on waiting twenty-five minutes) no precipitate was evident. When the solution became permanently blue, 2 g. of the sodium (0.22 atom) still remained unadded. The reaction ratio then is probably close to three atoms of sodium per mole of pinacol.

The remainder of the sodium was added, the mixture allowed to stand one and one-half hours with intermittent stirring and then decolorized by the addition of ammonium chloride. No precipitate, outside of a thin scum on the walls of the flask, was present; 20 cc. of water was added, and the ammonia allowed to evaporate. The ether extract of the residue, dried with anhydrous sodium sulfate and evaporated, yielded about 20 cc. of yellowish oil with an odor like methylphenylcarbinol. This oil was distilled through an Eastman column and the fraction boiling at 195–210° was identified as methylphenylcarbinol by its refractive index, specific gravity and by the preparation of its phenyl urethan (mixed melting point).

In two quantitative experiments 2.3387 and 2.5123 g. of acetophenone pinacol was placed in a reaction tube, ammonia condensed upon it and sodium (0.9493 and 0.9338 g.) in small pellets added slowly with agitation. At first the sodium was used up quickly and some hydrogen was evolved. After all the sodium had been added and the reaction was complete, ammonium chloride was added and the evolved hydrogen was collected separately. The results were as follows: hydrogen collected during addition of sodium to the pinacol (corrected to N. T. P.) 29.4 and 29.8 cc.; hydrogen collected during addition of ammonium chloride, 149 and 149 cc. From the latter figures it may be calculated that the amounts of sodium reacting with the pinacol were in the ratios of 2.90 and 2.64 atoms per mole.

Although the reaction between sodium and acetophenone pinacol is obviously complex, the principal results may be summarized by the equations

$$\begin{array}{l} C_6H_5CH_3COH \\ | \\ C_6H_5CH_3COH \end{array} + Na = \begin{array}{l} C_6H_5CH_3CONa \\ | \\ C_6H_5CH_3COH \end{array} + {}^1/_2H_2 \quad (1)$$

$$\begin{array}{l} C_6H_5CH_3CONa \\ | \\ C_6H_5CH_3COH \end{array} + 2Na + NH_3 = 2C_6H_5CH_3CHONa + NaNH_2 \quad (2)$$

That is, substitution of one of the hydroxyl hydrogens with sodium is followed by cleavage of the carbon–carbon bond and ammonolysis of the resulting organo-sodium compounds. The very noticeable decrease in the speed of reaction when one atomic equivalent of sodium had been added was probably due to completion of Reaction 1 followed by slow cleavage of the monosodium pinacolate. The subsequent increase in reaction rate may well be ascribed to the more rapid cleavage of the disodium pinacolate which would be formed from the monosodium compound as soon as appreciable quantities of sodium amide had been produced by Reaction 2. The cause of the discrepancy between the amounts of hydrogen collected and those calculated on the basis of Equation 1 is not known.

Summary

1. The disodium derivatives of pinacol and acetophenone pinacol may be prepared by the action of sodium amide on these glycols in liquid ammonia. These pinacolates give no evidence of dissociation into metal ketyls.

2. Sodium in liquid ammonia replaces only one of the hydrogen atoms of pinacol; it reacts extensively with acetophenone pinacol, not only replacing hydrogen, but also cleaving the carbon–carbon bond.

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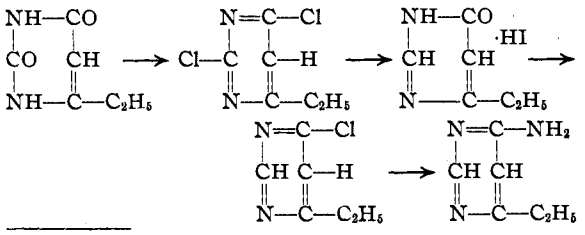
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE COLLEGE OF LIBERAL ARTS AND SCIENCES OF TEMPLE UNIVERSITY]

A Synthesis of 4-Ethyl-6-aminopyrimidine

BY WILLIAM T. CALDWELL AND WILLIAM M. ZIEGLER

Recently, R. R. Williams[1] suggested, as a probable structure of vitamin B_1, a formula derived from 4-ethyl-6-aminopyrimidine. For this reason, and since we found no record of this compound in the literature, we thought its synthesis of interest and accordingly have carried it out by a series of reactions summarized thus



Our method makes use of procedures, previously described, for the synthesis of analogously constituted compounds. However, noting that ethyl pseudo thiourea is probably more stable in alcohol than in water,[2] we condensed propionylacetic ester with ethyl pseudo thiourea in absolute methanol solution of potassium hydroxide, at 0°, with a yield of pure product greater than that obtained when the condensation was carried out in the usual way in aqueous medium.

Experimental Part

4-Ethyluracil.—This compound was prepared in 86.5% yield by hydrolyzing 2-ethylmercapto-4-ethyl-6-oxypyrimidine; the latter compound, melting at 89°, was obtained

(1) Williams, THIS JOURNAL, **57**, 229 (1935).

(2) Arndt, *Ber.*, **54**, 2241 (1921).

in 80% yield by condensing propionylacetic ester with ethyl pseudo thiourea hydrobromide in absolute methanol solution of potassium hydroxide. The same product, m. p. 89°, was formed, but our yields were not as good, when the reaction took place in aqueous potassium hydroxide.[3]

The 4-ethyluracil melted at 204–205°.

Anal. Calcd. for $C_6H_8O_2N_2$: C, 51.4; H, 5.7. Found: C, 51.4, 50.9; H, 6.2, 5.8.

2,6-Dichloro-4-ethylpyrimidine.—4-Ethyluracil (17 g.) was refluxed with 75 cc. of phosphorus oxychloride for one hour. After removing excess of the latter under diminished pressure, the residue was poured on ice, extracted with ether and dried over anhydrous sodium sulfate. After removing the ether, the residual oil was distilled at 90–95° at 4 mm.; at 103–107° at 7 mm.; yield, 17.5 g. of clear, colorless liquid.

Anal. Calcd for $C_6H_6N_2Cl_2$: Cl, 40.07. Found: Cl, 40.55, 40.25.

4-Ethyl-6-oxypyrimidine Hydriodide.—Hydriodic acid (90 cc.), b. p. 127°, was added to a mixture of 4 g. of red phosphorus and 17 g. of 2,6-dichloro-4-ethylpyrimidine.[4,5] A heavy precipitate soon formed which redissolved on heating. After refluxing for one-fourth hour, the mixture was diluted with 90 cc. of water, filtered and evaporated under diminished pressure, leaving a partially crystallized sirup which solidified on cooling. The solidified material was taken up in 50 cc. of hot absolute alcohol and then warm ether was added until precipitation began. After cooling in ice for several hours the yellow crystals were filtered off; yield 21.1 g.; m. p. 170.5–171.5°, after beginning to sinter at 160°.

Anal. Calcd. for $C_6H_8ON_2 \cdot HI$: I, 50.36. Found: I, 50.15, 50.06.

4-Ethyl-6-chloropyrimidine.—The above hydriodide (20.5 g.) was converted into 4-ethyl-6-chloropyrimidine by refluxing with 42 cc. of phosphorus oxychloride for one-half hour. After removing the excess phosphorus oxychloride, the residue was poured upon crushed ice, forming a black tar of unpromising appearance. However, upon treatment with a cold, saturated solution of sulfur dioxide, this viscous mass dissolved to form a bright yellow solution. To this iced solution, solid potassium hydroxide was added until just alkaline, the solution extracted with ether and the extract dried over sodium sulfate. After removal of the ether, the residue distilled at 193° at atmospheric pressure; yield 9.1 g.

Anal. Calcd. for $C_6H_7N_2Cl$: Cl, 24.87. Found: Cl, 24.28.

4 - Ethyl - 6 - aminopyrimidine.—4 - Ethyl - 6 - chloropyrimidine (8.5 g.) was dissolved in 250 cc. of saturated absolute alcoholic ammonia and heated in an autoclave for four hours at 150°. The excess ammonia and solvent were removed; the white crystalline residue was dissolved in water, treated with concentrated potassium hydroxide and extracted with ether. After removing the ether, the residual clear, colorless oil was slow in crystallizing; once crystals formed, however, there was no further difficulty in obtaining them from water. The compound, after recrystallization from water, yielded white, needle-like crystals of the trihydrate, m. p. 47.5–48°. When crystallizing from concentrated, warm aqueous solution on a watch glass, crystals start from a point and radiate outward in feathery form. The compound has a faint pyridine-like odor. An aqueous solution turns red litmus blue; yield, 7.9 g. of crude and 6.2 g. of pure hydrate.

0.1340 g. of hydrate lost 0.0400 g. of water in a desiccator over calcium chloride for one week. 0.0940 g. of dried compound took on 0.0400 g. of water.

Anal. Calcd. for $C_6H_9N_3 \cdot 3H_2O$: H_2O, 30.51. Found: H_2O, 29.85. M. p. of the anhydrous substance, 87.5–88°. Calcd. for $C_6H_9N_3$: C, 58.49; H, 7.37; N, 34.14. Found: C, 58.05, 57.86; H, 7.35, 7.37; N, 34.19, 33.75.

The compound forms a yellow picrate, m. p. 204–205°; a white hydrochloride, m. p. 198–199°; a yellow aurichloride, m. p. 150–151°. The aurichloride crystallized as long needles, if formed slowly, some of which were 35 mm. in length.

Anal. Calcd. for $C_6H_9N_3 \cdot HAuCl_4$: Au, 42.55. 0.1016 g. of the aurichloride gave 0.0434 g. Au. 0.0899 g. of the aurichloride gave 0.0384 g. Au. Found: Au, 42.71, 42.71.

Summary

4-Ethyl-6-aminopyrimidine and several intermediates have been prepared.

A slight modification in the method of condensing ethyl pseudo thiourea hydrobromide with a ketonic ester is reported.

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(3) Wheeler and Bristol, *Am. Chem. J.*, **33**, 445–446 (1905).
(4) Gabriel and Coleman, *Ber.*, **32**, 1533–1534 (1899).
(5) Schlenker, *ibid.*, **34**, 2823–2825 (1901).