[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE H. S. NEWCOMB COLLEGE, TULANE UNIVERSITY]

The Preparation of 4,4'-Dicyano-diphenyl and Certain Diketones of Diphenyl

BY CLARA DE MILT AND MILDRED SARTOR[1]

By the use of the Grignard reaction for the preparation of ketones from the cyanides, three ketones, derivatives of diphenyl, have been prepared from 4,4'-dicyano-diphenyl. Doebner[2] prepared this dicyanide from the 4,4'-disulfonic acid of diphenyl, but the over-all yield recorded was small. The dicyanide used in the preparation of the ketones was made from benzidine by means of the Sandmeyer reaction, as modified by Read and Clarke.[3] As preliminary experiments showed that the use of cuprous cyanide as a catalytic reagent gave low yields of the product, nickel cyanide was substituted for the usual copper salt. Korczynski[4] reported that the preparation of dicyanides by the use of nickel salts gave good yields, and noted the formation of molecular combinations of the diazonium salts with the catalysts to give colored precipitates.

The Grignard reactions for the preparation of the ketones proceeded without difficulty. The ketimide hydrochlorides were isolated from the hydrolysis mixture by filtration and were further hydrolyzed to the ketones by refluxing with very dilute acetic acid.

Of the three ketones prepared from 4,4'-dicyano-diphenyl, one, 4,4'-dibenzoyl-diphenyl, had been prepared by Wolfe[5] in 1881 and later by Schlenk and Brauns[6] by means of the Friedel–Crafts reaction. The other two ketones are not recorded in the literature.

Experimental

Preparation of the Dicyanide.—The relative molar concentrations of the reagents that gave the best yields of the dicyanide were one mole of benzidine to one mole of the nickel salt to four moles of potassium cyanide. An orange precipitate formed immediately. From this precipitate a yield of 66% of the dicyanide was obtained. This precipitate was not homogeneous and not stable in that the components present slowly changed into products of deeper color which were decomposed to form the desired dicyanide only with difficulty. Many variations of the procedure outlined above were carried out, but few of them appeared to increase the yield of the dicyanide.

Many attempts were made to decompose more effectively the precipitate which formed on the addition of the diazonium salt solution to the potassium nickelous cyanide solution. Of these, refluxing with butyl alcohol gave yields slightly lower than those with ethyl alcohol. The use of solutions of hydrochloric and acetic acids of concentrations varying from very dilute to twelve normal was unsuccessful, as any dicyano-diphenyl already present or formed during the refluxing was hydrolyzed to the corresponding dicarboxy acid. The use of glycerol, sodium hydroxide, acetone, ethyl acetate, nitrobenzene, and petroleum ether as solvents yielded no dicyanide; a dark brown, stable powder was recovered, practically unchanged in weight.

4,4'-Dicyano-diphenyl.—Five and five-tenths grams (0.03 mole) of benzidine was diazotized in the usual manner. The diazonium salt solution, neutralized with sodium carbonate, was added to a solution of 3.9 g. (0.03 mole) of nickel chloride and 7.8 g. (0.12 mole) of potassium cyanide with stirring. With constant stirring the solution gradually attained room temperature. After five hours the mixture was warmed gently on a water-bath for three hours, then allowed to stand overnight and the brown precipitate was filtered off. The 4,4'-dicyanodiphenyl obtained from the filtrate as a finely crystalline, yellow precipitate weighed 0.7 g. and gave a melting point of 234°, as recorded in the literature.

The brown precipitate, 12.5 g., was refluxed for twenty hours with 200 cc. of 95% ethyl alcohol. Three and five-tenths grams of a dark brown powder remained insoluble. From the alcohol filtrate, 3.6 g. of the dicyano-diphenyl was obtained. Recrystallization from benzene gave 3.4 g., melting at 232–234°. The total yield was 66%, based on the quantity of benzidine used.

4,4'-Dibenzoyl-diphenyl.—To an ether solution of phenylmagnesium bromide, prepared from 10.6 g. (0.068 mole) of bromobenzene, was added 5 g. (0.017 mole) of 4,4'-dicyanodiphenyl dissolved in benzene. A light orange-brown precipitate appeared immediately. The contents of the flask were refluxed for two hours. The mixture, following hydrolysis in hydrochloric acid solution, separated into two immiscible layers and a layer of solid settled out between them. This precipitate, washed twice with dilute acid solution and twice with dilute alkali, the ketimide hydrochloride, was further hydrolyzed by boiling with very dilute acetic acid for fifteen minutes. The ketone, 4,4'-dibenzoyl-diphenyl, weighed 5.9 g., a yield of 96%, based on the weight of the dicyanide used. Recrystallization from alcohol and pyridine gave a light tan, crystalline product melting at 218°. It was identified by its melting point and by analysis.

Anal. Calcd. for $C_{26}H_{18}O_2$: C, 86.2; H, 5.0. Found: C, 86.25; H, 6.05.

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[1] This paper is an abstract of a thesis submitted by Mildred Sartor in partial fulfillment of the requirements for the M.S. degree, Tulane University, 1940.

[2] Doebner, *Ann.*, **172**, 116 (1874).

[3] Read and Clarke, THIS JOURNAL, **46**, 1001 (1924).

[4] Korczynski, Mrozinski and Vielau, *Compt. rend.*, **171**, 182–184 (1920); Korczynski, *Bull. soc. chim.*, **29**, 283 (1921); Korczynski, Kniatowna and Kaminski, *ibid.*, **31**, 1179 (1922); Korczynski and Fandrich, *Compt. rend.*, **183**, 421 (1926).

[5] Wolfe, *Ber.*, **14**, 2031 (1881).

[6] Schlenk and Brauns, *ibid.*, **48**, 723 (1915).

The dioxime of this ketone, not recorded in the literature, prepared by the Bachmann–Boatner[7] method, is a white crystalline solid, melting at 247°.

Anal. Calcd. for $C_{26}H_{20}O_2N_2$: N, 7.14. Found: N, 7.2.

4,4′-Diphenacetyl-diphenyl.—The ketone was obtained in 94% yield by the action of benzylmagnesium bromide on the 4,4′-dicyanide of diphenyl. The product, recrystallized from ethyl acetate, is a tan crystalline solid, melting at 208–210°.

Anal. Calcd. for $C_{28}H_{22}O_2$: C, 86.1; H, 5.6. Found: C, 86.07; H, 6.7.

The dioxime, a white crystalline solid, melts at 202–205°.

Anal. Calcd. for $C_{28}H_{24}O_2N_2$: N, 6.62. Found: N, 6.65.

4,4′-Dipropionyl-diphenyl.—The ketone was prepared in 86% yield by the action of the 4,4′-dicyanide of diphenyl on ethylmagnesium bromide. Recrystallization from a solution of ethyl alcohol and pyridine gave tan crystals, melting at 163–165°.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.76. Found: C, 81.16; H, 6.81.

The dioxime was obtained as a very pale yellow powder, melting at 226–229°.

Anal. Calcd. for $C_{18}H_{20}O_2N_2$: N, 9.46. Found: N, 9.32.

Summary

By means of the Sandmeyer reaction with the use of nickel cyanide as the catalyst 4,4′-dicyano-diphenyl has been prepared from benzidine.

By the use of the Grignard reaction for the preparation of ketones, three ketones, 4,4′-dibenzoyl-diphenyl, 4,4′-diphenacetyl-diphenyl, and 4,4′-dipropionyl-diphenyl, have been prepared from 4,4′-dicyano-diphenyl. The ketones have been characterized by the preparation of the dioximes.

NEW ORLEANS, LOUISIANA RECEIVED MARCH 9, 1940

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[7] Bachmann and Boatner, THIS JOURNAL, **58**, 2097 (1936).

[CONTRIBUTION FROM THE INSTITUTE OF MATERIA MEDICA, SHANGHAI, CHINA]

Study of Gelsemine. I. The Reduction of Gelsemine

BY T. T. CHU AND T. Q. CHOU

Gelsemine, the principal alkaloid of *Gelsemium sempervirens*, was first investigated in 1870 by Wormley[1] and subsequently by many others.[2] Moore[3] was the first to obtain gelsemine in its pure state and assigned to it the formula $C_{20}H_{22}O_2N_2$, which was arrived at later by one of us.[4] Gelsemine also has been isolated recently from the Chinese drug, Ta-Ch'a-Yeh, identified as *Gelsemium elegans* Benth.[5] Knowledge of its chemistry however is still rudimentary. It is a monacidic and tertiary base, containing one hydroxyl group but no methoxyl or ethoxyl groups. When boiled with concentrated hydrochloric acid, it forms new bases by taking up one molecule of water or hydrogen chloride, while its alcoholic solution remains intact on boiling with sodium.[6]

The present communication describes a study of the reduction of gelsemine and some of its related reactions. First, it has been found that gelsemine is easily hydrogenated in the presence of Adams platinum catalyst, absorbing at most one mole of hydrogen with the quantitative formation of dihydrogelsemine. This crystallizes from acetone with one molecule of the solvent in prismatic needles or rhombic prisms, m. p. 224–225°, is optically active, having $[\alpha]^{17}_{D}$ +78.5° in chloroform, and is easily soluble in most organic solvents except petroleum ether. It forms well crystallized salts and a methiodide. It gives sensitive color reactions with oxidizing agents, but is more stable than gelsemine, because after boiling with concentrated hydrochloric acid or even with fuming hydriodic acid, it remains unchanged.

Second, when gelsemine is treated with zinc and hydrochloric acid in the presence of a little platinum or palladium chloride, an anomalous change takes place, the chief product appearing to be an isomer of gelsemine, $C_{20}H_{22}O_2N_2$, but differing from gelsemine in its melting point and specific rotatory power. This has been designated isogelsemine. When catalytically hydrogenated, it is reduced to the same dihydrogelsemine mentioned above. In addition to this isomeride, a small amount of a crystalline substance, having the composition $C_{18}H_{22}O_4N$, has been isolated. It is levorotatory, melts at 265–267° with decomposition, and forms a well crystallized hydrobromide and methiodide. Its aqueous solution

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[1] Wormley, *Am. J. Pharm.*, **41**, 1 (1870).

[2] A survey of literature can be found in (3) and (4).

[3] Moore, *J. Chem. Soc.*, **97** 2223 (1910).

[4] Chou, *Chinese J. Physiol.*, 131 (1931).

[5] Chou, *ibid.*, 79, (1936).

[6] Moore, *J. Chem. Soc.*, **99**, 1231 (1911).