The ether was removed under a slight vacuum at room temperature in a nitrogen atmosphere. The residue consisted of 0.46 g. (48.8% from the sulfhydrate) of minute clusters of opaque white crystals, m.p. 103.7–106.7°. An infrared spectrum showed the characteristic weak band of a thiol group at 2565 cm.$^{-1}$

Anal. Calcd. for $C_8H_7O_2BrS$: C, 38.88; H, 2.86; Br, 32.34; S, 12.98. Found: C, 38.56; H, 2.50; Br, 32.34; S, 13.20.

1,4-Piperazonium di-dl-cis-trans-chrysanthemummonocarboxylate. A solution of 1.65 g. of piperazine hexahydrate in 7 ml. of absolute ethanol was added to a solution of 2.87 g. of chrysanthemummonocarboxylic acid in 7 ml. of absolute ethanol and the resultant clear yellow liquid was allowed to stand overnight at room temperature. Concentration to about 10 ml. caused crystallization to occur. After the mixture had been cooled in a refrigerator, the crystals were collected by suction filtration, washed with ether, and air-dried. Crystallization from acetone afforded 1.25 g. (27.8%) of colorless needles, m.p. 129.5–130.5°.

Anal. Calcd. for $C_{24}H_{42}N_2O_4$: C, 68.21; H, 10.02; N, 6.63. Found: C, 68.61; H, 10.04; N, 6.48.

dl-cis-trans-Chrysanthemummonocarboxypiperidide. A solution of 1.45 g. of piperidine in 8 ml. of dry benzene was added to a solution of 1.59 g. of chrysanthemummonocarbonyl chloride in 10 ml. of the same solvent at room temperature. After standing overnight, the reaction mixture was filtered and the solvent removed in vacuum. The yellow residual oil was dissolved in 15 ml. of ether and washed successively with water, sulfuric acid (1*N*), sodium bicarbonate (1*N*), and water. Removal of the solvent gave 1.58 g. of crude product as a yellow oil. Vacuum distillation afforded 0.57 g. (28.5%) of colorless oil, b.p. 127° (0.33 mm.).

Anal. Calcd. for $C_{15}H_{25}NO$: C, 76.54; H, 10.71; N, 5.95. Found: C, 76.35; H, 11.10; N, 6.45.

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NATICK, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY UNIVERSITY OF GHENT]

Studies of the Grignard Reaction. II. Kinetics of the Reaction of Dimethylmagnesium with Benzophenone and of Methylmagnesium Bromide–Magnesium Bromide with Pinacolone

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The reaction of dimethylmagnesium with benzophenone is shown to occur with the transfer of only one of the two potentially reactive methyl groups, and proceeds faster than the corresponding reaction of methylmagnesium halides. Second order kinetics are found for the reaction of methylmagnesium bromide with pinacolone in the presence of equivalent amounts of magnesium bromide. These findings appear to support the mechanism proposed by Swain and Boyles.[1a]

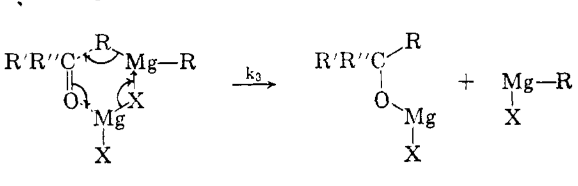
In a previous paper[1b] it was shown that the reaction of methylmagnesium halide with benzophenone and pinacolone follows a third-order law

$$V = k_3(\mathrm{Grignard})^2\,(\mathrm{ketone})$$

One possible way of explaining this result is to assume that the reactive species is $R_2Mg\cdot MgX_2$, which is believed to be a constituent of Grignard solutions.[2–8] According to the possible equilibrium

$$2\,\mathrm{RMgX} \rightleftharpoons \mathrm{R_2Mg\cdot MgX_2}, \text{ with } K = \frac{(\mathrm{RMgX})^2}{\mathrm{R_2Mg\cdot MgX_2}},$$

the reaction could be of third order and consistent with the process



$$V = k_3(\mathrm{ketone})(\mathrm{R_2Mg\cdot MgX_2}) = \frac{k_3}{K}\,(\mathrm{ketone})(\mathrm{Grignard})^2$$

This scheme can be excluded, however, as we have found[1b] that the reaction slows down with increasing concentration of Grignard reagent. Furthermore, it has been shown[9] that the equilibrium 2 RMgX $\rightleftharpoons$ $R_2Mg\cdot MgX_2$ is established very slowly, if at all.

Another possibility is that dialkylmagnesium is the reactive species:

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(1)(a) C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, 73, 870 (1951). (b) Part I, *J. Org. Chem.*, in press.

(2) A. Kirrmann and R. Hamelin, *Compt. Rend. Acad. Sciences*, 251, 2990 (1960); R. Hamelin, thesis, 1961, Paris.

(3) R. Dessy, *J. Org. Chem.*, 25, 2260 (1960).

(4) J. E. Nordlander, W. Young, and J. Roberts, *J. Am. Chem. Soc.*, 83, 495 (1961).

(5) See, however, A. Garett, A. Sweet, W. Marschall, D. Reley, and A. Tourna, *Record. Chem. Progr.*, 13, 155 (1952).

(6) The experiments of C. Noller and W. White [*J. Am. Chem. Soc.*, 59, 1354 (1937)] can be explained on the basis of the presence of $R_2Mg\cdot MgX_2$; see J. Aston and S. Bernhard, *Nature*, 165, 485 (1950).

(7) W. Slough and A. R. Ubbelohde, *J. Chem. Soc.*, 108 (1955).

(8) A. P. Terentjeff, *Z. Anorg. Chem.*, 156, 73 (1926).

(9) R. Dessy, G. Handler, J. Wotiz, and C. Hollingsworth, *J. Am. Chem. Soc.*, 79, 3476 (1957). R. Dessy and G. Handler; *J. Am. Chem. Soc.*, 80, 5824 (1958).

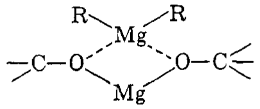
$$R_2Mg\cdot MgBr_2 \rightleftharpoons R_2Mg + MgBr_2$$

$$R_2Mg + \text{ketone} \longrightarrow \text{products}$$

Under these circumstances the entire process could also be of third order, if the second step is rate determining. Aston and Bernhard,[10] however, have shown that the reaction with dimethylmagnesium is much faster than with methylmagnesium iodide and that only one of the two potentially reactive alkyl groups reacts.

We have now attempted to determine the kinetics of the reaction of dimethylmagnesium with benzophenone and found, indeed, that the reaction is about ten times faster than the corresponding reaction of methylmagnesium bromide. Furthermore, it stops half-way when equivalent amounts of benzophenone and dimethylmagnesium are used. The results of Aston and Bernhard are thus confirmed and dialkylmagnesium is not an intermediate reactive species in the Grignard reaction.

When a double amount of dimethylmagnesium was employed the reaction was complete. Following the rate and calculating the third order constant the latter drops continuously (Table I). This could indicate a faulty choice of reaction order in that the true order should be greater. We prefer to ascribe it to complex formation of the dimethylmagnesium with the formed alcoholate, $(C_6H_5)_2COMgR$. A double molecule for this alcoholate is perhaps preferable $(RR'R''CO)_2Mg\cdot MgR''_2$, as this would be strongly stabilized by the following structural unit[11] and provides



an acceptable reason for the consumption of only one alkyl group of the dialkylmagnesium. Grignard solutions prepared in the presence of alcohols show indeed a remarkable inactivity,[11] even toward water. Interaction of the *p*-electrons of oxygen with the empty *d*-orbitals of the metal, weakening the $Mg^+—C^-$ dipole could be a factor to be taken into consideration.

The influence of magnesium halides on the Grignard reaction has been studied by Swain and Boyles,[1a] who showed that the reaction of Grignard reagents with ketone–magnesium bromide mixtures takes place *via* initial complex formation. If this does indeed occur, the kinetic pattern should fall to second order when magnesium bromide is added to the ketone before the reaction is started. We have found, indeed, that the Grignard reaction of methylmagnesium bromide with pinacolone–magnesium bromide mixtures follows a second order law $V = k_2$ (ketone) (Grignard), thus demonstrating that the mechanism is closely related to the following:

$$\text{Ketone} + MgBr_2 \underset{k_{-1}}{\overset{k_1\text{(rapid)}}{\rightleftharpoons}} (\text{ketone-}MgBr_2)$$

$$(\text{Ketone-}MgBr_2 + \text{“}RMgBr\text{”} \longrightarrow \text{product} + MgBr_2$$

The first step is a rapidly established equilibrium, which, in all likelihood, is strongly diplaced to the right; the second is rate controlling.

EXPERIMENTAL

Preparation of magnesium bromide solution. Bromine was allowed to react in ether with excess magnesium. The mixture was refluxed for several hours. Two layers, with the following compositions at 22°, are obtained: *Lower layer:* 448.0 mg./ml. $MgBr_2$ or 38.5 mg./100 g. solution (Menschutkin[12] quotes 39.2 g./100 g. solution). *Upper layer.* 37.9 mg. $MgBr_2$/ml.; Distribution coefficient: 0.0847. When pinacolone is added to this two phase system, the ketone distribution coefficient has the same value as that indicated for magnesium bromide. This shows the strong complexation between ketone and magnesium halide as discussed above.

Preparation of dimethylmagnesium. This reagent was prepared by the dioxane precipitation method. The procedure of Cope[13] was followed, except that in the present work only one equivalent of dioxane was used instead of an excess. It was indeed found that the halogen content of the solution had then dropped to zero. After eliminating the insoluble dioxane complexes by centrifugation, the clear supernatant was titrated for magnesium content.

Preparation of methylmagnesium bromide.[1b] Analysis of the magnesium used in the present experiments (and of part I[1b]) gave the following data[14]: Mn, 4 ppm.; Fe, 6 ppm.; Si, traces (?); Ni, none; Cr, traces (?); Al, traces; Ti, traces; V, traces.

Reaction of dimethylmagnesium with benzophenone. When 0.706 mmole of benzophenone and 0.768 meq. of dimethylmagnesium were brought together, only 54–55 % of benzophenone was consumed even after standing for several hours at room temperature (calculated when only one methyl group reacts: 52,5 %). On hydrolysis methane was formed. When a double amount of Grignard reagent was used, all the benzophenone was transformed into the corresponding carbinol. An example of the photometrically obtained results (see part I[1b]) is shown in Table I. The velocity constant was calculated, assuming third order kinetics.

Reaction of methylmagnesium bromide with pinacolone–magnesium bromide. At concentrations exceeding 2 mmole per 15 ml. of ether solvent two phase formation during the reaction occurs. Dilute solutions had therefore to be employed. The following procedure was adopted: 500 mg. (5 mmoles) of pinacolone was mixed with 28.0 ml. of magnesium bromide solution (37.9 mg./ml.) and diluted to 50.0 ml. with absolute ether. The reaction of 2.0 ml. of this solution with 1.0 ml. of the appropriate reagent solution was followed at low temperature as indicated in part I.[1b] Gas-liquid chromatographic analysis gave the amount of reacted product at several time intervals. Table II and III gives the data obtained. The mean-values of k_2 are the geometric mean values, while the scatter given is the standard deviation. The tem-

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(10) J. G. Aston and S. A. Bernhard, *Nature,* **165,** 485 (1950).

(11) E. Blues and D. Bryce-Smith, *Chem. & Ind.,* 1533 (1960).

(12) B. Menschutkin as quoted by A. Seidell in *Solubilities of Inorg. & Metalorg. Compounds,* Vol. I, Van Nostrand, New York, 1940, 936.

(13) A. Cope, *J. Am. Chem. Soc.,* **57,** 2238 (1935).

(14) I wish to thank Prof. Dr. J. Hoste and Dr. Fr. Verbeek (Analytic Department, University of Ghent) for these data.

TABLE I

REACTION OF DIMETHYLMAGNESIUM WITH BENZOPHENONE IN ETHER-BENZENE AT −15.2°[a]

Time	10.0	15.0	18.6	20.0	24.0	30.6	37.0	50.0	61.6	90	∞
X (% react.)	35.5	42.2	48.0	45.5	51.7	54.4	58.6	58.6	60.0	64.2	100
k_3	4.5	4.3	4.7	3.6	4.45	4.0	3.85	3.14	2.78	2.45	—

[a] Constants are calculated as for third-order reaction. a = conc. benzophenone = 0.123 mole l.$^{-1}$; b = conc. organometal = 0.126 mole/l.$^{-1}$ Solvent: 86.7% ether-13.3% benzene (by volume); temperature: −15.2° ± 0.1°.

TABLE II

SECOND-ORDER REACTION[a] OF METHYLMAGNESIUM BROMIDE WITH PINACOLONE–MAGNESIUM BROMIDE IN ETHER AT −2.2°

Time	36	68.4	91.4	115	121	165	201
X (% reaction)	7.2	14.1	18.6	21.7	25.2	30.9	34.9
$10^2 \cdot k_2$[b]	6.16	5.60	5.75	5.25	5.75	5.60	5.25
Time	240	300	400	540	720		
X (% reaction)	40.0	45.9	53.1	59.6	66.2	85.5	86.4
$10^2 \cdot k_2$	5.45	5.65	5.70	5.60	5.80	—	—

k_2 = 0.056 sec.$^{-1}$/mole^{-1} ± 0.002

[a] a = conc. pinacolone: 0.0666 mole/l.$^{-1}$; b = conc. organometal: 0.0573 mole/l.$^{-1}$; c = conc. magnesium bromide: 0.0864 mole/l.$^{-1}$ [b] Calculated as $k_2 = \frac{1}{t}\frac{2.303}{(a-b)}\log\frac{(a-x)b}{(b-x)a}$ where $(a - b) = 9.3\ 10^{-3}$; $\frac{2{,}3}{(a-b)} = 247.5$; $\log\frac{a}{b} = 0.0618$.

TABLE III

SECOND-ORDER REACTION[a] OF METHYLMAGNESIUM BROMIDE WITH PINACOLONE–MAGNESIUM BROMIDE AT 9.1°

Time	19.0	32.8	46.2	60.4	80.0	120	150.4
X (% reaction)	17.0	25.5	30.5	35.0	39.6	47.7	53.5
$10^2 \cdot k_2$	19.2	19.4	17.8	16.7	16.0	15.5	16.0
Time	180	255.6	270	346	435	∞	∞
X (% reaction)	55.8	64.0	65.2	70.0	74.0	83.1	82.9
$10^2 \cdot k_2$	14.5	15.5	15.8	16.7	14.8	—	—

k_2 = 0.165 sec.$^{-1}$ mole^{-1} ± 0.01

[a] a = 0.0666 mole/l.$^{-1}$; b = 0.0552 mole/l.$^{-1}$; $a - b$ = 0.0114 mole/l.$^{-1}$ $\frac{2.303}{(a-b)} = 202$. $\log a/b = 0.08205$. c = 0.0767 mole/l.$^{-1}$; temperature: 9.1° ± 0.1°.

perature of −2.2° (Table II) was obtained using an eutectic mixture of water/K_2CO_3[1b]; while the temperature of 9.1° (Table III) was provided by an ice-cooled thermostat.

The activation energy was found to be 14.5 ± 0.6 kcal./mole.

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