[Contribution from the Division of Agricultural Biochemistry, University of Minnesota]

THE REACTION OF ETHYL GLYCINATE HYDROCHLORIDE WITH PRIMARY, SECONDARY, AND TERTIARY GRIGNARD REAGENTS[1]

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Received December 16, 1940

INTRODUCTION

The study of the reaction between amino acid derivatives and the Grignard reagent began when, in 1905, Paal and Weidenkaff (1) reported on the reaction between glycine ester and phenylmagnesium bromide. They later (2, 3) published on the reaction of phenyl- and ethyl- magnesium bromides on ethyl diethylaminoacetate and of the aryl Grignard reagent on ethyl aspartate. In each instance the corresponding tertiary alcohol was obtained. In 1923 McKenzie, becoming interested in the mechanism of the elimination of the amino group of amino tertiary alcohols, used the reaction as a preparative method.

McKenzie and co-workers (4) treated a variety of amino acid esters, and in some instances the ester hydrochlorides, with several Grignard reagents. Phenylmagnesium bromide (4a, b, c) was usually employed, but benzyl (4c, d), *p*-tolyl (4f), ethyl (4e), and *n*-propyl (4e) Grignard reagents were also used. To obtain satisfactory yields of the amino tertiary alcohols large excesses of the Grignard reagent were required.

The most comprehensive work has been carried out by Fritz Bettzieche and coworkers (5). Bettzieche (5a) ran a series of comparative reactions with the amino acid ester and with its hydrochloride. An excess of the Grignard reagent was always employed, and it was found that the hydrochloride gave a better yield than the free ester. This fact, along with the absence of resinous by-products in most cases, led Bettzieche to conclude that the presence of the hydrochloride offered no complications. The benzoyl (5b) and *p*-toluenesulfonyl (5d) groups protected the amino group from the Grignard reagent and the amide linkage was not attacked under the conditions of the experiment. Dipeptide ester hydrochlorides and

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[1] Paper No. 1869 Journal Series Minnesota Agricultural Experiment Station, abstracted from a thesis presented by F. L. Greenwood to the faculty of the University of Minnesota in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

their benzoyl derivatives (5d) were also studied, but the only linkage attacked was the ester group.

Kanao and Shinozuka (6) report that the corresponding amino tertiary alcohols are obtained by the action of *n*-propyl- and of isoamyl- magnesium iodides on ethyl glycinate. Kapfhammer and Matthes (7) in addition to treating *l*-proline and *l*-oxyproline esters with the Grignard reagent used the diketopiperazine of the former. Barrow and Ferguson (8) proposed a more satisfactory method of isolating the amino tertiary alcohol resulting from the action of an alkyl Grignard reagent on an amino acid derivative.

DISCUSSION

As noted above Bettzieche (5) reported that the conversion of the amino acid esters to their hydrochlorides adequately protected the amino group from the Grignard reagent. McKenzie (4), likewise, did not report the evolution of any gas in reactions of this type. However, both groups of workers were forced to use large excesses of the Grignard reagent in order to obtain satisfactory yields of products. Tiffeneau, Lévy, and Ditz (9) also reported that the action of the Grignard reagent on the hydrochlorides of amino ketones presented no peculiarities. No experimental details are given, so one does not know how well the reactions proceeded. It would seem rather odd if the hydrogen atoms of an amine hydrochloride were not active toward the Grignard reagent since Houben, Boedler, and Fischer (10) have published evidence that somewhat similar hydrogen atoms are active toward the Grignard reagent. They found that all the hydrogen and ammonium halides brought about the decomposition of the Grignard reagent although some reacted more slowly than others. The hydrochloride of triethylamine was also found to effect the complete decomposition of the Grignard reagent.

Ivanoff and Spassoff (11) reported that various Grignard reagents with ethyl acetate gave rise to the hydrocarbon corresponding to the Grignard reagent. But only the secondary Grignard reagents were found to give an appreciable yield of hydrocarbon. The reaction, they said, must have involved enolization of the ester since the ester was completely recovered. They later (12) stated that the evolution of hydrocarbon is not necessarily due to enolization of the ester, and they reported the isolation of ketones from the reaction of ethyl acetate and isopropylmagnesium chloride. The hydrocarbon was now accounted for by reaction of the enolized ketone with the Grignard reagent.

From our study it seems quite definite that the conversion of amino acid esters to their hydrochlorides does not protect the amino group from the Grignard reagent. In all of the reactions studied large quantities of gas were collected, and apparently all three hydrogen atoms attached to the nitrogen atom are active and completely displaced by the Grignard reagent if the reaction-mixture is warmed for a sufficient time. The only hydrocarbon found in the reactions was the one corresponding to the Grignard reagent used.

As in the earlier work, it was necessary to use large excesses of the Grignard reagent to get good yields of products. The ester hydrochloride with *n*-propylmagnesium chloride gave good yields of the corresponding amino tertiary alcohol. This compound has been reported by Kanao and Shinozuka (6), who obtained it from glycine ester and *n*-propylmagnesium iodide. They gave no experimental details but analysis of the product checked satisfactorily.

Ivanoff and Spassoff (12) studied the reaction of ethyl acetate and isopropylmagnesium chloride. If the reaction products were distilled *in vacuo* the chief product was the ketol of methyl isopropyl ketone, but if the distillation was carried out at atmospheric pressure the main product was methyl isopropyl ketone. No tertiary alcohol was found in the reaction-mixture. In contrast to this, our work shows that with ethyl glycinate hydrochloride and the same Grignard reagent the main product is the amino tertiary alcohol. In one reaction a small amount of aminomethyl isopropyl ketone was isolated. Kanao and Shinozuka (6) state that ethyl glycinate hydrochloride and isoamylmagnesium chloride gave rise to the corresponding amino tertiary alcohol, for which they reported a satisfactory analysis. Again no experimental details were given.

Under the conditions we employed there appeared to be no reaction between the ester hydrochloride and *t*-butylmagnesium chloride other than the displacement of the active hydrogen atoms. No products could be isolated and nearly all of the nitrogen of the starting material was accounted for.

EXPERIMENTAL

Preparation of ethyl glycinate hydrochloride. The ester hydrochloride,m. p. 143–143.3°, was prepared from methyleneaminoacetonitrile (13), m.p. 127–127.5°, according to the method of Marvel (14).

Preparation of Grignard reagents. The Grignard reagents were prepared in a flask which had been flushed with dry nitrogen. The resulting solution was allowed to stand several days and then filtered into a bottle which had been flushed with nitrogen. The solutions were titrated according to the method of Gilman *et al.* (15) to obtain the concentration of Grignard reagent in the solution.

Reaction of n-*propylmagnesium chloride with ethyl glycinate hydrochloride* (I). The procedure finally adopted for this reaction was as described in (III). In this particular reaction the 180 cc. (containing 68.7 g. of *n*-propylmagnesium chloride; 0.668 mole) of Grignard solution was placed in a 500 cc. flask. The 23.3 g. (0.167 mole) of ethyl glycinate hydrochloride was added over a period of three hours. The ester hydrochloride was introduced through the free neck of the flask which was immediately stoppered, and a further addition not made until the reaction subsided. At the completion of the addition of the ester hydrochloride 150 cc. of dry ether was added, and the reaction-mixture stirred vigorously for one-half hour. The reaction-mixture was then stirred and refluxed for an additional hour. During the reaction 12.6 l. (24°/734 mm.) of gas was collected, but was not analyzed.

The reaction-mixture was decomposed and worked up as described in (III). The ether was distilled from the solution through column #2 (16) (a Fenske column of the total reflux type packed with single turn, one-eighth inch helices; 1.5 x 67 cm.; twelve theoretical plates). The residue was then distilled through column #1 (a column of the above-mentioned type; 1 x 45 cm.; nine theoretical plates). Sufficient material was not present to maintain a reflux but 1.8 g. of white solid, which was later shown to be 2-amino-1,1-di-*n*-propylethanol-1, was obtained.

From the aqueous layer was obtained 13.6 g. of amino tertiary alcohol hydrochloride, m.p. 105–107°. Total yield of the amino tertiary alcohol hydrochloride was 15.8 g. (52.1%).

Reaction of n-*propylmagnesium chloride with ethyl glycinate hydrochloride* (II). Since previous workers did not report any gas from this reaction it was thought that perhaps the gas might be due to reduction, and so a low-temperature reaction was carried out. The quantities of reactants were the same as used in (I). For the addition of the ester hydrochloride two concentric glass tubes were tapered and sealed at the bottom. They were ground in at the tapered portion and a hole drilled at the ground surfaces. Then by turning the hole of the inner tube to coincide with that of the other, solid was admitted to the flask.

The Grignard solution was cooled to $-10°$, and the temperature of the reaction-mixture was not allowed to rise above $-5°$ during the addition of the ester hydrochloride, which was effected in one and one-half hours. The reaction-mixture was held at $-10°$ for three hours and then warmed to 30° to drive out the dissolved gas. After warming the reaction-mixture, 10 l. (23°/738 mm.) of gas, which was not analyzed, had been collected.

The reaction-mixture was decomposed as before. The ether layer was extracted with water and the extracts added to the aqueous layer. The ether layer was then distilled through column #2, leaving practically no residue. Steam distillation of the aqueous layer was begun, but bumping became so violent that it became necessary to filter off and wash the magnesium hydroxide.[2] From the steam distillate was obtained 8.3 g. (27.3%) of amino tertiary alcohol hydrochloride, m.p. 108.2–108.7°.

Reaction of n-*propylmagnesium chloride with ethyl glycinate hydrochloride* (III). The procedure finally adopted was the following: A 1-l., three-necked flask was fitted with a mercury-seal stirrer and reflux condenser. In the other neck of the flask was placed a dropping-funnel fitted with a mercury-seal stirrer. A gas lead went from this funnel to the top of the condenser and thence to the gas-collecting carboys which were filled with saturated salt solution. The apparatus was flushed with nitrogen. In the 1-l. flask was placed 607 cc. (containing 137.3 g. of *n*-propylmagnesium chloride: 1.33 moles) of Grignard solution. Ethyl glycinate hydrochloride was forced through a #60 screen and 23.3 g. (0.167 mole) of this material placed in

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[2] This magnesium hydroxide was kept moist and then suspended in water and steam distilled. Some 2 l. of distillate was collected which was just acidified to Congo red with hydrochloric acid and evaporated to dryness on the steam-bath. Practically no residue was obtained, indicating that very little, if any, material was adsorbed on the base.

the dropping-funnel with sufficient dry ether to form a suspension. The stirrers were started and the ester hydrochloride suspension added at such a rate that refluxing was maintained, the addition requiring one and one-quarter hours. Soon after the addition of the ester hydrochloride began, the reaction-mixture became cloudy and solid separated. After the completion of the addition of the ester hydrochloride the reaction-mixture was stirred at room temperature for four hours and then refluxed for an additional hour. After cooling, the reaction-mixture was decomposed by pouring into a solution of 110 g. of ammonium chloride and 5 cc. of concentrated ammonium hydroxide in 400 cc. of water. Sufficient ice was present so that ice remained at the completion of the decomposition. The mixture was allowed to stand overnight.

The layers of the decomposition-mixture were separated, the aqueous layer (2.2 l.) divided in half, and each half extracted with one 200-cc. and three 100-cc. portions of ether. The extracts were combined with the ether layer and the solution dried with freshly heated potassium carbonate. The ether was filtered from the carbonate, the carbonate washed with dry ether and the washings added to the main solution. The ether was distilled off through column #2, and the residue washed into a 50 cc. Claisen flask with a little dry ether. After the removal of the ether 9.7 g. of a white solid (b.p. 76° at 4 mm.; m.p. 41.5°) was obtained. Kanao and Shinozuka (6) report b.p. 94.5-95° at 10 mm. and m.p. 58°. A residue of only a few drops remained in the flask. A benzenesulfonyl derivative of this material was prepared, which was soluble in alkali but insoluble in acid. A benzoyl derivative was also prepared and after recrystallization from 30% ethanol melted at 91-91.2°.

Anal. Calc'd for $C_{15}H_{23}NO_2$: C, 72.29; H, 9.24; N, 5.62.
Found: C, 72.89; H, 9.43; N (Dumas), 5.83.

To the aqueous layer was added 190 g. of sodium hydroxide dissolved in a small amount of water. This mixture was allowed to stand overnight. The supernatant liquid was then drawn off and the magnesium hydroxide centrifuged from the remainder of the solution. The precipitate was washed several times with water and the washings combined with the aqueous layer. This aqueous solution was now steam distilled until the distillate was no longer alkaline to litmus and only a few drops of acid required to acidify some 1500 cc. of distillate. The first 2 l. of distillate was aerated with a stream of nitrogen, the gas passing out through a condenser, to remove some of the ammonia. The steam distillate was just acidified to Congo red with hydrochloric acid and each 1700-cc. portion extracted with one 200-cc. and three 100-cc. portions of ether. The ether extracts (A) were combined and placed over 100 g. of freshly heated potassium carbonate.

The acidified steam distillate was evaporated to a small volume on a hot plate, the temperature of the solution during the evaporation being 50-60°. The small liquid residue was transferred to a beaker and dried in a forced draft oven at 55-60°. The solid residue was well ground in a mortar and extracted with a 200-cc., a 150-cc., and two 100-cc. portions of *n*-butyl alcohol (b.p. 117° at 742 mm.) and the residue finally washed with 100 cc. of boiling *n*-butyl alcohol. The extracts and washing were combined and 100 cc. of dry ether added to the solution. This solution was allowed to stand overnight in the cold room and then centrifuged from the ammonium chloride which separated. The resulting clear solution was vacuum distilled (bath temperature never above 55°) to a rather small volume and this poured into ether. After standing overnight in the cold room the solid was filtered off. The ether was distilled from the filtrate and the residue of *n*-butyl alcohol vacuum distilled practically to dryness. The distilling flask was rinsed with dry ether and the resultant solid combined with that obtained earlier.[3] Yield of 2-amino-1,1-di-*n*-propylethanol-1 hydrochloride: 10.7 g.; m.p., 106.5–107.5°. Total yield as amino alcohol hydrochloride: 22.8 g. (75.2%).

This hydrochloride, when isolated, is anhydrous, but on keeping in a corked vial it absorbs moisture, which brings about a lowering of the melting point. But on drying in an oven at 100° the melting point is restored to its original value. When the hydrochloride is freed of the last traces of ammonium chloride by recrystallization from dry benzene it melts at 108.7–109°.

Anal. Calc'd for $C_8H_{20}ClNO$: C, 52.89; H, 11.02; N, 7.71.
Found: C, 52.32; H, 11.12; N (Dumas), 7.58.

Amino nitrogen was determined on the hydrochloride by the Van Slyke method.

Theory: 14.8 cc. N and 15.3 cc. N.

Found: 14.3 cc. N and 14.8 cc. N.

Ether extract (A) was filtered, the carbonate washed with dry ether, the washings added to the filtrate, and the ether distilled off through column #2. The small residue was transferred to a distilling flask and 0.9 g. of liquid boiling at 77–80° and having the odor of ethyl alcohol was collected.

The alkaline aqueous residue remaining after the steam distillation was extracted with one 200-cc. and two 100-cc. portions of ether. The extracts were dried over potassium carbonate and the ether distilled through column #2, all the material distilling below 35° and leaving no residue.

The alkaline aqueous solution was just acidified with hydrochloric acid to Congo red. A solid separated, which was collected. This solid would not char in the hottest Bunsen flame. The filtrate was extracted with four 200-cc. and four 100-cc. portions of ether. The combined extracts were dried over calcium chloride and then distilled through column #2. From the residue a small amount of material (b.p. 75–80°; 3,5-dinitrobenzoate, m.p. 90–90.5°) with the odor and behavior of ethyl alcohol was obtained.

The acidified aqueous filtrate was analyzed for nitrogen (Kjeldahl) and found to contain nitrogen equivalent to 0.41 g. of ethyl glycinate hydrochloride.

During the addition of the ester hydrochloride to the Grignard solution, 12.61 l. (24°, 742 mm.) of gas was collected. This gas was analyzed with an Orsat apparatus, and carbon dioxide, carbon monoxide, oxygen, and olefins were found to be absent. For the absorption of olefins the percentages of sulfuric acid suggested by Matuszak (17) were used. Slow combustion of the gas remaining after absorption in the pipettes indicated propane, but the results were not absolutely conclusive. A sample of the gas was then liquefied with liquid oxygen and distilled through a Podbielniak column.[4] Distillation showed the gas to be composed of 38.8% non-condensables, 57.2% propane, and 4.0% ether. Thus, 12.73 g. of propane was obtained, which means that nearly two atoms of hydrogen were replaced by the Grignard reagent.

Reaction of isopropylmagnesium chloride with ethyl glycinate hydrochloride (IV). The reaction and treatment of the reaction-mixture were carried out as described

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[3] In another experiment, using the same quantities of reactants as used in this case, it was found that ether did not precipitate out all the amino tertiary alcohol hydrochloride, and to obtain all the product it was necessary to remove the solvent. In this experiment some material was accidentally lost but even so the yield of amino tertiary alcohol hydrochloride was 60.4%.

[4] We are indebted to M. C. Rogers for the distillation of the gas samples.

above (III). Ethyl glycinate hydrochloride (23.3 g.; 0.167 mole) and 614 cc. (containing 137.3 g. of isopropylmagnesium chloride; 1.33 moles) of Grignard solution were used. The addition of the ester hydrochloride suspension required one hour; the reaction-mixture was stirred for one and one-quarter hours more and then refluxed for an additional two and one-half hours.

From the combined ether layer and ether extracts (the aqueous layer was extracted with 3 l. of ether in 125-cc. portions) was obtained a residue which on distillation gave 6.2 g. of material boiling at 71–75° at 5 mm. The material remaining in the flask apparently condensed and 3.0 g. of a yellow, viscous liquid was collected at 75–175° at 5 mm. The material distilling at 71–75° at 5 mm. was not pure 2-amino-1,1-diisopropylethanol-1 but some of this material must have been present. A small amount of benzenesulfonyl derivative was obtained from this material, m.p. 103–103.8°. When mixed with the derivative (m.p. 103.9–104.5°) whose analysis is reported below (V), the melting point was 103–103.8°. A portion of the liquid boiling at 71-75° at 5 mm. was now dissolved in dry ether, and hydrogen chloride led into the cooled solution. To obtain a product, the solid must be filtered off after the addition of each small amount of hydrogen chloride. Otherwise, a dark, viscous oil results. Thus a white hydrochloride was obtained which after crystallization from dry benzene melted at 196–197°. This is apparently the hydrochloride of the amino tertiary alcohol.

Anal. Calc'd for $C_8H_{20}ClNO$: C, 52.89; H, 11.02; N, 7.71.
Found: C, 53.17; H, 11.44; N (Dumas), 7.39.

From the residue resulting from the evaporation of the acidified steam distillate 0.9 g. of material was extracted with *n*-butyl alcohol. This material could not be purified by solution in dry benzene, as it was insoluble in this solvent. However, extraction with acetone gave 0.68 g. of pure white flakes. This substance discolored at 145° and melted at 147-149° (decomp.). The material reacted with phenylhydrazine to give an oil which could not be crystallized. The substance is apparently the hydrochloride of aminomethyl isopropyl ketone.

Anal. Calc'd for $C_5H_{12}ClNO$: C, 43.64; H, 8.72; N, 10.18.
Found: C, 43.40; H, 9.04; N (Dumas), 10.31.

A benzenesulfonyl derivative, m.p. 81° (no range observable), was prepared.

Anal. Calc'd for $C_{11}H_{15}NO_3S$: C, 54.77; H, 6.22; N, 5.81.
Found: C, 54.18; H, 6.17; N (Dumas), 5.94.

No other products could be found. The final aqueous solution was found to contain nitrogen (Kjeldahl) equivalent to 1.94 g. of ethyl glycinate hydrochloride.

During the reaction 18.98 l. (24°, 742 mm.) of gas was collected. Analysis in the Orsat apparatus showed the absence of carbon dioxide, olefins, oxygen, and carbon monoxide. Combustion of the residue indicated propane, but again the data were not definitely conclusive. A portion of the gas was liquefied with liquid oxygen and distilled through a Podbielniak column. It was found to contain 37.4% non-condensables, 59.2% propane, and 3.4% ether. The 19.78 g. of propane liberated means that between two and three of the hydrogen atoms of the ester hydrochloride have been replaced.

Another reaction (V) between the ester hydrochloride and isopropylmagnesium chloride was carried out with the same quantities as described above (IV). The reaction-mixture was decomposed as soon as the solution could be cooled at the completion of the addition of the ester hydrochloride suspension. The layers of the decomposition-mixture were separated, the aqueous layer divided in half and each half extracted with one 250-cc., one 150-cc., and ten 125-cc. portions of ether. The latter extracts left no odor when several drops were evaporated. The extracts were combined with the ether layer and dried over sodium sulfate. The ether was then distilled off through column #2 until a residue of some 200 cc. remained. Ten cubic centimeters of this residue was placed in a test tube immersed in an ice-bath. The ether was driven off with a stream of nitrogen and a benzenesulfonyl derivative, m.p. 103.9–104.5°, of the residue prepared. This is apparently the derivative of the amino tertiary alcohol.

Anal. Calc'd for $C_{14}H_{23}NO_3S$: C, 58.94; H, 8.07; N, 4.91.
Found: C, 58.57; H, 7.70; N (Dumas), 5.04.

The ether solution was freed of ether and the residue weighed 20.2 g.

Aliquots of the aqueous layer from the decomposition-mixture were made alkaline with sodium hydroxide, the magnesium hydroxide filtered off and washed with hot water, the washings being added to the filtrate. The filtrate was evaporated on the steam-bath to a small volume. The small aqueous residue was transferred to a Kjeldahl flask, acidified with sulfuric acid and evaporated to dryness with a stream of clean air. Kjeldahl determinations on the residue indicated the absence of nitrogen.

Reaction of t-*butylmagnesium chloride with ethyl glycinate hydrochloride.* The reaction and treatment of the reaction-mixture were carried out as described above (III). The addition of the ester hydrochloride suspension to the 1060 cc. (containing 156 g. of *t*-butylmagnesium chloride; 1.33 moles) of Grignard solution required forty minutes. The mixture was stirred for three hours and then refluxed for two and one-half hours more. The only material that could be isolated from the reaction-mixture was a small amount of hexamethylethane which was probably formed during the preparation of the Grignard solution. When the magnesium hydroxide was centrifuged off it could not be washed free of a lavender color, which indicates that it probably contained some glycine.

The final aqueous solution contained nitrogen (Kjeldahl) corresponding to 17.04 g. of ethyl glycinate hydrochloride.

During the reaction 23.1 l. (24°, 742 mm.) of gas was collected. A portion of this gas was liquefied with liquid oxygen and distilled through a Podbielniak column. The gas was found to be composed of 32.7% non-condensables, 57.9% isobutane, and 9.4% ether. The 31.06 g. of isobutane obtained indicates that all three hydrogen atoms of the amine hydrochloride group are active and can be replaced by the Grignard reagent if the reaction is allowed to proceed for a sufficient time.

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REFERENCES

(1) PAAL AND WEIDENKAFF, *Ber.*, **38,** 1686 (1905).
(2) PAAL AND WEIDENKAFF, *Ber.*, **39,** 810 (1906).
(3) PAAL AND WEIDENKAFF, *Ber.*, **39,** 4344 (1906).
(4) (a) MCKENZIE AND RICHARDSON, *J. Chem. Soc.*, **123,** 86 (1923).
  (b) MCKENZIE AND WILLS, *J. Chem. Soc.*, **127,** 287 (1925).
  (c) MCKENZIE, ROGER, AND WILLS, *J. Chem. Soc.*, **1926,** 785.
  (d) MCKENZIE AND MILLS, *Ber.*, **62,** 287 (1929).
  (e) MCKENZIE AND LESSLIE, *Ber.*, **62,** 291 (1929).
  (f) MCKENZIE, MILLS, AND MYLES, *Ber.*, **63,** 906 (1930).
(5) (a) THOMAS AND BETTZIECHE, *Z. physiol. Chem.*, **140,** 244 (1924).
  (b) THOMAS AND BETTZIECHE, *Z. physiol. Chem.*, **140,** 279 (1924).
  (c) BETTZIECHE AND EHRLICH, *Z. physiol. Chem.*, **160,** 10 (1926).

(d) Bettzieche, Menger, and Wolf, *Z. physiol. Chem.*, **160,** 270 (1926).
(e) Bettzieche and Menger, *Z. physiol. Chem.*, **172,** 64 (1927).
(6) Kanao and Shinozuka, *J. Pharm. Soc. Japan,* **50,** 151 (1930).
(7) Kapfhammer and Matthes, *Z. physiol. Chem.*, **223,** 43 (1933).
(8) Barrow and Ferguson, *J. Chem. Soc.*, **1935,** 416.
(9) Tiffeneau, Lévy, and Ditz, *Bull. soc. chim.*, (5) **2,** 1853 (1935).
(10) Houben, Boedler, and Fischer., *Ber.*, **69,** 1784 (1936).
(11) Ivanoff and Spassoff, *Bull. soc. chim.*, (5) **1,** 1419 (1934).
(12) Ivanoff and Spassoff, *Bull. soc. chim.*, (5) **2,** 816 (1935).
(13) Adams and Langley, *Org. Syntheses*, Coll. Vol., **1,** 347 (1932).
(14) Marvel, *Org. Syntheses*, **14,** 46 (1934).
(15) Gilman *et al.*, *J. Am. Chem. Soc.*, **45,** 156 (1923).
(16) Whitmore and Lux, *J. Am. Chem. Soc.*, **54,** 3451 (1932).
(17) Matuszak, *Ind. Eng. Chem., Anal. Ed.*, **10,** 354 (1938).