to yield a residual oil. The addition of 50 cc. of ether yielded 0.7 g. of the crude reduction product melting at 90–115°. Recrystallization from absolute ethanol increased the melting point to 129–131.5°, and an additional recrystallization from benzene yielded the pure diacetamido compound IV melting at 132–133° and the melting point was not depressed when mixed with compounds under A and B.

Anal. Calcd. for $C_{15}H_{26}O_6N_2$: N, 8.48. Found: N, 8.58.

Preparation of DL-Lysine Dihydrochloride.—The purified diacetamido compound, V (33.6 g., m. p. 132–133°) was mixed with 200 cc. of concentrated hydrochloric acid. The resulting reaction mixture was refluxed for a period of eighteen hours. The resulting water-clear solution was concentrated *in vacuo* and a solid mass resulted. The residual solid was dissolved in 150 cc. of boiling 95% ethanol. After filtration the alcoholic solution was diluted with 50 cc. of ether and permitted to stand overnight. The white crystalline product was collected by filtration, washed with 80 cc. of ethanol–ether (50–50) solution, and dried *in vacuo*. The yield of DL-lysine dihydrochloride was 17.1 g. (77%) melting at 181–186° (dec.).

The dihydrochloride (2.9 g.) was converted to the monohydrochloride (m. p. 256–258° (dec.)). Mixed melting point with authentic sample (Eastman Kodak Co.) showed no depression.

Anal. Calcd. for $C_6H_{15}O_2N_2Cl$: C, 39.44; H, 8.27; N, 15.34; Cl, 19.4. Found: C, 39.13; H, 7.90; N, 15.67; Cl, 18.8.

Treatment of either the dihydrochloride or the monohydrochloride with an excess of benzoyl chloride yielded the dibenzoyl derivative melting at 145–146°. When mixed with an authentic sample of dibenzoyl-lysine, it melted at 145–146°.

Anal. Calcd. for $C_{20}H_{22}O_4N_2$: C, 67.76; H, 6.27; N, 7.91. Found: C, 68.01; H, 6.14; N, 7.85.

The dipicrate was prepared and melted at 185–187° (dec.) after drying.

Summary

1. A new synthesis of DL-lysine has been described.

2. An intermediate product, namely, ethyl α-carbethoxy-α-ϵ-diacetamidocaproate, has been prepared by three different synthetic routes.

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[CONTRIBUTION FROM THE RICHARDSON CHEMISTRY LABORATORY, TULANE UNIVERSITY]

Action of the Grignard Reagent on β-D-Glucose Pentaacetate

BY C. G. JEREMIAS[1] AND C. A. MACKENZIE

A number of authors have reported the formation of addition compounds between esters and Grignard reagents with the original ester being recovered on hydrolysis of the reaction product. Fischer[2] in 1912 claimed the formation of such products for glucose pentaacetate, acetobromoglucose, glucose tetraacetate and methyl tetraacetyl-β-D-glucoside when each compound was treated with methylmagnesium iodide. Analyses indicated addition compounds with the Grignard reagent and the ester combined in a 2:1 molar ratio. Hydrolysis of the products returned the original esters in good yields. In 1930 Fröschl and Zellner[3] reported similar results using methyl- and ethylmagnesium iodides. The 2:1 ratio resulted even when a large excess of the Grignard reagent was used. In all of the above work the reagents were mixed in a reaction vessel set in an ice-bath.

Different results were reported by Paal and Hörnstein.[4] They stated, without giving their experimental evidence, that the treatment of glucose pentaacetate with phenylmagnesium bromide resulted in the formation of a tertiary alcohol, diphenylmethylcarbinol. Hurd and Bonner,[5] have recently reported the same result for these reagents.

Discussion

The purpose of the present work was to test the behavior of glucose pentaacetate toward various Grignard reagents in an effort to determine if tertiary alcohols were generally formed in such reactions or if the addition type compounds first described by Fischer and Hess were to be expected.

We have used Grignard reagents prepared from methyl iodide, *n*-butyl bromide and bromobenzene. Molar ratios of Grignard reagent to ester of 2:1 and 10:1 were employed. The reagents were mixed at 0–5° and 25–35°.

The reaction, in general, proceeded in a normal fashion, that is, tertiary alcohols were formed. In view of the fact there was a marked decrease in the yield of tertiary alcohol at the lower temperature, it seems possible that the 2:1 addition compounds might be obtained if the reaction temperature should be decreased further. At the temperatures used, however, we obtained no evidence for the formation of the previously described addition compounds.

Glucose was obtained in a good yield as a product of the reaction. In connection with the isolation of this product, it is of interest to note that the Grignard reagent did not add to the glucose pentaacetate by opening its ring structure. Reaction was with the acetate groups only.

Experimental

The preparation of 5-methyl-5-nonanol, described below, is representative of the type of procedure employed.

Glucose pentaacetate (48.8 g., one eighth mole) was dissolved in 250 ml. of chloroform (1000 ml. of benzene or 2500 ml. of diethyl ether may be used in place of the chloroform). One quarter mole of *n*-butylmagnesium bromide (added as a solution of 0.5 *M* butylmagnesium bromide in ether) was placed in a three-liter three-neck flask. The

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[2] Fischer and Hess, *Ber.*, **45**, 912 (1912).

[3] Fröschl and Zellner, *Monatsh.*, **55**, 25 (1930).

[4] Paal and Hörnstein, *Ber.*, **39**, 1361 (1906).

[5] Hurd and Bonner, THIS JOURNAL, **67**, 1972 (1945).

flask was equipped with a condenser, a thermometer (not necessary unless it is desired to maintain a low temperature), a stirrer and a 500-ml. dropping funnel. The solution of the ester was added to the stirred Grignard solution at such a rate that gentle refluxing of the ether occurred. Cooling of the mixture with an ice-bath was sometimes necessary. After the addition was complete (about one hour), stirring was continued at room temperature for two hours. The mixture was hydrolyzed by pouring it onto cracked ice and sufficient dilute sulfuric acid was added to dissolve the precipitated magnesium hydroxide. The ether layer was separated, washed with a saturated sodium carbonate solution, and dried over anhydrous sodium sulfate. Removal of the ether and chloroform by distillation left a solid–liquid mixture. Petroleum ether (50 ml. 65–95° range) was added to the mixture to throw out of solution any dissolved solid. The solid was removed by filtration and washed with a little petroleum ether and the washings were added to the filtrate. Distillation of the filtrate gave 16.1 g. (81%) of crude product. Further fractionation gave 10.2 g. (51%) of 5-methyl-5-nonanol b. p. 91–92° (15 mm.).

The solid was recrystallized from ethyl alcohol. Recovery of pure glucose pentaacetate (identified by m. p. and mixed m. p. with an authentic sample) was 33.3 g. (87.5%). The same recovery of pentaacetate, but only 20% of carbinol, was isolated if reaction conditions were 0–5° and if the mixture was hydrolyzed immediately after the ester was all added (omit the two-hour stirring). Only 19 g. of crude pentaacetate was isolated if the Grignard reagent was added to the ester, but the yield of carbinol was 50%.

When a molar ratio of Grignard reagent (from methyl iodide, ethyl bromide, bromobenzene to β-D-glucose pentaacetate of 10:1) was used the procedure was the same except for the use of a 2 *M* Grignard diethyl ether solution. No pentaacetate was recovered nor was any sucrose octaacetate recovered when it reacted similarly with 10 moles of ethylmagnesium bromide. In these experiments 55–69% yields of tertiary alcohols were formed.

When an effort was made to duplicate the work of Fischer[2] with 5.0 g. of methyl iodide as the starting material, no carbinol was found and the recovery of pentaacetate was 60%.

When α- and β-D-glucose pentaacetate were compared in a reaction with ethylmagnesium bromide both gave the same result.

Formation of Glucosazone.—The aqueous layer from the preparation of 3-methyl-3-pentanol (a 10:1 ratio of Grignard reagent to ester was used) was treated with phenylhydrazine. The osazone formed had a m. p. of 205°. A mixed m. p. with glucosazone gave the same value.

Summary

The Grignard reagent reacts with β-D-glucose pentaacetate to form tertiary alcohols. No evidence was obtained for the formation of previously reported simple addition products which on hydrolysis would return the ester in its original form.

The Grignard reagent and β-D-glucose pentaacetate react in a molar ratio of 10:1 when the ester is added to the Grignard solution regardless of the ratio of reagents used.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MISSOURI]

The Bitter Principle of *Helenium Tenuifolium*

BY HERBERT E. UNGNADE AND EDWARD C. HENDLEY[1]

The common sneezeweed, *Helenium tenuifolium*[2] contains a colorless crystalline material with an intensely bitter taste which has been the subject of a number of investigations.[3,4,5]

The bitter principle can be obtained from the dried plant material by extraction with water,[4] chloroform[5] or benzene. The highest yields have been obtained by use of benzene and the product is easier to purify in this case.

A comparison by means of a standardized benzene extraction procedure shows that the leaves and flowers of the mature flowering plant contain the largest quantity of the bitter material which amounts to about 3% on a dry weight basis. Stems and roots contain only small amounts of the same material. Immature plants or second growth contain less than mature plants but proportionally more gum.

Purification of the plant extracts yields three substances melting at 152.3–153.3°, 155.3–156.3° and 192–195°. The first two of these are interconvertible. They possess identical absorption spectra and crystallographic constants which agree with those reported by Clark.[5] They must be regarded as crystalline modifications of isotenulin (I).

The high-melting material, m. p. 192–195°, is a benzene complex of Clark's tenulin (II). It is converted to (I) by refluxing with water. While this isomerization undoubtedly occurs when aqueous or wet solvents are used for extracting the plant, some isotenulin has been isolated even from extractions with dry benzene. It is therefore assumed that both (I) and (II) occur in the plant.

Isotenulin (I) is neutral, the *p*H of the saturated solution is 6.7. It consumes two moles of alkali on heating with aqueous alcoholic sodium hydroxide solution. One mole of alkali is accounted for by the acetoxyl group.[5] The product of the alkaline hydrolysis, desacetylisotenulin, isolated by Clark, allows for the loss of one mole of acetic acid. The function which reacts with the second mole of alkali is regenerated on acidification without isomerization because the hydrolysis product

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[1] From the Ph.D. Thesis of E. C. Hendley.

[2] The authors are indebted to Prof. W. E. Maneval of the Botany Department of the University of Missouri for the botanical identification of the plant.

[3] Weathers, *J. Dairy Sci.*, **16**, 401 (1933); MacDonald and Glaser, *Tenn. Agr. Exptl. Sta. Circ.*, **26**, 2 (1929); Herzer, *Proc. Assoc. Southern Agr. Workers*, **43**, 112 (1942).

[4] Buehler, Whitehead and Goodge, THIS JOURNAL, **59**, 2299 (1937).

[5] Clark, *ibid.*, **61**, 1836 (1939); **62**, 597, 2154 (1940).