

Recrystallization of the solid from ethanol gave II as white crystals, m.p. 77–79°, in 51% over-all yield.

2-Phenyl-5-(2'-pyridyl)-pentanol-2 (VIII).—To 100 ml. of a 2.0 *M* ethereal solution of phenylmagnesium bromide there was added dropwise with stirring a solution of 14.4 g. of 1-(2'-pyridyl)-4-pentanone⁴ in 100 ml. of dry ether. The mixture was boiled under reflux for one hour and was then decomposed by addition of an aqueous ammonium chloride solution. The ether layer was removed, dried and concentrated. The resulting residual oil crystallized after standing for a month. Recrystallization of this solid from pentane gave 11.0 g. (50%) of II as white crystals, m.p. 70–72°. The same product was obtained when the addition of methylmagnesium iodide to phenyl γ -(2-pyridyl)-propyl ketone³ was carried out in a similar manner.

5-(2'-Pyridyl)-pentanol-2, VII.—To 25 ml. of a 0.8 *M* ethereal solution of lithium aluminum hydride there was added dropwise with stirring a solution of 7.0 g. of 1-(2'-pyridyl)-pentanone-4 in 50 ml. of dry ether. After the solution had been boiled under reflux for fifteen minutes, moist ether was added and the precipitate of metallic hydroxides was removed. The ethereal solution was dried, concentrated and the residual oil was distilled yielding 5.0 g. (71%) of a colorless oil.

1-Phenyl-4-(2'-piperidyl)-butanol-1, IX.—A solution of 8.0 g. of 1-phenyl-4-(2'-pyridyl)-butanol-1,³ 0.1 g. of platinum oxide, 30 ml. of ethanol and 60 ml. of 1.7 *N* hydrochloric acid was subjected to hydrogenation at room temperature and 3 atm. pressure of hydrogen. The absorption of three molar equivalents of hydrogen was complete in three and one-half hours. The catalyst and part of the solvent were then removed, the aqueous solution was made basic, and the oil which separated was taken up in benzene. After removal of the benzene, the residue was distilled to yield 5.2 g. (63%) of a colorless viscous oil.

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The Synthesis of 2-Sulfanilamido-5-aminopyrimidine

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Although there are many substituted sulfanilamides and, indeed, many substituted sulfanilamidopyrimidines, there has been no record of the preparation of 2-sulfanilamido-5-aminopyrimidine. One reason for this is the fact that various devices for obtaining the compound by conventional or direct procedures all fail. From these may be singled out for mention the vain attempts to convert 2-amino-5-nitropyrimidine into a sulfonamide by the action of either *p*-nitrobenzenesulfonyl chloride or acetylsulfonyl chloride in pyridine, quinoline or other solvents, in the hot or cold, in spite of the fact that 2-acetamido-5-nitropyrimidine was easily obtained by warming with acetic anhydride. Other instances of a similar refractory behavior have been observed.¹ This paper describes the somewhat circuitous path by which the desired product was synthesized.

The author is grateful to Eli Lilly and Company for carrying out pharmacological tests, reports on which will appear elsewhere.

Experimental

2-Acetamido-5-benzamidopyrimidine.—The brownish solid residue obtained (after removing the solvent under diminished pressure without access of air) by catalytic reduction with platinum oxide instead of palladium on charcoal² of 30.7 g. of 2-acetamido-5-nitropyrimidine was treated in

(1) English, Clark, Shepherd, Marson, Krapcho and Roblin, *THIS JOURNAL*, **68**, 1041 (1946).

(2) Roblin, Winnek and English, *ibid.*, **64**, 509 (1942).

the cold with an excess (30 cc.) of benzoyl chloride followed by 310 cc. of 1.2 *N* aqueous potassium hydroxide, making sure that the mixture had an alkaline reaction. The buff or khaki-colored precipitate stood overnight in this alkaline medium and then was filtered off in a sintered glass funnel and washed well with cold water. A small sample was recrystallized from alcohol, using Darco, and yielded colorless to very pale yellow needles, that melted at 281–284° (uncor.) to a brown liquid; yield of crude product, 39.2 g. or 90%.

*Anal.*³ Calcd. for C₁₁H₁₂N₄O₂: N, 21.85. Found: N, 21.31.

2-Amino-5-benzamidopyrimidine.—The residue of 2-acetamido-5-benzamidopyrimidine (39 g.) was boiled for exactly 30 minutes with 170 cc. of 1.1 *N* aqueous potassium hydroxide. During this boiling, the character of the crystals changed in appearance; after cooling thoroughly, filtering through sintered glass and washing well with ice-water, 22 g. (air-dried) of olive colored crystals were obtained. This material was boiled with 900 cc. of water (with Darco); upon filtering and cooling, lustrous white crystals of 2-amino-5-benzamidopyrimidine (IV) separated; m.p. 214–217° (uncor.).

Anal. Calcd. for C₁₁H₁₀N₄O: N, 26.12. Found: N, 26.13.

2-Acetylsulfanilamido-5-benzamidopyrimidine.—A solution of 17 g. of acetylsulfanilamide in 35 cc. of dry pyridine was added slowly to a solution of 15.3 g. of 2-amino-5-benzamidopyrimidine in 50 cc. of dry pyridine in an ice-bath. After standing overnight at 45–50° there was a deposit of chunky crystals beneath a reddish-brown liquid. This cake of crystals was broken up with a stirring rod, shaken well and, after another four hours at 50°, had set to a thick porridge of crystals. The material was then heated for one hour on a steam-bath whereupon it became lighter in color, turning a canary yellow. After filtering off the solid and washing well with cold water, the creamy white product melted, after drying overnight at 110°, at 286–293° (uncor.); yield 68.2%. In several other runs, procedures and conditions were varied but yields remained at 68–69%.

Anal. Calcd. for C₁₉H₁₇N₅O₂S: N, 17.01. Found: N, 16.85.

2-Sulfanilamido-5-aminopyrimidine.—Although hydrolysis of 2-acetylsulfanilamido-5-benzamidopyrimidine to the final product proceeded satisfactorily with small amounts (5–10 g.) when refluxed overnight with twice the theoretical amount of 1.1 *N* 50% aqueous methanolic potassium hydroxide, it proved desirable to reflux a larger amount (38.9 g.) somewhat longer with 2.2 *N* 50% aqueous methanolic potassium hydroxide. After neutralizing with acetic acid, the product upon recrystallizing from water in which it is, surprisingly enough, even less soluble than "sulfadiazine" in the cold, was obtained as white needles; m.p. 256–259° (uncor.); yields 70–80%.

Anal. Calcd. for C₁₀H₁₁N₅O₂S: C, 45.28; H, 4.18; N, 26.40. Found: C, 45.19; H, 4.05; N, 26.58.

(3) All analyses by Clark Microanalytical Laboratory, Urbana, Illinois.

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Rhodanine Derivatives¹

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The compounds listed in Table I were prepared by the condensation of rhodanine or 3-substituted rhodanines with the appropriate aldehyde or ketone. The reactions, except as noted, were effected in an ethanol-ammonium hydroxide mix-

(1) The compounds were prepared under a contract with the Medical Division, Chemical Corps, U. S. Army.