## Experimental

**3,4-Dichlorobenzyl Cyanide.**—This nitrile was prepared in the usual manner from 3,4-dichlorobenzyl chloride and was obtained as a colorless liquid, b. p. 170° (12 mm.).

*Anal.* Calcd. for $C_8H_5Cl_2N$: N, 7.50. Found: N, 7.37, 7.51.

**2-(3,4-Dichlorophenyl)-4-diethylaminobutylamine.**—A solution of 128 g. (0.45 mole) of α-(3,4-dichlorophenyl)-γ-diethylaminobutyronitrile in 600 cc. of 15% methanolic ammonia was reduced in the presence of 30 g. of Raney nickel under fifty atmospheres pressure of hydrogen at 50°. The catalyst was removed by filtration and the residue distilled to give 124 g. (95.5%) of product, b. p. 125° (1 mm.).

*Anal.* Calcd. for $C_{14}H_{22}Cl_2N_2$: N, 9.77. Found: N (Dumas), 9.90; N (titration), 9.77.

**4-[2-(*p*-Chlorophenyl)-4-diethylaminobutylamino]-7-chloroquinoline.**—A mixture of 19.8 g. (0.1 mole) of 4,7-dichloroquinoline, 54 g. (0.211 mole) of 2-(*p*-chlorophenyl)-4-diethylaminobutylamine, and a pinch of potassium iodide was heated in a bath kept at 180°. The temperature of the reaction mixture was allowed to rise spontaneously to 198° and then kept at 180° so that the total time of heating at 180° or higher was thirty-five minutes. A solution of the viscous oil in 125 cc. of 40% acetic acid was added to excess, dilute sodium hydroxide and the liberated oil dissolved in ether. The ether solution was dried by shaking with potassium carbonate and set aside to crystallize. The 25.5 g. of white crystalline product, m. p. 122–125°, was recrystallized from Skellysolve C to give 25 g. (60%), m. p. 127–129°.

*Anal.* Calcd. for $C_{23}H_{27}Cl_2N_3$: C, 66.4; H, 6.50; N, 10.10. Found: C, 66.12; H, 6.59; N, 9.79.

**4-[2-(*p*-Chlorophenyl)-5-diethylaminopentylamino]-7-chloroquinoline.**—A mixture of 30 g. of phenol, 34 g. (0.126 mole) of 2-(*p*-chlorophenyl)-5-diethylaminopentylamine, 19.8 g. (0.1 mole) of 4,7-dichloroquinoline, and a pinch of potassium iodide was kept at 130–140° for three hours, dissolved in 125 cc. of 40% acetic acid, and added to excess, dilute sodium hydroxide. An ether solution of the liberated oil was washed well with 10% sodium hydroxide and then water, dried by shaking with potassium carbonate, and set aside to crystallize, yielding 29 g. of white crystalline product, m. p. 113–115°. Several recrystallizations from benzene–Skellysolve C gave 24.5 g. (57%), m. p. 119.5–121°.

*Anal.* Calcd. for $C_{24}H_{29}Cl_2N_3$: C, 66.98; H, 6.74; N, 9.77. Found: C, 66.98; H, 7.00; N, 9.89.

**7-Chloro-4-[4-diethylamino-2-(*p*-hydroxyphenyl)-butylamino]-quinoline.**—A solution of 30 g. (0.073 mole) of 7-chloro-4-[4-diethylamino-2-(*p*-methoxyphenyl)-butylamino]-quinoline in 450 cc. of 48% hydrobromic acid was refluxed for fifteen minutes and concentrated *in vacuo*. An aqueous solution of the residue was treated with charcoal and filtercel and added to excess ammonium hydroxide to precipitate a white solid weighing 26 g. (89.7%), m. p. 162–164°. Recrystallization from alcohol yielded 20 g., m.p. 163–164°. The product was soluble in dilute sodium hydroxide.

*Anal.* Calcd. for $C_{23}H_{28}ClN_3O$: C, 69.43; H, 7.04; N, 10.57. Found: C, 69.05; H, 7.12; N, 10.57.

**Acknowledgment.**—The authors wish to acknowledge, with appreciation, the advice of Drs. C. M. Suter and J. S. Buck. We wish to thank the Misses Bass, Rainey and Curran for the microanalyses recorded.

## Summary

The preparation of a series of 4-dialkylaminoalkylnitriles and amines is described in which a phenyl or substituted phenyl group is in the 2-position. These diamines have been condensed with 4,7-dichloroquinoline and 4,7-dichloro-3-methylquinoline to give a series of 7-chloro-4-substituted aminoquinolines and 7-chloro-3-methyl-4-substituted aminoquinolines. The preparation of an analogous series of 9-amino-6-chloro-2-methoxyacridine derivatives is reported.

RENSSELAER, N. Y. RECEIVED JULY 19, 1946

# NOTES

## The Preparation of β-Aminoethanephosphonic Acid

BY JACOB FINKELSTEIN

During the course of an investigation in this Laboratory it was desirable to prepare β-aminoethanephosphonic acid: $H_2NCH_2CH_2PO(OH)_2$ (I). The only compounds of this type reported are aminomethanephosphonic acid and its N substituted derivatives.[1] These substances were prepared from methylolamides $RCO—NR'CH_2OH$ which when treated with phosphorus trihalide produce intermediate dihalogen phosphorus esters, which rearrange spontaneously into phosphonic acid dihalides, and on hydrolyzing the phosphonic acids are obtained

$$RCONR'CH_2OH + PCl_3 \longrightarrow RCONR'CH_2OPCl_2 \longrightarrow RCONR'CH_2POCl_2 \longrightarrow RCONR'CH_2PO(OH)_2 \longrightarrow HNR'CH_2PO(OH)_2$$

This method is possibly not applicable to the preparation of compounds of the type $=N—(CH_2)_x—P^=$ where $x > 1$.

Nylen[2] has described the preparation of β-phosphonopropionic acid triethyl ester and its C-amide (β-carbamylethanephosphonic acid diethyl ester). This latter substance, when subjected to the Hofmann degradation, yielded the desired substance (I). The corresponding hydrazide was also prepared from the ester but would not undergo the Curtius rearrangement.

Nylen prepared the ester in 35% yield by the reaction of sodiodiethyl phosphite with ethyl β-

(1) U. S. Patent 2,304,156 and 2,328,358.

(2) Nylen, *Ber.*, **59**, 1119 (1926).

iodopropionate in ether. Upon distillation, it undergoes violent decomposition. For this investigation the ester was prepared in 78% yield from sodio-diethyl phosphite with ethyl β-bromopropionate in dry xylene. The product distilled very smoothly. The C-amide was obtained in the usual manner. The reactions may be summarized as follows

$$(C_2H_5O)_2OPNa + BrCH_2CH_2COOC_2H_5 \longrightarrow (C_2H_5O)_2OPCH_2CH_2COOC_2H_5 \longrightarrow (C_2H_5O)_2OPCH_2CH_2\cdot CONH_2 \longrightarrow (C_2H_5O)_2OPCH_2CH_2NH_2 \longrightarrow (HO)_2OPCH_2CH_2NH_2HCl \longrightarrow (HO)_2OPCH_2CH_2NH_2$$

The amino acid is a colorless, crystalline substance freely soluble in water and insoluble in alcohol. It is stable to hot hydrochloric acid and possesses a characteristic titration curve with one sharp break, at *p*H 7.5, due to the zwitterion effect.

### Experimental

**β-Phosphonopropionic Acid Triethyl Ester.**—To 68 g. of dry sodium ethoxide in 500 cc. of dry xylene, 138 g. of diethyl phosphite[3] is added slowly while stirring. When completely reacted, 181 g. of ethyl β-bromopropionate is added dropwise with vigorous stirring while the reaction mixture is kept in an ice–salt bath. After permitting the mixture to stand overnight to reach room temperature, it is warmed for two hours in a water-bath. After cooling, the sodium bromide is removed by filtering, the xylene distilled off *in vacuo* and the residual oil fractionated *in vacuo;* b. p. 141–143° at 9 mm. The ester is a clear, colorless liquid; yield, 78%.

**β-Aminoethanephosphonic Acid.**—To a solution of 30.8 g. of potassium hydroxide and 8 g. of bromine in 200 cc. of water at 0°, 10.45 g. of β-carbamylethanephosphonic acid diethyl ester is added and the mixture stirred until complete solution has occurred. After allowing the solution to stand overnight, at room temperature, 90 cc. of 48% hydrobromic acid is added when about one liter of carbon dioxide is evolved. The solution is evaporated to dryness *in vacuo* from a warm water-bath. The residue is treated with 75 cc. of water and filtered. The filtrate, at about *p*H 1, is heated in a sealed tube at 150–190° for two hours. The reaction mixture is then evaporated to dryness *in vacuo*, the residual cake extracted with 100 cc. of warm alcohol and the extract filtered. The filtrate is treated with excess aniline while stirring to precipitate the amino acid. After two recrystallizations from 50% alcohol, the product is pure; m. p. 281–282° (cor.), yield, 71%.

*Anal.* Calcd. for $C_2H_8NPO_3$: C, 19.20; H, 6.45; N, 11.20. Found: C, 19.21; H, 6.51; N, 10.55.

(3) Milobendzki and Sachnowski, *C. A.*, **13**, 2865 (1919).

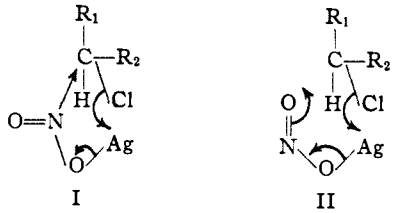
SCIENTIFIC DEPARTMENT
HOFFMANN-LA ROCHE, INC.
NUTLEY, N. J.

RECEIVED JULY 17, 1946

## Reaction of *d*-α-Phenethyl Chloride with Silver Nitrite

BY RICHARD H. EASTMAN AND SIDNEY D. ROSS

The reaction of silver nitrite with optically active β-*n*-octyl bromide has been shown[1] to lead to optically active β-nitro-*n*-octane and β-*n*-octyl nitrite. In view of the heterogeneous nature of this reaction it occurred to us that reaction complexes of the type I and II with the indicated electronic shifts would account for the retention of optical activity in the products



I II

equally as does the assumption of a simple displacement of chloride ion by nitrite ion, the sense of the attack of the latter determining whether nitro compound or nitrite is the product. As a test of our hypothesis we have carried out the reaction of silver nitrite with *d*-α-phenethyl chloride in benzene, in which case a retention of optical activity would be expected if cyclic complexes of the type shown were intermediates. Our choice of the optically active halide was dictated by the observation that if activity were retained in this case, the experiment would constitute good evidence for the hypothetical mechanism, since it has been shown[2] that in the reaction of benzyl chloride with mercuric salts, the mercuric ion simply removes the halogen leaving the alkyl residue as a carbonium ion or its equivalent. If the silver ion of the silver nitrite operates in this latter sense rather than in the former in the case of *d*-α-phenethyl chloride, the formation of α-phenethyl nitrite and α-nitroethylbenzene should be attended with racemization.

Our experiments show that racemization is the predominant course of the reaction in question.

### Experimental

***d*-α-Phenethyl Chloride.**—This material was obtained from *d*-α-phenethyl alcohol[3] ($[\alpha]^{32}D$ +29.8°) by the method of McKenzie and Clough.[4] Our material had b. p. 85–86° at 29 mm., $n^{25}D$ 1.5250 and $[\alpha]^{32}D$ + 37.0°.

***d*-α-Phenethyl Nitrite.**—A mixture of 3.5 g. of sodium nitrite, 10 cc. of water and 6.1 g. *d*-α-phenethyl alcohol ($[\alpha]^{32}D$ +29.8°) was cooled in an ice-bath and treated with 8.5 cc. of 6 *N* hydrochloric acid in portions during fifteen minutes with swirling. The layers were then separated, the product was diluted with ether, dried over sodium sulfate, freed from solvent and distilled through a two-foot Podbielniak column to yield 4.5 g. of *d*-α-phenethyl nitrite, a yellow oil of turpentine odor, of b. p. 70–71° at 16 mm.,[5] of $n^{25}D$ 1.4912, and of $[\alpha]^{31}D$ +39.9°.

**Reaction of *d*-α-Phenethyl Chloride with Silver Nitrite.**—Eight and one-half grams of *d*-α-phenethyl chloride ($[\alpha]^{32}D$ +37.0°) and 12.2 g. of silver nitrite (dried *in vacuo* over phosphorus pentoxide) were shaken together in 100 cc. of dry benzene for twelve hours. The silver halide was filtered off, the benzene was removed *in vacuo*, and the product was distilled through a two-foot Podbielniak column. The following fractions were obtained:

(1) Shriner and Young, THIS JOURNAL, **52**, 3332 (1930).

(2) Roberts and Hammett, *ibid.*, **59**, 1063 (1937).

(3) We wish to express our appreciation to George DeLaMater of Harvard University for providing us with the active phenethyl alcohols.

(4) McKenzie and Clough, *J. Chem. Soc.*, **103**, 687 (1913).

(5) *d*-α-Phenethyl nitrite has been previously reported as a yellow oil of b. p. 72.5–73° at 19 mm. [Holmberg, *Ber.*, **45**, 999 (1912)].

| Fraction | B. p. °C. | Mm. | Grams | $n^{25}D$ | $[\alpha]^{25}D$ |
|---|---|---|---|---|---|
| 1 | 45–46.5 | 4 | 1.3 | 1.4909 | +5.1 |
| 2 | 46.5–80 | 4 | 2.9 | 1.4932 | +5.1 |
| 3 | 80–89 | 4.5 | 0.7 | 1.5110 | ... |
| 4 | 89–95 | 5 | 1.9 | 1.5095 | +2.4 |

Fraction 1 was concluded to be essentially pure α-phenethyl nitrite. In order to establish the nature of fraction 4, 50 g. of *dl*-α-phenethyl chloride was treated with silver nitrite under the conditions described above, and from the crude reaction product there was obtained by repeated fractionation, in addition to 11.5 g. of α-phenethyl nitrite of b. p. 34–36° at 2 mm. and of $n^{25}D$ 1.4938, 2.5 g. of colorless oil of b. p. 90–95° at 3 mm. and of $n^{25}D$ 1.5210. The latter material, which corresponded roughly to fraction 4 above, was shown to contain largely α-nitroethylbenzene by conversion to the aci-form according to the method of Bamberger and Seligman.[6] The intermediate fractions gave precipitates of silver chloride when warmed with alcoholic silver nitrate solution and were concluded to contain, in addition to the other two components, unreacted α-phenethyl chloride.

(6) Bamberger and Seligman, *Ber.*, **36**, 707 (1903).

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASSACHUSETTS RECEIVED JULY 19, 1946

## Catalytic Decomposition of DDT

BY A. L. FLENNER

From work conducted on the stability of DDT to heating at 115°, Fleck and Haller[1] concluded that impurities present in technical DDT inhibit the action of catalytic substances in eliminating hydrogen chloride, and that removal of these impurities without simultaneous removal of catalytic substances produces an apparent instability of DDT. In the course of work on the manufacture and formulation of DDT, this Laboratory made a study of the stability of samples varying in degrees of purity.

It was found that Technical DDT, having a set point of 88°, and highly purified material, with a melting point of 108.5°, evolved no hydrogen chloride when heated for twenty-four hours at 115°, whereas material which had been once recrystallized from ethanol, and having a melting point of 105–107°, did evolve hydrogen chloride when heated under the same conditions. The material melting at 105 to 107° had not been filtered from a small amount of insoluble impurities during the recrystallization and it was thought that these impurities might be acting as catalytic decomposing substances. A portion of the partially purified material was therefore dissolved in ethanol, filtered, and then the solution evaporated to dryness to recover the DDT. When this filtered DDT, after drying, was subjected to heating at 115° for twenty-four hours, it was found to be stable since no hydrogen chloride was evolved, which indicates that the insoluble impurities acted as catalytic decomposition agents and their removal rendered the DDT stable under the test conditions. To obtain additional evidence, both technical DDT and purified DDT of m. p. 108.5° were heated in the presence of iron oxide at 115°. Hydrogen chloride was evolved almost immediately from different samples of the purified material, while from four to six hours were required to evolve hydrogen chloride from samples of technical DDT.

(1) Fleck and Haller, THIS JOURNAL, **68**, 142 (1946).

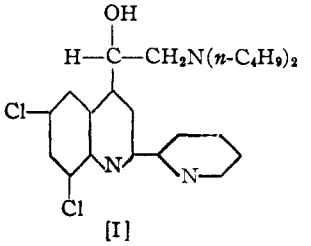
These results therefore verify those of Fleck and Haller[1] and it is concluded that there is some substance or substances present in technical DDT which act as an inhibitor to the catalytic elimination of HCl. Removal of these inhibiting substances will render the DDT susceptible to catalytic decomposition. It, therefore, seems quite possible that under conditions of use technical DDT may be more stable than purified or partially purified material since catalytic substances present in diluents and natural dusts may act to liberate hydrogen chloride slowly from spray deposits of the purified DDT. Although purified DDT is not being used extensively at the present time any future use under field conditions may require the addition of an inhibitor to protect it from catalytic decomposition.

PEST CONTROL RESEARCH LABORATORY
E. I. DU PONT DE NEMOURS & CO., INC.
WILMINGTON, DELAWARE RECEIVED AUGUST 5, 1946

## 6,8-Dichloro-2-(2'-pyridyl)-α-di-*n*-butylaminomethyl-4-quinolinemethanol[1a]

BY HENRY GILMAN, LEO TOLMAN AND SAMUEL P. MASSIE, JR.

In connection with studies on experimental avian malaria it was desirable to determine the activity of a 6,8-dichloro-4-quinolinemethanol having a nitrogen heterocycle in the 2-position. The compound selected was 6,8-dichloro-2-(2'-pyridyl) - α - di - *n* - butylaminomethyl-4-quinolinemethanol.[1b] This compound [I] was prepared *via* the Pfitzinger reaction by condensation of 5,7-dichloroisatin with methyl α-pyridyl ketone.[2] Ethyl 6,8-dichloro-2-(2'-pyridyl)-cinchoni-




[I]

nate was prepared incidental to an examination of its condensation with ethyl acetate to give the corresponding ketoester. The plan was to brominate the keto-ester as a means of preparing the 4-bromoacetyl compound. However, some orienting experiments showed that the condensation of the ethyl ester with ethyl acetate by means of sodium ethoxide was not so satisfactory as the reaction of diazomethane with the acid chloride.

### Experimental

**6,8-Dichloro-2-(2'-pyridyl)-cinchonic Acid.**—A mixture of 77 g. (0.36 mole) of 5,7-dichloroisatin,[3] 60 g. (1.08

(1) (a) The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Iowa State College; (b) the Survey Number assigned to this drug by The Survey of Antimalarial Drugs is SN-14,143-4. The activities of these compounds will be tabulated in a forthcoming monograph.

(2) See Winstein, Jacobs, *et al.*, THIS JOURNAL, **68**, 1831 (1946). Also, Lindwall, Bandes, and Weinberg *ibid.*, **53**, 317 (1931).

(3) Prepared in accordance with directions kindly provided by Drs. H. Sargent and T. C. Myers of the California Institute of Technology.

moles) of potassium hydroxide in 150 cc. of water, and two liters of ethanol was heated to reflux with stirring, and 44 g. (0.36 mole) of methyl α-pyridyl ketone was added rapidly. After working up the reaction product by customary procedures there was obtained 100 g. (87%) of product melting at 328–330°. An analytical sample of this acid was prepared by dissolving a small portion in hot dilute potassium hydroxide solution and heating with Norite. The warm filtrate was neutralized with acetic acid, and the solid obtained in this manner was filtered and washed with hot ethanol. After drying in the oven at 130°, the compound melted at 336–337°.

*Anal.* Calcd. for $C_{15}H_9O_2N_2Cl_2$: Cl, 22.18; N, 8.78. Found: Cl, 21.99; N, 8.95.

**Ethyl 6,8-Dichloro-2-(2'-pyridyl)-cinchoninate.**—The acid was esterified by heating 45 g. (0.14 mole) with 250 cc. of absolute ethanol, and 100 cc. of sulfuric acid at the reflux temperature for eight hours. Recrystallization from ethanol (1800 cc.) gave 35 g. (72%) of product melting at 113–114°. The same melting point was observed after recrystallization from ethyl acetate.

*Anal.* Calcd. for $C_{17}H_{12}O_2N_2Cl_2$: N, 8.05; Cl, 20.43. Found: N, 7.81; Cl, 20.19.

**6,8-Dichloro-2-(2'-pyridyl)-cinchoninyl Chloride.**—From twenty-five grams (0.078 mole) of 6,8-dichloro-2-(2'-pyridyl)-cinchoninic acid and 100 cc. of thionyl chloride there was obtained 28 g. (100%) of material melting at 255–263°. The melting point varied somewhat on different preparations. Another batch melted at 260–268°. The difference in melting points might be due to varying amounts of hydrogen chloride in the product.

**6,8-Dichloro-4-(α-bromoacetyl)-2-(2'-pyridyl)-quinoline.**—Twenty-five grams (0.074 mole) of 6,8-dichloro-2-(2'-pyridyl)-cinchoninyl chloride was added slowly to 0.3 mole of diazomethane in 900 cc. of dry methylene chloride[4] solution at 5°. Then, following standard procedures, 30 cc. of 48% hydrobromic acid was added. There was obtained 28 g. (95%) of material melting at 229–231°. Recrystallization of a small amount of this material from acetic acid and a few drops of 48% hydrobromic acid gave a product melting at 265–268°.

*Anal.* Calcd. for $C_{16}H_9ON_2BrCl_2 \cdot HBr$: N, 5.87; Cl, Br, 48.41. Found: N, 6.22 and 6.20; Cl, Br, 47.24.

A low combined-halogen analysis may be explained by the loss of some hydrogen bromide from the weakly basic product.

**α-Bromomethyl-6,8-dichloro-2-(2'-pyridyl)-4-quinoline methanol.**—A mixture of 20 g. (0.05 mole) of 6,8-dichloro-4-(α-bromoacetyl)-2-(2'-pyridyl)-quinoline, 11 g. of aluminum *i*-propoxide, and 200 cc. of anhydrous *i*-propanol was heated with a water-bath so that slow distillation occurred.[5] The residue was cooled and 100 cc. of 6 *N* hydrochloric acid was added slowly. The solid was filtered and washed with a little 6 *N* hydrochloric acid and about 200 cc. of water. After drying, the product weighed 16.5 g. (83%) and melted at 245–248°. From another preparation, the yield of carbinol melting over a wider range (245–250°) was 97%.

**6,8-Dichloro-2-(2'-pyridyl)-α-di-*n*-butylaminomethyl-4-quinolinemethanol.**—Five grams (0.012 mole) of α-bromomethyl-6,8-dichloro-2-(2'-pyridyl)-4-quinolinemethanol, 7.8 g. (0.06 mole) of di-*n*-butylamine and 20 cc. of toluene was heated in an oil-bath at 95–100° for fourteen hours.[5,6] The reaction mixture was poured into anhydrous ether and filtered. The filtrate was first distilled on a steam-bath at reduced pressure, and finally the residue was distilled at 0.5 mm. from a boiling water bath to remove the excess of di-*n*-butylamine. The viscous oil that remained was dissolved in a mixture of two parts anhydrous ether to one part acetone. The monohydrochloride was precipitated from this solution by the addition, with vigorous mechanical stirring, of 10-cc. portions of 0.26 *M* ethereal hydrogen chloride.[7] The first three portions of acid gave a total of 3.3 g. (57%) of material melting at 182–184°.[8] An analytical sample of this product melting at 188–190° was obtained by recrystallization from absolute ethanol–ethyl acetate solution.

*Anal.* Calcd. for $C_{24}H_{29}ON_3Cl_2 \cdot HCl$: N, 8.70; Cl, 22.05. Found: N, 8.71; Cl, 22.08 and 22.07.

**Methyl α-Pyridyl Ketone.**—Details are given for this preparation because of a 25% improvement in yield.[9] To 1.2 moles of sodium ethoxide in 1100 cc. of warm benzene, prepared from 27.6 g. (1.2 g. atoms) of sodium sand and 55.2 g. (1.2 mole) of absolute ethanol, was added with vigorous stirring a mixture of 120.2 g. (0.8 mole) of ethyl picolinate[10] and 140.8 g. (1.6 moles) of anhydrous ethyl acetate at a rate to maintain gentle refluxing. During the addition the sodium ethoxide disappeared; the mixture became clear, and then formed a thick yellow mush. The mixture was refluxed with stirring for twelve hours, cooled and poured into a cold solution of 40 g. of sodium hydroxide in 800 cc. of water. The light yellow solid was filtered off and 800 cc. of water was added to the filtrate. The benzene and aqueous layers were separated. The benzene layer was extracted with 400 cc. of water and the combined aqueous layers extracted with 100 cc. of benzene. The yellow precipitate was suspended in the aqueous solution and the mixture acidified with 350 cc. of concentrated hydrochloric acid. The solution was refluxed for two hours, cooled, made basic with solid sodium carbonate and extracted with 1500 cc. of ether in two portions. The ether was dried over anhydrous sodium sulfate. Removal of the ether and distillation of the residue at 79–80° (10 mm.) gave 72 g. (75%) of methyl α-pyridyl ketone.

(4) The authors are grateful to Dr. Robert E. Lutz for general directions on the use of methylene chloride in this reaction.

(5) This procedure followed a general method of Dr. Robert E. Lutz for the preparation of the corresponding 2-phenyl derivative.

(6) The temperature does not appear to be very critical in this condensation as good yields were obtained by heating at 70°. The period of heating was varied from six to fourteen hours without appreciable change in yield.

(7) It was found helpful in some cases where mixtures of amines were involved to effect separation by fractional precipitation of the hydrochlorides, using dilute ethereal hydrogen chloride.

(8) The melting points vary with the rate of heating. The melting points reported were taken by inserting the tube into the bath at 170° and heating the bath at 8° per minute. The pure compound also melted in twenty-eight seconds when inserted into a constant temperature bath of 198–199°.

(9) Kolloff and Hunter, THIS JOURNAL, **63**, 490 (1941).

(10) This ester was prepared in 73% yield by the esterification of picolinic acid with ethanol using hydrogen chloride.

CHEMICAL LABORATORY
IOWA STATE COLLEGE
AMES, IOWA

RECEIVED SEPTEMBER 3, 1946

## Antitubercular Studies. Bis-(*p*-aminophenyl) Derivatives of Ethyl Ether and Trichloroethane

BY EDITH GRAEF[1] AND ALFRED BURGER

On the basis of the observation[2] that the substitution of other "inhalation-anesthetic" groups for the trichloroethyl group in DDT led to compounds approaching, or rivaling, this insecticide in activity, it seemed advisable to substitute similar groups in 1,1,1-trichloro-2,2-bis-(*p*-aminophenyl)-ethane since one of its acyl derivatives had shown considerable antitubercular activity.[3]

As the first example in this series we have prepared α,α'-bis-(*p*-aminophenyl)-ethyl ether by condensation of 1-(*p*-acetamidophenyl)-ethyl bromide with sodium 1-(*p*-acetamidophenyl) eth-

(1) Du Pont Post-Graduate Fellow.

(2) Läuger, Martin and Müller, *Helv. Chim. Acta*, **27**, 892 (1944).

(3) Burger, Graef and Bailey, THIS JOURNAL, **68**, 1725 (1946).

oxide, and subsequent alkaline hydrolysis of the acetamido groups.

The relative insolubility of 1,1,1-trichloro-2,2-bis-(*p*-benzamidophenyl)-ethane[3] made it desirable to attempt the preparation of a soluble derivative of the parent amine of this compound. 1,1,1-Trichloro-2,2-bis-(*p*-phthalamidophenyl)-ethane[4] appeared suitable, but we did not succeed in purifying the product from the partial hydrolysis of the corresponding phthalimido compound.

### Experimental

**1-(*p*-Acetamidophenyl)-ethyl Bromide.**—This halide, previously described by Rousset,[5] was obtained from 1-(*p*-acetamidophenyl)-ethanol[5] which, in turn, could be prepared by reduction of *p*-acetamidoacetophenone with aluminum isopropoxide in the customary manner. A solution of 30 g. of 1-(*p*-acetamidophenyl)-ethanol in 300 cc. of dry chloroform was cooled to −10° in an ice–salt-bath. Phosphorus tribromide (10 cc.) was dropped in with constant stirring, the temperature being kept below 0°, and the solution was then allowed to warm to room temperature. Stirring was discontinued, the mixture allowed to stand overnight, the chloroform and excess phosphorus tribromide removed under reduced pressure, and the residue poured into 100 cc. of ice and water. The oil formed was extracted into ether; drying and evaporation of the ether extract yielded 24 g. (58%) of platelets which were recrystallized from ethanol. The crystals melted at 93–95° and darkened on standing.

**α,α′-bis-(*p*-Acetamidophenyl)-ethyl Ether.**—To 0.5 g. of sodium finely dispersed under xylene, was added a solution of 3.7 g. of 1-(*p*-acetamidophenyl)-ethanol in 50 cc. of dry ether at room temperature with mechanical stirring. When the spontaneous refluxing had ceased, a solution of 5 g. of 1-(*p*-acetamidophenyl)-ethyl bromide in 50 cc. of ether was added, and the mixture stirred overnight. It was washed with 50 cc. of water, the ether solution was dried over sodium sulfate, and the solvents were evaporated in a vacuum. The residual oil solidified on cooling and was crystallized from ethanol-acetone. It weighed 3 g. (44%) and melted at 109–111°.

*Anal.* Calcd. for $C_{20}H_{24}N_2O_3$: N, 8.23. Found: N, 8.51.

**α,α′-bis-(*p*-Aminophenyl)-ethyl Ether.**—A solution of 14 g. of α,α′-bis-(*p*-acetamidophenyl)-ethyl ether in 150 cc. of 15% ethanolic potassium hydroxide was refluxed for ten hours. The ethanol was distilled under reduced pressure, the residue taken up in water, and the solution acidified. The oil formed was separated and the acid solution extracted with ether which removed 4 g. of unhydrolyzed starting material. The aqueous layer was then made alkaline, the oil extracted into ether, dried, and fractionated. Six grams (57%) of a pale yellow oil boiling at 110–114° (70 mm.) was collected.

The **monohydrochloride** formed readily on treatment of an acetone solution of the oil with ethereal hydrogen chloride. It was recrystallized from ethanol–ether and melted at 186–187°.

*Anal.* Calcd. for $C_{16}H_{20}N_2O \cdot HCl$: N, 9.57. Found: N, 9.73.

**1,1,1-Trichloro-2,2-bis-(*p*-phthalimidophenyl)-ethane.**—A suspension of 100 g. of phthalanil and 50 g. of chloral in 500 cc. of 100% sulfuric acid was allowed to stand at room temperature for three days with occasional shaking. The solid gradually disappeared leaving a clear yellow-brown solution. This was poured onto 2000 g. of crushed ice, and the colorless precipitate thus formed was filtered. It weighed 112 g. (87%). Recrystallization from ethanol yielded colorless crystals, m. p. 97–99°.

*Anal.* Calcd. for $C_{30}H_{17}Cl_3N_2O_4$: N, 4.87. Found: N, 4.76.

(4) Suggested by Dr. Randolph T. Major.

(5) Rousset, *Bull. soc. chim.*, [3] **11**, 321 (1892).

Hydrolysis of the phthalimido groups patterned upon the method of Kuhara and Fukui[6] using a barium hydroxide-barium chloride solution led to an alkali-soluble product which, however, resinified during its isolation.

Succinanil and chloral could not be condensed under the same conditions.

(6) Kuhara and Fukui, *Am. Chem. J.*, **26**, 454 (1901).

COBB CHEMICAL LABORATORY
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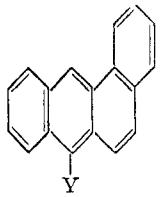
RECEIVED OCTOBER 1, 1946

## The Conjugation of Peptides with 1,2-Benzanthryl-10-isocyanate[1]

BY LARRY Q. GREEN AND HUGH J. CREECH

In connection with immunological studies[2] of hydrocarbon–protein conjugates,[3] it was found desirable to have as inhibitors some compounds with greater water solubilities than the amino acid conjugates[4] employed previously. It was thought that the use of di- and tripeptides or of dicarboxylic amino acids as components of the conjugates might solve this problem. Accordingly, 1,2-benzanthryl-10-isocyanate was coupled to glycylglycine, triglycine and glutamic acid in aqueous dioxane solution. As was the case with the glycine and ε-amino caproic acid conjugates prepared from this isocyanate, the new compounds were obtained only in an amorphous condition. Although the compounds were not isolated in an absolutely pure state because of their susceptibility to decomposition, they were suitable for the immunological tests.



I. Y = —NHCONHCH$_2$CONHCH$_2$COOH
II. Y = —NHCONHCH$_2$CONHCH$_2$CONHCH$_2$COOH
III. Y = —NHCONHCHCH$_2$CH$_2$COOH
|
COOH

### Experimental[5]

Glycylglycine, charring point 225°, was prepared by the hydrolysis of 2,5-diketopiperazine.[6] A solution of 375 mg. of this compound in 5 cc. of water adjusted to *p*H 9 with sodium hydroxide was added slowly with stirring to a solution of 500 mg. of 1,2-benzanthryl-10-isocyanate in 50 cc. of purified dioxane. After ten minutes at room temperature, 150 cc. of water was added to the light yellow suspension and the mixture was heated to 40° whereupon most of the precipitate went into solution. Normal

(1) Aided by a grant from the International Cancer Research Foundation. This article was prepared at the present address of one of us (H. J. C.), The Lankenau Hospital Research Institute and The Institute for Cancer Research, Philadelphia 30, Pa.

(2) Manuscripts in course of preparation; also, Creech and Franks, *Am. J. Cancer*, **30**, 555 (1937).

(3) Creech and Jones, THIS JOURNAL, **63**, 1661, 1670 (1941).

(4) Fieser and Creech, *ibid.*, **61**, 3502 (1939).

(5) Analyses by Miss E. Werble.

(6) Fischer, *Ber.*, **34**, 2868 (1901).

hydrochloric acid was added to the filtrate causing the formation at *p*H 3 of a gelatinous yellow precipitate which was washed twice with a liter of slightly acidified water. The precipitate was removed and dried in a vacuum desiccator; the slightly brown powder was ground and washed with ether.[7] The **1,2-benzanthryl-10-carbamidoacetoglycine** (I) thus obtained in 82% yield darkened at 210° and had not completely melted at 260°.

*Anal.* Calcd. for $C_{23}H_{19}O_4N_3$: C, 68.9; H, 4.78; N, 10.45. Found: C, 67.8; H, 4.88; N, 10.43.

Chloroacetylglycylglycine, prepared from 2,5-diketopiperazine and chloroacetyl chloride,[8] was treated with ammonium hydroxide to give triglycine[9] which turned yellow at 215° and melted with decomposition at 240°. This compound was conjugated with the isocyanate under conditions similar to those used above to form **1,2-benzanthryl-10-carbamidoacetoglycylglycine** (II) obtained in 68% yield as a slightly brown powder which darkened at 200° and decomposed at 250°.

*Anal.* Calcd. for $C_{25}H_{22}O_5N_4$: C, 65.6; H, 4.84. Found: C, 66.36, 66.15; H, 4.78, 4.81.

For the preparation of α-(1,2-benzanthryl-10-carbamido)-glutaric acid (III), 1(+)-glutamic acid was employed. The procedures of coupling and isolation were the same as those used before. The brown product, obtained in 44% yield, darkened slightly at 235°, softened at 247° and melted at 252–254° with decomposition.

*Anal.* Calcd. for $C_{24}H_{20}O_5N_2$: C, 69.2; H, 4.83; N, 6.74. Found: C, 68.92; H, 4.90; N, 6.46.

(7) Attempts to crystallize this compound from aqueous dioxane or from other solvents were not successful; usually such attempts led to serious decomposition.

(8) Fischer, *Ber.*, **39**, 2931 (1906).

(9) Fischer, *ibid.*, **37**, 2500 (1904).

DEPARTMENT OF CHEMISTRY
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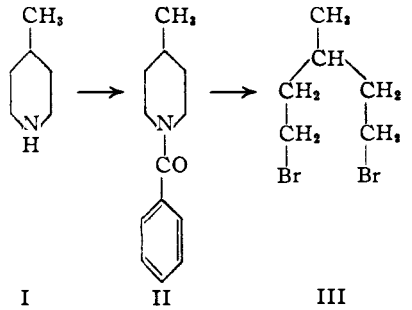
RECEIVED JULY 23, 1946

## 1,5-Dibromo-3-methylpentane

BY NELSON J. LEONARD AND ZENO W. WICKS[1]

1,5-Dibromo-3-methylpentane (III) has not been prepared previously. This compound is of interest as an intermediate in the synthesis of certain heterocycles,[2] and as a building unit for certain saturated isoprenoid molecules in which synthesis may be effected by combination of alternating symmetrical six- and four-carbon units rather than the customary unsymmetrical five- and five-carbon units.

4-Methylpiperidine (I) was converted to 1-benzoyl-4-methylpiperidine (II) by a Schotten–Baumann reaction with benzoyl chloride,[3] and this, in turn, by a von Braun reaction with phosphorus pentabromide, gave III.[4]



I II III

**1-Benzoyl-4-methylpiperidine** (II).—To a mixture of 340 g. of I (3.4 moles), 180 g. of sodium hydroxide (4.5 moles), and 1400 ml. of water, 476 g. of benzoyl chloride (3.4 moles) was added with stirring at 35–40° during one hour. The non-aqueous layer and the ether extracts of the aqueous layer were combined and evaporated to dryness. The solid residue was recrystallized from ethanol as colorless prisms; m. p. 83.5–84°; yield, 635 g. (92%).

*Anal.* Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.92; H, 8.26; N, 6.72.

**1,5-Dibromo-3-methylpentane** (III).—During cooling and stirring, 575 g. of phosphorus tribromide (2.15 moles) was added to 426.5 g. of II (2.10 moles), followed by 325 g. of bromine (2.13 moles). The reaction mixture was distilled under reduced pressure from 65 (30 mm.) to 112° (20 mm.), until a yellow solid collected in the condenser and extensive decomposition occurred in the distilling flask. The total distillate was poured onto ice, the mixture stirred for several hours and allowed to stand overnight. The oily layer was separated and boiled with 625 ml. of 40% hydrobromic acid solution under reflux for four hours. After steam distillation, the oily layer in the distillate was separated and washed twice with 10% sodium carbonate, once with water, dried over Drierite, then distilled *in vacuo*. The product boiled at 97–98.5° (10 mm.); yield, 333 g. (65%); $n^{20}D$ 1.5073; $d^{20}_4$ 1.607.

*Anal.* Calcd. for $C_6H_{12}Br_2$: C, 29.53; H, 4.96; Br, 65.51; $MR_D$, 45.44. Found: C, 29.68; H, 5.19; Br, 65.38; $MR_D$, 45.21.

(1) Present address: Interchemical Corporation, New York, N. Y.

(2) *Cf.* Prelog and Seiwerth, *Ber.*, **72**, 1638 (1939).

(3) "Organic Syntheses," Coll. Vol. I, 1941, p. 101; Adams and Leonard, THIS JOURNAL, **66**, 257 (1944).

(4) "Organic Syntheses," Coll. Vol. I, 1941, p. 428.

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
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RECEIVED JULY 26, 1946

## Osmotic and Activity Coefficients of Lithium Nitrate Solutions

BY R. A. ROBINSON

Vapor pressure measurements of lithium nitrate solutions have been made by the isopiestic method[1] at 25° up to a concentration of 3.8 *M*. The range has now been extended by further measurements in more concentrated solution. Lithium nitrate was prepared by double recrystallization from the salt obtained from a sample of lithium carbonate which had been purified by the method outlined by Caley and Elving.[2]

TABLE I

| $m_{LiNO_3}$ | $m_{NaCl}$ | $m_{LiNO_3}$ | $m_{NaCl}$ | $m_{LiNO_3}$ | $m_{NaCl}$ |
|---|---|---|---|---|---|
| 3.316 | 3.676 | 3.500 | 3.877 | 3.607 | 3.996 |
| 3.864 | 4.273 | 4.661 | 5.136 | 4.750 | 5.221 |
| 5.292 | 5.796 | 5.554 | 6.061 | 5.614 | 6.132 |
| $m_{LiNO_3}$ | $m_{H_2SO_4}$ | $m_{LiNO_3}$ | $m_{H_2SO_4}$ | $m_{LiNO_3}$ | $m_{H_2SO_4}$ |
| 5.456 | 4.246 | 6.925 | 5.161 | 8.682 | 6.202 |
| 9.522 | 6.691 | 10.33 | 7.124 | 11.22 | 7.635 |
| 11.78 | 7.909 | 11.94 | 8.012 | 12.29[a] | 8.161 |
| 13.36 | 8.757 | 13.72 | 8.966 | | |

[a] In equilibrium with saturated solution.

(1) R. A. Robinson, THIS JOURNAL, **57**, 1165 (1935).

(2) H. S. Booth, "Inorganic Syntheses," Vol. I, McGraw-Hill Book Co., Inc., New York, N. Y., 1939.

Solutions were equilibrated against sodium chloride or sulfuric acid solutions and the following pairs of solutions (Table I) were found to have equal vapor pressure at 25°.

Osmotic and activity coefficients were evaluated relative to the corresponding values for the reference electrolytes[3] with the following results (Table II).

TABLE II

| $m$ | $\varphi$ | $\gamma$ | $m$ | $\varphi$ | $\gamma$ |
|---|---|---|---|---|---|
| 0.1 | 0.938 | 0.788 | 4.0 | 1.270 | 1.125 |
| .2 | .935 | .752 | 5.0 | 1.352 | 1.310 |
| .3 | .940 | .736 | 6.0 | 1.426 | 1.515 |
| .5 | .954 | .726 | 7.0 | 1.490 | 1.734 |
| .7 | .970 | .729 | 8.0 | 1.544 | 1.960 |
| 1.0 | .997 | .743 | 9.0 | 1.593 | 2.202 |
| 1.5 | 1.043 | .783 | 10.0 | 1.637 | 2.455 |
| 2.0 | 1.088 | .835 | 11.0 | 1.674 | 2.711 |
| 2.5 | 1.134 | .896 | 12.0 | 1.704 | 2.967 |
| 3.0 | 1.181 | .966 | 13.0 | 1.735 | 3.242 |
| 3.5 | 1.227 | 1.044 | 13.5 | 1.754 | 3.398 |

The saturated solution contained 45.87% of lithium nitrate. Campbell[4] gives 46.0% as the solubility. The water activities corresponding to the above osmotic coefficients are higher by approximately 0.0020 over the range 2 to 9 $M$ than those measured by Pearce and Nelson,[5] the difference rising to 0.0080 at 12.87 $M$.

(3) S. Shankman and A. R. Gordon, THIS JOURNAL, **61**, 2370 (1939); P. Olynyk and A. R. Gordon, *ibid.*, **65**, 224 (1943); R. A. Robinson, *Trans. Roy. Soc., N. Z.*, **75**, 203 (1945); R. H. Stokes and B. J. Levien, THIS JOURNAL, **68**, 333 (1946).

(4) A. N. Campbell, THIS JOURNAL, **64**, 2680 (1942).

(5) J. N. Pearce and A. F. Nelson, *ibid.*, **54**, 3544 (1932).

CHEMISTRY DEPARTMENT
AUCKLAND UNIVERSITY COLLEGE
AUCKLAND, NEW ZEALAND RECEIVED AUGUST 2, 1946

## Ultraviolet Absorption Spectra of Mescaline Sulfate and β-Phenylethylamine Sulfate

BY KURT SALOMON AND ALBERT F. BINA

The following is a report on the results of a spectrographic study of the absorption spectra of mescaline sulfate (3,4,5-trimethoxy-β-phenylethylamine sulfate) and β-phenylethylamine sulfate.

Mescaline has specific pharmacological properties, such as production of color hallucinations in man, while β-phenylethylamine does not exhibit the aforementioned effects. It has been shown by various workers[1,2,3] that the introduction of methoxy groups in the phenylethylamine molecule greatly influences the metabolic fate of this compound by rendering it more resistant to oxidation. Further information about the interrelationship of methoxy groups and the physical and chemical properties of the molecule is therefore desirable.

Only a few experimental studies concerning the influence of methoxy groups on the ultraviolet absorption spectra of benzene and its derivatives have been reported. Hillmer and Schornig[4] have established the fact that introduction of methoxy groups into the benzene ring in presence or absence of various side chains produces simplification of the fine structure of the absorption curve as well as a shifting of the maxima toward the visible region. This shift was in the order of magnitude of ten to twenty millimicrons, depending on the number of methoxy groups introduced and the character of the side chain present. Furthermore, they state that the intensity of the absorption increases with the introduction of methoxy groups. Our results are in agreement with their findings.

(1) K. H. Slotta and J. Müller, *Z. physiol. Chem.* (Hoppe-Seyler's), **238**, 14 (1936).

(2) D. Richter, *Biochem. J.*, **31**, 2022 (1937).

(3) F. Bernheim and M. L. C. Bernheim, *J. Biol. Chem.*, **123**, 317 (1938).

### Experimental

The ultraviolet absorption spectra were measured with a Beckman Quartz Spectrophotometer. Measurements were made in 80% ethyl alcohol. Crystalline mescaline sulfate was used in these experiments; the melting point of this preparation was 181–184° (uncor.).[5] The β-phenylethylamine used was obtained from Eastman Kodak Company with the information that it has a boiling point from 89–90.5° at 15 mm. pressure. The measurements on this compound were made immediately after redistillation *in vacuo*. In order to produce β-phenylethylamine sulfate for measurements, 0.1 cc. of concentrated sulfuric acid was added to the β-phenylethylamine solution to be measured. The concentrations of mescaline sulfate used were in the range of 25 micrograms per ml. ($8 \times 10^{-5}$ molar) to 100 micrograms per ml. ($32 \times 10^{-5}$ molar). The concentrations of β-phenylethylamine sulfate were in the range of 400 micrograms per ml. ($36 \times 10^{-4}$ molar) to 800 micrograms per ml. ($72 \times 10^{-4}$ molar).

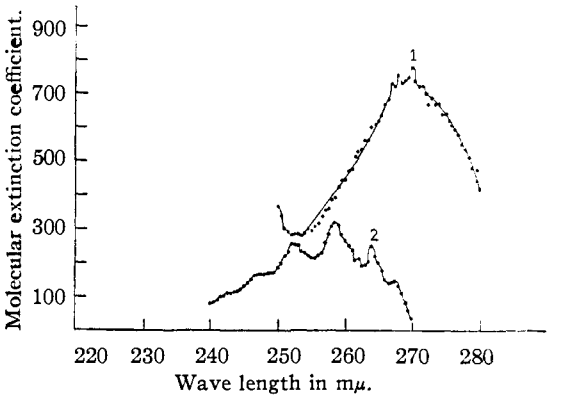


Fig. 1.—1, Mescaline sulfate in 80% ethyl alcohol; 2, β-phenylethylamine sulfate in 80% ethyl alcohol.

Preliminary experiments show that mescaline can be extracted from an alkaline water solution into isobutyl alcohol. The amount of mescaline can then be estimated by measuring the intensity of absorption at the absorption peak. The absorption spectrum of mescaline is identical in ethyl alcohol and in isobutanol.

(4) A. Hillmer and P. Schornig, *Z. physik. Chem.*, **A167**, 407 (1933).

(5) The mescaline sulfate was kindly furnished by Hoffmann-LaRoche, Inc., Nutley, New Jersey.

CONTRIBUTION FROM THE
BIOCHEMICAL LABORATORY OF THE
DEPARTMENTS OF NEUROPSYCHIATRY AND RADIOLOGY
WASHINGTON UNIVERSITY MEDICAL SCHOOL
ST. LOUIS, MO. RECEIVED APRIL 8, 1946

## Claisen Condensation by *t*-Butylmagnesium Chloride

BY H. D. ZOOK, W. J. MCALEER AND LEVONNA HORWIN

*t*-Butylmagnesium chloride reacts with esters of higher molecular weight acids to give 35–45% yields of symmetrical ketones. This reaction was first described by Petrov[1] as a new abnormal Grignard reaction occurring by the following scheme.

$$2RCOOC_2H_5 \longrightarrow RCOR + CO_2 + (C_2H_5)_2O$$

We have found that the ketones are not the initial products of the reaction but result from the hydrolysis of β-ketoesters formed by a Claisen type condensation of the ester by the basic Grignard reagent.

$$2RCH_2CO_2C_2H_5 \xrightarrow{(CH_3)_3CMgCl} RCH_2COCHRCO_2C_2H_5 \xrightarrow{H_2O} (RCH_2)_2CO$$

*i*-Propylmagnesium bromide and mesitylmagnesium bromide previously have been shown to effect Claisen condensations of certain esters.[2]

That the β-ketoester is the intermediate product is shown by the complete solubility of the reaction product in a small amount of ether. Mild hydrolysis gives a copious precipitation of the symmetrical ketone which is only sparingly soluble in ether. With lower esters the β-keto ester can be isolated by fractional distillation. Thus, *t*-butylmagnesium chloride and ethyl propionate give a 50% yield of ethyl propionylpropionate.

Contrary to Petrov,[3] it was found that the reaction of the Grignard reagent with the ester does not require temperatures of 110–120° but proceeds smoothly at room temperature with the evolution of isobutane and isobutene.

The symmetrical ketone is not the exclusive product of the reaction as claimed.[1] Yields from eight runs of *t*-butylmagnesium chloride on the methyl and ethyl esters of myristic and palmitic acids were all below 50%. Normal addition of the Grignard reagent to the ester to give the expected ketone, RCOR′, followed by reduction of this ketone to the secondary alcohol also occurs as a simultaneous reaction.[4] High vacuum distillation of the mother liquors from the crystallization of myristone in one experiment gave a 40% of *t*-butyltridecylcarbinol.

### Experimental

Grignard reagents were prepared at 15° from carefully fractionated *t*-butyl chloride in dry ether. The solutions were forced with nitrogen through fine glass wool filters and titrated in the usual manner.

**Condensation of Methyl Myristate.**—The usual apparatus for the Grignard reaction and an atmosphere of nitrogen were employed. A solution of 490 cc. (1.08 moles) of *t*-butylmagnesium chloride was added with stirring over a period of seven hours to 77 g. (0.32 mole) of the ester in 200 cc. of dry ether. Heat and gas were evolved at once. The flask was cooled in a water-bath to prevent refluxing. Stirring was continued overnight and finally the water bath heated to 40° to drive out the remainder of the gases. The total gases from the reaction were shown by distillation and absorption methods to consist of 0.09 mole of isobutene and 0.17 mole of isobutane. The reaction mixture was hydrolyzed with excess dilute hydrochloric acid and the organic layer concentrated to an oil by removal of most of the ether. Cooling the ether solution at several concentrations failed to give a precipitate.

The oil was dissolved in 400 cc. of ethanol and refluxed overnight with 200 cc. of 10% sodium hydroxide. Most of the ethanol was removed under vacuum and the residue diluted with 500 cc. of water and extracted with 500 cc. of ether. Much white solid was present at the interface. The ether layer and solid were washed well with water and filtered to give 22 g. (35%) of myristone, melting point and mixed melting point with an authentic sample 77–78°; oxime, m. p. and mixed m. p. 50–51°. Concentration of the mother liquor gave a 5.5 g. (9%) second crop, m. p. 75–77°. Further concentration gave 44 g. of oil which would not solidify at 0°. Acidification of the alkaline layer gave 6 g. (8%) of myristic acid, m. p. 53–55° after one crystallization from ethanol.

High vacuum distillation of the non-crystallizable oil gave six fractions totaling 37 g. (40%) of *t*-butyltridecylcarbinol, b. p. 87–90° at $10^{-4}$ mm., $n^{20}D$ 1.4490–1.4491, m. p. 12–14°. The alcohol was dehydrated by passing the vapors at 1 mm. through a 1.7 × 50 cm. column packed with alumina and heated to 280–300°. The olefin distilled at 60–67° at $10^{-4}$ mm., $n^{20}D$ 1.4465–1.4478. Titration with bromine by the Francis method[5] gave a mol. wt. of 255 (calcd. for $C_{18}H_{36}$: mol. wt., 252). Oxidation of 16.5 g. of the olefin by the procedure of Armstrong and Hilditch[6] using 40 g. of potassium permanganate in saturated acetone solution gave 1.5 g. (21%) of trimethylacetic acid, b. p. 95–98° at 60 mm., 155–160° at 740 mm.; neutral equivalent, 105; calcd. for $C_5H_{10}O_2$, 104; anilide, m. p. and mixed m. p. 129–130°; S-benzylthiouronium salt, m. p. and mixed m. p. 145–146°. Also obtained was 4.9 g. (35%) of *n*-tridecanoic acid, b. p. 118° at 0.5 mm., m. p. 38–40°[7]; neutral equivalent, 211; calcd. for $C_{13}H_{25}O_2$, 214; *p*-phenylphenacyl ester, m. p. 84–85°.[8]

**Condensation of Ethyl Propionate.**—To 102 g. (1 mole) of the ester dissolved in 100 cc. of dry ether was added 770 cc. (1.7 moles) of *t*-butylmagnesium chloride solution. The mixture was cooled in a water bath to prevent refluxing, stirred until solid and allowed to stand for five days. Hydrolysis with excess dilute hydrochloric acid and careful fractionation of the organic layer through a 10-plate column gave 23 g. (20%) of ethyl-*t*-butylcarbinol, b. p. 44–45° at 15 mm., $n^{20}D$ 1.4215–1.4218; α-naphthylurethan, m. p. 109–110°[9] and 39 g. (50%) ethyl propionylpropionate, b. p. 62–63° at 5 mm., $n^{20}D$ 1.4230–1.4232. The ketoester gave a deep blue color with dilute ferric chloride solution. Identification was made by hydrolysis of 5 g. of the ketoester by warming one hour on the steam-bath with 60 cc. of 5% potassium hydroxide solution. Obtained was 1.7 g. of diethyl ketone, b. p. 101° at 740 mm.; 2,4-dinitrophenylhydrazone, m. p. 154–155°; mixed m. p. with an authentic sample 155–156°.

DEPARTMENT OF CHEMISTRY
PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PA.

RECEIVED JULY 24, 1946

(1) A. D. Petrov, *Sci. Records Gorky State Univ.*, **7**, 3 (1939); *C. A.*, **35**, 435 (1941).

(2) Conant and Blatt, THIS JOURNAL, **51**, 1227 (1929); Spielman and Schmidt, *ibid.*, **59**, 2009 (1937); Hauser and Hudson's chapter in "Organic Reactions," Vol. I, John Wiley and Sons, New York, N. Y., 1942, p. 277.

(3) Petrov, Karasev and Cheltzova, *Bull. soc. chim.*, [5] **3**, 169 (1936).

(4) *Cf.* Whitmore and Forster, THIS JOURNAL, **64**, 2966 (1942).

(5) Francis, *Ind. Eng. Chem.*, **18**, 821 (1926).

(6) Armstrong and Hilditch, *J. Soc. Chem. Ind.*, **44**, 43T (1925).

(7) Pool and Ralston, *Ind. Eng. Chem.*, **34**, 1104 (1942).

(8) Price and Griffith, THIS JOURNAL, **62**, 2884 (1940).

(9) Whitmore, Meyer, Pedlow and Popkin, *ibid.*, **60**, 2788 (1938).