The fermentation was carried out in a 400-liter resin-lined tank using the synthetic medium described by Stone and Farrell[1] and culture Q-176 of *Penicillium notatum*. The precursor, γ-chlorocrotylmercaptoacetic acid, was employed at a concentration of 250 mg. per liter. The assay of the beer at harvest (sixty-four hours) was 250 Oxford units per ml. When processed by the carbon–acetone method,[2] 44 g. of crude sodium salt was obtained; bio-assay, 625 Oxford units per mg.; purity indicated by hydroxylamine assay,[3] 24%. The crude penicillin was purified by partition chromatography[4,5,6] of the free acid on an ether–silica column using *p*H 6.2 potassium phosphate buffer. A peak fraction in the eluates[7] which included 70% of the activity was titrated to *p*H 7.0 with 1% potassium hydroxide solution and dried from the frozen state. The resulting amorphous potassium salt crystallized when treated with dry acetone. It was recrystallized by dissolving it in 90% acetone and adding 3 volumes of dry acetone. The yield of recrystallized potassium salt was 4.2 g.; bio-assay, 1900 Oxford units per mg.

Anal. Calcd. for $C_{14}H_{18}N_2O_4ClS_2K$: C, 40.32; H, 4.35; S, 15.38; Cl, 8.50. Found: C, 40.32; H, 4.35; S, 15.22; Cl, 8.37.

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(1) Stone and Farrell, *Science*, **104**, 445 (1946).

(2) Whitmore, Wagner, Noll, Bassler, Fleming, Carnahan, Weisgerber, Oakwood, Herr, Patterson, Haggard, Mraz, Hoover, DiGiorgio, Weisel, Lovell, Walter and Ropp, *Ind. Eng. Chem.*, **38**, 942 (1946).

(3) Ford, *Anal. Chem.*, **19**, 1004 (1947).

(4) Gordon, Martin and Synge, *Biochem. J.*, **37**, 79 (1943).

(5) Harris and Wick, *Ind. Eng. Chem.*, *Anal. Ed.*, **18**, 276 (1946).

(6) Behrens, Corse, Edwards, Garrison, Jones, Soper, Van Abeele and Whitehead, *J. Biol. Chem.*, **175**, 793 (1948).

(7) The optical rotation was found to be a convenient measurement for use in grouping the eluate fractions.

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Some New Derivatives of 4-Methylimidazole

During a search for compounds which possess antihistaminic activity, a brief study was made of substances which contained the imidazole nucleus. A few compounds were synthesized by treatment of 4-(chloromethyl)-imidazole hydrochloride[1] with an appropriate secondary amine or thiourea. The intermediate 4-(hydroxymethyl)-imidazole hydrochloride was prepared by the method of Totter and Darby.[2] None of the compounds listed below inhibited the effect of histamine on isolated intestinal strips of guinea pigs.

Typical Procedure.—The 4-(aminomethyl)-imidazoles were prepared by heating under reflux for two hours a mixture of 0.025 mole of 4-(chloromethyl)-imidazole hydrochloride, 0.075 mole of the secondary amine and 75 cc. of absolute alcohol. The resultant solution was first made alkaline with aqueous ammonia and the ammonium chloride that formed was removed by filtration. After evaporation under reduced pressure to remove the solvent and the excess amine, the residue was dissolved in absolute alcohol, from which the hydrochloride was obtained as a sticky solid by the addition of an ether solution of anhydrous hydrogen chloride. In all cases two or three recrystallizations from alcohol–ether gave pure products in the form of hygroscopic white powders.

4-(Diethylaminomethyl)-imidazole Dihydrochloride.—Yield, 90%; m. p. 200° with softening at 172°.

Anal. Calcd. for $C_8H_{15}N_3\cdot 2HCl$: N, 18.6; Cl, 31.3. Found: N, 18.4; Cl, 31.2.

4-(1-Piperidylmethyl)-imidazole Dihydrochloride.—Yield, 45.5%; m. p. 223.6–227.1°.

Anal. Calcd. for $C_9H_{15}N_3\cdot 2HCl$: N, 17.7; Cl, 29.6. Found: N, 17.9; Cl, 29.5.

4-(4-Morpholinylmethyl)-imidazole Dihydrochloride.—Yield, 66.7%; m. p. 173°.

Anal. Calcd. for $C_8H_{13}N_3O\cdot 2HCl$: C, 39.9; H, 6.25; N, 17.5; Cl, 29.6. Found: C, 39.4; H, 6.69; N, 16.5; Cl, 29.5.

S-(4-Imidazolylmethyl)-isothiourea Dihydrochloride.—A solution of 3.5 g. (0.05 mole) of thiourea in 100 cc. of absolute alcohol was brought to a boil and then treated with 7.6 g. (0.05 mole) of 4-(chloromethyl)-imidazole hydrochloride. The resultant mixture was heated under reflux for ten minutes, and the solid which precipitated upon cooling was collected. A practically quantitative yield was obtained of milky, white prisms which, after recrystallization from dilute alcohol, melted at 227.6–229.6°.

Anal. Calcd. for $C_5H_8N_4S\cdot 2HCl$: N, 24.4; Cl, 31.0. Found: N, 24.3; Cl, 30.9.

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RECEIVED JUNE 9, 1948

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(1) Pyman, *J. Chem. Soc.*, **99**, 674 (1911).

(2) Totter and Darby, "Organic Syntheses," **24**, 69 (1944).

Dichromate Salts of 2-Benzyl and 4-Benzylpyridine

2-Benzylpyridinium Dichromate.—2-Benzylpyridine (25 g., 0.15 mole), dissolved in hot water (600 ml.) containing sufficient sulfuric acid to yield a clear solution, was treated with a solution of chromic anhydride (30 g., 0.30 mole) in water (200 ml.). A red oil was deposited which even on seeding could not be induced to crystallize. However, upon solution in acetone (100 ml.) and reprecipitation by addition of water (600 ml.) the oil readily crystallized in bright orange prisms. By several recrystallizations from hot water (any traces of tar being removed by filtration) the melting point was raised to 95–96°, uncor., with decomposition. There was no evidence of hydration.

The salt was analyzed for chromium by ignition; the neutralization equivalent was determined in water using phenolphthalein, the color change being from orange to yellow (dichromate to chromate) and finally back to orange (red of indicator plus yellow of chromate).

Anal. Calcd. for $C_{24}H_{24}Cr_2N_2O_7$ (*i. e.*, $(C_{12}H_{11}N)_2\cdot H_2Cr_2O_7$): Cr, 18.7; neut. equiv., 139.0. Found: Cr, 18.9, 18.9; neut. equiv., 136.7, 136.8.

4-Benzylpyridinium Dichromate.—4-Benzylpyridine (5 g., 0.03 mole) dissolved in dilute sulfuric acid (25 ml.) and treated with a solution of chromic anhydride (5 g., 0.05 mole) in water (5 ml.) precipitated a red oil. By solution in acetone (15 ml.) and pouring into water (50 ml.) the salt soon crystallized in orange flakes (7.7 g., 94% yield) melting at 110–115° uncor. with decomposition. By further recrystallization from water (as for the isomer above) the melting point of the salt was raised to 115–115.5°, uncor., with decomposition.

Anal. Calcd. for $C_{24}H_{24}Cr_2N_2O_7$ (*i. e.*, $(C_{12}H_{11}N)_2\cdot H_2Cr_2O_7$): Cr, 18.7; neut. equiv., 139.0. Found: Cr, 18.8, 18.9; neut. equiv., 138.7, 139.1.

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RECEIVED MAY 14, 1948

1,2-Di-(4-ketocyclohexane)-ethane

1,2-Di-(4-hydroxycyclohexane)-ethane was obtained by high-pressure hydrogenation of *p*,*p*′-dihydroxystilbene

(10 g.)[1] in 100 cc. of methanol at 200° (330 atm.) with 3 g. of W-3 Raney nickel. The reduction was complete in four hours. The product remaining after removal of catalyst and solvent weighed 10.04 g. and melted at 128–138°.[2] It consisted of a mixture of isomers.

Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.59; H, 12.01.[3]

The mixture of isomers (1.0 g.) was adsorbed on aluminum oxide (General Chemical Co., Reagent) from benzene solution. Elution with benzene gave 0.13 g. of crude material (m. p. 102–115°) which was obtained pure after one crystallization from Skellysolve B and melted at 123.5–124.5°.

Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.19; H, 11.69.

Fractional crystallization of the original mixture (1.0 g.) from benzene yielded 0.41 g. of material melting at 139–145°. Further crystallizations from benzene and ethyl acetate raised the melting point to 144–145°. A mixture of the pure isomers melted at 133–143°.

Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.05; H, 11.56.

1,2-Di-(4-ketocyclohexane)-ethane was prepared by oxidation of the crude mixture of isomers (1.0 g.) dissolved in 20 cc. of benzene and 3 cc. of acetic acid, with a solution of 4.4 g. of sodium dichromate and 5.9 cc. of concentrated sulfuric acid in 20 cc. of water at room temperature. The benzene extract of the reaction mixture yielded 0.65 g. of crude diketone melting at 89–93.5°. Several crystallizations from Skellysolve C gave a constant melting product, m. p. 94.5–96°, yield 0.45 g.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.64; H, 9.97. Found: C, 75.55; H, 10.19.

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[1] The author is indebted to Dr. W. M. Hoehn, formerly with the George Breon Co., Kansas City, Mo., for the gift of this material.

[2] All melting points uncorrected.

[3] Analyses by K. T. Zilch and E. W. Crandall.

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RECEIVED APRIL 12, 1948

Preparation of 2-Methyl-4-methoxy-5-isopropylpropiophenone and 2-Methyl-4-methoxy-5-isopropylphenylethylcarbinol[1]

2-Methyl-4-methoxy-5-isopropylpropiophenone.—Twenty-six and eight-tenths grams (0.13 mole) of 2-methyl-4-hydroxy-5-isopropylpropiophenone, which was prepared by the Fries rearrangement[2] of 2-isopropyl-5-methylphenylpropionate, was treated with 32.8 g. (0.26 mole) of dimethyl sulfate in aqueous sodium hydroxide to yield 21.0 g. of the desired methyl ether, b. p. 169–171° (20 mm.).

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.09. Found: C, 76.20; H, 9.21.

2-Methyl-4-methoxy-5-isopropylphenylethylcarbinol.—To a refluxing solution containing 19.8 g. (0.09 mole) of 2-methyl-4-methoxy-5-isopropylpropiophenone in 150 ml. of absolute ethanol was added in small pieces through the top of the condenser a total of 14.5 g. (0.63 mole) of sodium. The reaction mixture was set aside at room temperature for twenty-four hours, and then 150 ml. of water were cautiously added. The alkaline solution was extracted with ether, and the ether extracts were washed with water until the ether layer was neutral to litmus. After removing the ether by distillation, the yellow oily residue was distilled under reduced pressure to yield 13.2 grams of the carbinol; b. p. 156–159° (8 mm.).

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.67; H, 9.90. Found: C, 75.73; H, 9.89.

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[1] Author's present address: Wallace and Tiernan Products, Inc., Belleville, New Jersey.

[2] K. W. Rosenmund and W. Schnurr, *Ann.*, **460**, 56 (1938).

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RECEIVED JUNE 2, 1948

Benzyl Chloromethyl Selenide

A new compound, benzyl chloromethyl selenide, was prepared by the authors[1] as an intermediate in the preparation of β,β'-diseleno-dialanine. The purpose of the present report is to present some of the properties of this new compoumd.

Preparation.—Seventy-three grams of benzyl seleno was mixed with 25 g. of polyoxymethylene in a flask equipped with a mechanical stirrer. The mixture was cooled in a water-bath and saturated with dry hydrogen chloride with occasional stirring. Thirty grams of calcium chloride was added and the mixture was allowed to stand at room temperature for twenty-four hours. The solid material was removed by filtration and the orange-colored filtrate was distilled *in vacuo* collecting the fraction that boiled at 121° at 5 mm.; yield, 53.3 g., 57%.

Anal. Calcd. for C_8H_9ClSe: C, 43.7; Cl, 16.2, Se, 36.0. Found: C, 43.4; Cl,[2] 16.0; Se,[3] 36.1.

Physical Properties.—It forms long pale-yellow needles below 37° and a yellow liquid with disagreeable odor above 38°; b. p. 121° at 5 mm.; sp. gr. 1.03^{43}; refractive index, 1.5587^{52}. It is soluble in acetone, benzene, ethyl ether, petroleum ether and ethyl alcohol but insoluble in water.

Chemical Properties.—Cleavage with hydriodic acid produces benzyl iodide, m. p. 24.1°; chloromethyl iodide, b. p. 109° and selenols (qualitative identification with mercuric chloride).

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RECEIVED FEBRUARY 13, 1948

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[1] L. R. Williams and A. Ravve, THIS JOURNAL, **70**, 1244 (1948).

[2] O. Kamm, "Qualitative Organic Analysis," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1932, p. 200.

[3] W. O. Robinson, H. C. Dudley, K. T. Williams and H. G. Byers, *Ind. Eng. Chem., Anal. Ed.*, **6**, 274 (1934).