124°); *p*-nitrobenzoate, m.p. 112–113° (lit. 114–115°); methiodide, m.p. 102–103° (lit. 103–104°). The benzyl bromide derivative was also prepared by reaction of the pyridine compound with an excess of benzyl bromide at room temperature. The crystalline derivative which separated was recrystallized twice from ethanol; m.p. 155–156°.

Anal. Calcd. for $C_{15}H_{18}NOBr$: C, 58.44; H, 5.89; N, 4.54. Found: C, 58.64; H, 5.95; N, 4.60.

2-Methyl-3-(β-ethoxyethyl)-4,6-dichloropyridine (II).—One-hundred and fifteen grams of 2-methyl-3-(β-ethoxyethyl)-4,6-dihydroxypyridine (I) was dissolved in 540 ml. of phosphorus oxychloride. The solution was heated in a glass-lined bomb nearly full for six hours at 140° under a nitrogen pressure of about 400 p.s.i. The excess phosphorus oxychloride was removed under reduced pressure and the residue was poured into an excess of crushed ice. No precipitate formed. The mixture was diluted, and partially neutralized with 30% sodium hydroxide solution to about *p*H 3. The solution was extracted several times with chloroform, which extract was washed, dried, and concentrated, leaving a brown, oily residue. It was distilled under reduced pressure; b.p. 96–97° (1 mm.). The yield of 2-methyl-3-(β-ethoxyethyl)-4,6-dichloropyridine (II) was 106 g. (90%).

RAHWAY, N. J. RECEIVED DECEMBER 8, 1950

Concerning *trans*-Acylation in Azlactone Synthesis

BY SERGE N. TIMASHEFF AND F. F. NORD

Although it is considered that in the synthesis of azlactones[1] no *trans*-acylation occurs,[2] Bennett and Niemann have reported that in the preparation of some azlactones of fluorinated benzene they were able to detect products of *trans*-acylation by means of ultraviolet absorption analysis[3] and in one instance by isolation. These authors reported that in the product obtained some benzamido groups from the expected phenyloxazolone had become replaced by acetamido groups from the acetic anhydride in which medium the reaction is carried out.

Realizing the significance of such a *trans*-acylation in the recently reported synthesis of thiophene azlactones,[4] a similar study was carried out using the first member of this series, namely, 2-phenyl-4-(2-thenal)-5-oxazolone. The ultraviolet absorption spectra of both the crude phenyloxazolone and the purified material along with that of the methyl compound are presented in Fig. 1. It can be seen that the curves of the absorption spectra of the phenyloxazolone preparations are very similar, both possessing peaks at 270 and 394 mμ. The crude preparation displayed neither a peak nor a plateau in the region of 362–364 mμ, which is characteristic for the methyloxazolone. Thus, it can be concluded that in the case of the phenyloxazolone derived from thiophene-2-aldehyde[5] *via* the Erlenmeyer–Plöchl synthesis using acetic anhydride as the medium, no *trans*-acylation occurs.

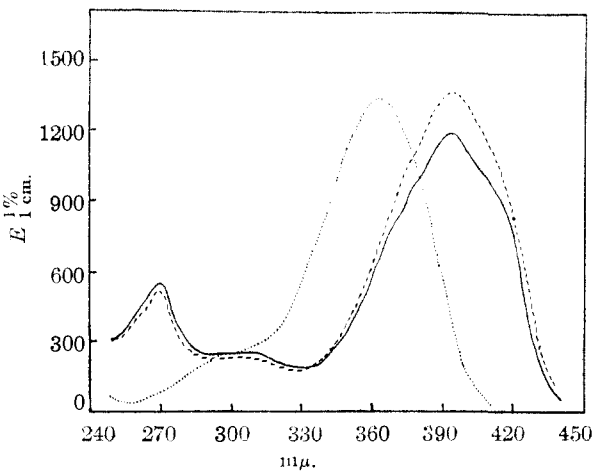


Fig. 1.—Ultraviolet spectra of thiophene azlactones: ....., methyloxazolone; - - - - - -, phenyloxazolone (purified); ——, phenyloxazolone (crude).

(1) J. Plöchl, *Ber.*, **16**, 2815 (1883); E. Erlenmeyer, *Ann.*, **275**, 1 (1893).

(2) J. W. Cornforth, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 733, 784.

(3) E. L. Bennett and C. Niemann, THIS JOURNAL, **72**, 1803 (1950).

(4) B. F. Crowe and F. F. Nord, *J. Org. Chem.*, **15**, 81 (1950).

(5) W. J. King and F. F. Nord, *ibid.*, **13**, 635 (1948).

DEPARTMENT OF ORGANIC CHEMISTRY AND ENZYMOLOGY
FORDHAM UNIVERSITY
NEW YORK 58, N. Y. RECEIVED DECEMBER 11, 1950

The Synthesis of DL-Aspartic Acid-4-C^{14} [1]

BY S. C. WANG, T. WINNICK AND J. P. HUMMEL

Aspartic acid, labeled in the carboxyl adjacent to the substituted methylene group, has been synthesized in one step from ethyl formylaminomalonate and methyl bromoacetate-1-C^{14} (purchased from Tracerlab, Inc.). The procedure required no special equipment. The yield of the purified product was 63%. The specific radioactivity was about 16,000 counts per minute per mg., starting from 0.025 mole of methyl bromoacetate containing 1 mc. of C^{14}.

The position of the labeling, already established by the method of synthesis, was further confirmed by the Van Slyke ninhydrin–carbon dioxide method. Both carboxyls of aspartic acid are ninhydrin-labile.

Attempts were also made to prepare aspartic acid by the reduction of ethyl oxalacetate-4-C^{14} oxime with sodium amalgam. Only a 42% yield was obtained in this reduction. The potassium salt, from which the oxime was made, was prepared in 87% yield from sodium acetate-1-C^{14} by converting the latter to ethyl acetate with diethyl sulfate and condensing the ethyl acetate with ethyl oxalate in the presence of potassium.

(1) For detailed descriptions order Document 3125 from American Documentation Institute, 1719 N Street, N. W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.05 for photocopies (6 × 8 inches) readable without optical aid.

RADIATION RESEARCH LABORATORY AND
DEPARTMENT OF BIOCHEMISTRY
STATE UNIVERSITY OF IOWA COLLEGE OF MEDICINE
IOWA CITY, IOWA RECEIVED JANUARY 12, 1951

The Structure of Ethylketene Dimer

BY R. L. WEAR

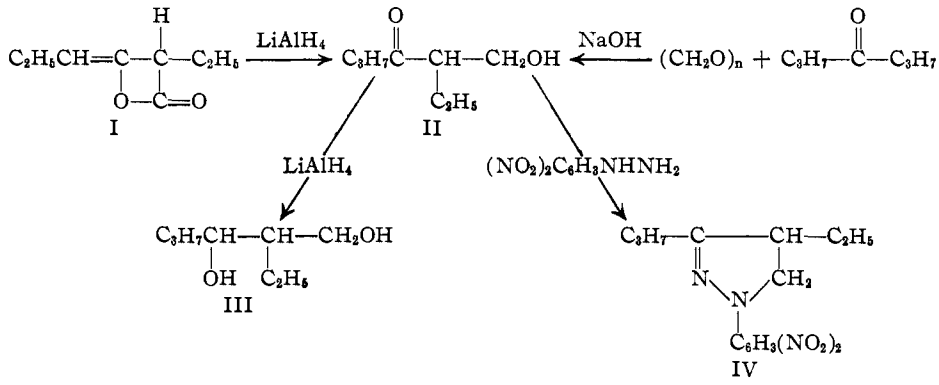
The structure of alkylketene dimers, prepared by the dehydrohalogenation of acyl halides, continues to be of interest.[1,2]

(1) C. D. Hurd and C. A. Blanchard, THIS JOURNAL, **72**, 1461 (1950).

(2) J. D. Roberts, R. Armstrong, R. F. Trimble, Jr., and M. Burg, *ibid.*, **71**, 843 (1949).

In this Laboratory it has been found that the lithium aluminum hydride reduction of ethylketene dimer (I) produced 3-(hydroxymethyl)-4-heptanone (II) in 55% yield. This result is consistent with the β,γ-unsaturated β-lactone structure for the dimers, but not with the 1,3-cyclobutanedione or acyl ketene structures.[3]

To identify II, it was reduced with lithium aluminum hydride. A high yield of 2-ethyl-1,3-hexanediol (III) was obtained; however, this is not an unequivocal proof of the identity of II. Therefore excess di-*n*-propyl ketone was condensed with paraformaldehyde in the presence of a small amount of methanolic sodium hydroxide, a general procedure stated to give monomethylol ketones.[4] The product was shown to be identical with II.



Experimental

Ethylketene Dimer (I).—The preparation was carried out as described by Sauer.[5] Eighty grams (0.75 mole) of butyryl chloride was dehydrohalogenated with 78 g. (0.77 mole) of triethylamine. A 65% yield of product (34.2 g.) was collected at 92–95° (31 mm.), $n^{24}D$ 1.4385.

Preparation of 3-(Hydroxymethyl)-4-heptanone (II) **by Lithium Aluminum Hydride Reduction of Ethylketene Dimer.**—The reaction was carried out in a 3-necked flask equipped with a gas inlet and dropping funnel, a ground-glass sealed stirrer and a condenser protected with a drying tube. The apparatus was dried several hours in a 125° oven before use. Powdered lithium aluminum hydride (3.0 g., 0.079 mole) was dissolved in 200 ml. of anhydrous ether. With a slow stream of nitrogen flowing through the apparatus, 14.0 g. (0.10 mole) of ethylketene dimer dissolved in 30 ml. of anhydrous ether was added dropwise. The mixture refluxed during the addition. Stirring was continued for an additional 30 minutes. The mixture was cooled with ice and cautiously hydrolyzed by slowly adding 15 ml. of methanol. Then 180 g. of 10% sulfuric acid was added, the ether layer separated and the aqueous layer extracted with two portions of ether. The combined ether layers were washed with saturated aqueous sodium bicarbonate and water, dried, and the ether flask distilled. The pleasant-smelling residual liquid was distilled from a Claisen flask. The material distilling at 70–76° (1 mm.) was collected. The yield was 8 g. (55%). Redistillation through a 10-plate column gave a high recovery of liquid distilling at 58.5–59° (0.5 mm.), 75° (1.5 mm.), $n^{23}D$ 1.4389. *Anal.* Calcd. for $C_8H_{16}O_2$: C, 66.62; H, 11.18. Found: C, 66.2; H, 11.0.

The reaction of this compound with 2,4-dinitrophenylhydrazine reagent produced a pyrazoline (IV), which is characteristic of methylol ketones.[6] The orange crystals melted at 118.5–119.5° after recrystallization from absolute ethanol. *Anal.* Calcd. for $C_{14}H_{18}N_4O_4$: C, 54.89; H, 5.92; N, 18.29. Found: C, 54.70; H, 5.99; N, 18.2.

Preparation of 3-(Hydroxymethyl)-4-heptanone (II) **from Di-*n*-propyl Ketone and Paraformaldehyde.**—Di-*n*-propyl ketone (45.7 g.), 3.0 g. of paraformaldehyde and a small amount of phenolphthalein indicator were heated to 50°. Small amounts of methanolic sodium hydroxide were added when necessary to keep the mixture slightly alkaline to the indicator. After several minutes the paraformaldehyde dissolved. The mixture was then cooled in ice for two hours and allowed to stand overnight. After neutralizing with acetic acid, the mixture was filtered and the filtrate distilled. Excess di-*n*-propyl ketone was collected up to 50° (20 mm.). The product then distilled at 72–73° (1.3 mm.), $n^{24}D$ 1.4387. The yield was 6.0 g. (42%). The pyrazoline derivative prepared from 2,4-dinitrophenylhydrazine reagent melted at 118–119.5°. A mixture of the two pyrazolines melted at 118.5–120°.

Preparation of 2-Ethyl-1,3-hexanediol (III) **by Lithium Aluminum Hydride Reduction of 3-(Hydroxymethyl)-4-heptanone** (II).—II (7.5 g.) was reduced with lithium aluminum hydride (1.5 g.) in a manner similar to that described above. Distillation of the crude product yielded 6.0 g. (79%) of III, b.p. 91–93° (1.5–2 mm.), $n^{16}D$ 1.4535. The bis-phenylurethan, fine white needles after recrystallization from benzene, melted at 130–131°. *Anal.* Calcd. for $C_{22}H_{28}N_2O_2$: N, 7.3. Found: N, 7.5.

The bis-phenylurethan prepared from a commercial sample of 2-ethyl-1,3-hexanediol gave a mixed m.p. of 129–130° with the above derivative.

Acknowledgment.—I wish to thank Messrs. B. W. Nippoldt, P. B. Olson and J. G. Gagnon of our Analytical Section for the analyses.

CONTRIBUTION NO. 27 FROM
THE CENTRAL RESEARCH DEPARTMENT
MINNESOTA MINING AND MANUFACTURING COMPANY
ST. PAUL, MINN. RECEIVED JANUARY 2, 1951

(3) The lithium aluminum hydride reduction of γ-valerolactone gives 1,4-pentanediol: see R. F. Nystrom and W. G. Brown, THIS JOURNAL, **70**, 3738 (1948).

(4) W. M. Quattlebaum, Jr., U. S. Patent 2,064,564.

(5) J. C. Sauer, THIS JOURNAL, **69**, 2444 (1947).

(6) G. T. Morgan and E. L. Holmes, *J. Chem. Soc.*, 2667 (1932).

The Resolution of Methylethylphenylcarbinol

BY HAROLD H. ZEISS

The resolution of the mixed aliphatic–aromatic tertiary alcohol, methylethylphenylcarbinol (I),[1] is achieved by the methods employed in the separation of the enantiomorphs of methylethylisobutylcarbinol.[2] Past attempts to resolve I by other approaches are reported to be unsuccessful.[3] The carbinol is prepared by the reaction of methyl ethyl ketone with phenylmagnesium bromide and is converted to hydrogen 2-phenylbutyl-2-phthalate (II) by the addition of its potassium salt to phthalic anhydride in benzene solution. The acid ester is isolated easily and in pure form by crystallization from benzene.[4] When II and an equimolecular amount of brucine are combined in acetone, brucine 2-phenylbutyl-2-phthalate (III) crystallizes from solution as clusters of transparent prisms. A systematic fractional crystallization of III from acetone, according to the triangle

(1) An optical rotation of $\pm 14°$ is erroneously reported for I in "Beilstein," (1) Vol. VI, p. 258.

(2) W. von E. Doering and H. H. Zeiss, THIS JOURNAL, **70**, 3966 (1948); **72**, 147 (1950).

(3) E. S. Wallis and F. H. Adams, *ibid.*, **55**, 3838 (1933).

(4) M. P. Balfe, M. A. Doughty, J. Kenyon and R. Poplett, *J. Chem. Soc.*, 605 (1942), have previously reported II without description of preparation or properties.