4. In concentrated alkaline solutions, both phenolsulfonephthalein and *o*-cresolsulfonephthalein are converted largely into the colorless tribasic salts of the carbinolcarboxylic acid, although the reaction proceeds very much more rapidly with the former.

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DI-NORMAL-BUTYL ETHER AS A SOLVENT FOR THE GRIGNARD REAGENT

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The need for a solvent with a higher boiling point than that of diethyl ether for the preparation and use of the Grignard reagent has long been felt. The low boiling point of diethyl ether with the consequent loss of it in handling and danger of the formation of explosive mixtures of its vapor and air has limited the use of the Grignard reagent in commercial work to very rare cases. Numerous papers describing the use of higher aliphatic ethers, various phenyl ethers and high boiling hydrocarbons have appeared in the literature.[1]

It seemed likely that a suitable substitute for diethyl ether would be di-*n*-butyl ether, which has occasionally been used as a solvent in the Grignard reaction. This ether may be prepared in a pure condition easily and cheaply fron *n*-butyl alcohol and its boiling point is high enough so that it can be conveniently handled without excessive loss due to evaporation. Furthermore, distillation alone gives an ether free from moisture and butyl alcohol, thus avoiding the difficulties met in the purification of ordinary ethyl ether. While it has been suggested as a solvent in this reaction, there is very little information in the literature concerning the yields of the Grignard reagents from different halogen compounds or of the yields of products that may be obtained from Grignard reagents in this solvent. Gilman and McCracken[1] report a yield of 55.9% of phenylmagnesium bromide from bromobenzene and magnesium in di-*n*-butyl ether.

The present investigation has shown that the yields of the Grignard reagent from several typical halogen compounds when di-*n*-butyl ether is the solvent are nearly equal to those obtained in diethyl ether. It has also been shown that in a typical reaction of the Grignard reagent, such as that with carbon dioxide, as good a yield of product can be obtained in di-*n*-butyl ether as when diethyl ether is used. For a reaction such as that between the Grignard reagent and ethylene oxide, where an elevated temperature is needed to complete the reaction, di-*n*-butyl ether is more

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[1] A review of this topic is given in a recent paper by Gilman and McCracken, *Rec. trav. chim.*, **46**, 463 (1927).

convenient to use than is the usual mixture of ether and benzene. For the preparation of primary alcohols from the Grignard reagent and formaldehyde di-*n*-butyl ether has a decided advantage over diethyl ether since in the higher boiling solvent a temperature can be reached which will bring about depolymerization of paraformaldehyde in the reaction mixture. This obviates the necessity of depolymerizing the paraformaldehyde as a separate operation. One disadvantage that should be mentioned is that di-*n*-butyl ether cannot be used conveniently as a solvent in reactions used for the preparation of neutral substances which boil too close to its own boiling point (141°). The di-*n*-butyl ether may be recovered from these reaction mixtures with very little loss and after distillation is again ready for use.

Experimental Part

1. Preparation of Grignard Reagents in Di-*n*-butyl Ether.—In determining the yields of various Grignard reagents in di-*n*-butyl ether a standard procedure essentially the same as that devised by Gilman and his students[2] was used. A 200-cc., three-necked flask was fitted with a mechanical stirrer, separatory funnel, reflux condenser and thermometer. In the flask was placed about 40 cc. of di-*n*-butyl ether, 1.5 g. of magnesium turnings and a crystal of iodine. The theoretical amount of halogen compound dissolved in enough di-*n*-butyl ether to make a total volume of 30 cc. was placed in the separatory funnel. A small amount of the solution of the halogen compound was added and the reaction flask was heated until the reaction started. This temperature varied somewhat with the different halogen compounds. When the reaction was once started, stirring was begun and the remainder of the solution of the halogen compound was added at a rate which allowed the reaction to proceed smoothly. After addition of the last of the solution of the halogen compound stirring was continued until the mixture had cooled to room temperature. The reaction mixture was then rapidly transferred to a volumetric flask and the reaction vessel rinsed with more solvent. The level of the liquid in the volumetric flask was brought up to the mark by the addition of more solvent and aliquot parts were titrated with standard acid.

The di-*n*-butyl ether used in these experiments was prepared from *n*-butyl alcohol and sulfuric acid. It was washed with sodium hydroxide solution and distilled twice. The fraction boiling at 140–142° was collected. The halogen compounds and magnesium were of the ordinary grade used for the preparation of the Grignard reagent.

The results of the experiments are listed in the following table.

TABLE I

YIELDS OF GRIGNARD REAGENT FROM VARIOUS HALOGEN COMPOUNDS AND MAGNESIUM IN DI-*n*-BUTYL ETHER

Halogen compound	Yield, %	Halogen compound	Yield, %
Ethyl bromide	91–93	*Iso*butyl bromide	82–86
n-Propyl bromide	89–90	*n*-Heptyl bromide	73–81
*Iso*propyl bromide	79–80	Cyclohexyl bromide	80–83
n-Butyl bromide	86–87	Bromobenzene	70–77
sec.-Butyl bromide	68–72	α-Bromonaphthalene	63–71
		β-Phenylethyl bromide	68–71

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[2] Gilman, Wilkinson, Fishel and Meyers, THIS JOURNAL, **45**, 150 (1923); Gilman and Meyers, *ibid.*, **45**, 159 (1923); Gilman and McCracken, *ibid.*, **45**, 2462 (1923).

The yields recorded in the table are the upper and lower yields (to the nearest whole number) of a number of runs.

2. **Reactions of the Grignard Reagent in Di-*n*-butyl Ether.** ***dl*-Methylethylacetic Acid.**—The standard procedure for the preparation of an acid from the Grignard reagent was followed[3] except that di-*n*-butyl ether was substituted for diethyl ether. The yield of *dl*-methylethylacetic acid (b. p. 173–175°) from 274 g. of *sec.*-butyl bromide was 135 g. (66% of the theoretical amount). In diethyl ether the yield has been found to be 135–136 g.

***n*-Nonyl Alcohol.**—The general procedure for the preparation of *n*-hexyl alcohol from *n*-butyl bromide[4] was followed with the exception that di-*n*-butyl ether was used as a solvent in place of the usual solvents, ether followed by benzene. The Grignard reagent was prepared from 179 g. of *n*-heptyl bromide in about 300 cc. of di-*n*-butyl ether. This solution was cooled to 0° and with stirring an excess of ethylene oxide was added. The temperature was maintained at 0° for one hour after the addition of the ethylene oxide and then allowed to rise to 40° and maintained at that point for one hour. Finally the mixture was heated on the steam-bath for two hours and then decomposed and the product was isolated according to the procedure used for *n*-hexyl alcohol. The yield of *n*-nonyl alcohol boiling at 95–100° (12 mm.) was 95 g. (65% of the theoretical amount).

Cyclohexyl Carbinol.—The proportions of the reagents used were those described for this preparation by Adams and Noller.[5] The general procedure was the same except that the Grignard reagent was prepared in di-*n*-butyl ether. The solution was heated to 100–110° and 100 g. of dry paraformaldehyde was added in small portions to the well stirred solution over a period of about two hours. The product was isolated as described for the preparation in diethyl ether. The yield of cyclohexyl carbinol (b. p. 88–93° (18 mm.)) from 163 g. of cyclohexyl bromide was 70 g. (60% of the theoretical amount). In diethyl ether the yield has been found to be 61–65% of the theoretical amount.

Summary

1. Di-*n*-butyl ether may be used in place of diethyl ether as a solvent for the preparation of the Grignard reagent without materially reducing the yield.

2. The three typical reactions of the Grignard reagent which were studied have been found to give as good yields in di-*n*-butyl ether as when diethyl ether is used as a solvent. In two of these reactions the procedure is simplified by the use of the higher boiling solvent.

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[3] Gilman and Parker, "Organic Syntheses," John Wiley and Sons, Inc., New York, **5**, 75 (1925).

[4] Dreger, "Organic Syntheses," John Wiley and Sons, Inc., New York, **6**, 54 (1926).

[5] Adams and Noller, "Organic Syntheses," John Wiley and Sons, Inc., New York, **6**, 22 (1926).