(unpublished) results indicate that the amino acid must not be allowed to remain too long upon the resin else it becomes difficult to remove it completely. This suggests the very important problem of elution. Work with the resins seems to indicate that the exchange or acid-binding is quite reversible in the absence of side-reactions. It may be mentioned that these resins are prepared with formaldehyde and if there remains in the resin any residual formaldehyde or if any residual reactive groups are present then chemical reaction with amino acids might be expected. This point is made here not because we have any definite evidence bearing upon it but because we feel that it should be borne in mind. There also exist the possibilities of using the resins for the chromatographic separation of amino acid esters, or acyl derivatives; or of influencing the ionization of the amino acids by the use of alcohol or other solvent mixtures[23] or by modifying the amino acid by means of formol,[24] so that differences between individual amino acids may be accentuated for the purpose of separating them.

(23) Th. Wieland, *Naturwissenchaften*, **30**, 374 (1942); also ref. 8.

(24) G. Schramm and J. Primosigh, *Ber.*, **76**, 373 (1943). See also Englis and Fiess[10] who made some studies of this kind but who used probably too dilute a formaldehyde solution and too low a *p*H.

**Acknowledgment.**—We wish to record our indebtedness to Professor Hubert B. Vickery for encouragement and advice in this work.

## Summary

The responses toward several amino acids of a cation-exchange and an acid-binding synthetic organic resin have been examined. The influence of the following factors upon the responses have been investigated: type of resin, particle size, length of adsorption column, rate of flow, concentration of amino acid in solution, hydrogen ion concentration of the solution. The investigation has been extended to several binary and two ternary mixtures of amino acids, and evidence regarding their separability has been obtained. An attempt has been made to explain the effects observed. The problems involved in separating amino acids on exchange-resins have been considered as well as the factors needing further investigation.

NEW HAVEN, CONNECTICUT RECEIVED MARCH 20, 1945

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

# Preparation of (+)2-Methylbutanal-1

BY ELMER J. BADIN AND EUGENE PACSU

It was necessary in connection with other investigations to know the properties of the optically active aldehyde, (+)2-methylbutanal-1, and its derivatives; the optical rotations for the aldehyde obtained by Ehrlich[1] and by Levene and Kuna[2] were at variance with one another. The aldehyde was prepared by oxidizing amyl alcohol fractions containing various percentages of active 2-methylbutanol-1 and inactive 3-methylbutanol-1 obtained by fractionation of fusel oil. In this work the procedure of Ehrlich, involving oxidation with sodium dichromate in sulfuric acid solution, was modified by reducing the oxidation time and by fractionating the oxidation products to isolate the aldehyde instead of first preparing the bisulfite addition compound and hydrolyzing it with sodium carbonate. The latter step was avoided to prevent racemization of the aldehyde which presumably occurred during the hydrolysis by others of the bisulfite addition compound. By these modifications both the yield and purity of the product were greatly improved.

## Experimental

**Preparation of Active Amyl Alcohol.**—The optically active amyl alcohol was prepared by fractionation of fusel oil with $[\alpha]_D$ −1.40° through a twelve theoretical plate glass helix packed column. In one series of distillations there was obtained an alcohol with $[\alpha]_D$ −5.42°, b. p. 128–129°, $d^{20}_4$ 0.8186. This was accomplished by carrying out eight complete distillations and by taking from three to five cuts per distillation. Based on an optical rotation of $[\alpha]_D$ −6.0°[3] for pure (−)2-methylbutanol-1, this alcohol contained 90.3% (−)2-methylbutanol-1 and 9.7% 3-methylbutanol-1. Other fractions obtained had 29.8% of the active alcohol with $[\alpha]_D$ −1.79° and 59.2% of the active alcohol with $[\alpha]_D$ −3.55°.

**Oxidation of Active Amyl Alcohol.**—Sixty grams (0.682 mole) of the active amyl alcohol, $[\alpha]_D$ −5.42°, was placed in a one-liter flask equipped with a dropping funnel, electric mercury seal stirrer, and a modified Claisen distillation head packed with saddles and fitted to a downward condenser. A sulfuric acid solution of 68 g. (0.227 mole) of sodium dichromate dihydrate, 55 ml. of concentrated sulfuric acid, and 400 ml. of water was prepared. The alcohol was heated to incipient boiling and the sodium dichromate solution added at a constant rate to the vigorously stirred alcohol over a period of twenty-two minutes. Volatile products were allowed to distil out as formed; the bath surrounding the reaction flask was maintained at 95° throughout the oxidation. After addition of all the dichromate solution the bath was heated to 140° over a period of fifteen minutes to remove the remainder of the products.

The organic layer of the distillate was dried twice with anhydrous sodium sulfate and magnesium sulfate and then fractionated. The cut boiling below 95° was collected and dried with calcium chloride and sodium sulfate and redistilled; 23 g. of aldehyde with b. p. 90–92°, $d^{25}_4$ 0.8055, $[\alpha]_D$ +28.50° (homogeneous, 1-dm. tube) was obtained. The yield of the aldehyde was 52% of the theoretical based on the amount of the alcohol oxidized.

(1) Ehrlich, *Ber.*, **40**, 2556 (1907).

(2) Levene and Kuna, *J. Biol. Chem.*, **110**, 323–328 (1935).

(3) Whitmore and Olewine, THIS JOURNAL, **60**, 2569–2570 (1938).

In addition there was obtained 15.0 g. of unchanged alcohol and 9.5 g. of a high-boiling material of b. p. 179–185°. This latter fraction was a mixture of the acids formed during the oxidation and their esters with the alcohols present in the starting material. It had an 18% acid and an 82% ester content based on its acid value and saponification value.

An oxidation of 88 g. (1 mole) of alcohol with $[\alpha]_D$ −3.55° corresponding to 59.2% (−)2-methylbutanol-1 gave 35 g. of aldehyde with rotation $[\alpha]_D$ +17.73°, 14.5 g. of unchanged alcohol and 24 g. of high boiling residue. The yield of aldehyde was 49% of the theoretical.

Similarly, a third oxidation of 88 g. (1 mole) of amyl alcohol with $[\alpha]_D$ −1.79° corresponding to 29.8% (−)2-methylbutanol-1 yielded 30 g. of aldehyde with $[\alpha]_D$ +8.72°, 11 g. of unchanged alcohol and 21 g. of high boiling material. The aldehyde was obtained in 40% yield. The rotations of the three aldehydes *versus* the rotations of the alcohols from which they were prepared is shown graphically in Fig. 1. Since the aldehydes were susceptible to oxidation by atmospheric oxygen, they were stored in a nitrogen atmosphere in glass-stoppered flasks. Ehrlich,[1] by oxidation of an alcohol with $[\alpha]_D$ −5.47°, obtained only a 15% yield of aldehyde with $[\alpha]_D$ +23.6°. The extrapolated value for pure (+)2-methylbutanal-1 from Fig. 1 is $[\alpha]_D$ +31.2° as compared with the 24% lower value of $[\alpha]_D$ +23.6° obtained by Ehrlich. No experimental details are given for comparison in the work of Levene and Kuna.[2]

The unrecrystallized 2,4-dinitrophenylhydrazones of the three aldehydes obtained had $[\alpha]_D$ +30.3° ($c$ = 4.89, acetone, 1-dm. tube), m. p. 125.5–126.5° from the aldehyde with $[\alpha]_D$ +28.50°; $[\alpha]_D$ +17.5° ($c$ = 4.84, acetone, 1-dm. tube), m. p. 111.5–113.5° from the aldehyde with $[\alpha]_D$ +17.5°; $[\alpha]_D$ +8.06° ($c$ = 4.96, acetone, 1-dm. tube), m. p. 114–115.5°, from the aldehyde with $[\alpha]_D$ +8.72°. For the determination of the constants of the 2,4-dinitrophenylhydrazone of pure (+)2-methylbutanal-1, the 2,4-dinitrophenylhydrazone ($[\alpha]_D$ +30.3°) from the aldehyde of rotation $[\alpha]_D$ +28.50° was recrystallized three times, once from 80% ethanol and twice from 90% ethanol when a melting point of 132.5–133° was obtained. The rotation of this derivative was $[\alpha]_D$ +32.1° ($c$ = 4.99, acetone, 1-dm. tube); the value obtained by extrapolation from the curve of $[\alpha]_D$ of the derivative *versus* $[\alpha]_D$ of the aldehyde was $[\alpha]_D$ +32.2°.

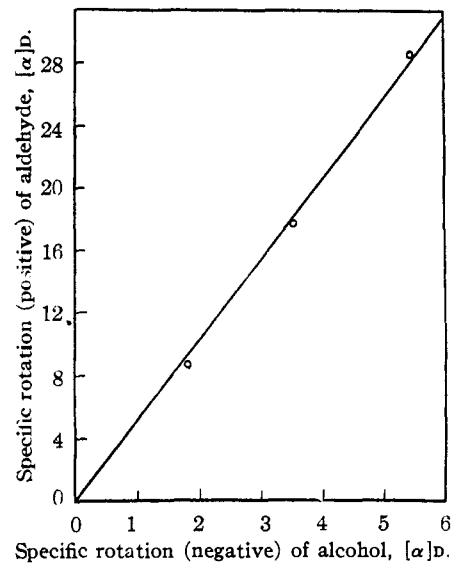

Fig. 1.

*Anal.* Calcd. for $C_{11}H_{14}N_4O_4$: C, 49.57; H, 5.30; N, 21.04. Found: C, 49.35; H, 5.32; N, 21.50.

## Summary

The optically active aldehyde, (+)2-methylbutanal-1, has been prepared by oxidation of active amyl alcohol and the optical rotation of the pure aldehyde and the properties of its 2,4-dinitrophenylhydrazone determined.

PRINCETON, NEW JERSEY RECEIVED MARCH 20, 1945

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

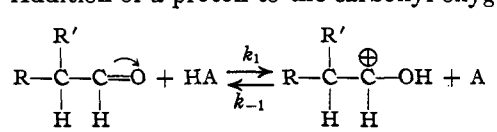
# Kinetics and Mechanism of the Acid Catalyzed Racemization of (+)2-Methylbutanal-1

BY ELMER J. BADIN AND EUGENE PACSU

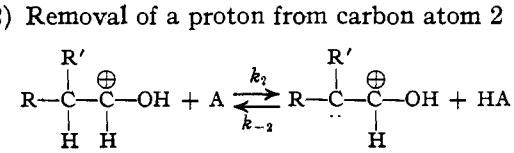
In probing the mechanism of hydrogenation and dehydrogenation of aldehydes and alcohols,[1] it was found necessary to prepare the optically active aldehyde, (+)2-methylbutanal-1. This aldehyde was found to racemize readily on a nickel catalyst surface. A study of the acid catalyzed racemization of this aldehyde was undertaken since no data on the rate of racemization of an aldehyde have previously been reported. The study has permitted further information to be obtained in regard to the extent and nature of solvation in acid catalyzed reactions in addition to information regarding the racemization reaction.

The rate in alkaline medium was found to be much greater than in acid solution; work in this investigation has dealt mainly with the rate of acid catalyzed racemization in aqueous dioxane solvents. Results indicated that the general mechanism applying for acid catalysis was best represented by the following steps where HA represents a molecule of acid and A its conjugate base.

(1) Addition of a proton to the carbonyl oxygen




(2) Removal of a proton from carbon atom 2




(1) Badin and Pacsu, THIS JOURNAL, 66, 1963 (1944).