{14}O\overset{\underset{\displaystyle |}{(CH_2)_5CH_3}}{C}HCO_2C_2H_5 \quad (X)$$

$$\xrightarrow[C_2H_5OH]{C_2H_5ONa} \begin{array}{l} CH_3CH_2CO_2C_2H_5 + \\ CH_3CH_2C^{14}O_2C_2H_5 + \\ CH_3(CH_2)_6CO_2C_2H_5 + \\ CH_3(CH_2)_6C^{14}O_2C_2 \end{array}$$

The esters constitute two pairs (VII and X or VIII and IX) comprised of chemically but not

reactions are illustrated below using structure II as an example.

$$CH_3CH_2C^{14}OCl + CH_3(CH_2)_6COCl \xrightarrow{(C_2H_5)_3N} CH_3CH=C^{14}=O + CH_3(CH_2)_5CH=C=O \longrightarrow$$

$$\begin{array}{cc} CH_3CH=C^{14}-CH(CH_2)_5CH_3 & \quad or \quad CH_3(CH_2)_5CH=C-CHCH_3 \\ \quad\quad | \quad\quad\quad | & \quad\quad\quad\quad\quad | \quad\quad | \\ \quad\quad O-C=O & \quad\quad\quad\quad\quad O-C^{14}=O \\ \quad\quad XI & \quad\quad\quad\quad\quad XII \\ \quad\quad \downarrow C_2H_5OH & \quad\quad\quad\quad\quad \downarrow C_2H_5OH \\ \quad\quad X & \quad\quad\quad\quad\quad VIII \end{array}$$

$$\xrightarrow{C_2H_5ONa \downarrow C_2H_5OH}$$

$$CH_3CH_2C^{14}O_2C_2H_5 + CH_3(CH_2)_6CO_2C_2H_5$$

isotopically equivalent components. Regardless of the ratio of formation, (VII + X)/(VIII + IX), the equivalence of the carbonyl groups in VI would be expected to make VII/X and VIII/IX equal to unity.[9] Cleavage of the β-ketoester mixture derived from the dimer with sodium ethoxide would result in the formation of *radioactive* ethyl caprylate. If all of the mixed dimer had

In the present investigation, the carbonyl-labeled propionyl chloride was prepared from carboxyl-labeled propionic acid which was made from ethylmagnesium chloride and radioactive carbon dioxide.[10] The mixed dimer was made following the directions of Sauer[7] and was separated from the simultaneously formed methyl- and hexylketene dimers by fractional distillation. The mixed dimer was degraded through the substituted acetoacetic esters as outlined above. Since the separation of a small amount of ethyl propionate from ethyl alcohol is not possible by

(9) It is recognized that differences in the zero-point energies of $C^{12}$–$C^{14}$ and $C^{12}$–$C^{12}$ bonds may prevent the bonds of an isotopic cyclobutanedione-1,3 ring from cleaving so as to give exactly the expected product ratios. An effect of this type has been reported by Calvin (paper presented at the Chicago Meeting of the American Chemical Society, April 21, 1948) for the decarboxylation of carboxyl-labeled malonic acid. In the present case, the error so introduced should probably not amount to more than 5%.

(10) The carbon dioxide was prepared from $C^{14}$-barium carbonate supplied by the Clinton Laboratories, Oak Ridge, Tenn., and obtained on allocation from the U. S. Atomic Energy Commission.

distillation the mixture of esters was saponified and the resulting propionic and caprylic acids separated by fractional distillation. The radioactivity analyses were made by the previously reported procedure.[11] The results are summarized in Table I.

TABLE I

RADIOACTIVITY ANALYSES

| Compound | Measured activity, counts/min.[a] | No. of tagged positions per molecule | Counts/ min./ mg. of BaCO₃/ tagged position[b] |
|---|---|---|---|
| Methylketene dimer | 372 | 2 | 390 |
| Hexylketene dimer | 10[c] | 2[d] | 28 |
| CO₂ from decarboxylation of ethyl α-capryloyl-caprylate | 5 | 1[e] | 2 |
| Mixed dimer (methyl- and hexyl- ketenes) | 105 | 1 | 400 |
| Acetoacetic esters from mixed dimer | 94 | 1 | 420 |
| CO₂ from decarboxylation of acetoacetic ester mixture | 806 | 1 | 280 |
| Propionic acid | 374 | 1 | 390 |
| Caprylic acid (Frac. 1) | 8.6 (2)[f] | 1 | 6[g] |
| (Frac. 2) | 9.7 (3)[f] | 1 | 8[g] |
| (Frac. 3) | 8.8 (2)[f] | 1 | 6[g] |
| Propionic acid[h] | 294 | | |
| Caprylic acid[h] (Frac. 1) | 6.2 | | |
| (Frac. 2) | 4.1 | | |

[a] Activity (corrected for background) of "infinitely thick" barium carbonate samples having a cross-sectional area of 2.90 cm.² measured with a Lauritsen electroscope (see Ref. 11) or a methane-filled windowless counter ("Nucleometer") manufactured by the Radiation Counter Laboratories. [b] Corrected for self absorption, calculated from (specific activity) × (number of carbon atoms)/ (number of labeled positions). [c] The activity of this material must be due to impurities since the activity of the carbon dioxide from the decarboxylation of a sample of ethyl α-capryloylcaprylate prepared from the dimer was much lower. [d] Two tagged positions were assumed since the carbonyl groups are equivalent in this compound. [e] The number of tagged positions is taken as unity since the specific activity of the carbonyl positions is the important consideration and the activity would not be increased even if both carbonyl positions were decarboxylated at once. [f] Values in parentheses are corrected for the efficiency of the separation of the propionic and caprylic acids. The correction factor was taken as (6.2 + 4.1) (374)/2 (294) = 6.6 counts/min. [g] Corrected for efficiency of the separation process. [h] Blank separation using radioactive and non-radioactive caprylic acids.

The activity of the caprylic acid (corrected for the efficiency of the separation of propionic and caprylic acids in the apparatus used) from the degradation of the mixed dimer was 1.5% of the activity per labeled carbon atom of the mixed dimer. From this value, the maximum amount of the material in the mixed dimer with structure VI which is convertible to acetoacetic esters with alcohol is 3%.

With the knowledge that practically none of the

(11) Roberts, Bennett, Holroyd and Fugitt, *Anal. Chem.*, **20**, 904 (1948).

mixed dimer has the VI structure it is possible to determine the composition of the forms XI and XII (or the corresponding unsymmetrical compounds derived from I or III) of the dimer by radioactive analysis of the carbon dioxide formed by decarboxylation of the acetoacetic acids resulting from the hydrolysis of the mixture of esters, VIII and X. The carbon dioxide so formed had 67% of the activity of the acetoacetic ester mixture and hence the composition of the original mixed dimers must be 33% of XI and 67% of XII.

In order to effectively utilize the information obtained from the radiochemical work a comparison was made between the physical properties of diketene, methylketene dimer, hexylketene dimer and the mixed dimer. The dipole moments (Table II) which were determined in benzene solution are large and quite close together. If the hypothesis is accepted that all of the compounds have similar structures the increase in moment (0.25 D) in going up the series from diketene to hexylketene dimer may well be due to induced moments in the long alkyl side chains. The molar refractivities of the compounds (Table II) are in best agreement with the lactone structures although some exaltation is noticed as might be expected for small ring structures.

The ultraviolet absorption spectra (Fig. 1) were determined in cyclohexane and may be taken as indicating that diketene is different in structure from the other aldoketene dimers. The spectrum of diketene has previously been interpreted by Calvin, Magel and Hurd[12] as being in agreement with expectations for form II. The differences in
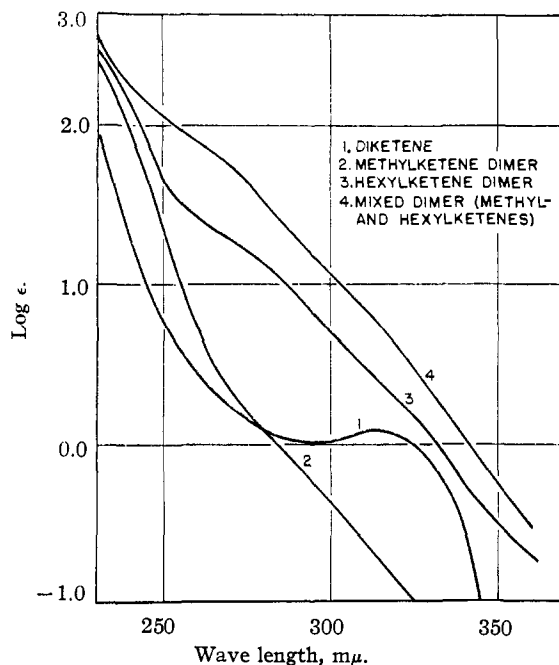


Fig. 1.—Ultraviolet spectra.

1. DIKETENE
2. METHYLKETENE DIMER
3. HEXYLKETENE DIMER
4. MIXED DIMER (METHYL- AND HEXYLKETENES)

(12) Calvin, Magel and Hurd, THIS JOURNAL, **63**, 2174 (1941).

<div align="center">

Table II

Molar Refractivities, Polarizations and Dipole Moments of Aldoketene Dimers

</div>

| Compound | $n^{25}$D | $d^{25}_4$ | $MR$D | Calculated $MR$D for structures corresponding to | | | | $P_\infty$ b | $\mu$(Debye) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | | | | I | II or III | IV | V | | |
| Diketene[a] | 1.4313 | 1.0626 | 20.49 | 20.18 | 20.30 | 19.00 | 20.08 | 234.6 | 3.23[c] |
| Methylketene dimer[a] | 1.4322 | 0.9864 | 29.49 | 29.44 | 29.56 | 28.26 | 29.34 | 252.7 | 3.30 |
| Mixed dimer[a] (methyl- and hexylketenes) | 1.4453 | 0.9130 | 53.16 | 52.59 | 52.71 | 51.41 | 52.49 | 292.8 | 3.42 |
| Hexylketene dimer[a] | 1.4517 | 0.8959 | 75.95 | 75.74 | 75.86 | 74.68 | 75.64 | 338.6 | 3.58 |

[a] Non-radioactive materials prepared by the methods of Sauer (ref. 7). [b] Data for calculation of $P_\infty$ given in Table III [c] Oesper and Smyth, This Journal, **64**, 768 (1942), report 3.31 D in benzene solution.

ultraviolet spectra between diketene and the higher aldoketene dimers might be due to considerably higher proportions of substances corresponding to III in the higher dimers although this conclusion may not be safe in view of the small extinction coefficient of the 312 m$\mu$ absorption maximum of diketene and the unknown influence which substitution of alkyl groups might have on the spectrum of II.

The infrared and Raman spectra of all four dimers have been obtained by Dr. R. C. Lord, Jr., Mr. R. S. McDonald, and Mr. E. J. Slowinski, to whom we are much indebted. The spectra, which will be published in detail later, are in satisfactory agreement with those previously reported[3,13,14] although the infrared spectrum of diketene shows a double peak at about 1060 cm.$^{-1}$ which has been reported earlier as a single shoulder on the 1020 cm.$^{-1}$ bond by Whiffen and Thompson.[13]

The infrared and Raman absorption of all of the dimers are similar and seem to be consistent with the lactone structures, II and III. The absence of absorption at 2153 cm.$^{-1}$ and above 3200 cm.$^{-1}$ typical of C=C=O and OH groups, respectively, appears to exclude structures I and V for all of the compounds. The presence of three widely separated C—H stretching frequencies at 2972, 3024 and 3120 cm.$^{-1}$ is in agreement with the conclusion that diketene is not a single pure compound since none of the structures I–V have more than two different varieties of C–H bonds.

The physical evidence is generally consistent with the hypothesis that the aldoketene dimers prepared in the present work have similar structures. The physical evidence in conjunction with the tracer study favors the assignment of structures of the type II or III which may be in equilibrium as suggested by Miller and Koch.[3]

**Acknowledgment.**—We wish to acknowledge the assistance of Miss Winifred Bennett with the radioactivity analyses and Mr. D. R. Smith with the preparation of the radioactive propionyl chloride.

<div align="center">

Experimental

</div>

**Preparation of Mixed Dimer of Methyl- and Hexylketenes.**—The preparation was carried out as described by Sauer.[7] The procedure is described in detail since consistent yields were not always obtained using other condi-

tions. A solution containing 37 g. (0.4 mole) of carbonyl-labeled propionyl chloride (0.015 mc. of C[14]) and 65 g. (0.4 mole) of caproyl chloride in 500 ml. of dry ether was placed under nitrogen in a 2-l. three-necked flask equipped with Dry Ice condenser, efficient sealed stirrer and dropping funnel. To the stirred solution was added dropwise 80.9 g. (0.8 mole) of purified triethylamine[7] over a period of three hours. The reaction mixture was allowed to stand at room temperature for three days and the solution of the ketene dimers separated from the amine salt by inverted filtration. The ethereal solution was concentrated under reduced pressure and finally distilled at 0.1 mm. using a Dry Ice-cooled receiver. The distillate was fractionated under reduced pressure using a 1.5 × 35 cm. Vigreux column equipped with a total condensation partial take-off distilling head. The yields were: methylketene dimer, b. p. 41–49° (11.5 mm.), 5.5 g. (24.5%); hexylketene dimer, b. p. 148° (1.3 mm.), 12.0 g. (24%); and mixed dimer, b. p. 86–89.5° (1.3 mm.), 18.6 g. (25.5%). Intermediate fractions amounted to 7.1 g. and 5.2 g. of brown viscous residue remained.

**Degradation of Mixed Dimer.**—The mixed dimer (10.4 g., 0.057 mole) was refluxed with 23 g. of absolute alcohol containing dry hydrogen chloride for five hours. The alcohol was removed by distillation and the residual mixture of ethyl $\alpha$-propionylcaprylate and ethyl $\alpha$-caproyl-propionate distilled under reduced pressure. After collection of a forerun of 1.9 g., b. p. 60–105° (0.5 mm.), the ester mixture distilled at 105° (0.5 mm.). The yield was 9.1 g. (70%). The mixture of ethyl $\alpha$-propionylcaprylate and ethyl $\alpha$-caproylpropionate was analyzed.

*Anal.* Calcd. for $C_{13}H_{24}O_3$: C, 68.38; H, 10.60; OC$_2$-H$_5$, 19.74. Found: C, 68.53; H, 10.37; OC$_2$H$_5$, 19.55.

The mixture of ethyl $\alpha$-propionylcaprylate and ethyl $\alpha$-caproylpropionate (4.5 g., 0.0197 mole) was refluxed with a solution of 0.3 g. of sodium in 50 ml. of dry alcohol for five hours. Sodium hydroxide solution was added and the mixture was refluxed for an additional two hours to hydrolyze the ethyl propionate and ethyl caprylate. The solution was evaporated under reduced pressure and the residue acidified with phosphoric acid and boiled for an hour. The solution was made basic and any non-acidic material steam-distilled. The residual solution was acidified and extracted continuously for three days with methylene chloride. The methylene chloride solution was dried over calcium sulfate and the solvent removed through a glass helices-packed column. The residue was transferred to a small flask and fractionated through a small center-tube column.[15] The yield of propionic acid, b. p. 135–136°, was 0.62 g. (43%). The yield of caprylic acid, b. p. 231–227°, was 1.34 g. (47%). Intermediate fractions amounted to 0.07 g.

As a test of the efficiency of the column, a mixture of 1.3 g. of radioactive propionic acid and 2.0 g. of caprylic acid was fractionated. The recoveries were: 1.03 g. (80%) of propionic acid and 0.91 g. (45%) of caprylic acid. Radioactivity analyses of the products are given in Table I.

To determine the composition of the possible unsymmetrical forms of the mixed dimer such as XI or XII, 0.116

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(13) Whiffen and Thompson, *J. Chem. Soc.*, 1005 (1946).

(14) Taufen and Murray, This Journal, **67**, 754 (1945).

(15) The fractionating section of this column was similar to that described by Naragon and Lewis, *Ind. Eng. Chem., Anal. Ed.*, **18**, 448 (1946).

## TABLE III

DIELECTRIC CONSTANTS, DENSITIES AND POLARIZATIONS
IN BENZENE AT 25°

| $f_2$ | $\epsilon$ | $d$ | $P_2$ |
|---|---|---|---|
| Diketene | | | |
| 0.00000 | $(2.2725)^a$ | 0.87222 | $P_1 = 26.6720$ |
| .006407 | 2.3642 | .87355 | 228.4 |
| .013211 | 2.4659 | .87485 | 228.4 |
| .022613 | 2.6109 | .87625 | 226.8 |
| .032564 | 2.7604 | .87793 | 220.5 |
| .040303 | 2.8783 | .87911 | 216.3 |
| .060383 | 3.1746 | .88246 | 203.8 |
| Methylketene dimer | | | |
| 0.00542 | 2.3497 | 0.87307 | 239.7 |
| .011488 | 2.4550 | .87396 | 258.6 |
| .022082 | 2.6462 | .87533 | 264.4 |
| .032160 | 2.8227 | .87677 | 258.9 |
| .041811 | 3.0214 | .87811 | 260.8 |
| .057532 | 3.3055 | .88022 | 250.1 |
| Mixed dimer of methyl- and hexylketenes | | | |
| 0.006361 | 2.3748 | 0.87293 | 292.7 |
| .009736 | 2.4376 | .87330 | 302.6 |
| .011827 | 2.4634 | .87317 | 291.0 |
| .014545 | 2.5165 | .87324 | 298.3 |
| Hexylketene dimer | | | |
| 0.004751 | 2.3555 | 0.87291 | 336.4 |
| .009643 | 2.4398 | .87272 | 335.4 |
| .021604 | 2.6502 | .87369 | 331.4 |
| .039671 | 2.9547 | .87438 | 321.3 |
| .047347 | 3.2051 | .87491 | 346.6 |
| .062258 | 3.3259 | .87472 | 311.7 |

$^a$ Hartshorn and Oliver, *Proc. Roy. Soc. (London)*, **A123**, 664 (1929).

g. of the mixture of ethyl α-propionylcaprylate and ethyl α-caprylylpropionate was hydrolyzed by refluxing with a carbon dioxide-free solution of sodium hydroxide prepared by dissolving 0.05 g. of clean sodium in 10 ml. of boiled alcohol and diluting with 10 ml. of boiled water. The hydrolysis mixture was acidified with dilute perchloric acid and heated to boiling. The evolved carbon dioxide was swept out with nitrogen and precipitated as barium carbonate which was analyzed in the usual manner.[11]

**Ultraviolet Absorption Spectra.**—The ultraviolet spectra were determined in purified cyclohexane solution using a Beckman Quartz Spectrophotometer.[16]

**Dipole Moments.**—The dielectric constants were measured at a frequency of 954 kilocycles using a modification of the heterodyne heat apparatus described by Smyth.[17] The standard condenser was a General Radio Type 722-N. The dielectric cell was similar to the one described previously.[18] The replaceable capacity of the cell at 25° was 123.50 $\mu\mu$ fd. and the volume about 40 ml. The pycnometers were of the graduated type described by Robertson.[19]

The dipole moments were obtained from the dielectric constants and densities of dilute solutions using the customary equations.[17] Values of $P_\infty$ were obtained by least squares extrapolation of $P_2$ to infinite dilution and the sum of the electronic and atomic polarizations at infinite wave length was assumed to be equal to the experimental value of the molar refraction for the sodium D line, $MR_D$. The data are given in Tables II and III.

## Summary

The isotopic tracer technique has been used to demonstrate that the mixed aldoketene dimer of methyl- and hexylketenes prepared by the Wedekind reaction does not have a cyclobutanedione-1,3 structure.

The physical properties of several aldoketene dimers indicate that these substances probably have structures similar to diketene and are best formulated as vinylaceto-β-lactone or β-crotonolactone derivatives.

(16) Cary and Beckman, *J. Optical Soc. Am.*, **31**, 682 (1941).

(17) Smyth, in Weissberger, "Physical Methods of Organic Chemistry," Vol. 2, Interscience Publishers, Inc., New York, 1946, Chap. XX.

(18) Rogers and Roberts, THIS JOURNAL, **68**, 843 (1946).

(19) Robertson, *Ind. Eng. Chem., Anal. Ed.*, **11**, 464 (1939).

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# The Binding of Organic Ions by Proteins. Effect of Temperature

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The affinity of serum albumin for organic ions has been found to depend on the charge and structure of the anion, as well as on the pH and nature of the buffer and on the concentration of the protein.[1–6] From the magnitude of the effects of these different factors, it has been possible to obtain some insight into the molecular nature of the anion–protein complex. Since entropy and enthalpy changes accompanying a chemical transformation are frequently also very illuminating in this respect, it has seemed appropriate to examine also the temperature dependence of the binding process.

In his exploratory work on sulfonamide–plasma protein complexes, Davis[1] observed no marked change in degree of binding with rise in temperature. Similarly Putnam and Neurath[7] in their electrophoretic investigations of complexes between albumin and sodium dodecyl sulfate obtained no indication of a temperature dependence.

(1) B. D. Davis, *J. Clin. Invest.*, **22**, 753 (1943).

(2) P. D. Boyer, F. G. Lum, G. A. Ballou, J. M. Luck and R. G. Rice, *J. Biol. Chem.*, **162**, 181 (1946).

(3) I. M. Klotz, F. M. Walker and R. B. Pivan, THIS JOURNAL, **68**, 1486 (1946).

(4) J. D. Teresi and J. M. Luck, *J. Biol. Chem.*, **174**, 653 (1948).

(5) I. M. Klotz, H. Triwush and F. M. Walker, THIS JOURNAL, **70**, 2935 (1948).

(6) I. M. Klotz and J. M. Urquhart, *J. Phys. and Colloid Chem.*, **3**, in press (1949).

(7) F. W. Putnam and H. Neurath, *J. Biol. Chem.*, **159**, 195 (1945).