The aqueous solution gave 0.30 g. or a 12% yield of acid melting at 219–220°. This acid was shown to be 1,4-diphenyl-2-butene-1,4-dicarboxylic acid.[13]

Summary

It has been shown that the more reactive organometallic compounds dehydrogenate some partially reduced nuclear and open-chained compounds smoothly and under very mild conditions. Illustrations are the conversion of 1,4-dihydronaphthalene to naphthalene, 1,4-diphenylbutene-2 to 1,4-diphenylbutadiene-1,3, and 1,4-dihydrodibenzofuran to dibenzofuran.

Intermediate compounds have been isolated and a mechanism considered.

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[13] Schlenk and Bergmann, *Ann.*, **463**, 100 (1928).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Relative Reactivities of Organometallic Compounds. XIX. Hydrogenolysis of RM Compounds

BY HENRY GILMAN, ARTHUR L. JACOBY AND HELEN LUDEMAN

Introduction

The smooth and ready dehydrogenation by organometallic compounds described in the preceding[1] paper suggested that the more reactive organometallic compounds might undergo easy hydrogenolysis. This has been found to be the case. Actually, some of the organoalkali compounds are cleaved by hydrogen under extremely mild conditions: room temperature, atmospheric pressure and in the absence of any catalyst. Apparently there is no report of any other class of organic compounds reacting with hydrogen under such mild conditions. Not only do some organometallic compounds undergo easier reduction than any other type of organic compound, but they also appear to be oxidized at least as readily as any other class.

Relative Rates of Hydrogenolysis of RM Compounds Having Different Metals.—The varying rates of hydrogenolysis of organoalkali and other reactive organometallic compounds suggested the possibility of a correlation with the relative reactivities of organometallic compounds established with other reactants. Earlier studies by others pointed to such a relationship. Ipatieff and Rasuwajeff[2a] showed that under elevated pressures (60 atmospheres), elevated temperatures (225 and 350°) and in the absence of catalysts, the rate of hydrogenolysis of the triphenyl derivatives of phosphorus, arsenic, antimony and bismuth increased in the order: P, As, Sb, Bi. Then Zartman and Adkins,[3] in an examination of the hydrogenation of some more reactive RM compounds, found that the order of increasing ease of hydrogenation of R_3Sb, R_4Pb, R_2Zn and R_2Mg compounds was: Sb, Pb, Zn, Mg. These authors used not only elevated temperatures and pressures but also a nickel catalyst. Two reactions were noted, depending on the kind of RM compound used

$$R_2M + H_2 \longrightarrow R{\cdot}R + M$$
$$R_2M + H_2 \longrightarrow 2RH + MH_2$$

For example, tetraphenyllead gave biphenyl and lead, both a catalyst and hydrogen being necessary, and diphenylmagnesium gave benzene and magnesium hydride. Ipatieff and co-workers[2b] observed the following reaction with tetraalkyl- and tetraaryllead compounds in the absence of a catalyst, but in a glass and not a copper reaction vessel.

$$R_4Pb + 2H_2 \longrightarrow 4RH + Pb$$

We have found that the order of increasing ease of hydrogenolysis of some very reactive organometallic compounds is: Ca, Li, Na, K, Rb, Cs. This order together with the orders established by Ipatieff and by Adkins follows almost exactly the order of increasing chemical reactivity of the organometallic compounds as established in other reactions. It is interesting to note that here, as in the recent study[4] on the relative reactivities of organoalkali compounds, there is only a small difference between the relative reactivities of organopotassium and organorubidium compounds.

The preponderant reaction which takes place with organoalkali compounds is

$$RM + H_2 \longrightarrow RH + MH$$

The rate of hydrogenolysis varies somewhat with the medium, as illustrated in Fig. 1. The

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

[2] (a) Ipatieff and Razuwajeff, *Ber.*, **63**, 1110 (1930); (b) Ipatieff, Razuwajeff and Bogdanov, *ibid.*, **63**, 335 (1930).

[3] Zartman and Adkins, THIS JOURNAL, **54**, 3398 (1932).

[4] Gilman and Young, *J. Org. Chem.*, **1**, 315 (1936).

curves indicate that the rate-controlling factor in petroleum ether suspension may be the rate of diffusion of hydrogen through the petroleum ether; and with benzene, a first-order reaction in which the concentration of hydrogen is constant. Obviously, the high reactivity of organoalkali compounds made it desirable to work with suspensions in benzene and petroleum ether.

Relative Rates of Hydrogenolysis of RLi Compounds Having Different Radicals.—Under corresponding conditions, and in benzene, the times in hours required for the hydrogenolysis of some organolithium compounds were: phenyl (32.2 hours), methyl (38.5), α-naphthyl (40), *n*-butyl (61), *n*-heptyl (66), *n*-lauryl (91), *p*-tolyl (150). This order follows somewhat the tendency of corresponding organoalkali compounds to metalate systems like dibenzofuran and dibenzothiophene.[5]

Effect of Catalysts on Rates of Hydrogenolysis.—It seemed of interest to examine the effect of some catalysts on the rates of hydrogenolysis. For this purpose, platinum and palladium were selected because of their general accelerating effect on organic reductions. Neither catalyst appeared to have any significant effect on the rate of hydrogenolysis of phenyllithium and phenylsodium.

Experimental Part

The organoalkali compounds were prepared in accordance with general procedures, details of which have been given in earlier publications from this Laboratory. Phenylpotassium was prepared by stirring for forty-eight hours 75 cc. of dry benzene, 4.0 g. (0.10 g. atom) of cut potassium and 6.9 g. (0.22 mole) of di-*n*-butylmercury. The reaction started promptly with the appearance of a precipitate of phenylpotassium, but with very little noticeable warming. Related reactions were used for the syntheses of phenylrubidium and phenylcesium.

Depending upon the particular organometallic compound, comparative runs were made at atmospheric pressure; at pressures slightly above atmospheric pressure (about 785 mm.); and at 100 lb. (7 atm.) pressure in a shaking machine. The rate of hydrogenolysis was determined by disappearance of the color test,[6] or by noting the time for absorption of 90% of the hydrogen. The latter procedure was used rather than the time for complete absorption because the reaction was observed to be erratic toward the end and variations were then noted with individual experiments. Rates determined by disappearance of the color test were confirmed by carbonation; no acid was obtained in those cases where no color test was observed.

In some experiments, the lithium hydride was analyzed by hydrolysis, the evolved hydrogen being measured, and the lithium hydroxide being titrated with standard acid. The results of two analytical experiments showed: 0.00072 mole of hydrogen and 0.00078 equivalent of lithium hydroxide; and, 0.00027 mole of hydrogen and 0.00024 equivalent of lithium hydroxide. The benzene formed by hydrogenolysis was isolated in yields upward of 60% and characterized as *m*-dinitrobenzene.

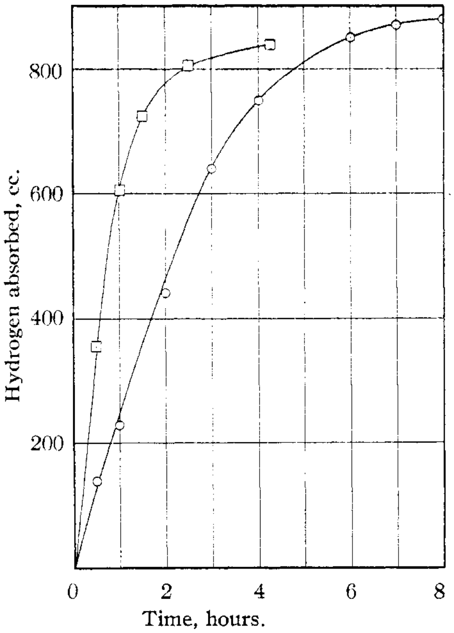

Fig. 1.—Rates of hydrogenolysis of phenylsodium: ⊡, benzene as medium; ⊙, petroleum ether (b. p. 115–130°).

TABLE I

REDUCTION RATES IN BENZENE SUSPENSION

Organometallic compound	Av. time (hours) for complete redn. at 100 lb.	Av. time (hours) for 90% redn. at pres. sl. above atm.
C_6H_5CaI	Incomplete, 150	..
C_6H_5Li	32.2	..
C_6H_5Na	0.5	1.9
C_6H_5K	..	0.54
C_6H_5Rb	..	.42
C_6H_5Cs	..	.2

Typical of results obtained for 90% reduction at pressures a few millimeters above atmospheric pressure are phenylsodium, one and eight-tenths and two hours, respectively; and phenylpotassium, one-half and fifty-eight hundredth hours, respectively. Also, in the series of RLi compounds having different R groups, phenyllithium was reduced completely at 100 lb. (7 atm.) pressure in thirty-one hours, thirty-one and one-half hours and thirty-four hours, respectively.

Summary

The more reactive organoalkali compounds are

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(5) Gilman and Jacoby, *J. Org. Chem.*, **3**, in press (1938). Also, unpublished studies by R. L. Bebb.

(6) Gilman and Schulze, THIS JOURNAL, **47**, 2002 (1925).

reduced more easily than any reported type of organic compound. Reduction is effected at room temperature, atmospheric pressure and in the absence of any catalyst. The reaction is $RK + H_2 \longrightarrow RH + KH$.

The order of increasing ease of hydrogenolysis of the phenyl derivatives is: Ca, Li, Na, K, Rb, Cs. This series follows essentially the series of relative reactivities as established by other reactants.

The rates of hydrogenolysis appear to be unaffected by the presence of platinum and palladium.

The rates of hydrogenolysis have been established for a series of RLi compounds having different R groups.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Urethans as Local Anesthetics. IV. Alkyl N-(*p*-Aminobenzyl)-carbamates

BY R. L. SHRINER AND JAMES M. CROSS

A study of the local anesthetic action of *p*-aminophenyl urethans (Formula I) showed that their anesthetic potency was high but that they were very irritating whether applied topically or intracutaneously.[1] It seemed possible that the irritation might be due to the *p*-phenylenediamine grouping present as a portion of the molecule since other derivatives of this compound have been found to cause irritation.[2]

In molecules of the type of alkyl N-(*p*-aminobenzyl)-carbamates (II) the urethan grouping is separated from the benzene ring by a methylene

I $H_2NC_6H_4NHCOOR$

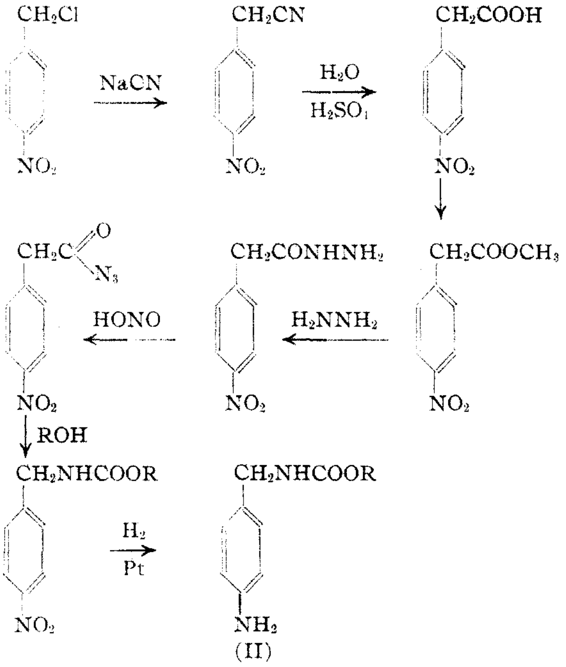
II $H_2NC_6H_4CH_2NHCOOR$

III $H_2NC_6H_4COO(CH_2)_xNR_2$

group and the *p*-phenylenediamine group is no longer present. The structure of urethans of type II is related to compounds of the novocaine type (III) in that each contains a *p*-aminophenyl radical attached to a carbon atom. Since the alkyl *p*-aminobenzoates are not especially irritating, it was considered of interest to synthesize the urethans of type II in order to determine whether this structure would be non-irritating to the tissues but still retain the superiority in topical and injection anesthetic potency of the urethans of type I over those of the *p*-aminobenzoates of type III.

The urethans were synthesized by means of the reactions summarized in Chart I.

CHART I



Although the final compounds are new, each of the individual steps in the above synthesis represents well-known reactions which were adapted to the present compounds with slight modifications which are given in the experimental part.

Through the courtesy of the Lilly Research Laboratories the pharmacological action of 1% aqueous solutions of the hydrochlorides of this series of urethans was determined. The data obtained are summarized in Table I.

The pharmacological data in Table I show that these urethans cause some local anesthesia when injected intracutaneously but that they are not especially active when applied topically. All of these urethans were irritating both to the skin and eyes and this fact probably accounts for the somewhat erratic results. These urethans are

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[1] Horne, Cox and Shriner, THIS JOURNAL, **55**, 3435 (1933).

[2] Hanzlik, *J. Ind. Hyg.*, **4**, 386, 448 (1923); Erdmann and Bakken, *Arch. Exptl. Path. Pharm.*, **53**, 402 (1905).