the separation of radium from barium on a commercial basis could be much more easily effected by this column method than by the current procedure based on fractional crystallization. The method is simple to operate and thus may be easily adapted to remote control. The use of this separation method for the quantitative analysis of radium has not been investigated, but it is probably applicable.

OAK RIDGE NATIONAL LABORATORY
OAK RIDGE, TENNESSEE RECEIVED MAY 24, 1948

NEW COMPOUNDS

1-(4-Chloromercuriphenylazo)-naphthol-2

This substance, synthesized in an effort to obtain a colored compound capable of attachment to biological tissue through mercaptan groups only, has been applied successfully in biological investigations.[1,2]

Synthesis.—35.4 g. of *p*-aminophenylmercuric acetate (m. p. 166–167°), prepared by direct mercuration of aniline according to the method of Dimroth,[3] was diazotized at −5° in 500 ml. of 50% acetic acid with 7.0 g. of sodium nitrite, according to the method of Jacobs and Heidelberger.[4] The filtered diazonium salt was coupled to 2-naphthol (15 g. of 2-naphthol, 180 g. of sodium hydroxide, in 2 l. of iced water). After standing a few hours, the precipitate was collected by filtration, washed, dissolved in 200 ml. of glacial acetic acid, filtered, and precipitated by dilution to 2 l. This precipitate was collected, washed, and dissolved by refluxing with 3 l. of 60% ethanol in a water-bath. The hot solution was filtered, the clear filtrate was brought to a boil under reflux, and to it was added 5.8 g. sodium chloride in 150 ml. of 60% ethanol. A cottony red precipitate of 1-(4-chloromercuriphenylazo)-naphthol-2 formed immediately. Refluxing was continued for thirty minutes, the precipitate, 3.6 g. (6.2%), collected by hot filtration and washed several times with boiling 50% ethanol. The precipitate was recrystallized three times from *n*-butyl alcohol (0.9 g. per l. of boiling alcohol) with 95% yield of fine red needle-like crystals which were virtually insoluble in water, but slightly soluble in cold alcohols, chloroform, toluene and decahydronaphthalene, melting with blackening at 291.5–293° (cor.).

Anal. Calcd. for $C_{16}H_{11}ClHgN_2O$: C, 39.76; H, 2.29; Cl, 7.34; Hg, 41.5; N, 5.80. Found: C, 39.36; H, 2.24; Cl, 7.12; Hg, 42.0; N, 6.01.[5]

Degradation.—The product was split by sodium hydrosulfite, yielding 1-amino-2-hydroxynaphthalene.

(1) Bennett, *Anat. Rec.*, **100**, (suppl.) 7, 100 (1948).
(2) Bennett, in press.
(3) Dimroth, *Ber.*, **35**, 2032 (1902).
(4) Jacobs and Heidelberger, *J. Biol. Chem.*, **20**, 513 (1915).
(5) The analyses were preformed by Mr. Nagy of the Microchemical Lab., Massachusetts Institute of Technology.

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RECEIVED MAY 19, 1948

β-Glyceryl Phenyl Ether and 1,3-Dichloro-2-phenoxypropane

These compounds were prepared as intermediates in an effort, which proved unsuccessful, to synthesize phenyl cyclopropyl ether by the procedure described by Krantz and Drake[1] for the synthesis of methyl cyclopropyl ether.

β-Glyceryl Phenyl Ether.—The reduction of phenoxymalonic ester[2] by lithium aluminum hydride,[3] with alkaline hydrolysis of the intermediate aluminate, furnished the crude product, m. p. 59–66° in 95% yield. On recrystallization from benzene it was obtained as colorless needles, m. p. 68°. *Anal.*[4] Calcd. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.07; H, 7.19.

1,3-Dichloro-2-phenoxypropane. A. From β-Glyceryl Phenyl Ether and Thionyl Chloride.—A solution of 40 g. of β-glyceryl phenyl ether in 40 g. of pyridine, dissolved with the aid of heat, was added dropwise, keeping the temperature below 20°, to 200 g. of thionyl chloride. The flask, with reflux condenser attached, was heated very gently to start the evolution of sulfur dioxide and eventually more strongly until the temperature of the vapor in the flask reached 70°. Excess thionyl chloride was removed under reduced pressure. Water was then cautiously added to the residue, the mixture extracted with ether and the extract washed once with dilute alkali. The final purification was by fractional distillation under reduced pressure, using a 30″ wire-spiral column which resulted in a 75% yield of 1,3-dichloro-2-phenoxypropane, b. p. 103.5–104° (1 mm.), $n^{25}D$ 1.5358. *Anal.* Calcd. for $C_9H_{10}OCl_2$: C, 52.76; H, 4.92; Cl, 34.58. Found: C, 52.67; H, 5.15; Cl, 34.57.

B. From Benzene Diazonium Chloride and 1,3-Dichloropropan-2-ol.—Dry benzene diazonium chloride[5] prepared from 22 g. of aniline hydrochloride was added in small portions over a period of one-half hour, keeping the temperature below 25°, to 200 g. of redistilled 1,3-dichloropropan-2-ol (b. p. 173–175°). Stirring was continued until the evolution of nitrogen and hydrogen chloride ceased (about seventeen hours). Most of the excess dichloropropanol was removed by distillation at 10 mm. pressure and the residue was then fractionated at a lower pressure using the 30″ column. The yield of the desired product was 5.8 g., b. p. 99.5–100° (0.5 mm.), $n^{25}D$ 1.5369. *Anal.* Found: C, 53.20; H, 4.92; Cl, 34.27. The ultraviolet absorption spectrum, exhibiting a maximum at 270 mμ, was virtually identical with that of material prepared by Method A.

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RECEIVED JUNE 14, 1948

(1) Krantz and Drake, U. S. Patent 2,330,979.
(2) Niederl and Roth, THIS JOURNAL, **62**, 1154 (1940).
(3) Nystrom and Brown, *ibid.*, **69**, 1197 (1947).
(4) Performed by Wm. Saschek.
(5) Pray, *J. Phys. Chem.*, **30**, 1478 (1926).
(6) Present address: Department of Chemistry, University of California at Los Angeles.

γ-Chlorocrotylmercaptoacetic Acid and γ-Chlorocrotylmercaptomethylpenicillin

One hundred thirty-five grams of 1,3-dichloro-2-butene (du Pont, Organic Chemicals Department) was added to a solution of 85 g. of sodium hydroxide and 108 g. of mercaptoacetic acid (85%) in 1.0 liter of water over a period of two hours. Rapid mechanical stirring was used and the mixture was held at 45–50° during the addition of the halide and for four hours thereafter. The mixture was extracted with ethylene dichloride and the aqueous layer was acidified with concentrated hydrochloric acid. The resulting oil was extracted with ethylene dichloride. After removal of the solvent the residual liquid was vacuum distilled. The main fraction boiled at 108–111° (0.6 mm.) and was a yellow liquid with a pronounced skunk-like odor; yield 128 g. (77%).

Anal. Calcd. for $C_6H_9ClO_2S$: C, 39.89; H, 5.02; neut. eq., 180.7. Found: C, 39.91; H, 5.04; neut. eq., 180.6.

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.

(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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RECEIVED JUNE 14, 1948

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.

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

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

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.

CALCO CHEMICAL DIVISION
AMERICAN CYANAMID COMPANY
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RECEIVED JUNE 9, 1948

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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WILMINGTON, DELAWARE HENRY C. WALTER

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