In every instance the results appear to be in good accord with the theory that the tautomer of lower oxido-reduction potential is the one which will predominate in the equilibrium mixture.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS.
RECEIVED MARCH 31, 1934

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Mechanism of the Reaction of Dimethyl Sulfate with Arylmagnesium Halides

BY ARTHUR C. COPE[1]

The reaction of dimethyl sulfate with Grignard reagents furnishes a valuable method for the synthesis of methyl hydrocarbons. The discoverers of the reaction[2] represented it by the equation

$$(CH_3)_2SO_4 + RMgX \longrightarrow RCH_3 + CH_3OSO_2OMgX \qquad (1)$$

While the equation is still commonly written in this manner, the reaction has also been represented[3] as requiring two moles of dimethyl sulfate, one mole being utilized in the production of methyl halide

$$2(CH_3)_2SO_4 + RMgX \longrightarrow RCH_3 + CH_3X + (CH_3OSO_2O)_2Mg \qquad (2)$$

Evidence that two moles of the alkylating agent are necessary to complete the reaction is afforded by the work of Rossander and Marvel[4] and Gilman and Heck,[5] who found that alkyl halides (R′X) as well as alkyl hydrocarbons (R—R′) are formed through the reaction of alkyl *p*-toluene sulfonates with Grignard reagents (RMgX).

While the complete reaction (2) seems to be well established, there is little evidence as to its mechanism. In the case of alkyl sulfonates, when one mole of $CH_3C_6H_4SO_2OR'$ is used the products are R—R′, RH and R′X. Rossander and Marvel[4] explained the formation of the alkyl halide by a cleavage of the Grignard reagent at the Mg—X bond[6]

$$CH_3C_6H_4SO_2OR' + RMgX \longrightarrow R'X + CH_3C_6H_4SO_2OMgR$$

Hydrolysis of the new magnesium derivative produced in this manner would account for the formation of RH. Gilman and Heck[5] preferred to explain the formation of the alkyl halide by a reaction of the halomagnesium salt produced in the alkylation process

$$CH_3C_6H_4SO_2OR' + CH_3C_6H_4SO_2OMgX \longrightarrow R'X + (CH_3C_6H_4SO_2O)_2Mg$$

Hydrolysis of unreacted Grignard reagent would account for the formation of RH.

In this investigation an attempt has been made to determine the mechanism of the reaction of dimethyl sulfate with arylmagnesium halides. The Grignard reagents and dimethyl sulfate were allowed to react in equimolecular proportions, and then the yields of all of the products formed were determined by a method which is described in the experimental part. The data obtained are summarized in Table I.

Since two moles of dimethyl sulfate are required to complete the reaction (equation 2) a portion of the Grignard reagents was recovered. In three of the cases the recovered Grignard reagent contained much more basic magnesium than halogen; in other words, part of it was present as R_2Mg. Since the diarylmagnesium could hardly have been formed through reaction of the arylmagnesium halide with dimethyl sulfate, the presence of R_2Mg in the original Grignard reagent is established. Independent chemical evidence is thus obtained in support of Schlenk's conclusion[7] that Grignard reagents exist in the equilibrium: $2RMgX \rightleftharpoons R_2Mg + MgX_2$. The increase in the ratio of basic magnesium to halogen produced in the Grignard reagents through partial reaction with dimethyl sulfate must be attributed to a relatively rapid removal of magnesium halide from this equilibrium to form methyl halide. The results of experiments in which magnesium bromide and iodide were allowed to react with dimethyl sulfate substantiate the conclusion that the magnesium halides in equilibrium with the Grignard reagents are a principal source of the methyl halide, since methyl halides were pro-

---

(1) National Research Fellow in Chemistry.

(2) Werner and Zilkens, *Ber.*, **36**, 2116, 3618 (1903); Houben, *ibid.*, **36**, 3083 (1903); **37**, 488 (1904).

(3) "Organic Syntheses," 1931, Vol. XI, p. 66.

(4) Rossander and Marvel, THIS JOURNAL, **50**, 1491 (1928).

(5) Gilman and Heck, *ibid.*, **50**, 2223 (1928).

(6) Such a cleavage had been postulated previously by Kenyon, Phillips and Turley, *J. Chem. Soc.*, **127**, 399 (1925).

(7) Schlenk and Schlenk, *Ber.*, **62**, 920 (1929).

TABLE I

REACTION OF DIMETHYL SULFATE AND HALOMAGNESIUM COMPOUNDS IN EQUIVALENT PROPORTIONS

										Yield of RCH_3, %		Reactants accounted for, %		
Magnesium compound	Moles	Equivalents of X^-	Moles of dimethyl sulfate	CH_3X, %	R_2Mg, %	RMgX, %	$RMgOSO_2OCH_3$, %	CH_3OSO_2OMgX, %	$(CH_3OSO_2O)_2Mg$, %	Based on basic Mg	Based on CH_3X	Mg	X	SO_4
C_6H_5MgBr	0.05	0.055	0.05	60.1	20.9	37.3	4.7	5.9	88.8	37.1	39.9	98.8	95.8	99.4
2,4-$(CH_3)_2C_6H_3MgBr$	.05	.0545	.05	50.2	0	38.4	9.3	14.2	74.8	52.3	49.8	95.6	95.3	98.3
Mesityl MgBr	.05	.058	.05	53.0	0	32.2	18.8	22.6	58.5	49.0	47.0	95.3	93.0	99.9
C_6H_5MgI	.05	.0518	.05	85.2	45.0	11.3	21.9	2.0	72.0	21.8	14.8	92.2	95.2	95.9
2,4-$(CH_3)_2C_6H_3MgI$[a]	.05	.0599	.05	91.0	26.8	14.6	30.0	2.7	79.6	28.6	9.0	91.6	90.6	112.3[a]
$MgBr_2$	.025	.05	.05	92.9				4.2	90.8[b]			99.2	97.1	95.0
MgI_2	.025	.05	.05	97.0				0.3	95.5[c]			95.8	97.3	95.8

[a] Data obtained from this Grignard reagent are not quantitatively significant. [b] *Anal.* Calcd. for a mixture of 92.6% $Mg(CH_3SO_4)_2$ and 7.4% CH_3OSO_2OMgBr: Mg, 10.04; S, 25.18. Found: Mg, 10.11; S, 25.01. [c] *Anal.* Calcd. for $Mg(CH_3SO_4)_2$: Mg, 9.94; S, 26.01. Found: Mg, 10.55; S, 25.46.

duced practically quantitatively and quite rapidly, especially from magnesium iodide. No attempt was made to determine whether the reaction proceeds in steps or directly to the final products.

$$(CH_3)_2SO_4 + MgX_2 \longrightarrow CH_3X + CH_3OSO_2OMgX \quad (3)$$

$$(CH_3)_2SO_4 + CH_3OSO_2OMgX \longrightarrow CH_3X + (CH_3OSO_2O)_2Mg \quad (4)$$

$$2(CH_3)_2SO_4 + MgX_2 \longrightarrow 2CH_3X + (CH_3OSO_2O)_2Mg \quad (3a)$$

An appreciable quantity of arylmagnesium methyl sulfate, $RMgOSO_2OCH_3$, was formed from each of the Grignard reagents. Since the yield of this product is much higher from phenylmagnesium iodide (21.9%) than from the bromide (4.7%), while the diphenylmagnesium content of the two reagents is similar, in the latter case at least a part of this product must be formed through the previously postulated cleavage of RMgX[4,6,8] at the Mg—X bond

$$(CH_3)_2SO_4 + RMgX \longrightarrow CH_3X + CH_3OSO_2OMgR \quad (5)$$

The arylmagnesium methyl sulfates can also be formed from the R_2Mg present in the Grignard reagents. This was proved by carrying out the reaction of dimethyl sulfate with diphenylmagnesium.

$$(CH_3)_2SO_4 + R_2Mg \longrightarrow CH_3OSO_2OMgR + RCH_3 \quad (6)$$

The product obtained contained magnesium methyl sulfate, indicating either that part of the new magnesium derivative had reacted further with dimethyl sulfate

$$(CH_3)_2SO_4 + CH_3OSO_2OMgR \longrightarrow RCH_3 + (CH_3OSO_2O)_2Mg \quad (7)$$

or that the sum of (6) and (7) had occurred initially

$$2(CH_3)_2SO_4 + R_2Mg \longrightarrow 2RCH_3 + (CH_3OSO_2O)_2Mg \quad (6a)$$

Since the magnesium halides and diphenylmagnesium have been found to react with dimethyl sulfate, while evidence is presented by the quantitative data that RMgX reacts according to equations (1) and (5), the most satisfactory explanation of the mechanism of the reaction of arylmagnesium halides with dimethyl sulfate is that all of the components of the equilibrium $2RMgX \rightleftharpoons R_2Mg + MgX_2$ react with the dimethyl sulfate but at different rates. The methyl halide produced must be formed largely from the magnesium halide (equations 3 and 4); however, a part is derived from the cleavage of RMgX at the Mg—X bond,[4] at least with the iodides (equation 5). A part of the methyl halide undoubtedly is formed according to (4), following the normal alkylation reaction (1), but it should be noted that this cannot be the only source,[5] since in three cases the yield of methyl halide exceeds the yield of methyl hydrocarbon. Hydrolysis of the reaction mixture would yield RH from R_2Mg, RMgX and $RMgOSO_2OCH_3$. However, even when an excess of dimethyl sulfate is used, some of the unmethylated hydrocarbon (RH) is formed.[9] Since RMgX and R_2Mg should be removed completely by an excess of dimethyl sulfate, the RH produced under these circumstances probably results from the hydrolysis of the arylmagnesium methyl sulfate, as these salts are very insoluble and would not be expected to

---

(8) Suter and Gerhart, THIS JOURNAL, **55**, 3496 (1933), have described the reaction of *n*-butylmagnesium bromide and dibutyl sulfate as: $(C_4H_9)_2SO_4 + C_4H_9MgBr \longrightarrow C_4H_9MgOSO_3OC_4H_9 + C_4H_9Br$. If this formulation is correct, they have prepared an alkylmagnesium alkyl sulfate in the pure state. In view of the complexity of the reaction of arylmagnesium halides and dimethyl sulfate observed in the present work, such a simple course of reaction appears unlikely. One would expect that a mixture of dibutylmagnesium, butylmagnesium butyl sulfate, magnesium butyl sulfate, butyl bromide and *n*-octane would be formed. Decision must await publication of their experimental data.

(9) Smith and Lund, *ibid.*, **52**, 4146 (1930); Smitb and MacDougall, *ibid.*, **51**, 3003 (1929).

react completely with dimethyl sulfate under the mild conditions employed. The yield of arylmagnesium methyl sulfate is much smaller from the arylmagnesium bromides than from the iodides (*cf.* Table I; 9% from xylylmagnesium bromide compared to 30% from xylylmagnesium iodide). This explains why Maxwell and Adams[10] obtained higher yields of pseudocumene from xylylmagnesium bromide than Smith and Lund[9] did from the iodide. It should be emphasized that at least two moles of dimethyl sulfate must be employed to one of the halide used in preparing the Grignard reagent, since practically all of the halogen is eventually converted to methyl halide.[11]

Experimental Part

The Grignard reagents used in this investigation were prepared under nitrogen in the usual manner. After dilution to a concentration of approximately one molar, they were filtered into a nitrogen-filled graduate, which was then connected to a buret. The reagents were standardized by acid titration,[12] and the total halogen in the solutions was determined by the Volhard method. These values indirectly gave the total magnesium in solution, since the excess of halogen over basic magnesium represents magnesium halide. The position of the equilibrium $2RMgX \rightleftharpoons R_2Mg + MgX_2$ was also determined for each of the Grignard reagents. This was done by Schlenk's method[7] as modified by Noller[13] except that the precipitate formed on adding dioxane to the Grignard reagents was separated by centrifuging rather than by filtration. The following values represent the percentage of the basic magnesium of the Grignard reagents present as R_2Mg (the values enclosed in parentheses are those given by Schlenk[14]): phenylmagnesium bromide, 71.5% (70); 2,4-dimethylphenylmagnesium bromide, 56%; mesitylmagnesium bromide, 36%; phenylmagnesium iodide, 61% (62); 2,4-dimethylphenylmagnesium iodide, 45%.

Quantitative Reactions with Dimethyl Sulfate

In each experiment exactly 0.05 mole of the Grignard reagent was introduced into a dry nitrogen-filled 200-cc. three-necked flask. With the arylmagnesium bromides the flask was fitted with a mercury-sealed stirrer, Friedrichs reflux condenser, dropping funnel and a tube through which a slow stream of nitrogen was admitted. The reflux condenser was connected to a train of four Erlenmeyer flasks containing a solution of alcoholic sodium hydroxide prepared by dissolving 5.8 g. of sodium in 100 cc. of 90% alcohol. This solution served to remove methyl bromide from the gas stream. A solution of 0.05 mole of dimethyl sulfate in 25 cc. of dry ether was added to the Grignard reagent during ten minutes. The condenser was then turned off and the flask immersed in an oil-bath which was heated to 50° during five minutes and kept at that temperature for one hour. During the hour 50 cc. of ether was added to the reaction mixture through the separatory funnel and 70 to 80 cc. of ether distilled into the absorption train. The train was then disconnected and the flask cooled, after which the salt was separated by filtration through a sintered glass funnel under nitrogen. The salt was washed with sufficient dry ether to bring the total volume of the filtrate to 200 cc. (received in two 100-cc. volumetric flasks).

The reaction products were thus separated into three groups; gaseous (methyl bromide), ether soluble (R_2Mg, $RMgX$, RCH_3 and RH), and ether insoluble (magnesium methyl sulfate, bromomagnesium methyl sulfate, and arylmagnesium methyl sulfate). The method used in the analysis of these fractions may be illustrated by the results obtained with phenylmagnesium bromide. The sodium hydroxide solution was boiled to remove alcohol and ether, cooled, acidified with nitric acid and made up to 500 cc. A 50-cc. aliquot required 30.05 cc. of 0.1 *N* silver nitrate, corresponding to a yield of 60.1% of methyl bromide. One-fifth of the ethereal filtrate neutralized 58.2 cc. of 0.1 *N* sulfuric acid, equivalent to a recovery of 58.2% of the original basic magnesium; the same sample required 37.3 cc. of 0.1 *N* silver nitrate, corresponding to 37.3% of 0.05 mole of C_6H_5MgBr; consequently the remaining 20.9% basic magnesium was present as $(C_6H_5)_2Mg$. The values for R_2Mg thus obtained are minima, and do not take into account the fact that the "RMgX" recovered may be present largely as R_2Mg and MgX_2. In the two cases where % R_2Mg is given as zero, this merely means that the ratio of basic magnesium to halogen was unity. The salt weighed 6.60 g.; 1.00 g. neutralized 3.55 cc. of 0.1 *N* sulfuric acid, indicating the presence of 0.50 g. (4.7% of 0.05 mole) of $C_6H_5MgOSO_2OCH_3$ in the total sample; the same sample required 4.46 cc. of 0.1 *N* silver nitrate, indicating the presence of 0.63 g. (5.9% of 0.05 mole) of $BrMgOSO_2OCH_3$. The remaining 5.47 g. of salt was assumed to be magnesium methyl sulfate (88.8% of the theoretical 0.025 mole). This assumption is warranted because in each case the sum of the equivalents of sulfate so obtained (in this case $88.8 + 5.9 + 4.7 = 99.4\%$ of 0.05 mole) is equal to the amount of dimethyl sulfate originally introduced. The yield of the remaining product, RCH_3, can be calculated in two ways; first it is equal to 100% minus the total recovered basic magnesium (in this case $100 - (20.9 + 37.3 + 4.7) = 37.1\%$); second it is equal to 100% minus the yield of methyl bromide (in this case $100 - 61.1 = 39.9\%$). The discrepancy in the yields of RCH_3 as calculated by the two methods represents the extent to which side reactions not considered in equations (1) to (6) occur, such as the reaction of the second methyl group of dimethyl sulfate, either to produce methyl halide or methyl hydrocarbon. In the recorded data these discrepancies are within the limits of experimental error, but in preliminary runs in which higher boiling solvents were used the discrepancy was 20% or more, indicating the necessity of milder conditions of reaction.

---

[10] Maxwell and Adams, THIS JOURNAL, **52**, 2962 (1930).

[11] The use of an insufficient quantity of dimethyl sulfate probably accounts for the anomalous formation of 2-iodofuran from 5-iodofuryl-2-magnesium iodide and dimethyl sulfate reported by Gilman and Wright, *ibid.*, **55**, 3308 (1933).

[12] Gilman, Zoellner and Dickey, *ibid.*, **51**, 1576 (1929).

[13] Noller, *ibid.*, **53**, 639 (1931).

[14] Schlenk, *Ber.*, **64**, 735 (1931).

The data recorded represent single experiments which were reproduced in each case within 2%; the analytical determinations in any single run were accurate to 0.5%.

The same experimental conditions could not be employed with the arylmagnesium iodides, because the use of a higher boiling solvent necessary for the removal of methyl iodide brought about secondary reactions, and operation in vacuum was not practical experimentally. The methyl iodide consequently was determined as a constituent of the ethereal filtrate. The apparatus was altered in that a nitrogen atmosphere was maintained by introducing nitrogen under a pressure of 1 cm. of mercury at the top of the reflux condenser. In the case of phenylmagnesium iodide the dimethyl sulfate was added during ten minutes, the solution refluxed for five minutes, then cooled in ice and filtered as before. The yield of methyl iodide was determined by adding one-fifth of the ethereal filtrate to 75 cc. of water, distilling into an excess of alcoholic silver nitrate, and weighing the silver iodide formed. The discrepancy in the yields of RCH_3 as calculated by the two methods was 7% in this case, indicating that the method is less accurate than that used with the bromides. No conditions were found which gave quantitative results with xylylmagnesium iodide. In the experiment recorded the addition of dimethyl sulfate was made in eight minutes while the mixture was cooled in ice, followed by five minutes of stirring at 0°. The 20% discrepancy in the yields of RCH_3 as calculated by the two methods in this case is due to the considerable excess of magnesium iodide present in the solution of xylylmagnesium iodide due to coupling in the preparation of the Grignard reagent. Magnesium iodide is capable of reaction with the second methyl group of dimethyl sulfate to form methyl iodide; this was proved by treating 0.05 mole of magnesium iodide[15] with 0.05 mole of dimethyl sulfate; 148% of 0.05 mole of methyl iodide was produced.

Evidence for the Existence of $RMgOSO_2OCH_3$.—It has been assumed to this point that the ether-insoluble basic constituent of the mixed magnesium salts precipitated during the reaction was the arylmagnesium methyl sulfate. An attempt was made to prepare phenylmagnesium methyl sulfate through the reaction of diphenylmagnesium and dimethyl sulfate. An ether solution containing 0.012 mole of diphenylmagnesium (prepared by precipitating phenylmagnesium bromide with dioxane) was treated with 0.012 mole of dimethyl sulfate; there was no noticeable heat of reaction. After ninety minutes of refluxing the salt was filtered, washed with ether under nitrogen and dried in vacuum at 55° for thirty minutes; yield 1.70 g. Analysis showed 66.46% SO_4; calcd. for $C_6H_5MgOSO_2OCH_3$, 45.21%; calcd. for $(CH_3OSO_2O)_2Mg$, 77.94%. Therefore on the basis of the sulfate analysis the salt was composed of 35% $C_6H_5MgOSO_2OCH_3$ and 65% $(CH_3OSO_2O)_2Mg$. Analysis for total magnesium gave 10.71%; calcd. for the above mixture 10.42%. It was possible to check this composition of the salt by analysis for basic magnesium by acid titration; 1.00 g. of the salt neutralized 18.2 cc. of 0.1 *N* sulfuric acid, indicating the presence of 38.4% of $C_6H_5MgOSO_2OCH_3$. This check furnishes evidence for the existence of phenylmagnesium methyl sulfate, and furthermore proves that it can be determined quantitatively by acid titration.

Summary

Independent chemical evidence has been obtained that Grignard reagents exist in the equilibrium $2RMgX \rightleftharpoons R_2Mg + MgX_2$, as proposed by Schlenk. The products obtained in the reaction of dimethyl sulfate with arylmagnesium halides are best explained by assuming that all three components of this equilibrium react simultaneously but at different rates with the dimethyl sulfate.

CAMBRIDGE, MASSACHUSETTS RECEIVED APRIL 2, 1934

---

[15] Magnesium iodide and magnesium bromide etherates were prepared by the method of Menschutkin, *Z. anorg. Chem.*, **49**, 40 (1906), and solutions in a mixture of benzene and ether were standardized by titration for halogen. In the reaction of magnesium bromide and dimethyl sulfate benzene was added to the reaction mixture, which was then heated at 95° for thirty minutes. The reactions with magnesium iodide were carried out as with phenylmagnesium iodide, except that the solutions were refluxed for fifteen minutes after the dimethyl sulfate was added.