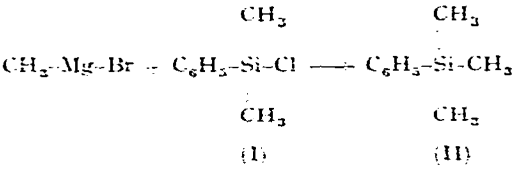
The standardization of solutions of methyllithium and methylmagnesium derivatives[*]

Of the various procedures employed for determining the concentrations of solutions of Grignard reagents[1] and organolithium compounds[2] perhaps the most common is the hydrolysis of an aliquot of the reagent followed by an acid–base titration to determine the total amount of basic material obtained from the aliquot of reagent. This procedure suffers from the disadvantage that bases present in the original solution of the organometallic reagent (*e.g.* from partial oxidation or hydrolysis of the reagent or from cleavage of the solvent) are not distinguished from the base produced by hydrolysis during the analytical procedure. As a result the molar concentration of the organometallic reagent determined by this procedure may be significantly greater than the correct value. Various procedures to avoid this potential error include the iodometric titration of organomagnesium derivatives[1,3], the generation of methane from methyl reagents[1-3], and the use of a double titration for organolithium reagents where the organolithium reagent is destroyed prior to one titration by reaction with a halide such as benzyl chloride or 1,2-dibromoethane[2]. Since we have found these methods troublesome, especially for methylmagnesium derivatives, we were prompted to look for an alternative analytical procedure and report here a method which works equally well for ether solutions of methylmagnesium bromide, dimethylmagnesium or methyllithium.

The procedure utilizes the previously studied[3] reaction of a methylmagnesium derivative with the commercially available[**] dimethylphenylchlorosilane (I) to form phenyltrimethylsilane (II). The reaction,



$$CH_3\text{-}Mg\text{-}Br + C_6H_5\text{-}\underset{CH_3}{\overset{CH_3}{Si}}\text{-}Cl \longrightarrow C_6H_5\text{-}\underset{CH_3}{\overset{CH_3}{Si}}\text{-}CH_3$$

(I) (II)

effected in ether solution at room temperature with an excess of the chlorosilane (I), is complete in less than 1 h. After the ether solution has been washed with aqueous ammonium chloride, the quantity of the silane (II) produced can be determined by gas chromatography employing cumene as an internal standard. In practice, an aliquot of an ethereal solution containing excess chlorosilane and a known weight of the internal standard, cumene, is added to an aliquot of an ether solution of methyllithium or the methylmagnesium derivative. After the reaction is complete and the reaction mixture has been washed, the ether solution is separated and analyzed by gas chromatography. Since this procedure relies on the determination of a specific product formed from the methyl organometallic derivative, the molar concentration or reagents determined by this method cannot be larger than the correct value, a possibility that is the usual source of concern in synthetic work.

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[**] Dow-Corning Corporation, Midland, Michigan.

Experimental

Analysis for methylmagnesium bromide. A stock solution was prepared by diluting a mixture of 10.9245 g (64 mmoles) of freshly distilled (b.p. 85–87°/32 mm, lit.[4] b.p. 192–194°/760 mm) dimethylphenylchlorosilane (I) and 4.2514 g of cumene (isopropylbenzene) with anhydrous ether to a total volume of 50 ml. An ethereal solution which was 2.80 *M* in methylmagnesium bromide, as determined by hydrolysis and subsequent acid–base titration, was prepared in the usual way. For standardization a 2.0 ml aliquot (*ca.* 5.6 mmoles) of the methylmagnesium bromide solution was added to 10.0 ml of the aforementioned stock solution [containing *ca.* 13 mmoles of dimethylphenylchlorosilane (I) and 850.3 mg of cumene]. The resulting solution was stirred for 40 min under a nitrogen atmosphere during which time a white precipitate (presumably inorganic magnesium salts) separated and then poured into approximately 15 ml of saturated, aqueous ammonium chloride. After the organic phase had been separated and the aqueous phase had been washed with two 15-ml portions of ether, the combined ether layers were dried over magnesium sulfate and analyzed by gas chromatography*. The calculated yield of phenyltrimethylsilane (II) was 815 mg corresponding to a 2.71 *M* concentration of the Grignard reagent. The identity of the product (II) was established by comparison of retention times with an authentic sample. The gas chromatograph was calibrated with a known mixture of cumene and the silane (II); the ratio, area of silane/area of cumene, had to be multiplied by 1.065 to give the correct ratio, weight of silane/weight of cumene, on our equipment. The retention times of the various components were: cumene, 14.2 min; the silane (II), 19.2 min; the chlorosilane (I), 42.6 min. The saturated, aqueous ammonium chloride used in the isolation procedure was found to hydrolyze the chlorosilane (I) so that this component normally was not present in ether solutions being analyzed by gas chromatography.

In a comparable experiment, 2-ml aliquots of the reaction mixture were quenched in 5-ml portions of aqueous ammonium chloride after various periods of time and the product mixture was analyzed as previously described. The calculated concentrations after 20, 40, and 60 min were 2.67, 2.71 and 2.72 *M*. In a similar set of experiments employing an ethereal solution which was 2.55 *M* (acid–base titration) in methylmagnesium bromide, the ratio of peak areas for the standard and the silane (II) was found to change after 15 min but was constant for aliquots removed after 40, 90 and 180 min; the calculated concentration of methylmagnesium bromide was 2.30 *M*. Consequently, a reaction time of 1 h for this standardization procedure appears to be adequate when excess chlorosilane (I) is being used with reasonably concentrated solutions (*i.e.* 1 *M* or greater) of methylmagnesium halides. In doubtful cases, the reaction time can be extended to several hours.

As an alternative procedure, 9.71 ml (*ca.* 17 mmoles) of the previously mentioned 2.80 *M* etheral methylmagnesium bromide was treated with a solution of 6.221 g (36 mmoles) of the chlorosilane (I) and 3.6840 g of cumene in 20 ml of ether. The mixture was stirred for 2 h under a nitrogen atmosphere and then quenched and analyzed as in previous cases. The calculated concentrations from duplicate runs were 2.71 and 2.74 *M*.

Analysis of dimethylmagnesium and methyllithium solutions. The above procedure

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* The analyses were performed on an F and M, Model 720, gas chromatograph fitted with a column packed with Silicone Fluid, No. 710, suspended on Chromosorb P.

was followed with reaction times ranging from 2–4.5 h. Although these reactions with the chlorosilane (I) appear to be much more rapid than the reaction with methylmagnesium bromide, we did not establish minimum reaction times in these cases. Aliquots (2 ml or *ca.* 1.7 mmoles) of an ether solution which was 0.84 M (acid–base titration) in dimethylmagnesium were added to 10 ml of an ethereal solution containing 6.2 mmoles of the chlorosilane (I) and 456.2 mg of cumene. The concentration found in duplicate runs was 0.78 M, two moles of the silane (II) being formed for each mole of dimethylmagnesium added. Similarly, 2-ml (*ca.* 2.8 mmoles) aliquots of ethereal methyllithium (1.40 M by acid–base titration and 1.34 M by a double titration employing ethylene dibromide) were added to 10 ml of an ethereal solution containing 6.0 mmoles of the chlorosilane (I) and 417.2 mg of cumene. The concentrations found in duplicate runs were 1.36 M and 1.35 M.

Reaction of the chlorosilane (I) with magnesium methoxide. Since reaction of the methyllithium and methylmagnesium compounds with oxygen could lead to the presence of a metal methoxide in the organometallic solution, we examined the reaction of the chlorosilane (I) with methoxide ion to establish that the product of this reaction would not interfere with the analytical procedure. To 10 ml of an ethereal solution containing 13 mmoles of the chlorosilane and 850 mg of cumene was added 1.12 g (13 mmoles) of magnesium methoxide and 10 ml of methanol. The resulting solution was stirred for 4 h and then an aliquot was examined by gas chromatography. The solution no longer contained the chlorosilane (I) (retention time 47.7 min) but did contain a new peak (retention time 41.7 min) believed to be dimethylphenylmethoxysilane. Subsequent treatment of this solution with aqueous ammonium chloride did not hydrolyze this new component in the time required for separation of the ether solution as was the case with the chlorosilane (I). However, since the retention time of this component is much greater than the retention time of the silane (II) no complication is caused in the analytical procedure.

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