Tyson's procedure was modified in that a temperature of 325° rather than of 350–360° was found sufficient. The yield of crude 1-methylindole obtained from the reaction of methyl iodide with the potassium salt of indole was 77% of the theoretical. The products from several runs for each indole were combined, refluxed with Raney nickel and then distilled. Since 3,3-dimethylpseudoindole trimerizes, even at room temperature, it was prepared and hydrogenated immediately. The trimer, m. p. 217–222°, was also hydrogenated and found to give the same product as the monomer. The crude 2,3-dimethylindole was purified by shaking it with Raney nickel in dioxane for five hours at room temperature under 415 p.s.i. of hydrogen. The final yield (22.6 g.) of pure 2,3-dimethylindole, b. p. 164–167° (20 mm.), m. p. 106–107°, was 61% of the theoretical.

The indolines were obtained by fractionation, through a Fenske column, of the reaction mixtures from hydrogenation. Indoline distilled at 119° (24 mm.), n^{25}_{D} 1.5883, and had a neut. equiv. of 119 (calcd. 119). 1-Methylindoline distilled at 82–83° (6 mm.), n^{25}_{D} 1.5670, picrate m. p. 163–164°. 3,3-Dimethylindoline showed m. p. 31–33°, b. p. 105–106° (12 mm.), n^{25}_{D} 1.5513; benzene sulfonamide, m. p. 102–102.5°, neut. equiv. 151.7 (calcd. 147). 2,3-Dimethylindoline had b. p. 110–112°, n^{25}_{D} 1.5524, m. p. acid oxalate 134–136°.

Summary

The extent of the hydrogenation of an ester of the type of *n*-octyl caprylate to 1-octanol over copper chromium oxide at 260° increases from 20% at 10 atm. to 99% at 250 atm. of hydrogen. Thus the process may be used for the conversion of an alcohol, RCH_2OH, to the corresponding ester, RCO_2CH_2R, as well as the hydrogenation of an ester to alcohol.

The extent of the hydrogenation of indole and of 1-methylindole to the corresponding indolines, over copper chromium oxide at 150–170°, increases from 50% at 30 atm. to 90% at 400 atm. of hydrogen. The equilibrium between 2,3-dimethylindole and the corresponding indoline is even more unfavorable to complete hydrogenation, the ratio of the indole to the indoline at equilibrium being about 3 to 2 at 250 atm. of hydrogen. In contrast, the hydrogenation of 3,3-dimethylpseudoindole, with the double bond in the 1,2 rather than in the 2,3 position as with the other indoles studied, goes to completion under 35 atm. of hydrogen.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Organolithium Compounds with Hydroxyl, Nitrilo and Sulfonamido Groups

BY HENRY GILMAN AND DONALD S. MELSTROM

The halogen–metal interconversion reaction is particularly suitable, in connection with studies concerned with physiological action, for the preparation of organolithium compounds containing a functional group which under ordinary conditions reacts with RLi compounds. Some of the functional groups present in molecules which have been prepared in accordance with the reaction

$$RX + n\text{-}C_4H_9Li \longrightarrow RLi + n\text{-}C_4H_9X$$

are amino,[1a] azomethylene,[1b] phenolic hydroxyl[1c] and carboxyl.[1c]

We are now reporting the preparation of RLi compounds from bromophenyl alcohols like *m*- and *p*-bromobenzyl alcohols, *p*-bromophenethyl alcohol and *p*-bromo-α-methylbenzyl alcohol. The yields of interconversion products, as determined by carbonation and isolation of the corresponding carboxylic acids, range from 18 to 52%. However, the actual yields of RLi compounds are greater, since the interconversion products when treated in another study with triphenyllead chloride instead of with carbon dioxide were converted into the expected unsymmetrical organolead compounds in yields of 41 to 63%. Also, the halogen–metal interconversion product of *o*-bromobenzyl alcohol, although not studied by carbonation of the reaction product, gave a 70% yield of triphenyl-*o*-hydroxymethylphenyllead by reaction with triphenyllead chloride. Incidentally, improved directions are given for the preparation of *p*-bromobenzyl alcohol.

The isolation of terephthalic acid by carbonation of the interconversion product of *p*-bromobenzonitrile and *n*-butyllithium indicates that *p*-carboxybenzonitrile was formed and underwent hydrolysis incidental to working up the reaction products. Carbonation of the interconversion product from *p*-bromobenzenesulfonamide and *n*-butyllithium gave *p*-carboxybenzenesulfonamide which was slightly contaminated with what may be a reduction product. It is interesting to note in this connection that carbonation of the interconversion product from *p*-iodo-N,N-diethylbenzenesulfonamide gave directly a 72% yield of *p*-carboxy - N,N - diethylbenzenesulfonamide, the melting point of which was unchanged after crystallization.[1c]

Experimental

Preparation of *p*-Bromobenzyl Alcohol.—Ziegler and Tiemann[2] prepared this alcohol from *p*-bromophenylmagnesium bromide and formaldehyde. They obtained a 61% yield of product distilling over the range 125–140° (11 mm.), but their yield of pure compound (crystallized from ethanol) is not reported. We tried this method, patterning the procedure after that described for cyclo-

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[1] (a) Gilman and Stuckwisch, THIS JOURNAL, 63, 2844 (1941), and 64, 1007 (1942); (b) Gilman and Spatz, *ibid.*, 62, 446 (1940), and 63, 1553 (1941); (c) Gilman and Arntzen, *ibid.*, 69, 1537 (1947). For general references, see pp. 538–539 of Gilman, "Organic Chemistry," Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943.

[2] Ziegler and Tiemann, *Ber.*, 55, 3406 (1922).

TABLE I

REACTIONS OF RX COMPOUNDS WITH n-C_4H_9Li

RX	RX in ether mole	RX in ether cc.	n-C_4H_9Li in ether mole	n-C_4H_9Li in ether cc.	Temp. of reaction, °C.	Time of addition, min.	Stirring period, min.	Product	M. p. of product, °C.	Literature m. p., °C.	Yield of crude product g.	Yield of crude product %
p-$BrC_6H_4CH_2OH$	0.018	30	0.036	240	Room	10	60	p-$HOCH_2C_6H_4COOH$	160–173	181[a]	0.5[b]	18[c,d]
m-$BrC_6H_4CH_2OH$[e]	.0267	20	.054	70	Room	2	30	m-$HOCH_2C_6H_4COOH$	114.5–115[f]	111[g]	1.3	32
p-$BrC_6H_4CH_2CH_2OH$	.05	30	.1	120	Room	10	60	p-$HOCH_2CH_2C_6H_4COOH$	127–128[h]		4.4	52
p-$BrC_6H_4CH(OH)CH_3$[i]	.05	30	.1	195	Room	10	30	p-$CH_3CH(OH)C_6H_4COOH$	138–139[j]	137–138[k]	3.8	45
p-$BrC_6H_4SO_2NH_2$	.018	20	.036	70	Room	5	15	p-$HOOCC_4H_4SO_2NH_2$	284–286[l]	Dec. 280[m]	0.5	14[n]
p-BrC_6H_4CN	.05[o]	35	.05	65	−70	Rapidly	5	p-$C_6H_4(COOH)_2$[p,q]	Subl. *ca.* 300	Subl. *ca.* 300	1.4	17[r]

[a] Löw, *Ann.*, **231**, 373 (1885). [b] There was also recovered 15% of p-bromobenzyl alcohol. [c] The low yield may have been in part due to the prompt formation of bulky, insoluble $LiOCH_2C_6H_4CO_2Li$-p which interfered with effective carbonation of all the interconversion product. [d] The actual yield of interconversion product is higher, as shown by its reaction with triphenyllead chloride to give triphenyl-p-hydroxymethylphenyllead in 57 to 63% yield, based on p-bromobenzyl alcohol. [e] Prepared from m-bromotoluene by a series of reactions like those detailed in the text for p-bromobenzyl alcohol from p-bromotoluene. [f] Crystallized from benzene containing a few drops of absolute ethanol. *Anal.* Calcd. for $C_8H_8O_3$: neut. equiv., 152. Found: neut. equiv., 153. [g] Langguth, *Ber.*, **38**, 2063 (1905). [h] Crystallized from very dilute ethanol. *Anal.* Calcd. for $C_9H_{10}O_3$: neut. equiv., 166. Found: neut. equiv., 163, 164. [i] Prepared by the procedure of Ziegler and Tiemann, *Ber.*, **55**, 3406 (1922). [j] Crystallized once from dilute ethanol and then from benzene containing a small amount of absolute ethanol. *Anal.* Calcd. for $C_9H_{10}O_3$: neut. equiv., 166. Found: neut. equiv., 168, 169. [k] Emerson, *et al.*, THIS JOURNAL, **68**, 674 (1946). [l] Softened at 200–280°, melted and simultaneously sublimed completely away on the block at 284–286°. [m] Decomposes at 280°, without melting, according to Palmer, *Am. Chem. J.*, **4**, 164 (1882). [n] There was also recovered 59% of p-bromobenzenesulfonamide. [o] The p-bromobenzonitrile was added as a suspension in ether, and the reverse order of addition was employed (RX to R'Li). [p] p-Cyanobenzoic acid was undoubtedly formed but underwent hydrolysis during working up. [q] Characterized by conversion to dimethyl terephthalate (mixed m. p.). [r] From the neutral layer there was obtained a mixture which appeared to consist largely of p-bromobenzonitrile and p-bromo-n-valerophenone.

hexylcarbinol.[3] The yields were unsatisfactory, since from the Grignard reagent (prepared from one mole of p-dibromobenzene and one gram atom of magnesium) and an excess of formaldehyde, the total amount of p-bromobenzyl alcohol (purified by steam distillation followed by crystallization from petroleum ether), melting at 76–77°, was 34 g. (18%).

Secondly, a procedure of Bodroux[4] involving the conversion of p-bromobenzyl chloride to the acetate and hydrolysis of the acetate with alcoholic potassium hydroxide was examined. Here, too, the yields were low, varying from 6 to 28%. However, the difficulty in this case may have been due to the presence of impurities in the commercially available p-bromobenzyl chloride, for a modification of the procedure, using p-bromobenzyl bromide prepared by photobromination of p-bromotoluene,[5] was successful.

To a solution of 135 g. (0.54 mole) of pure, crystalline p-bromobenzyl bromide in 375 g. of glacial acetic acid was added 132 g. (0.6 mole) of lead oxide (PbO). The mixture was heated gently while the reaction was swirled at intervals to prevent local overheating, until all of the lead oxide had gone into solution. The solution was then heated at reflux for twenty-five minutes, during which time a white, crystalline precipitate of lead bromide deposited. After cooling and filtering, the filtrate was first diluted with 100 cc. of water and then treated with a cold solution of 225 g. of sodium hydroxide in 600 cc. of water.[6] The oily layer was then taken up in 200 cc. of ether, the ether layer separated, and the aqueous layer extracted with an additional 50 cc. of ether. The crude acetate, remaining after removal of the ether, was treated with 55 g. of potassium hydroxide in 275 cc. of methanol. The solution of methanolic alkali should be cooled before it is added to the acetate, in order to moderate the violent reaction which sometimes occurs on mixing. After the spontaneous reaction had ceased (slight heating may be necessary to start the reaction if the solutions are very cool), refluxing was continued for twenty minutes. Methanol was then distilled off until foaming became so pronounced that the distillation had to be stopped. Water was now added to dissolve the inorganic salts, and the oily layer was separated and combined with the ether extract of the aqueous layer. After drying, and heating with Norit, the solvents were removed, and the residual oil was crystallized from petroleum ether (b. p., 60–68°) containing a few cc. of benzene to give 61 g. (61%) of p-bromobenzyl alcohol melting at 77–78°.

Preparation of p-Bromophenethyl Alcohol.—This alcohol was prepared in accordance with procedures patterned after those used by Dreger[7] for the synthesis of n-hexyl alcohol. To p-bromophenylmagnesium bromide (prepared from one mole of p-dibromobenzene and 1.17 g. atoms of magnesium) was added 1.35 moles of ethylene oxide. The yield of alcohol was 40%, and its identity was established by conversion to the phenylurethan[8] (melting at 126°) by treatment with phenyl isocyanate.

General Procedure for the Interconversions.—The solution of butyllithium[9] in ether was added, over a short period of time, to a solution of the RX compound in ether. This is the preferred order of addition where the functional group of the RX compound has an active hydrogen.[1c] After stirring the mixture, it was carbonated by pouring over solid carbon dioxide. The product was obtained by acidification of a sodium hydroxide extract. Details are given in the accompanying table.

p-Bromobenzenesulfonamide and n-Butyllithium.—The crude p-carboxybenzenesulfonamide obtained by interconversion at room temperature and carbonation (Table I) was not susceptible to purification by recrystallization. Some of the acid obtained from another preparation by the same method was converted to the ethyl ester, which melted at 108–109°. The melting point reported for p-carbethoxybenzenesulfonamide[10] is 110–111°. From these results it appears that the product from the interconversion reaction is largely p-carboxybenzenesulfonamide

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(3) Gilman and Catlin, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 188.

(4) Bodroux, *Bull. soc. chim.*, [3] **21**, 289 (1899).

(5) Weizmann and Patai, THIS JOURNAL, **68**, 150 (1946); Fiekers and Di Geronimo, *ibid.*, **70**, 1654 (1948).

(6) If too much sodium hydroxide is used, a precipitate of lead hydroxide is formed, and then enough acetic acid must be added to redissolve the precipitate.

(7) Dreger, ref. 3, p. 306.

(8) Taylor and Hobson, *J. Chem. Soc.*, 184 (1936).

(9) The titer of the butyllithium solutions was determined by the analytical procedure of Gilman and Haubein, THIS JOURNAL, **66**, 1515 (1944).

(10) Remsen, *Ann.*, **178**, 301 (1875).

together with a small amount of impurity probably resulting from reduction of the sulfonamide by *n*-butyllithium.

Only unchanged starting material was obtained from a reaction carried out at −70°.

***p*-Bromobenzonitrile and *n*-Butyllithium.**—Terephthalic acid, isolated after interconversion at −70° and carbonation (Table I), owes its formation to hydrolysis of *p*-carboxybenzonitrile, for on working up the carbonation product the ether suspension was extracted with dilute potassium hydroxide solution and the basic extract was heated on the steam plate for about one hour to remove dissolved ether.

Neither *p*-carboxybenzonitrile nor terephthalic acid was obtained from a second experiment in which the *p*-bromobenzonitrile, dissolved in a mixture of benzene and ether (rather than suspended in ether alone), was added to a solution of *n*-butyllithium in ether at −70°. It was shown earlier[11] that no acidic fraction (exclusive of valeric acid formed from *n*-butyllithium) was obtained from carbonation of an attempted interconversion reaction in which *p*-bromobenzonitrile, dissolved in a mixture of toluene and ether, was added to a solution of *n*-butyllithium in ether at 0°. It is probable, on the basis of other studies,[12] that benzene and toluene suppress the interconversion reactions.

Summary

In connection with studies concerned with physiological action, it has been shown that the halogen-metal interconversion reaction can be used for the preparation of organolithium compounds containing the alcoholic hydroxyl (as $-OLi$), nitrilo, and sulfonamido (as $-SO_2NHLi$ or $-SO_2NLi_2$) groups. Incidental to the hydroxyl studies, there was developed a satisfactory synthesis of *p*-bromobenzyl alcohol.

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[11] W. A. Gregory, unpublished studies, Iowa State College.

[12] Gilman and Moore, THIS JOURNAL, **62**, 1843 (1940); Gilman, Langham and Moore, *ibid.*, **62**, 2327 (1940); Gilman, Moore and Baine, *ibid.*, **63**, 2479 (1941).

AMES, IOWA RECEIVED JULY 17, 1947

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Catalytic Hydrogenation of 2-Naphthol to 1,2,3,4-Tetrahydro-2-naphthol

BY HYP J. DAUBEN, JR.,[1a] BLAINE C. MCKUSICK[1b] AND GEORGE P. MUELLER[1c,d]

During a search for compounds with favorable insect repellent properties,[2] it became apparent that alcohols as a group and 2-phenethanols in particular possessed appreciable repellency times. Of the 2-phenethanols prepared and tested, 1,2,3,4-tetrahydro-2-naphthol represented not only the most effective repellent in this class but one of the few compounds of any type with the requisite properties of low irritancy, low toxicity and complete protection from mosquito bites for many hours even under tropical conditions.[3]

In response to requests from different investigators[3] in the repellency field, large quantities of 1,2,3,4-tetrahydro-2-naphthol were prepared. By repeated preparations of this material it became possible to define, within narrow and reproducible limits, the conditions for rapid production of a pure product in good yields and to determine the nature and amounts of by-products.

Partial catalytic hydrogenation of 2-naphthol has been shown to furnish 1,2,3,4-tetrahydro-2-naphthol and 5,6,7,8-tetrahydro-2-naphthol in varying relative amounts depending on the catalyst and conditions used. Stork[4] and Adkins and Krsek[5] have demonstrated recently that hydrogenation, using Raney nickel catalysts, gives yields of 66–87% of 5,6,7,8-tetrahydro-2-naphthol and 6–33% of 1,2,3,4-tetrahydro-2-naphthol. The same authors showed that the addition of small amounts of basic promoters altered the relative rates so that 65% yields of the 1,2,3,4-tetrahydro isomer could be realized. Earlier work by the Adkins group[6] with copper–chromium oxide catalyst led to the isolation of 1,2,3,4-tetrahydro-2-naphthol as the major product in 76–88% yields. Purification of this product was performed by fractional distillation and no mention was made of the formation of other products. The present studies, using copper–chromium oxide catalyst and improved methods of purification, confirm the yield but indicate the formation of 5,6,7,8-tetrahydro-2-naphthol and naphthalene as minor by-products.

Hydrogenation of purified 2-naphthol was conducted at 200° without solvent and reaction ceased with the absorption of 2 moles of hydrogen. Total impurities in the crude hydrogenation product were estimated by cryoscopic determination. Approximately 8.5 mole per cent. total impurities were indicated and this value agrees fairly well with those obtained by actual isolation; purified 2-naphthol (14.90 kg.) gave 79.0% (11.76 kg.) of pure 1,2,3,4-tetrahydro-2-naphthol, 5.1% (0.76 kg.) of pure 5,6,7,8-tetrahydro-2-naphthol and

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[2] This work was carried out as part of the program at Harvard University with Paul D. Bartlett as official investigator under contracts NDCrc-136 and OEMsr-1304 with the Office of Scientific Research and Development.

[3] Testing was done at the Experiment Station of U. S. Department of Agriculture, Bureau of Entomology and Plant Quarantine, Orlando, Florida. Extensive evaluation of the compound was made by this group and by Jachowski and Pijoan at the Naval Medical Research Institute, Bethesda, Maryland, *cf. Science*, **104**, 266–269 (1946).

[4] Stork, THIS JOURNAL, **69**, 576 (1947).

[5] Adkins and Krsek, *ibid.*, **70**, 412 (1948).

[6] Musser and Adkins, *ibid.*, **60**, 665 (1938); Adkins and Reid, *ibid.*, **63**, 741 (1941).