(22.7 g., 0.1 mole), cobaltous chloride (0.68 g., 0.05 mole), and anhydrous ether (100 ml.) during the course of 1 hr. The reaction mixture was refluxed for 2 hr. and was then decomposed in the usual manner. The ether-water insoluble material was collected by filtration, and the tetraphenylethylene thus obtained was recrystallized from 95% ethanol (m.p. 222–223°).

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

Studies of the Grignard Reaction. I. Kinetics of the Normal Grignard Addition Reactions on Benzophenone and Pinacolone

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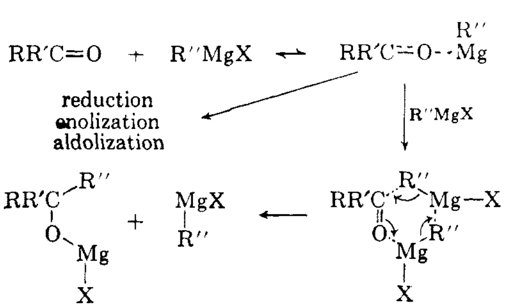
The kinetics of the reaction of methylmagnesium bromide with benzophenone and pinacolone have been studied. A third-order reaction law was found: V = k_3 (ketone) (Grignard).[2] The dependence of the velocity constant k_3 on the initial concentration of Grignard reagent is believed to be caused by complexation.

Several mechanisms for the Grignard addition reaction are proposed in the literature.[1-5] With the exception of Petit,[5] most authors agree that the participation of *two* molecules of Grignard reagent is necessary. This conclusion is based on the results of Pfeiffer and Blank[6] who isolated insoluble ketone-Grignard complexes and who found in this case that only the addition of a *second* molecule of the Grignard reagent yielded the expected carbinols.[7]

The most generally accepted scheme is the Swain mechanism.[1]



Solvation is here neglected although this factor can play an important role.[2] In any case, the structure of the intermediate[2] can be put into another form, or the occurrence of a hexagram[3] can be discussed, but all the proposed schemes appear to follow a kinetic equation of the form;

$$V = \frac{d(P)}{dT} = \frac{k_1k_2(G)^2(K)}{k_{-1} + k_2(G)},$$

where it is supposed that $K + G \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C; C + G \xrightarrow{k_2} P$ and where K_2 = ketone, G = Grignard reagent, C = complex, and P = product.[2] Therefore the reaction will be of second or third order, depending on whether k_{-1} is much smaller or much greater than k_2 (G).

Direct kinetic investigations of the Grignard reaction with nitriles have been carried out[9,10] but the corresponding investigation of the reaction with ketones is much more difficult because the velocity of the reaction is very high. Only one such study has apparently been reported.[11] According to this and in contradiction to the generally accepted Swain scheme,[1] the reaction with acetone and ethyl acetate was only first order with respect to the Grignard reagent.

We have studied the kinetics of the reaction of methyl Grignard reagents (bromide and iodide) with benzophenone and pinacolone. These ketones and Grignard reagents were chosen because side-reactions (reduction, enolization etc.) are impossible or negligible and because the reaction could be conveniently followed at low temperatures.[12] We found that the reaction was in all cases of third order. With a twenty-fold excess of Grignard reagent and after (graphically) correcting the reaction rate, the reaction reduced to (pseudo) first order. The whole process can thus be fitted to

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(1) C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, **73**, 870 (1951).

(2) R. N. Lewis and J. R. Wright, *J. Am. Chem. Soc.*, **74**, 1253 (1952).

(3) E. Royals, *Advanced Organic Chemistry*, Prentice-Hall, New York (1954).

(4) M. Kharasch and O. Reinmuth, *Grignard Reactions of Non-metallic Substances*, Prentice-Hall, New York (1952).

(5) G. Petit, *Bull. Soc. Chim. France*, **5**, 130 (1948).

(6) P. Pfeiffer and H. Blank, *J. Prakt. Chem.*, 2, **153**, 242-56 (1939).

(7) This inference has been questioned by Nesmeyanov and co-workers.[8]

(8) A. N. Nesmeyanov and V. A. Sazanova, *Chem. Abstr.*, **37**, 2723 (1943).

(9) J. Vekemans and A. Bruylants, *Bull. soc. chim. Belg.*, **68**, 541 (1959).

(10) C. G. Swain, *J. Am. Chem. Soc.*, **69**, 2406 (1947).

(11) J. E. Brugger, M. S. thesis, Pennsylvania State College (1946), as quoted by J. G. Aston and S. A. Bernhard, *Nature*, 1, 485 (1950).

(12) With acetone and methylmagnesium bromide the reaction was almost complete within ten seconds even at −15°.

the equation $V = k_3$ (ketone) (Grignard).[2] Tables I, II, and III show the results obtained at different temperatures and with variable concentrations.

TABLE I

THIRD-ORDER VELOCITY CONSTANTS. REACTION OF METHYLMAGNESIUM BROMIDE WITH BENZOPHENONE IN ETHER-BENZENE (86.5/13.5)

No.	Concn., Grignard	Concn., Ketone	Temp.	k_3	Number of Determinations
1	0.333	0.350	−15.2	0.172 ± 0.005	10
2	0.331	0.331	−15.2	0.165 ± 0.002	7
3[a]	0.333	0.0167	−15.2	0.165	7
4	0.159	0.167	−15.2	0.36 ± 0.01	8
5	0.0935	0.0920	−15.2	0.425 ± 0.009	10
6	0.333	0.333	−21.4	0.100 ± 0.004	12

[a] Calculated from first-order reaction as mentioned in Experimental.

TABLE II

THIRD-ORDER VELOCITY CONSTANTS. REACTION OF METHYLMAGNESIUM BROMIDE WITH PINACOLONE IN ETHER

No.	Concn., Grignard	Concn., Ketone	Temp.	k_3	Number of Determinations
7	0.288	0.253	−15.2	0.062 ± 0.001	18
8	0.336	0.405	−15.2	0.075 ± 0.002	16
9	0.346	0.412	−15.2	0.068 ± 0.001	4
10	0.554	0.600	−15.2	0.043 ± 0.002	5
11	0.728	0.832	−15.2	0.025 ± 0.001	11
12	0.0505	0.0594	−2.2	2.97 ± 0.075	11
13	0.288	0.253	−2.2	0.265 ± 0.028	17
14	0.732	0.832	−2.2	0.087 ± 0.001	9

TABLE III

THIRD-ORDER VELOCITY CONSTANTS. REACTION OF METHYLMAGNESIUM IODIDE WITH PINACOLONE IN ETHER

No.	Concn., Grignard	Concn., Ketone	Temp.	k_3	Number of Determinations
15	0.224	0.280	−15.2	0.053 ± 0.0014	7
16	0.558	0.574	−15.2	0.012 ± 0.0004	12
17	0.647	0.664	−15.2	0.014 ± 0.0004	8
18	0.224	0.280	−2.2	0.212 ± 0.0032	9
19	0.314	0.314	−2.2	0.138 ± 0.002	14
20	0.531	0.562	−2.2	0.066 ± 0.003	10
21	0.647	0.664	−2.2	0.065 ± 0.001	7

It was further found that the constant k_3 is dependent upon Grignard concentration. Although the third-order law is followed for any given initial concentration, there is a gradual drop of the k_3 value with increasing initial concentrations of Grignard reagent. Run 3 of Table I shows that the ketone concentration is not responsible for this behavior.

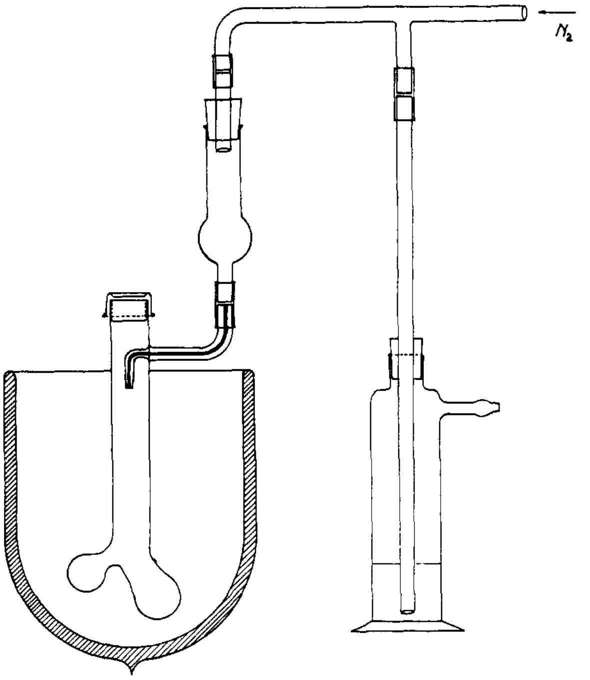

Fig. 1. Apparatus used for kinetic measurements

It is seen that this effect occurs analogously at different temperatures so that the activation energy can be calculated. The values obtained are: 11.1 ± 0.4 kcal./mole for benzophenone and methylmagnesium bromide; 14.4 ± 0.2 kcal./mole for pinacolone and methylmagnesium bromide; 15.6 ± 0.4 kcal./mole for pinacolone and methylmagnesium iodide. The dependence of the velocity constant of the Grignard reagent concentration is probably due to a concentration-dependent self-association as well as with other Grignard reagent forms which are believed to exist, and with the reaction products as the reaction proceeds. These kinetic data support the reaction mechanism of Swain.[1] Unfortunately, as indicated before, the reaction with acetone[12] could not be followed and the effort to establish this mechanism for an even wider variety of ketone structure must be deferred.

EXPERIMENTAL

Temperature control and reaction flask. The reaction flask was of the Zerewitinoff type (Fig. 1), and was continuously rinsed with dry oxygen-free nitrogen. After introducing each reagent in a compartment, the vessel was stoppered, the nitrogen stream flowing from this moment on through the safety outlet. The reaction was started by vigorous shaking, and interrupted with a 10% ammonium chloride solution. Temperature control to ± 0.1° was obtained by using eutectic mixtures of ice and sodium chloride (−21.4°), ammonium chloride (−15.2°), and sodium carbonate (−2.2°). The appropriate solutions were cooled sufficiently, while stirring, by adding liquid air or Dry Ice. The resulting slurry provided a constant temperature for several hours.

Preparation of methylmagnesium bromide. Gaseous methyl bromide was led (after drying by passage through a tower of potassium hydroxide pellets) into ether and excess magnesium ("Merck" Späne nach Grignard). After all the

TABLE IV

Run 1

a = concentration of benzophenone = 0.333 mole/l.
b = concentration of methylmagnesium bromide = 0.350 mole/l.
Temperature −21.4° ± 0.1°

$$\text{Calculation of } k_3 = \frac{1}{2t}\left[\frac{1}{(C-x)^2} - \frac{1}{C^2}\right];\ \text{where } C = \sqrt[3]{ab^2} = 0.344$$

Time (sec.)	10.0	19.2	22	28	31.5	40.0	60.0	90.0	120.0	180.0
X (% reaction)	17.0	27.0	29.6	33.4	36.0	38.0	44.7	53.0	57.0	65.0
k_3[sec.$^{-1}$ (moles/l.)$^{-2}$]	0.172	0.177	0.194	0.186	0.196	0.169	0.158	0.166	0.150	0.167

$k_3 = 0.172 \pm 0.005$

TABLE V

Run 5

Time (sec.)	45	60	92	121	180	208	270	330	520	890
X (% reaction)	12.4	15.6	23.9	27.7	32.9	35.7	43.6	47.3	55.6	63.0
k_3[sec.$^{-1}$(moles/l.)$^{-2}$]	0.40	0.40	0.46	0.44	0.39	0.40	0.46	0.455	0.45	0.41

$k_3 = 0.425 \pm 0.009$

bromide was added, keeping the temperature below 0°, the reaction mixture was stirred for 6 hr. at room temperature and about 10% of the ether was evaporated *in vacuo*, removing at once any unchanged methyl bromide. The usual procedure (refluxing reaction) gave up to 20% *excess* free bromide ion. Only the described method gave equivalent amounts of basic magnesium and bromide (checked by acid and Volhard titration). The concentration was kept about 1*M*. Clear supernatant solutions free of colloidal magnesium were obtained after the reaction mixture was permitted to stand undisturbed. Methylmagnesium iodide solution was obtained in the same way.

Reaction with benzophenone. Solutions of benzophenone (Merck "purissimum" dried on phosphorus pentoxide) were made in ether-benzene (4:1). In each run 2 ml. of this solution could be mixed with about 1 ml. of the Grignard solutions. After interruption of the reaction, the aqueous layer was extracted with ether. The volume of the extract was adjusted to 25.0 ml., and 0.10 ml. (or 1.0 ml. for run 3) of this was deluted to 10 ml. with methanol. The benzophenone concentration was followed photometrically at several wave lengths as a function of the time interval preceeding quenching. It was found very helpful to determine the initial concentration of Grignard reagent by reaction with excess ketone and quantitative analysis of the reaction mixture after infinite reaction time. Pinacolone was chosen as the ketone for this determination because it provided an easy gas-liquid chromatographic analysis. Tables IV and V give the data obtained for runs 1 and 5.

The data for run 3 of Table I are graphically represented in Fig. 2 (full line). This line deviates from what would be expected for a first-order course because the twenty-fold excess of Grignard reagent is not sufficiently high and the concentration of this reagent changes sufficiently during the reaction to have an effect upon its velocity. At the end of the reaction the Grignard reagent concentration in this case has fallen to a nineteen-fold excess which represents a 5% concentration drop. As the reaction velocity is related to the square of the Grignard reagent concentration, a correction of 10% was introduced on the graph. A perfect first-order course with a half-time of 38.0 sec. is now obtained (dotted) line). The velocity constant for this reaction was found to be $k_1 = 0.0182$ sec.$^{-1}$ which led to the value of

$$k_3 = 0.165\ \text{sec.}^{-1}\left(\frac{\text{moles}}{\text{l.}}\right)^{-2}$$

It is perhaps not without significance that the reaction mixture of benzophenone with methylmagnesium halide takes on a yellow color, which persists as long as the reaction is not completed. With benzylmagnesium halide[13] the reaction mixture was deep purple-blue. Some authors have observed the appearance of such colors at room temperature when benzylmagnesium chloride was added to benzophenone solutions,[14] but they attributed this rather to the abnormal

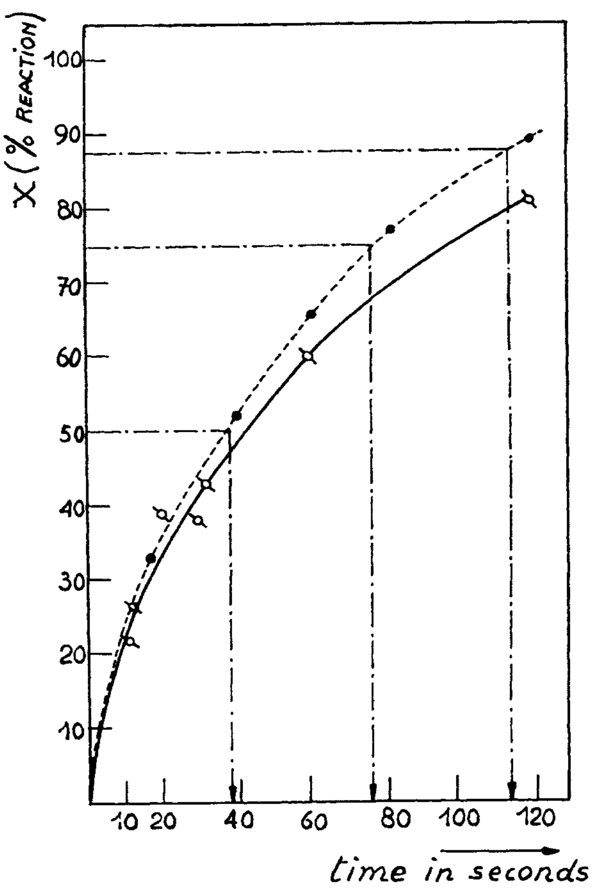

Fig. 2. Reaction of a twenty-fold excess of methylmagnesium bromide on benzophenone (run 3, Table I)

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[13] This was used immediately after preparation and before magnesium chloride precipitation started.

[14] H. Gilman and R. E. Fothergill, *J. Am. Chem. Soc.*, 51, 3149 (1929).

(radical) side reaction forming benzopinacol. The reaction on a preparative scale, however, (with 5% excess methylmagnesium bromide) under the same reaction conditions gave almost 100% of the expected carbinol.

Reaction with pinacolone. Pinacolone (3,3-dimethyl-2-butanone) was prepared following the literature.[15] The fraction with b.p. 106.0–106.5° was free of side products (2,3-dimethyl-2-butene principally) as checked by gas-liquid chromatography. The same procedure was followed as for benzophenone and the reaction mixture was directly analyzed by gas-liquid chromatography (Griffin Mark II, silicone oil 550, temp. 130–145°) by comparing with known mixtures of pinacolone and *t*-butyldimethylcarbinol.

Reaction on preparative scale gave 95% of the carbinol (b.p. 131°/760 mm.). With excess Grignard reagent no pinacolone was recovered. These facts show that only the normal addition reaction takes place, enolization and aldolization being negligible. When pinacolone was in excess the reaction constant was calculated using the equation[16]

$$k_3t = \frac{1}{a-b}\left[\frac{1}{b-x} - \frac{1}{b}\right] + \frac{203}{(a-b)^2}\,\mathrm{l.g}\,\frac{a(b-x)}{b(a-x)}$$

Acknowledgment. I thank Prof. H. Kwart for help with the presentation of this paper.

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(15) H. Gilman, *Org. Syntheses,* Coll. Vol. I, 451 (1932).

(16) J. Jungers *et al. Cinétique Chimique Appliquée* p. 84 (1958). Editions TECHNIP, Paris XVIème.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Addition of Benzylmagnesium Chloride and *p*-Chlorobenzylmagnesium Chloride to Phenyl Duryl Ketone[1]

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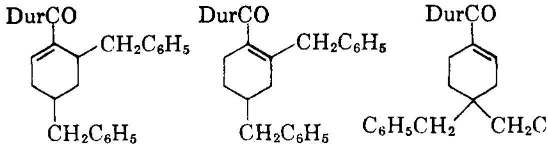
Conditions have been found under which phenyl duryl ketone reacts with two moles of benzylmagnesium chloride; the product has been shown to be duryl 2,4-dibenzyl-2,3,4,5-tetrahydrophenyl ketone. *p*-Chlorobenzylmagnesium chloride behaves in a similar way. Evidence is presented which shows that the addition of the second mole of reagent occurs before hydrolysis of the reaction mixture is begun.

Condensation of phenyl duryl ketone with benzylmagnesium chloride is known to bring about benzylation at the *para-* position of the phenyl ring.[4] If the reaction is carried out under a nitrogen atmosphere and the reaction mixture is heated under reflux for two hours, dibenzylation occurs—*i.e.*, the enolate produced by the first addition reacts with a second mole of the reagent. The dibenzyl ketone is obtained in 14% yield along with the monobenzyl ketone (15%). Chemical and spectroscopic evidence indicates that the dibenzyl ketone is a duryl dibenzyltetrahydrophenyl ketone with the double bond in conjugation with the carbonyl group. It undergoes the normal reactions of an α,β-unsaturated ketone and is reduced by lithium aluminum hydride to a duryl dibenzylcyclohexyl ketone; oxidation by alkaline hydrogen peroxide converts it into an epoxy ketone. The infrared spectrum has a carbonyl band at 1655 cm.$^{-1}$ and an olefinic band at 1638 cm.$^{-1}$ in agreement with the chemical evidence.

As the first benzyl group adds to the *para-* position of the phenyl radical, it may be assumed that one benzyl group of the dibenzyl compound is in the 4- position of the cyclohexene ring. Accordingly the most probable structures for this ketone are I, II, and III.



I II III

NMR data eliminate formula II as a possibility; the spectrum of the diaddition product (16%, carbon disulfide) has a band in the vinyl proton region at 3.66 τ that does not appear in that of the duryl dibenzylcyclohexyl ketone. This conclusion is supported by the position of the vinyl proton band in the spectrum (19%, carbon disulfide) of 1-duroylcyclohexene (3.83 τ). The ultraviolet spectrum (ethanol) has a peak at 237 mμ(ϵ 10,000) which would be expected for structures I and III but not for structure II.[5]

Dehydrogenation of the dibenzyl ketone with palladium-on-charcoal gave a diaryl dibenzyl ketone, which has been shown to have structure IV. The NMR spectrum (30%, carbon disulfide) has bands at 5.57 and 6.20 τ that can be assigned to the *ortho-* and *para-*benzylic protons, respectively.

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[1] This investigation was supported in part by a grant from the Office of Ordnance Research, U. S. Army (Contract No. DA-11-220-ORD-874).

[2] Atomic Energy Commission Predoctoral Fellow, 1951–1953.

[3] Chas. Pfizer and Co. Fellow, 1960–1961.

[4] R. C. Fuson and B. C. McKusick, *J. Am. Chem. Soc.,* 65, 60 (1943).

[5] A. E. Gillam and E. S. Stern, *Electronic Absorption Spectroscopy in Organic Chemistry,* Edward Arnold Ltd., London, 1957 (2nd ed.), p. 105.