ing overnight deposited yellow needles. After recrystallization from 50% ethanol the melting point was 147–148°. The reported[5] melting point for the 2,4-dinitrophenylhydrazone of L-glyceraldehyde is 147–148°.

2,3-Dibenzoyl-4,5-Isopropylidene-D-Arabinose Dibenzyl Thioacetal.—4,5-Isopropylidene-D-arabinose dibenzyl thioacetal (86 g.) was dissolved in anhydrous pyridine (200 cc.) and after cooling to −15° benzoyl chloride (60 cc.) was added dropwise with stirring. The mixture was then allowed to stand at room temperature for 48 hours. The reaction mixture was added to ice water with stirring and after about 30 min. the sirupy product crystallized. The solid mass was broken up, filtered and washed with water to remove most of the pyridine. After air drying, the crude product was recrystallized from methanol in the presence of decolorizing charcoal. The material was recrystallized twice more from methanol with very little loss; yield 117 g. (91%), m.p. 103.5–104°; $[\alpha]^{22}D$ +81.5° (*c* 1.9, chloroform). *Anal.* Calcd. for $C_{36}H_{36}S_2O_6$: C, 68.82; H, 5.73; S, 10.19; benzoyl, 33.4. Found: C, 68.7; H, 5.9; S, 10.1; benzoyl, 33.2.

Monobenzoyl-D-Arabinose Dibenzyl Thioacetal.—2,3-Dibenzoyl-4,5-isopropylidene-D-arabinose dibenzoyl thioacetal (45 g.) was dissolved in ethanol (250 cc.). Dilute (5%) hydrochloric acid (70 cc.) was added and the solution heated on the steam-bath for one hour. The reaction mixture was cooled and neutralized with saturated sodium bicarbonate solution and the mixture concentrated under reduced pressure until viscous. Chloroform was added and the mixture warmed for a few minutes to hasten solution and then filtered. The chloroform solution was dried over anhydrous sodium sulfate, treated with charcoal, and then filtered. The colorless filtrate was concentrated to dryness and the viscous, colorless sirup triturated with hot ether. The sirup crystallized and after filtration and washing with ether it was recrystallized from absolute ethanol containing about 10% petroleum ether; yield was 25 g. (71%), m.p. 112–112.5°; $[\alpha]^{23}D$ −25.4° (*c* 2.1, chloroform). *Anal.* Calcd. for $C_{26}H_{28}S_2O_5$: S, 13.2. Found: S, 13.2.

A sample (0.5 g.) was heated on the steam-bath for 30 min. with 2% sodium hydroxide solution (40 cc.). The hot solution was filtered rapidly through a preheated funnel and a precipitate separated which was filtered and washed with water until the washings were neutral. After drying the product weighed 0.3 g. (79%), m.p. 147–148°. A mixed melting point determination with authentic D-arabinose dibenzyl thioacetal showed no depression.

2,3-Dibenzoyl-D-arabinose Dibenzyl Thioacetal.—2,3-Dibenzoyl-4,5-isopropylidene-D-arabinose dibenzyl thioacetal (50 g.) was heated on the steam-bath for one hour in 80% acetic acid (500 cc.). The solvent was removed under reduced pressure and the nearly colorless sirup dissolved in ether and the solution washed with saturated bicarbonate and then with water. The ethereal solution was then dried over anhydrous sodium sulfate in the presence of decolorizing charcoal. After filtration the solvent was removed and a perfectly colorless sirup was obtained that would not crystallize after three months. On prolonged standing in an evacuated desiccator over phosphorus pentoxide, the sirup became a colorless glass; yield was 44 g. (93%); $[\alpha]^{26}D$ +56.5° (*c* 1.7, chloroform). It was insoluble in water and soluble in all the usual organic solvents, including warm petroleum ether.

Anal. Calcd. for $C_{33}H_{32}S_2O_6$: C, 67.35; H, 5.44; S, 10.9; benzoyl, 35.7. Found: C, 67.2; H, 5.6; S, 10.9; benzoyl, 35.3.

A sample (0.5 g.) of 2,3-dibenzoyl-D-arabinose dibenzyl thioacetal was dissolved in anhydrous acetone (350 cc.) containing anhydrous cupric sulfate (15 g.) in suspension. The mixture was agitated for 5 days at room temperature, then filtered and the filter washed with dry acetone. The solvent was removed from the filtrate and the gummy residue triturated with a little methanol. Immediate crystallization occurred. The product was recrystallized from methanol. A mixed melting point determination with authentic 2,3-dibenzoyl-4,5-isopropylidene-D-arabinose dibenzyl thioacetal showed no depression.

Lead Tetraacetate Oxidation of 2,3-Dibenzoyl-D-Arabinose Dibenzyl Thioacetal.—Oxidation of a sample (0.2536 g.) of the above compound with 90 ml. of 0.048 *M* lead tetraacetate in glacial acetic acid, made up to 100 ml. with the same solvent showed that 0.09, 1.6, 1.9, 2.4, 2.9, 3.2, 4.4, 4.6 and 4.9 molecular equivalents of the oxidant were consumed in 1/12, 1/4, 3/4, 2, 3.5, 5.5, 24, 28.5 and 48 hours, respectively. The analytical results thus indicated that oxidation of the divalent sulfur atoms occurred.

In another experiment a sample of the above compound was oxidized in glacial acetic acid with one molecular equivalent of lead tetraacetate. The oxidant was consumed but formaldehyde could not be detected. Two molecular equivalents of lead tetraacetate were consumed with the formation of a high yield (93%) of formaldimethone. The authenticity of the latter compound was determined by a mixed melting point of 188–190°. The reported m.p. is 189–190°.

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S-(*n*-Butyl)-homocysteine (Butionine)

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Ethionine is known to act as an antagonist to the utilization of methionine[1,2]; to some extent, it can be utilized by the living cell instead of the latter amino acid.[2,3] It seemed, therefore, interesting to study a higher homolog of ethionine, such as S-(*n*-butyl)-homocysteine (Butionine). This substance, however, proved to cause no response on the part of *Escherichia coli*.[2]

β-Butylthio-ethanol.—Butyl bromide (12 ml.) was added at 0° to a solution of 15.6 g. of β-thioethanol and 13 g. of potassium hydroxide in 65 ml. of alcohol. The mixture was refluxed for three hours and, after addition of water, extracted with ether; b.p. 118° (28 mm.); yield 17.5 g. (65%). This method is preferable to that of Whitner and Reid[4] who prepared the compound from ethylene chlorohydrin and butyl mercaptan (b.p. 92–93° (3 mm.)).

Anal. Calcd. for $C_6H_{14}OS$: S, 23.9. Found: S, 23.7.

β-Butylthioethyl Chloride.—At 0° with agitation, 17.5 g. of β-butylthioethanol was added to 10.5 ml. of phosphorus trichloride. After two hours, at room temperature, the upper layer was treated with ice-water and extracted with ether; b.p. 96° (26 mm.); yield 10.5 g. (54%) (literature,[4] b.p. 68° (6 mm.)).

Anal. Calcd. for $C_6H_{13}ClS$: Cl, 23.0. Found: Cl, 23.1, 23.2.

Diethyl (β-Butylthioethyl)-phthalimidomalonate.—An intimate mixture of 10.5 g. of β-butylthioethyl chloride and 25.6 g. of diethyl sodiophthalimidomalonate[5] was heated at 160° for six hours and then at 200° for 15 minutes. The mass was triturated with hot water and the oily reaction product extracted with ether; b.p. 265–270° (13 mm.); yield 12.6 g.

Anal. Calcd. for $C_{21}H_{27}NO_6S$: C, 60.0; H, 6.4; N, 3.3 S, 7.6. Found: C, 60.3; H, 6.6; N, 3.7; S, 7.6.

S-(*n*-Butyl)-homocysteine.—To the foregoing product in 12 ml. of alcohol, 33.6 ml. of 5 *N* sodium hydroxide was added. With evolution of heat, a salt crystallized out. The mass was heated on the water-bath for two hours, di-

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(2) E. D. Bergmann, B. E. Volcani and R. Ben-Ishai, *ibid.*, in press (1952).

(3) S. A. Stekol, K. Weiss and S. Weiss, THIS JOURNAL, **72**, 2309 (1950).

(4) T. C. Whitner and E. E. Reid, *ibid.*, **43**, 636 (1921).

(5) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 384.

luted with 50 ml. of water, cooled at 0° and after neutralization with 2 *N* hydrochloric acid, precipitated by addition of 12 ml. of concentrated hydrochloric acid. After twelve hours, a resinous product had separated, which was freed from the supernatant liquid by decantation and heated on the steam-bath for 45 minutes with 120 ml. of 20% hydrochloric acid and for further two hours with 60 ml. of concentrated hydrochloric acid. The filtered solution was evaporated *in vacuo* to dryness and the residue taken up in 40 ml. of 50% alcohol. When pyridine was added to the solution, well-shaped needles separated which were recrystallized from water; m.p. 240° (dec.); yield 2.8 g. (21.4%, calculated on β-butylthioethyl chloride).

Anal. Calcd. for $C_8H_{17}NO_2S$: C, 50.3; H, 8.9; N, 7.3. Found: C, 50.4; H, 8.8; N, 7.1.[6]

Also **β-ethylthio-ethanol** can be produced by the above method more easily than by condensation of ethylene chlorohydrin with ethyl mercaptan[7]: to a solution of 82 g. of β-thioethanol and 4 g. of sodium hydroxide in 200 ml. of water, 154 g. of diethyl sulfate was added with stirring at 50°. The mixture was heated for six hours at 100° and extracted with ether; b.p. 99° (28 mm.); yield 71.5 g. (64%).

Anal. Calcd. for $C_4H_{10}OS$: S, 30.2. Found: S, 30.5.

(6) The amino-acid has been obtained by a different method, by E. Borek and H. Waelsch, *J. Biol. Chem.*, **147**, 135 (1949); *cf.* M. D. Armstrong and J. D. Lewis, *J. Org. Chem.*, **16**, 749 (1950).

(7) W. Steinkopf, J. Herold and J. Stoehr, *Ber.*, **53**, 1007 (1920).

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Some Heterocyclic Secondary Amines[1]

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Four unsymmetrically substituted heterocyclic secondary amines which involve the 2-pyridyl, 2-pyrimidyl and 2-thiazolyl radicals have been prepared as part of a program on the synthesis of basically substituted heterocyclic compounds containing the amidine structure. These compounds were prepared by the reaction of the sodium salt of a primary amine with an "active" heterocyclic halide. The sodium salt of the amine was employed since it has been established[3] that the ring nitrogen of 2-aminopyridine, for example, is capable of substitution *via* the imino form of the amine. The necessity of employing the sodium salt of the amine has been demonstrated during the course of this investigation.[4]

Although the method of synthesis employed appears to be straightforward, the actual preparation of pure samples of these amines has involved considerable difficulty. It has been impossible to develop one set of conditions which would satisfactorily lead to all the desired products. Thus the sodium salt of 2-aminopyridine reacted with 2-chlorothiazole in refluxing benzene to produce a 40% yield of 2-pyridyl-2′-thiazolylamine. Similarly, the sodium salt of aniline reacted with 2-chloropyrimidine to give a 22% yield of 2-anilinopyrimidine.[5] In contrast, the reaction of the sodium salt of 2-aminopyrimidine with 2-chlorothiazole in benzene led to no reaction; the same reactants in *p*-cymene produced an insoluble and infusible substance which probably arose from ring rupture. This latter reaction was successfully carried out in 9.5% yield by the direct reaction of the sodium salt of the amine with the heterocyclic halide. Correspondingly, the sodium salts of 2-aminopyrimidine and 2-aminopyridine did not produce 2-pyridyl-2′-pyrimidylamine when refluxed in benzene with 2-bromopyridine and 2-chloropyrimidine, respectively; however, the direct reaction of the sodium salt of 2-aminopyrimidine with 2-bromopyridine produced a 27% yield of 2-pyridyl-2′-pyrimidylamine.

Experimental[6]

Sodium Salts of 2-Aminopyrimidine and 2-Aminopyridine.—2-Aminopyrimidine (19.02 g., 0.2 mole) was added over a 10-minute period to a solution of sodium amide[7] (0.2 mole) in approximately 200 ml. of anhydrous liquid ammonia. After 2 additional hours of stirring, the solvent was evaporated, the gray-white sodium salt pulverized, extracted with two 100-ml. portions of anhydrous benzene and dried under vacuum over phosphorus pentoxide; yield 19 g. (85%).

The sodium salt of 2-aminopyridine was prepared in an analogous manner except for the extraction process which was omitted; this salt was dark blue in color.

2-Pyridyl-2′-thiazolylamine.—The sodium salt of 2-aminopyridine (35.9 g., 0.3 mole) was refluxed in 50 ml. of anhydrous benzene with stirring for one-half hour in order to ensure complete reaction. 2-Chlorothiazole[8] (30 g., 0.25 mole) in 40 ml. of anhydrous benzene was added over a 10-minute period to the warm suspension of the sodium salt while the reaction flask was being cooled in a cold water-bath. The reaction mixture was then stirred and heated at gentle reflux for 10 hours. The dark brown mixture was cooled and extracted with 250 ml. of a 1:1 mixture of concentrated hydrochloric acid and water. The acidic extract was cooled and adjusted to a *p*H 10 with 48% sodium hydroxide. The tan colored precipitate was filtered, washed with four 50-ml. portions of cold water and dried at 100°; yield 22 g., m.p. 191.8–193°. Recrystallization from 95% ethanol after treatment with charcoal gave 17.9 g. (40.3%) of light tan colored needles, m.p. 195.8–196.6°, sublimation at 15 mm. pressure and recrystallization from ethanol gave colorless needles which had essentially the same melting point as the discolored crystals. *Anal.* Calcd. for $C_8H_7N_3S$: C, 54.22; H, 3.98; N, 23.72; S, 18.09. Found: C, 54.32; H, 4.13; N, 23.75; S, 17.95.

2-Pyridyl-2′-pyrimidylamine.—The sodium salt of 2-aminopyrimidine (22.65 g., 0.193 mole) and 2-bromopyridine[9] (30.6 g., 0.193 mole) were heated in an oil-bath at 150–170° for 45 minutes. The cooled reaction mixture was thoroughly extracted by shaking with several portions of cold water; the addition of a cold 1:1 mixture of ethanol and ether converted the sticky mixture into a light cream colored powder which was filtered, washed with ether and dried under vacuum over phosphorus pentoxide; yield 9.1 g. (27.2%), m.p. 149.6–151.7°. Recrystallization from ethanol gave light cream colored hexagonal plates, m.p. 149.3–152.1°; vacuum sublimation under 2 mm. pressure produced

(1) Abstracted, in part, from a thesis presented by W. K. Detweiler to the Graduate Faculty of Lehigh University in partial fulfillment of the requirements for the Ph.D. degree, June, 1951.

(2) The Wm. S. Merrell Company Research Assistant in Organic Chemistry, 1948–1951.

(3) A. E. Tschitschibabin, R. A. Konowalowa and A. A. Konowalowa, *Ber.*, **54**, 814 (1921).

(4) The direct fusion of 2-chloropyrimidine with 2-aminopyridine for 42 hours at approximately 100° gave an ionic halogen compound which upon treatment with base liberated a substance which melted at 182–184°; in contrast, the reaction of the sodium salt of the amine with the same halide gave 2-pyridyl-2′-pyrimidylamine which melted at approximately 150–152°. The higher melting material was not investigated further but may have been an isomeric material formed by reaction of a ring nitrogen.

(5) This reaction was run in order to determine the stability of 2-chloropyrimidine in the presence of a sodium salt of an active primary amine.

(6) All melting points have been corrected for thermometer stem-emergence.

(7) Prepared according to T. H. Vaughn, R. R. Vogt and J. A. Nieuwland, THIS JOURNAL, **56**, 2120 (1934).

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