tion in an aqueous 7.4% borax solution is given as $[\alpha]_D$ 28.3°[7] and $[\alpha]^{26}_D$ 28.5°.[5]

The acetyl derivative prepared by heating with acetic anhydride and sodium acetate had m. p. 123–123.5° (cor.) and $[\alpha]^{25}_D$ 21.53° (*c*, 1.97) in chloroform. The hexaacetate of *d*-mannitol has been reported to have m. p. 122° $[\alpha]^{20}_D$ 24.4° in chloroform[8] and m. p. 123.5–124.5°, $[\alpha]^{27}_D$ 21.3° in chloroform.[5] A mixed m. p. with an authentic sample of mannitol hexaacetate gave no depression.

To determine in which part of the seed the mannitol was present, 680 g. of the whole seeds was separated into shells and kernels and each extracted as above. Mannitol could be isolated only from the shells.

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[7] E. Fischer, *Ber.*, **23**, 385 (1890).

[8] E. Pacsu and F. V. Rich, THIS JOURNAL, **55**, 2023 (1933).

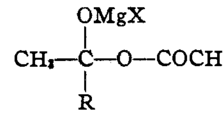
SCHOOL OF PHARMACY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN
RECEIVED NOVEMBER 13, 1944

The Preparation of Ketones from Grignard Reagents

BY MELVIN S. NEWMAN AND WILLIAM T. BOOTH, JR.

We have found that excellent yields of methyl ketones may be obtained by the addition of Grignard reagents to an ether solution of acetic anhydride at about −70°. Primary, secondary, tertiary aliphatic, and aromatic Grignard reagents give 70–79% yields of the corresponding methyl ketones while the allyl and benzyl reagents give 42 and 52%, respectively.[1]

We attribute the success of these reactions at low temperature to the thermal stability of the complex, I, formed by the addition of one molecule



$$CH_3-\overset{\displaystyle OMgX}{\underset{\displaystyle R}{\overset{|}{\underset{|}{C}}}}-O-COCH_3$$

I

of Grignard reagent to one of the carbonyl groups of acetic anhydride, and to its decreased solubility. These factors both tend to reduce the further reaction of I with more Grignard reagent to form tertiary alcohol. At the low temperature involved there is probably no cleavage of this complex to form ketone which might further react.

The success of the above reactions led to the hope that good yields of ketones may be obtained also from acid chlorides and esters in a similar manner. These possibilities are being examined as well as the effect of low temperatures on other preferential Grignard reactions.

Experimental

In a typical experiment, 0.2 mole of a titrated Grignard reagent was added slowly during one hour to a stirred solution of 40 g. of acetic anhydride in 100 cc. of dry ether in a 500-cc. 3-necked flask cooled by a mixture of Dry Ice and acetone in a Dewar flask. The added reagent was cooled by dripping through a tube externally cooled with Dry Ice. After stirring for two to three hours the cooling bath was removed and the mixture was treated with ammonium chloride solution. After washing out the acetic anhydride and acid with alkali the ether was fractionated and the ketones distilled. For the most part the ketones were identified by boiling point and index of refraction, although a few derivatives were made. The following Grignard reagents gave the corresponding methyl ketones in the following yields: *n*-butylmagnesium chloride, 79%; *n*-butylmagnesium bromide, 79%; *s*-butylmagnesium bromide, 78%; *t*-butylmagnesium chloride; 77%; phenylmagnesium bromide, 70%; benzylmagnesium chloride, 52%; and allylmagnesium bromide, 42%. With phenylmagnesium bromide and propionic anhydride a 59% yield of propiophenone was obtained.

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[1] Fournier, *Bull. soc. chim.*, (3) **31**, 483 (1904); (3) **35**, 19 (1906); (4) **7**, 836 (1910), treated a series of primary halide Grignard reagents with a series of anhydrides at about −20° and reported general yields in the range 25–50%. We have found that on adding butylmagnesium bromide to acetic anhydride at −33° the yield of somewhat impure ketone is less than 40%.

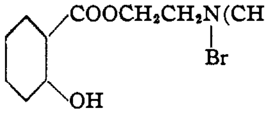
DEPARTMENT OF CHEMISTRY
OHIO STATE UNIVERSITY
COLUMBUS 10, OHIO
RECEIVED SEPTEMBER 20, 1944

Some New Esters of Choline

BY M. WEIZMANN AND E. BOGRACHOV

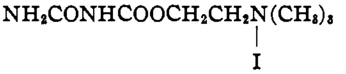
For a pharmacological and physiological study[1] esters of choline were required which were expected to be less easily saponified under biological conditions than acetyl-choline. To this end the derivatives of salicylic acid and of allophanic acid have been synthesized.

As the quaternary ammonium chlorides corresponding to acetyl-choline proved too hygroscopic, the bromides and iodides have been prepared. Salicyloyl chloride reacts with the hydroxyl group of trimethyl-(β-hydroxyethyl)-ammonium bromide and iodide in the normal way, and from the ester-bromide so obtained



the sulfate is prepared by interaction with silver sulfate.

For the preparation of the allophanic acid ester β-iodo-ethyl allophanate was prepared from ethylene iodohydrin and cyanic acid according to Béhal.[2] The halogenated ester was then treated with trimethylamine



$$NH_2CONHCOOCH_2CH_2\underset{\displaystyle I}{\underset{|}{N}}(CH_3)_3$$

Experimental

(1) Trimethyl-(β-hydroxy-ethyl)-ammonium Bromide (I).—Trimethylamine (75 g.) is added to a concentrated aqueous solution of ethylene bromohydrin (125 g.) at ice temperature. The mixture is kept overnight at below 5°, evaporated to dryness *in vacuo* and the residue recrystallized from alcohol; yield, 172 g. *Anal.* Calcd. for $C_5H_{14}ONBr$: C, 32.6; H, 7.6; N, 7.6. Found: C, 32.6; H, 7.6; N, 7.5.

The iodide (II) was prepared and recrystallized in the same way; yield, 94%. *Anal.* Calcd. for $C_5H_{14}ONI$: N, 6.1; I, 55.0. Found: N, 6.1; I, 54.9.

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[1] A. Schweitzer, M. Weizmann and S. Wright, *Cardiologia*, Vol. II, fasc. 4/5, 1938.

[2] Béhal, *Bull. soc. chim.*, [4] **25**, 477 (1919).

(2) **The Methobromide of β-Dimethylaminoethyl Salicylate.**—The bromide I (36.8 g.), salicyloyl chloride (45 g., large excess) and dried benzene (75 g.) are heated on the water-bath until the evolution of gaseous hydrochloric acid ceases. The benzene is decanted, replaced by anhydrous acetone and the mixture boiled for one hour. This procedure is repeated and the solid phase subsequently recrystallized from alcohol as white prisms, m. p. 176°, readily soluble in water, difficultly in alcohol; yield, 80%. *Anal.* Calcd. for $C_{12}H_{13}O_3NBr$: Br, 26.3. Found: Br, 26.4.

The corresponding iodide, prepared analogously from II, forms, after recrystallization from alcohol, white needles, m. p. 147–148°; yield, 88%. *Anal.* Calcd. for $C_{12}H_{18}O_3NI$: N, 4.0; I, 36.2. Found: N, 3.9; I, 36.0.

(3) **The Methosulfate of β-Dimethylaminoethyl Salicylate.**—To a solution of the methobromide (61 g.) in water (300 cc.), silver sulfate (35 g.) was added and the mixture shaken for four hours. Upon evaporation *in vacuo*, microscopic needles of m. p. 300° were obtained. *Anal.* Calcd. for $C_{24}H_{36}O_{10}N_2S$: N, 5.1; SO_4, 17.6. Found: N, 5.1; SO_4, 17.6.

(4) **β-Iodo-ethyl Allophanate.**—Cyanuric acid (35 g.) is heated in a current of dry carbon dioxide and the gaseous cyanic acid formed absorbed at 0° in ethylene iodohydrin (255 g.). During this operation, which requires approximately one hour, a voluminous precipitate is formed which is collected and recrystallized from alcohol or boiling water: needles, m. p. 182°; yield, 60%. *Anal.* Calcd. for $C_4H_7O_3N_2I$: N, 10.8; I, 49.0. Found: N, 10.8; I, 49.5.

(5) **The Methiodide of β-Dimethylaminoethyl Allophanate.**—A suspension of the preceding substance (5 g.) in water (60 cc.) is saturated with gaseous trimethylamine at room temperature. The mixture is heated for ten hours at 100° in a sealed tube, filtered from traces of solid material and evaporated to dryness *in vacuo*. By recrystallization from alcohol, the residue is obtained in form of needles, m. p. 254–255° (dec.); yield, 4 g. *Anal.* Calcd. for $C_7H_{16}O_3N_3I$: N, 13.3; I, 40.1. Found: N, 13.2; I, 40.0.

LABORATORY OF ORGANIC CHEMISTRY
HEBREW UNIVERSITY
JERUSALEM, PALESTINE

RECEIVED JULY 31, 1944

NEW COMPOUNDS

Thiomesitaldehyde

Because of the excessive crowding about the functional group there was some question as to whether mesitaldehyde could be converted to thiomesitaldehyde by the general method for transforming aromatic aldehydes to their sulfur analogs. Moreover, it was of interest to determine whether thiomesitaldehyde, once formed, would exist in the monomeric or the trimeric form.

A solution of 24 g. of mesitaldehyde in 250 ml. of absolute ethanol was saturated with dry hydrogen chloride. Hydrogen chloride and hydrogen sulfide were then passed into the solution for two hours at 0–5°. The white powder, produced in this way, was isolated and recrystallized from nitromethane; m. p. 184–185°; yield 8.5 g. Recrystallization from glacial acetic acid yielded a pure sample of thiomesitaldehyde in the form of beautiful white crystals; m. p. 186–187°.

Anal. Calcd. for $C_{30}H_{36}S_3$: C, 73.13; H, 7.37; mol. wt., 492. Found: C, 73.51; H, 7.38; mol. wt. (ebullioscopic in chloroform), 483.

Thiomesitaldehyde not only exists as a trimer but behaves normally in other respects. For example, heating with copper–bronze by the method of Klinger[1] converts it to 1,2-dimesitylethylene. An intimate mixture of 1.64 g. of the thioaldehyde and 1.4 g. of copper–bronze powder was heated for thirty minutes in an oil-bath at 220–230°. The crude stilbene, obtained by extracting the resulting mass with high-boiling petroleum ether, was purified by recrystallization from aqueous acetic acid and then from ethanol; m. p. 125–128°; yield 0.55 g. Repeated recrystallization from ethanol and the use of Norite gave pure 1,2-dimesitylethylene; m. p. 131–132°.[2]

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[1] Klinger, *Ber.*, **9**, 1893 (1876); see also Wood, Bacon and Meibohm, THIS JOURNAL, **63**, 1334 (1941).

[2] Fuson, Denton and Best, *J. Org. Chem.*, **8**, 64 (1943).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS
REYNOLD C. FUSON
CHRIS E. BEST

RECEIVED OCTOBER 2, 1944

1,1-Di-(*p*-chlorophenyl)-1,2,2,2-tetrachloroethane

1,1-Di-(*x*-chlorophenyl)-2,2,2-trichloroethane prepared from chlorobenzene and chloral according to Zeidler[1] was dehydrochlorinated by refluxing for ten hours a solution of 15 g. (0.042 mole) in 400 cc. of absolute ethanol containing 8.0 g. (0.14 mole) of potassium hydroxide. About half of the alcohol was removed by distillation and the residue poured into 600 cc. of cold water, the crystalline precipitate was collected by suction filtration, washed with water until free of hydroxide and chloride ions, dried in air and crystallized from about 75 cc. absolute ethanol; yield, 11 g., 81% of the theoretical, melting 86–87°.

Anal. Calcd. for $C_{14}H_8Cl_4$: Cl, 44.61. Found: Cl, 44.64, 44.64.

This product corresponds to the 1,1-di-(*x*-chlorophenyl)-2,2-dichloroethylene obtained by a similar procedure by Zeidler.[1] The structure of this compound was established by oxidizing 1.0 g. in a mixture of 5 g. of chromic acid and 30 cc. of glacial acetic by refluxing for four hours. This solution was poured into 200 cc. of cold water, suction filtered and the solid washed with water, dried in air and crystallized from absolute ethanol; 0.8 g. of *p,p'*-dichlorobenzophenone, m. p. 143–144°, mixed melting point with an authentic sample, 143–144°, was obtained. This product proves the structure of the ethylene derivative to be 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene which in turn establishes Zeidler's 1,1-di-(*x*-chlorophenyl)-2,2,2-trichloroethane as 1,1-di-(*p*-chlorophenyl)-2,2,2-trichloroethane (DDT). Several attempts to oxidize the latter with chromic acid in acetic acid to *p,p'*-dichlorobenzophenone gave no identifiable products.

1,1-Di-(*p*-chlorophenyl)-1,2,2,2-tetrachloroethane is readily made either by chlorination of the trichloroethane compound or the dichloroethylene derivative. Ten grams (0.028 mole) of 1,1-di-(*p*-chlorophenyl)-2,2,2-trichloroethane (m. p. 105–106°) in 65 cc. of carbon tetrachloride containing 0.5 g. phosphorus trichloride was placed in a cylindrical flask 1.5" o.d. and 7.5" high. A 45° side-arm near the top was attached to a reflux condenser. Chlorine gas was passed vigorously for three hours through a sintered-glass gas bubbler with an outlet 1" in diameter placed near the bottom of the flask while the solution was refluxed gently. To accelerate the chlorination a 150-watt bulb was located about 8" from the flask. On evaporation of the solution with vacuum a semi-solid residue of 16 g. remained. This was crystallized from 100 cc. of absolute ethanol and 0.2 g. of Norit. The crude product was twice recrystallized with 60 and 50 cc. portions of absolute alcohol to yield 8 g. of colorless crystals, resembling granulated sugar in appearance, m. p. 91–92°; yield 73%.

Anal. Calcd. for $C_{14}H_8Cl_6$: Cl, 54.76. Found: Cl, 54.38, 54.46.

Two grams (0.006 mole) of 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene in 20 cc. of chloroform was chlorinated in the same way as before but without radiation. Additional solvent was added to replace that evaporated. Evaporation of the solution with vacuum and two crystallizations

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[1] Zeidler, *Ber.*, **7**, 1181 (1874).