alcohol, the solution is filtered free from inorganic material, and subjected to complete distillation under reduced pressure at 40°. The residue is fractionated. The fraction boiling between 135–160° at 2–5 mm. consists chiefly of the hydroxy-lactone. It weighs 14 g. (35%). Fractionation at reduced pressure yields the pure lactone which boils at 145–148° at 2–4 mm.

Preparation of Isocrotonolactone.—Seventy-one grams of phosphorus pentoxide is added, 10 to 20 g. at a time, to a solution of fifty grams of β-hydroxybutyrolactone in 200 cc. of dioxane. The mixture is allowed to stand for an hour (in one experiment the mixture stood overnight without ill effect). The dioxane solution is then decanted into a Claissen flask. The residue is extracted twice with absolute alcohol, the alcohol extracts being added to the dioxane solution. The solvent is removed under reduced pressure (10–15 mm. with water-bath at 70–80°), and the residue is distilled at 7 mm. The boiling range of 22 g. of material obtained in this way was 80–86° (53%).

Anal. Calcd. for $C_4H_4O_2$: H, 4.78; C, 57.1. Found: H, 5.16; C, 57.05.

The lactone was then transformed into DL-erythronic lactone by the procedure of Braun. From 78 g. of the unsaturated lactone of boiling range 82–86° at 7 mm. there was obtained 49 g. of crude DL-erythronic lactone, m. p. 88–90°; a yield of 45%.

Summary

1. New procedures which shorten the time of preparation and increase yields have been devised for the preparation of the following compounds: ethyl γ-bromo-crotonate, ethyl γ-chlorocrotonate, γ-bromo-crotononitrile, β-hydroxy-butyrolactone, and isocrotonolactone.

2. Braun's synthesis of DL-threonic acid has been greatly modified. The over-all yield by the new procedure is 5.3% (calculated from allyl alcohol) as against 2.2% (calculated from glycerol dichlorohydrin) by Braun's procedure.

3. The preparation of β-hydroxy-butyrolactone and isocrotonolactone from vinylacetic acid as reported in this article is a much more dependable process than the procedure in which these substances are made from glycerol monochlorohydrin.

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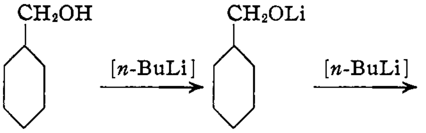
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

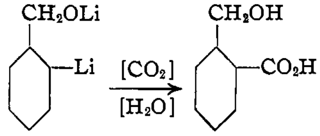
Metalation of Alcohols and Amines

BY HENRY GILMAN, G. E. BROWN, F. J. WEBB AND S. M. SPATZ

Halogen-metal interconversion reactions have been noted in a great variety of reactions, and are of particular interest with polyfunctional compounds.[1] Hydrogen-metal interconversion reactions or metalations are also very common, but because they generally take place at a somewhat slower rate than halogen-metal interconversion reactions there is a greater opportunity for secondary reactions with polyfunctional compounds.

We are now reporting preliminary observations on the metalation of some selected simple alcohols and amines, and will report later on polyfunctional compounds having alcohol and amino groups. Metalation takes place with all the chief types of aromatic alcohols and amines: primary, secondary and tertiary. An illustration is the metalation of benzyl alcohol.





In accordance with the general rules postulated for interconversions with organometallic compounds,[1] metalation occurs *ortho* to the group containing the hetero element. The only exception now known is the metalation of dibenzothiophene by phenylcalcium iodide, where metalation takes place in the 3- and not in the 4-position.[2,3]

Poly-metalation is to be expected with the more reactive organometallic compounds, and was observed earlier in the dibenzofuran series.[4] It may be stated that, in general, halogen-metal interconversions, hydrogen-metal interconversions as well as the numerous other interconver-

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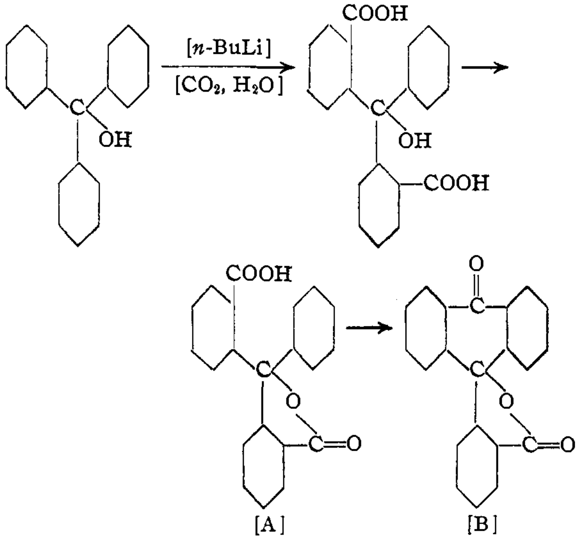
(1) Gilman, "Metalation and Related Interconversion Reactions," Eighth National Organic Chemistry Symposium, St. Louis, Dec. 30, 1939. See also recent papers in THIS JOURNAL on interconversion reactions with organometallic compounds.

(2) Gilman, Jacoby and Pacevitz, *J. Org. Chem.*, **3**, 120 (1938).

(3) Under generally drastic conditions of high temperature and pressure, Houben and co-workers [*Ber.*, **37**, 3978 (1904); **42**, 3729, 4488, 4815 (1909); **46**, 3833 (1913)] have obtained predominantly *para*-amino acids by interaction of carbon dioxide with the complexes derived from various secondary and tertiary amines with Grignard reagents. Under corresponding conditions they did not isolate acidic material from primary aromatic amines.

(4) Gilman and Young, THIS JOURNAL, **56**, 1415 (1934); **57**, 1121 (1935).

sions involving organometallic compounds can be correlated with the relative reactivities of organometallic compounds.[5] A case of dimetalation is reported now with triphenylcarbinol.



The acid isolated was the lactone of triphenylcarbinol-2,2′-dicarboxylic acid [A], which was characterized by dehydration to the oxanthrone [B]. It is of interest that this dimetalation took place with a quantity of *n*-butyllithium sufficient to react with but one of the three phenyl groups in triphenylcarbinol.

Metalation is probably one of the oldest reactions in organic chemistry. Davy[6] in 1837, incidental to attempts to obtain improved yields of his newly discovered potassium, fused potassium tartrate with carbon and obtained a highly reactive substance which yielded acetylene when treated with water. It is quite likely that an ethynylpotassium was formed as an intermediate. The halogen-metal interconversion reaction is also quite old, and an early reference is the work of Kalle on the reaction between benzenesulfonyl chloride and diethylzinc to yield zinc benzenesulfinate and ethyl chloride.[7]

Experimental Part

Benzyl Alcohol.—A solution of 10.8 g. (0.1 mole) of benzyl alcohol was added dropwise to a cold, stirred solution of approximately 0.2 mole of *n*-butyllithium in 400 cc. of ether. After refluxing for forty-two hours, the mixture was carbonated by pouring jet-wise on crushed carbon dioxide; acidified with iced dilute hydrochloric acid; and extracted with ether. Extraction of the ether layer with sodium bicarbonate solution, followed by acidification, yielded 1.5 g. of a yellow solid melting in the range 65–115°. This was evidently a mixture of phthalide[8] and *o*-carboxybenzyl alcohol[8] since heating with sodium hydroxide solution and then acidification gave 1.3 g. of *o*-carboxybenzyl alcohol, m. p. 120.5–121.5°, in a yield of 8.7%, or 21.5% based on the benzyl alcohol which had reacted.

Anal. Calcd. for $C_8H_8O_3$: neut. equiv., 152. Found: neut. equiv., 150.4.

On resolidification, the compound melted at 73–74°, showing the conversion to phthalide. Oxidation with alkaline permanganate gave phthalic acid which was identified by comparison with an authentic specimen.

From the neutral fraction there was recovered 6.5 g. or 60% of benzyl alcohol.

Benzyl Methyl Ether.—An orienting experiment showed that ethers of alcohols can also be metalated. A diethyl ether solution of 0.1 mole *n*-butyllithium and 12.2 g. (0.1 mole) of benzyl methyl ether was refluxed for twenty hours, then carbonated and worked up in a customary manner. The acid obtained, probably *o*-carboxybenzyl methyl ether, melted at 94–95° after recrystallization from petroleum ether (b. p., 60–68°).

Anal. Calcd. for $C_9H_{10}O_3$: neut. equiv., 166. Found: neut. equiv., 166.

Benzohydrol.—The usual initial vigorous reaction (due to replacement of active hydrogen by lithium) took place when 0.1 mole of *n*-butyllithium was filtered into an ether solution of 9.2 g. (0.05 mole) of benzohydrol. Ether was added to bring the total volume to 250 cc. The solution gradually turned brownish-red and after several hours became deep red. After refluxing for forty-six hours carbonation was effected by solid carbon dioxide. The yield of 2-phenylphthalide[9] (formed by lactonization of the *o*-carboxybenzohydrol) was 1.95 g. or 18.6%. This product melted at 114.5°, and was oxidized by alkaline potassium permanganate to *o*-benzoylbenzoic acid[9] (m. p., 126.5°).

Triphenylcarbinol.—The suspension resulting from mixing 13 g. (0.05 mole) of triphenylcarbinol with slightly more than 0.1 mole of *n*-butyllithium was stirred, and refluxed for forty-eight hours prior to carbonation. The alkaline extract of the hydrolyzate yielded 1.2 g. of a product melting at 187–215°. Recrystallizations from acetic acid raised the melting point to 240°.

Inasmuch as a first experiment with triphenylcarbinol gave no acid, the reaction was repeated using 0.5 g. of copper bronze as a catalyst. It was shown earlier that various catalysts can be used to retard and accelerate organometallic reactions.[10] The catalyst not only improved the yield (to 2.3 g.), but also gave a purer acid. It is now known that the interconversion reactions are affected not only by catalysts, but also by solvents, concentration of reactants, time and temperature. Apropos the first negative experiment with triphenylcarbinol, it should be recalled that the formation of organolithium

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(5) See pp. 435–439 in Gilman, "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938.

(6) Davy, *Ann.*, **23**, 144 (1837).

(7) Kalle, *ibid.*, **119**, 153 (1861).

(8) Hessert, *Ber.*, **10**, 1445 (1877).

(9) Rotering and Zincke, *ibid.*, **9**, 631 (1876).

(10) Gilman, St. John, St. John and Lichtenwalter, *Rec. trav. chim.*, **55**, 577 (1936).

compounds is a little more erratic[11] than that of the corresponding Grignard reagents, and that one advantage to the use of carbonation in these preliminary studies is to get the extra check afforded by the odor of *n*-valeric acid formed by carbonation of the slight excess of *n*-butyllithium.

The acid melting at 240° was shown to be the lactone of triphenylcarbinol-2,2′-dicarboxylic acid,[12] and was characterized by conversion to 9-phenyl-9-hydroxanthr-10-one-2′-carboxylic acid lactone[12] melting at 234°. The yield of pure lactone-acid was 0.8 g. or 4.85%; or 52.5% if allowance be made for the recovery of 11.8 g. of triphenylcarbinol.

Aniline.—A mixture of 4.6 g. (0.05 mole) of aniline and slightly more than 0.15 mole of *n*-butyllithium was refluxed for fifty hours and then carbonated to yield 4.2% of anthranilic acid. Characterization was completed by diazotization and coupling with β-naphthol to the red 1-(*o*-carboxyphenylazo)-2-naphthol melting at 271°, using the method of mixed melting points with an authentic specimen.[13] There was recovered 2.9 g. of aniline, and the yield of anthranilic acid on the basis of aniline not recovered is 13.7%.

The larger than usual excess of *n*-butyllithium was used here to take care, if necessary, of the two active hydrogens attached to the nitrogen. It is quite likely that experiments now in progress will reveal the possibility of first replacing such hydrogens by metals other than lithium or by the use of organometallic compounds other than those of lithium.

Diphenylamine.—An ether solution of 13.5 g. (0.08 mole) of diphenylamine and 0.16 mole of *n*-butyllithium was stirred and refluxed for eighteen hours. Carbonation, followed by hydrolysis, yielded 1.85 g. or 10.9% of N-phenylanthranilic[14] acid melting at 182°. Recrystallization from a hot methanol–water mixture gave 1.45 g. or an 8.5% yield of the pure compound melting at 183.5°. The yield of N-phenylanthranilic acid based on the quantity of diphenylamine actually reacting was 30.3%.

In a second experiment the yield was somewhat improved by a longer period of refluxing. When the reactants were refluxed for twenty-four hours, the yield was 14.7%, or 38.2% based on the diphenylamine actually reacting.

N-*n*-Butylaniline.—Fifteen grams (0.1 mole) of freshly distilled N-*n*-butylaniline was heated for twenty hours with a slight excess over two equivalents of *n*-butyllithium in 275 cc. of ether. Subsequent to carbonation and hydrolysis, there was isolated a 2% yield of N-*n*-butylanthranilic acid.

N-*n*-Butylanthranilic Acid.—A solution prepared from 10 g. (0.073 mole) of anthranilic acid and 5 g. of potassium carbonate was refluxed for sixteen hours with 10 g. (0.073 mole) of *n*-butyl bromide. After cooling, the precipitate was dissolved in potassium hydroxide, and the oily material extracted with benzene. Neutralization of the alkaline layer precipitated the N-*n*-butylanthranilic acid which after crystallization from dilute methanol melted at 80–81° and weighed 6.4 g.

Anal. Calcd. for $C_{11}H_{15}O_2N$: N, 7.25. Found: N, 7.36.

A mixed melting point with the acid isolated from the metalation of N-*n*-butylaniline showed no depression.

Triphenylamine.—A reaction mixture of 12.25 g. (0.05 mole) of triphenylamine, 0.1 mole of *n*-butyllithium and 0.5 g. of copper bronze was stirred and refluxed for forty-five hours prior to carbonation. The yield of acidic material was 2.16 g. In addition, 9.6 g. or 78.5% of the triphenylamine was recovered. The mixture of acids has not as yet been resolved.

Piperidine.—An ether solution of 17 g. (0.2 mole) of piperidine and 0.42 mole of *n*-butyllithium was refluxed for twenty hours. On working up by customary procedures, subsequent to carbonation, there was obtained 21.6 g. or an 89% yield of piperidine hydrochloride in addition to a small quantity of an as yet unidentified oil. It is quite likely that more reactive organometallic compounds can effect such secondary reactions on piperidine as dehydrogenation[15] and cleavage.

Acknowledgment.—The authors are grateful to F. W. Moore and W. Harber for assistance.

Summary

It is shown that *n*-butyllithium metalates some typical primary, secondary and tertiary aromatic amines and some typical primary, secondary and tertiary aromatic alcohols.

AMES, IOWA

RECEIVED JANUARY 29, 1940

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[11] Gilman, Zoellner and Selby, THIS JOURNAL, **55**, 1252 (1933).

[12] Scholl and Donat, *Ann.*, **512**, 24 (1934); Cook, *J. Chem. Soc.*, 65 (1928).

[13] Anschütz and Schmidt, *Ber.*, **35**, 3469 (1902).

[14] N-Phenylanthranilic acid was characterized by conversion to N,N-diphenylanthranilic acid in accordance with the directions of Goldberg and Nimerovsky, *ibid.*, **40**, 2448 (1907).

[15] Gilman and Bradley, THIS JOURNAL, **60**, 2333 (1938).