senting as low as 0.0002–0.0003 mg. of lead per liter are arcked (equivalent to 1 part per 3 to 5 billion of urine). Moreover, 0.1-cc. portions of fresh urine always give a lead line, and since some of these in our experience contain as little as 0.01 mg. of lead per liter, the indicated sensitivity without resort to other than the routine procedures of the method as described, is of the order of 1 part per 100 million.

Summary

1. A method is described for the quantitative spectrographic determination of minute quantities of lead in urine.
2. This method is suitable for the determination of lead in samples so small that a chemical method cannot be used.
3. Concentrations of lead in urine as low as 1 part per 100 million can easily be detected. Concentrations which can be measured accurately by the technique described lie between 0.01 and 0.20 mg. per liter.
4. For amounts of lead up to 0.10 mg. per liter the accuracy of the method is ±0.01 mg. per liter. For amounts above 0.10 and up to 0.20 mg. per liter the error is somewhat greater.
5. The method may be made applicable to the measurement of lead in all kinds of biological material.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Reaction of Alkyl Sulfates and *p*-Toluenesulfonates with the Grignard Reagent and the Preparation of Dialkylmagnesium Compounds

BY C. M. SUTER AND HOWARD L. GERHART

This investigation was a result of the observation that in the reaction of equimolecular quantities of *n*-butyl sulfate and *n*-butylmagnesium bromide there was no appreciable decrease in the amount of basic magnesium. This reaction was first[1] formulated as

$$n\text{-}C_4H_9MgBr + (n\text{-}C_4H_9)_2SO_4 \longrightarrow n\text{-}C_4H_9MgOSO_3C_4H_9 + n\text{-}C_4H_9Br$$

but further investigation has shown that only a small percentage of the basic magnesium is present in the precipitate formed in the reaction. If any large amount of *n*-butylmagnesium *n*-butyl sulfate is produced it undergoes disproportionation.[2]

$$2n\text{-}C_4H_9MgOSO_3C_4H_9 \longrightarrow (n\text{-}C_4H_9)_2Mg + Mg(n\text{-}C_4H_9SO_4)_2$$

The results of some preliminary experiments comparing the behavior of *n*-butyl sulfate, methyl sulfate and methyl *p*-toluenesulfonate with typical Grignard reagents are listed in Table I. In these experiments only the amount of basic magnesium remaining in solution was determined.[3]

Benzene, *n*-butylbenzene and *n*-butyl bromide were isolated from the phenylmagnesium bromide–*n*-butyl sulfate reaction mixture by fractionation of the ether solution after hydrolysis. Fractionation before hydrolysis gave *n*-butyl bromide and *n*-butylbenzene.

TABLE I

Magnesium compound	Ester	Decrease in basic magnesium, % 1 mole ester 15 min. reflux	2 moles ester 2 hrs. reflux
n-C_4H_9MgBr	$(n\text{-}C_4H_9)_2SO_4$	<5	30
n-C_4H_9MgCl	$(n\text{-}C_4H_9)_2SO_4$	<5	43 (3 hrs.)
C_6H_5MgBr	$(n\text{-}C_4H_9)_2SO_4$	36	58
n-C_4H_9MgBr	$(CH_3)_2SO_4$	18	66
C_6H_5MgBr	$(CH_3)_2SO_4$	52	100
C_6H_5MgBr	$CH_3OSO_2C_7H_7$	42	100

In Table II are given more complete data for the reaction of a number of esters with two Grignard reagents. Since the chief reaction involves the formation of an alkyl bromide, one mole of ester was used per equivalent of halogen present in the Grignard solution. The phenylmagnesium bromide was 0.63 N in basic magnesium[3] and 0.68 N in bromide ion; the *n*-butylmagnesium bromide, 0.59 N and 0.62 N in these components. A volume of solution containing 0.03 equivalent of halogen was used for each reaction. The reaction time was one hour except where otherwise specified.

The figures given in the fourth column represent a purely arbitrary method of expressing the variation in reactivity of the alkyl sulfates and

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(1) Suter and Gerhart, THIS JOURNAL, **55**, 3496 (1933).

(2) This paper as originally submitted for publication contained a discussion of the structure of the Grignard reagent in the light of its reaction with alkyl sulfates. The subsequent appearance of the work of Cope, *ibid.*, **56**, 1578 (1934), which contains an excellent discussion of this topic makes its treatment here unnecessary.

(3) Gilman, Zoellner and Dickey, *ibid.*, **51**, 1576 (1929).

TABLE II

REACTIONS OF PHENYLMAGNESIUM BROMIDE

Ester	Decrease in Basic Mg, %	Decrease in Br, %	Ratio of reactivity, Br⁻/basic Mg	Ester accounted for, %
$(CH_3)_2SO_4$	37.2	72	1.9	105[a]
$(C_2H_5)_2SO_4$	21.9	75	3.4	96
$(n\text{-}C_4H_9)_2SO_4$	24.8	70	2.8	94
$CH_3OSO_2C_7H_7$	40.1	62	1.5	99
$C_2H_5OSO_2C_7H_7$	29.6	74	2.5	102
$n\text{-}C_4H_9OSO_2C_7H_7$	32.5	69	2.1	99
REACTIONS OF *n*-BUTYLMAGNESIUM BROMIDE				
$(CH_3)_2SO_4$	16.8	80	4.8	96
$(C_2H_5)_2SO_4$	8.1	86	10.6	94
$(n\text{-}C_4H_9)_2SO_4$	3.1	70	23	73[b]
$(n\text{-}C_4H_9)_2SO_4$	2.8	82	29	85[c]
$CH_3OSO_2C_7H_7$	26	68	2.6	93
$n\text{-}C_4H_9OSO_2C_7H_7$	3.1	63	20	66[d]

[a] Second methyl group may have reacted to slight extent. [b] Time eighty minutes. [c] Time two hours. [d] In four hours 90% of bromine had reacted when a 10% excess of the ester was added.

sulfonates toward the magnesium–carbon and magnesium–bromide bonds. The difference in reactivity of the *n*-butyl esters toward the two Grignard reagents is quite striking.

By the use of slightly more than one mole of ethyl sulfate per equivalent of halogen, a solution containing nearly pure di-*n*-butylmagnesium resulted. In each experiment the *n*-butylmagnesium bromide solution contained 0.03 equivalent of halogen as in the experiments of Table II. The data are given in Table III.

TABLE III

Expt.	$(C_2H_5)_2SO_4$, mole	Reaction time, hrs.	Decrease in Basic Mg, %	Decrease in Br⁻, %
1	0.030	1	8.1	86
2	.0324	2	8.6	95
3	.0324	6	8.2	95
4	.034	2	...	96

Of the 4% of the bromine not converted into ethyl bromide in Expt. 4 approximately half was in the precipitate,[2] probably as $C_2H_5OSO_3MgBr$. In an experiment similar to (2), 17% of the basic magnesium was found to be in the precipitate. With *n*-butyl sulfate practically all of the basic magnesium remained in solution but the formation of alkyl bromide was considerably slower.

As has already been reported[1] it is possible to obtain by the action of magnesium upon *n*-butyl sulfate in anhydrous ether a solution exhibiting the properties of the Grignard reagent. This reaction apparently does not occur unless a small amount of magnesium halide is present as a catalyst. The Grignard reagent is not chiefly $n\text{-}C_4H_9MgOSO_3C_4H_9$ as was first thought, but a mixture of di-*n*-butylmagnesium and magnesium *n*-butyl sulfate. It seems probable that these products result from the following reactions which explain how a small amount of iodine will convert a relatively large amount of alkyl sulfate into the dialkylmagnesium

$$MgI_2 + 2(n\text{-}C_4H_9)_2SO_4 \longrightarrow 2n\text{-}C_4H_9I + Mg(n\text{-}C_4H_9SO_4)_2$$

$$2n\text{-}C_4H_9I + 2Mg \longrightarrow (n\text{-}C_4H_9)_2Mg{\cdot}MgI_2 \rightleftharpoons (n\text{-}C_4H_9)_2Mg + MgI_2$$

The same type of reaction has been carried out with *n*-butyl *p*-toluenesulfonate but the yields of di-*n*-butylmagnesium were only 30–35% as compared with 75–80% for *n*-butyl sulfate.

In a preliminary experiment in which methyl sulfate was used the yield of dimethylmagnesium was low due to the formation of ethane which was evolved rapidly toward the end of the reaction.

$$2(CH_3)_2SO_4 + (CH_3)_2Mg \longrightarrow 2C_2H_6 + Mg(CH_3SO_4)_2$$

Experimental

Materials.—The *n*-butyl sulfate was prepared by the action of sulfuryl chloride or *n*-butyl chlorosulfonate upon *n*-butyl sulfite.[4] The other esters were Eastman Kodak Company products.

Quantitative Study of the Reactions.—The Grignard reagents for the experiments of Table **I** were made in approximately 0.05 molar quantities in a 125-cc. graduated flask under nitrogen. The concentration of basic magnesium was determined by acid titration[5] and the proper amount of alkyl sulfate added. After refluxing for a given time a filtered portion of the reaction mixture was titrated to determine the extent of the reaction.

The Grignard reagents for the experiments of Tables II and III were prepared in 0.5 mole quantities, the solutions diluted with dry ether, filtered and standardized by titration with standard sulfuric acid and silver nitrate. For each experiment an amount of solution containing 0.03 mole of halogen was measured from a buret into a 200-cc. flask. The alkyl sulfate or sulfonate was then added through a small separatory funnel, the last traces being washed into the flask with 10 cc. of dry ether, and the reaction mixture kept at the boiling point for a specified time. The entire reaction mixture was then hydrolyzed and titrated as in the standardization.

Isolation of Reaction Products. A. From *n*-Butyl Sulfate and *n*-Butylmagnesium Bromide.—By hydrolysis of the reaction mixture from 0.25 mole of each reactant there was obtained a small amount of *n*-butane, b. p. 0°, and 29.5 g. or 86% of the theoretical amount of *n*-butyl bromide, b. p. 98–101°. When ice water was used in the hydrolysis the grayish solid which precipitated contained when dry 14.5% magnesium instead of the 12.4% required for the basic salt, $HOMgOSO_3C_4H_9$, indicating the presence of some magnesium hydroxide. Heating the pre-

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[4] Levaillant, *Compt. rend.*, **189**, 465 (1929); **190**, 54 (1930); **197**, 648 (1933).

[5] Gilman and co-workers, THIS JOURNAL, **45**, 153 (1923); **51**, 1577 (1929).

cipitate to a high temperature caused decomposition with formation of a combustible gas, carbonaceous matter and magnesium sulfate.

B. From *n*-Butyl Sulfate and Phenylmagnesium Bromide.—From 0.5 molar quantities of the reactants there were isolated after hydrolysis 18.7 g. of benzene, b. p. 80–82°, n^{21}_{D} 1.4951; 24.2 g. of *n*-butyl bromide, b. p. 98–101°, n^{21}_{D} 1.4383; and 10.5 g. of *n*-butylbenzene, b. p. 180°, n^{22}_{D} 1.4955. The *n*-butylbenzene was further identified by oxidation to benzoic acid.

In the reaction of 1 mole of *n*-butyl sulfate with 0.5 mole of phenylmagnesium bromide nineteen hours of refluxing was required before reaction was complete as judged by absence of Grignard reagent. From this was obtained an 84% yield of *n*-butyl bromide, b. p. 97–101°, and a 42% yield of *n*-butylbenzene, b. p. 176–180°. There also remained a small amount of unreacted *n*-butyl sulfate.

C. Methyl Sulfate and Methyl *p*-Toluenesulfonate with Phenylmagnesium Bromide.—From the reaction of 0.97 mole of methyl sulfate with the Grignard reagent from 0.48 mole of bromobenzene a 62% yield of toluene, b. p. 105–110°, resulted. Fractionation of a mixture of toluene and ether containing a known quantity of toluene under the same conditions gave a 90% recovery. Werner and Zilkens[6] report a 31% yield for equimolecular quantities of the reactants.

Substitution of methyl *p*-toluenesulfonate for methyl sulfate in the above reaction gave a 70% yield of toluene. Gilman and Beaber[7] report a 38% yield for equimolecular quantities of the reactants.

Reaction of *n*-Butyl Sulfate with Magnesium + Magnesium Iodide.—A large number of experiments was performed to determine the most satisfactory method for obtaining a high yield of di-*n*-butylmagnesium from *n*-butyl sulfate and magnesium in ether to which a small amount of iodine had been added. The following procedure gave the best results.

A mixture of 1.26 g. of magnesium (0.05 mole + 5% excess) and 1.27 g. (0.01 atom) of iodine was covered with 60 cc. of ether in a graduated flask and warmed slightly until the iodine was converted into magnesium iodide. To the mixture was then added over a period of three hours 10.5 g. (0.05 mole) of *n*-butyl sulfate, and refluxing continued for an additional hour. Titration of portions of the filtered reaction mixture indicated a 78–80% yield of di-*n*-butylmagnesium.

Decreasing the amount of iodine to one-half the quantity given above decreased the yield slightly to 70–75% and another hour of refluxing was necessary. The reaction proceeds slowly with even a trace of iodine present but the slow destruction of the di-*n*-butylmagnesium by the *n*-butyl sulfate decreases the yield of the former and makes the time of the reaction inconveniently long.

Analysis of the precipitate formed during the reaction indicated it to be practically pure *magnesium n*-butyl sulfate.

Anal. Calcd. for $Mg(C_4H_9SO_4)_2$: Mg, 7.35. Found: Mg, 6.9.

It was readily soluble in water and gave no test for sulfate ion unless heated with acid. In calculating the yield of di-*n*-butylmagnesium the volume occupied by the precipitated magnesium *n*-butyl sulfate was taken into consideration. Its density determined in benzene suspension was 1.17.

The di-*n*-butylmagnesium was identified by conversion into *n*-butylmercury chloride,[8] m. p. 126–127°, and by the preparation of *n*-butyl alcohol by oxidation with oxygen. From a 0.2-mole run there was obtained a 70% yield of *n*-butyl alcohol, b. p. 116–118°, n^{22}_{D} 1.4018, calculated on the basis of the *n*-butyl sulfate used. Care was taken to keep the reaction mixture cold during hydrolysis to prevent formation of *n*-butyl alcohol from the magnesium *n*-butyl sulfate.

The preparation of di-*n*-butylmagnesium from *n*-butyl *p*-toluene-sulfonate by the same procedure as outlined above gave a 30–35% yield as determined by titration.

Reaction of Methyl Sulfate with Magnesium + Magnesium Iodide.—The use of the same procedure as given for *n*-butyl sulfate gave a 28% yield of dimethylmagnesium and a large volume of gaseous products. Combustion analysis[9] of the saturated hydrocarbons which constituted practically all of the gas gave 96.1% ethane and the remainder methane. Any ethylene present was removed with the ether and hence was not determined. The amount of ethane evolved was approximately 50% of the theoretical amount.

Summary

1. The reaction of a number of alkyl sulfates and *p*-toluenesulfonates with phenyl and *n*-butylmagnesium bromide has been studied quantitatively. The results are summarized in tables.

2. *n*-Butyl sulfate is converted into di-*n*-butylmagnesium and magnesium *n*-butyl sulfate by reaction with magnesium and magnesium iodide. Ethane is formed as the chief product when methyl sulfate is treated in the same way.

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(6) Werner and Zilkens, *Ber.*, **36**, 2116 (1903).

(7) Gilman and Beaber, THIS JOURNAL, **47**, 518 (1925).

(8) Marvel, Gauerke and Hill, *ibid.*, **47**, 3011 (1925).

(9) We are indebted to Mr. Robert Christ for this analysis.