[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

DIKETONES. I. THE REACTION BETWEEN 4-PHENYLSEMICARBAZIDE AND ACETYLACETONE

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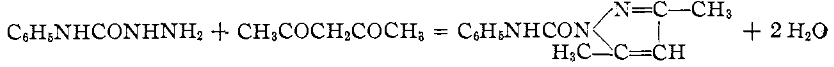
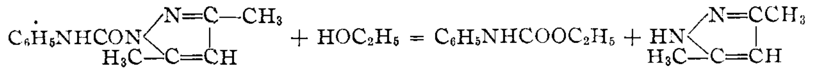
Two earlier attempts[2] were made in this Laboratory to solve the problem presented in the reaction between 4-phenylsemicarbazide and acetylacetone. Posner[3] worked out the reaction between semicarbazide and acetylacetone, obtaining 3,5-dimethylpyrazole-1-carbonamide. In our reaction two compounds are produced: one with a low melting point and very soluble in organic solvents; the other of high melting point and insoluble in organic solvents. The amount of either can be greatly increased by small changes in conditions. The low melting compound seemed to be a pyrazole on account of its pleasant odor but it could not be purified. At 60–70° it melted to an opaque liquid and above 200° to a clear liquid. Nitrogen determinations were too high. In the present study a purification method was found and a correct nitrogen analysis obtained by increasing the length of the combustion tube 100%. The reaction is carried out in alcoholic solution with very little water present. Purification was effected by extraction with petroleum ether, since both hot alcohol and hot water decompose the product. The investigation of the high melting compound (m. p. 255–257°) is reserved for future study.

The low melting compound (m. p. 69°) was proved to be a new substance, 1-phenylcarbamyl-3,5-dimethylpyrazole, according to the following equation



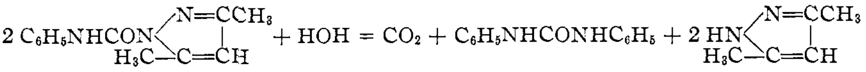
$$C_6H_5NHCONHNH_2 + CH_3COCH_2COCH_3 = C_6H_5NHCON\left\langle\begin{matrix}N=C-CH_3\\ |\\ H_3C-C=CH\end{matrix}\right. + 2\,H_2O$$

We were able to split off the long side chain, C_6H_5NHCO, with boiling alcohol, obtaining phenylurethan and 3,5-dimethylpyrazole



$$C_6H_5NHCON\left\langle\begin{matrix}N=C-CH_3\\ |\\ H_3C-C=CH\end{matrix}\right. + HOC_2H_5 = C_6H_5NHCOOC_2H_5 + HN\left\langle\begin{matrix}N=CCH_3\\ |\\ H_3C-C=CH\end{matrix}\right.$$

Boiling water reacts with two molecules, giving carbanilide, carbon dioxide and dimethylpyrazole



$$2\,C_6H_5NHCON\left\langle\begin{matrix}N=CCH_3\\ |\\ H_3C-C=CH\end{matrix}\right. + HOH = CO_2 + C_6H_5NHCONHC_6H_5 + 2\,HN\left\langle\begin{matrix}N=CCH_3\\ |\\ H_3C-C=CH\end{matrix}\right.$$

Bromine reacts with the phenylcarbamyl derivative in methyl alcoholic solution, substituting the hydrogen atom in Position 4. Boiling water

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[1] Mr. R. D. Norton, Research Assistant, Rockefeller Fund.

[2] O. A. Pickett, *Thesis*, **1916**; E. O. Moehlmann, Master's *Thesis*, **1923**.

[3] Posner, *Ber.*, **34**, 3980 (1901).

splits this product, giving 3,5-dimethyl-4-bromopyrazole, described by Morgan and Ackerman.[4]

Experimental Part

1-Phenylcarbamyl-3,5-dimethylpyrazole, $C_{12}H_{13}ON_3$.—Nine and five-tenths g. of 4-phenylsemicarbazide hydrochloride was dissolved in the least possible amount of water and mixed with 45 cc. of alcohol. Another solution was made of 4.6 cc. of acetylacetone, 30 cc. of alcohol and 5 g. of sodium acetate dissolved in the least possible amount of water. The second solution was slowly added with stirring to the first. A white precipitate of microscopic crystals formed at once as a rule. After standing for thirty minutes this was filtered off. Water was added to the filtrate and a second precipitate was filtered and added to the original product. The yield was about 9 g. On heating it melted to an opaque liquid at 60–70° and to a clear liquid above 200°. Petroleum ether extracted only the low melting compound. Upon its evaporation with an air jet long, white needles separated. These melted to a clear liquid at 69°. The product possesses the pleasant odor of dimethylpyrazole. As much as 8.5 g. of the pure product has been obtained with the above quantities. The amount of water used greatly affects the yield. The product is insoluble in water but soluble in the usual organic solvents.

Anal. Calcd. for $C_{12}H_{13}ON_3$: N, 19.53. Found: 19.49, 19.86.

In order to get good analyses it was necessary to use a combustion tube 155 mm. in length.

Proof of Structure

Reaction with Boiling Alcohol.—One g. of the product was dissolved in 25 cc. of absolute alcohol and boiled under a reflux for an hour. The alcohol was evaporated off on the steam-bath and a viscous liquid remained which crystallized on cooling. This solid was treated with hot water, an oily substance remaining insoluble. This was filtered off and it crystallized on standing. The filtrate was concentrated over steam to a very small volume. On cooling flake-like crystals separated. They melted at 106–107° and had a very pleasant odor. This compound was 3,5-dimethylpyrazole, described by Rosengarten.[5] Its picrate and double silver salt were prepared in order to more fully identify it. The picrate formed fine, yellow needles melting at 166–167°. The double silver nitrate salt was formed by treating the compound with silver nitrate in water solution. The voluminous precipitate was recrystallized from hot water, forming long, white needles melting at 162°. Rosengarten gives 152°.

Anal. Calcd. for $(C_5H_8N_2)_2 \cdot AgNO_3$: Ag, 29.79. Found: 29.36, 29.45.

The oily substance which crystallized on cooling was recrystallized from petroleum ether. The ether was warmed slightly and decanted from an oily substance which settled out on the bottom of the beaker. If the solution is heated too much and agitated, the impurity also goes into solution. Long, white needles were obtained on cooling the ether, melting at 51–52°, which is the melting point of phenylurethan. The latter was more fully identified by boiling with aniline, forming carbanilide, melting at 238°.

Reaction with Boiling Water.—The phenylcarbamyl derivative was boiled with water under a reflux for an hour. The condenser was connected with a tube containing lime water. Carbon dioxide was evolved, as evidenced by the formation of calcium carbonate. A second product condensed in considerable quantity in the condenser. This proved to be carbanilide, melting at 238°.

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[4] Morgan and Ackerman, *J. Chem. Soc.*, **123**, 1316 (1923).

[5] Rosengarten, *Ann.*, **279**, 237 (1894).

Anal. Calcd. for $C_{13}H_{12}ON_2$: N, 13.20. Found: 13.15.

The carbanilide was converted into acetanilide (m. p. 116°) by heating with acetic anhydride.

The aqueous solution in the flask was concentrated to small volume and dimethylpyrazole crystallized out.

Reaction with Ammoniacal Silver Nitrate.—The phenylcarbamyl derivative was boiled with an ammoniacal alcoholic silver nitrate solution under a reflux for an hour. A grayish powder separated. This was analyzed for silver.

Anal. Calcd. for $C_5H_7N_2Ag$: Ag, 53.19. Found: 52.94.

In this product an atom of silver has replaced the side chain attached to nitrogen. The silver was removed with hydrochloric acid and dimethylpyrazole obtained.

1-Phenylcarbamyl-3,5-dimethyl-4-bromopyrazole, $C_{12}H_{12}ON_3Br$.—One g. of the phenylcarbamyl derivative was dissolved in 25 cc. of absolute methyl alcohol and 0.75 g. of bromine, dissolved in a little methyl alcohol, was added dropwise with stirring. White, plate-like crystals formed. These were filtered off and washed with methyl alcohol. They melted at 100–101°.

Anal. Calcd. for $C_{12}H_{12}ON_3Br$: Br, 27.21. Found: 26.83.

The bromo derivative was hydrolyzed with boiling water. The product containing the bromine melted at 123° and proved to be 3,5-dimethyl-4-bromopyrazole, described by Morgan and Ackerman,[4] who gave 118° as the melting point. However, we brominated dimethylpyrazole according to their directions and obtained the melting point 123°.

Summary

1. 1-Phenylcarbamyl-3,5-dimethylpyrazole is formed by the action of 4-phenylsemicarbazide on acetylacetone, together with a substance of high melting point.

2. It yields with boiling alcohol phenylurethan and 3,5-dimethylpyrazole.

3. It yields with boiling water carbanilide, carbon dioxide and 3,5-dimethylpyrazole.

4. With bromine in alcoholic solution it gives a monobromo derivative with bromine in position 4.

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