The Reaction of Chloral with Cyclohexylmagnesium Bromide

BY VAUGHN W. FLOUTZ

The action of chloral with various organomagnesium halides gives a number of reaction products depending principally upon the nature of the organomagnesium halide employed. Secondary alcohols which contain the trichloromethyl and alkyl groups have been prepared by several investigators.[1,2,3] In some instances the reported yields of such alcohols have been low,[2] and in one case[4] leading to the synthesis of trichloroisopropanol, trichloroethanol was formed in isolable quantity. A recent study[5] of the interaction of chloral and ethylmagnesium halides has shown that trichloroethanol is produced in yields up to 65%, but that no significant quantities of secondary alcohol are formed. Secondary alcohols containing the trichloromethyl group together with an aryl group are formed readily in good yield by the Grignard reaction.[6,7] Unpublished research by the author has shown that trichloromethylphenylcarbinol and trichloromethyl-*o*-tolylcarbinol can be prepared in yields as high as 70%. With the exception of trichloromethylbenzylcarbinol described first by Howard,[2] and more recently by Gilman and Abbott,[5] attempts to prepare secondary alcohols from chloral and phenyl substituted alkylmagnesium halides have proved unsuccessful. In this connection Dean and Wolf[8] have shown that β-phenylethylmagnesium bromide, γ-phenylpropylmagnesium bromide, and δ-phenylbutylmagnesium bromide react with chloral to give trichloroethanol, styrene and its homologs, and 1,4-diphenylbutane and its homologs, but no detectable secondary alcohol.

The object of this study was to investigate the behavior of cyclohexylmagnesium bromide with chloral.

Procedure.—The Grignard reagent was prepared by adding a 0.2-mole portion of cyclohexyl bromide dissolved in a like volume of anhydrous ether to 0.2 g.-atom of magnesium turnings in 200 ml. of anhydrous ether under an atmosphere of nitrogen. In the normal addition, 0.2 mole of freshly distilled chloral dissolved in a like volume of anhydrous ether was added slowly to the Grignard reagent and the mixture finally refluxed for one-half hour. In the inverse addition the Grignard reagent was removed and slowly added to 0.2 mole of freshly distilled chloral dissolved in 75 ml. of anhydrous ether. In both types of addition very little solid separated in the course of the reaction. The reaction mixture was treated with 1 *N* hydrochloric acid and the ether layer was separated and washed in turn with sodium bicarbonate solution, sodium bisulfite solution, and water, then dried over anhydrous sodium sulfate.

The dried ether was removed by distillation and the residue was heated in an oil-bath to a bath temperature of 110°. This gave a distillate which was found to be principally cyclohexene. The hydrocarbon was identified by its conversion to 1,2-dibromocyclohexane, boiling point 116–118° at 29 mm. In determinations carried out subsequent to the identification of cyclohexene, it was found advisable to add the cyclohexene distillate to the ether first removed by distillation, and treat the resulting ether solution with a slight excess of bromine. Following this the ether solution was washed with sodium bicarbonate solution and water. The dried ether was removed by distillation and the residue subjected to fractional distillation under diminished pressure to obtain the 1,2-dibromocyclohexane.

The residue from the removal of the cyclohexene was fractionated under diminished pressure. The first fraction collected gave upon redistillation an oily liquid distilling at 66–69° at 25 mm. This product was identified as trichloroethanol through the preparation of the *m*-nitrobenzoate, melting point 75°, and the α-naphthyl urethan, melting point 119°. Dicyclohexyl, boiling point 122–125° at 20 mm., was isolated from a higher boiling fraction.

From a number of determinations the average yields of trichloroethanol, 1,2-dibromocyclohexane, and dicyclohexyl were, where normal addition was followed, 12.5 g., 14.5 g. and 1 g.; where inverse addition was followed, 15.5 g., 21 g. and 2 g., respectively.

This investigation shows that the interaction of cyclohexylmagnesium bromide and chloral produces no secondary alcohol. Cyclohexene, trichloroethanol, and dicyclohexyl are formed in the reaction. Inverse addition gives in general better yields, but does not change the nature of the reaction products.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF AKRON
AKRON, OHIO

RECEIVED JULY 23, 1943

---

[1] Henry, *Compt. rend.*, **138**, 205 (1904).

[2] Howard, THIS JOURNAL, **48**, 774 (1926).

[3] Howard, *ibid.*, **49**, 1068 (1927).

[4] Kharasch, Kleiger, Martin and Mayo, *ibid.*, **63**, 2305 (1941).

[5] Gilman and Abbott, *J. Org. Chem.*, **8**, 224 (1943).

[6] Savarian, *Compt. rend.*, **146**, 297 (1908).

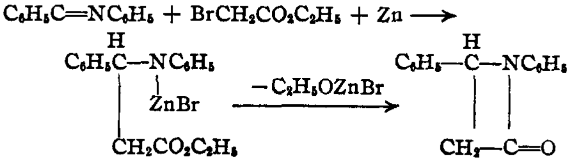
[7] Fritzman, *J. Russ. Phys.-Chem. Soc.*, **7**, 1046–1048 (1906).

[8] Dean and Wolf, THIS JOURNAL, **58**, 332 (1936).

The Reformatsky Reaction with Benzalaniline

BY HENRY GILMAN AND MERRILL SPEETER

There appears to be no report on a Reformatsky reaction with an anil linkage.[1] We have observed that a mixture of ethyl bromoacetate and zinc adds to the anil linkage of benzalaniline to give a 56% yield of the β-lactam of β-anilino-β-phenylpropionic acid [A]



$$C_6H_5\overset{H}{C}{=}NC_6H_5 + BrCH_2CO_2C_2H_5 + Zn \longrightarrow C_6H_5\overset{H}{C}(CH_2CO_2C_2H_5){-}N(ZnBr)C_6H_5 \xrightarrow{-C_2H_5OZnBr} C_6H_5{-}\overset{H}{C}{-}NC_6H_5,\ CH_2{-}C{=}O$$

A

The structure of the lactam was established by the method of mixed melting points with a sample prepared by adding ketene to benzalaniline.[2]

Hydrolysis of the reaction mixture apparently is unnecessary to obtain the lactam. This indicates that the intermediately formed zinc complex can lose C_2H_5OZnBr (when ethyl bromoacetate is used) to cyclicize to the lactam.

---

[1] See the excellent recent survey of the Reformatsky reaction by Shriner in Adams, "Organic Reactions," John Wiley and Sons, New York, N. Y., 1942, Vol. I, pp. 1–37.

[2] Staudinger, *Ber.*, **50**, 1037 (1917).

The extent of addition to the anil linkage is significantly increased when ethyl α-bromopropionate is used. In this case there is obtained an 85% yield of the β-lactam of α-methyl-β-anilino-β-phenylpropionic acid. The Reformatsky reaction with anils appears to be broad in scope, and more complete details will be published later.

Experimental

β-Lactam of β-Anilino-β-phenylpropionic Acid.—A solution of 36.2 g. (0.2 mole) of benzalaniline in 200 cc. of sodium-dried toluene was heated to boiling with 13.5 g. (0.21 g. atom) of sandpapered zinc foil and a crystal of iodine. Three cc. of ethyl α-bromoacetate was added and on stirring an exothermic reaction set in. Twenty more cc. (a total of 0.21 mole) of the bromo-ester was now added at such a rate as to maintain gentle refluxing. When the addition was completed, the mixture was boiled gently for one-half hour. Hydrolysis was effected with 200 cc. of concd. ammonium hydroxide. The toluene layer was then washed with water, dilute hydrochloric acid, sodium bisulfite solution, and again with water. After distillation of the solvent, and two recrystallizations from methanol, a 56% yield of lactam melting at 153-154° was obtained.

Ketene[3] was treated with 0.1 mole of benzalaniline following the directions of Staudinger.[2] After a number of recrystallizations from methanol, the product melted at Staudinger's value of 153-154°. A mixed melting point determination showed the compounds to be identical.

Reaction without Hydrolysis.—A mixture of 11.1 cc. (0.1 mole) of ethyl α-bromoacetate and 18.1 g. (0.1 mole) of benzalaniline in 100 cc. of toluene reacted with 6.6 g. (0.1 g. atom) of zinc. After the reaction, the mixture was diluted with 500 cc. of dry ether. The precipitate was allowed to settle and the supernatant liquid then decanted. After distillation of the solvent, the residue was twice recrystallized from anhydrous methanol. The melting point of the product was 154°, and there was no depression when this compound was mixed with lactam prepared from ketene.

β-Lactam of α-Methyl β-Anilino-β-phenylpropionic Acid.—Using the same general procedure as in the first reaction, but substituting 0.21 mole of ethyl α-bromopropionate for the ethyl α-bromoacetate, an 85% yield of lactam melting at 109-110° was obtained. Crystallization was from methanol.

Reaction with Benzyl α-Bromoacetate.—A solution of 18.1 g. of benzalaniline (0.1 mole) in 100 cc. of toluene reacted with 6.6 g. of zinc (0.1 g. atom) and 23 g. (0.1 mole) of benzyl α-bromoacetate. The product was isolated and purified by the procedure of the first reaction. A 40% yield of lactam melting at 153-154° was obtained. This compound was identified by a mixed melting point determination with the lactam obtained from ketene.

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA

RECEIVED AUGUST 16, 1943

---

(3) Hurd, "Organic Syntheses," **4**, 39 (1925).

4-Phenylphenyl Iodoacetate

BY LEE C. HENSLEY AND STEWART E. HAZLET

Bromine previously[1] has been shown to convert 4-phenylphenyl chloroacetate to 4-phenylphenyl bromoacetate by a reaction in specially prepared acetic acid in the presence of a trace of iron. We have now prepared the corresponding iodoacetate by the reaction of potassium iodide with the chloro or bromo compound.

Preparation of 4-Phenylphenyl Iodoacetate from 4-Phenylphenyl Bromoacetate.—Four and seventy-five hundredths grams of the bromoacetate was dissolved in 40 ml. of acetone. This solution was added in small portions to 275 ml. of acetone saturated with potassium iodide and containing an excess of 0.5 g. of undissolved potassium iodide. At first a cloudiness appeared but, as more of the solution containing the ester was added, small granules formed and precipitated. The mixture was set aside at room temperature for thirty-six hours; Norite was added and the mixture was then allowed to stand for an additional six hours. Boiling, filtering, and removing about one-half of the acetone on the steam-bath followed. The remaining solution was poured into 600 ml. of water, and a flocculent precipitate was formed. This product represented a 77.8% yield of 4-phenylphenyl iodoacetate; m. p. 113-114°. Two recrystallizations from methanol followed by two from 70-90° ligroin raised the melting point to 113.5-114.3°.

Anal. Calcd. for $C_{14}H_{11}O_2I$: I, 37.53. Found: I, 37.76.

Preparation of 4-Phenylphenyl Iodoacetate from 4-Phenylphenyl Chloroacetate.—The same procedure, applied to the bromoacetate, gave 18.3% yield of the iodo product.

DEPARTMENT OF CHEMISTRY
STATE COLLEGE OF WASHINGTON
PULLMAN, WASHINGTON

RECEIVED AUGUST 9, 1943

---

(1) Hazlet, Hensley and Jass, THIS JOURNAL, **64**, 2449 (1942).

[BUREAU OF AGRICULTURAL AND INDUSTRIAL CHEMISTRY
AGRICULTURAL RESEARCH ADMINISTRATION, UNITED
STATES DEPARTMENT OF AGRICULTURE]

The Hydrolysis of Nicotinonitrile by Ammonia

BY CHARLES F. KREWSON AND JAMES F. COUCH

It is well known that the action of potassium or sodium hydroxide on nitriles leads directly to the formation of the corresponding acids.[1] The amides, postulated as intermediate products in this reaction, are obtained when hydrogen peroxide is added to the mixture.[2]

The action of ammonium hydroxide has not been extensively studied. Schlieper reported that it did not react with valeronitrile. The idea that ammonium hydroxide reacts with nitriles to form amidines possibly stems from Bernthsen's[3] discovery that amine hydrochlorides react with certain nitriles to form amidine hydrochlorides. Ammonium chloride, however, did not react in this way. We have found that ammonium hydroxide reacts with nicotinonitrile to form nicotinamide.

Procedure.—A mixture of nicotinonitrile (20 g.) prepared either by the Woodward, Badgett and Willaman process[4] or from nicotinamide by the method of LaForge,[5] and 120 ml. (9 moles) of concentrated ammonium hydroxide solution in a cylindrical glass bulb made of 60-mm. Pyrex glass tubing, to one end of which is sealed a short piece of 10-mm. tubing, is cooled in ice, and the small tube drawn down to a spiral capillary. The bulb is then placed in a 500-cc. steel bomb along with 100 cc. of concen-

---

(1) (a) A. Schlieper, *Ann. Chem. Pharm.*, **59**, 1-23 (1846); (b) E. Frankland and H. Kolbe, *ibid.*, **65**, 288-304 (1848).

(2) (a) Br. Radziszewski, *Ber.*, **17**, 1289-1290 (1884); **18**, 355-356 (1885); (b) L. McMaster and F. B. Langreck, THIS JOURNAL, **39**, 103-109 (1917); (c) L. McMaster and C. R. Noller, *J. Indian Chem. Soc.*, **12**, 652-653 (1935); *C. A.*, **30**, 1736 (1936).

(3) A. Bernthsen, *Ann. Chem. Pharm.*, **184**, 321-370 (1876); **192**, 1-60 (1878); *Ber.*, **10**, 1235 (1877).

(4) In course of publication.

(5) F. B. LaForge, THIS JOURNAL, **50**, 2477 (1928).