It is significant that in almost every case unreacted benzophenone could be recovered, even when an excess of the Grignard reagent was used. Although the unreacted Grignard could be detected[18] only where it was in excess, it was undoubtedly present in every case. The failure of the color test can be attributed to the fact that the Grignard was tied up as the addition complex with benzophenone, and to the fact that the Michler ketone used in the test is even less reactive than benzophenone, the reaction rates being in the ratio of 0.313:1.[19]

The good yields obtained in anisole and phenetole can be explained by a faster, and therefore more complete, reaction. The reaction in ether can be speeded up with an excess of Grignard, as is evident from a comparison of runs 16 and 18. The yield has been increased to 80% by allowing a 4:1 excess of ethylmagnesium bromide to stand for 24 hours at 0° with benzophenone.[20] The fact that the order of mixing had little effect on the yield is further evidence of a slow reaction.

Increasing the reaction temperature, contrary to expectation, decreased the yields in each of the following pairs: 1 and 15, 3 and 16, 9 and 10, 17 and 19. The inference here is that the magnesium alcoholate produced is decomposed by heating. Perhaps even room temperature is too high.

In reactions subject to a good deal of steric hindrance the use of anisole as a solvent has resulted in a marked increase in yield (Table II). In these reactions it is probable that anisole not only increases the reaction rate, but decreases the proportion of by-products.

Two unexpected products, benzopinacol and 1,1-diphenylpropene, have been isolated from ethylmagnesium bromide and benzophenone. The benzopinacol seems to be due to some unidentified impurity in one lot of magnesium, and is associated with dark-colored Grignard solutions. Kharasch and Sayles[29] have observed such coupling reactions in the presence of manganous, ferric, cobaltous or cuprous chlorides. It is possible that our magnesium contained one of these metals. Benzopinacol was not found when the Grignard reagent was added to the ketone (inverse addition). Diphenylpropene, the dehydration product of ethyldiphenylcarbinol, seems to result from heating the reaction mixture. It was previously observed by Kharasch and Sayles, and probably constitutes the unidentified material observed by Pfeiffer and Blank.[3]

The factors which seem to have the most effect in producing good yields are: an excess of Grignard reagent,[3] a stoichiometric amount of magnesium bromide,[5] a low temperature combined with a long reaction time,[20] a solvent of low basicity like anisole. It is to be hoped that the best yields will result from a combination of all of these factors.

[29] M. S. Kharasch and D. L. Sayles, *ibid.*, **64**, 2972 (1942).

NEWARK, DELAWARE RECEIVED AUGUST 9, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

Reactivity of Substituted Benzophenones in the Grignard Reaction[1]

BY RICHARD N. LEWIS[2] AND JAMES R. WRIGHT

The relative reactivities of benzophenone and seven of its *p*-substitution products toward methylmagnesium iodide have been investigated. Relative rate constants were calculated from the relative amounts of carbinol and methane produced in competition experiments with α-naphthol. It was found that the reaction rate is increased by electron-withdrawing groups.

Hibbert,[3] in 1912, devised a rapid method for the determination of the relative reactivities of ketones toward methylmagnesium iodide. The method is based on competition between the condensation of the Grignard reagent with the ketone and its reaction with α-naphthol to produce methane. If the Grignard reagent and α-naphthol are present in equal amounts an almost quantitative yield of methane is obtained; but if a carbonyl compound is added, part of the Grignard reagent is used up in the formation of an alcohol. The more reactive the ketone the less methane will be formed, provided that the ratio of ketone to naphthol and Grignard is constant.

The object of the present work was to establish the relative reactivity of a series of *p*-substituted benzophenones in the Grignard reaction, in order to learn something about the nature of the reaction. Hibbert's procedure was followed rather closely. In brief, the ketone and α-naphthol in a 4:1 mole ratio[4] were dissolved in phenetole, and an insufficient amount of methylmagnesium iodide in phenetole was added. The amount of methane produced is shown in Table I.

It is not possible to calculate rate constants from this work, but by making certain assumptions the ratios of rate constants can be determined. We assume that both ketone and naphthol react by second order reactions; then, letting (K), (N) and (G) represent concentrations of ketone, naphthol and Grignard, and the subscripts, o and f, the original and final concentrations

$$d(K)/dt = k(K)(G);\ d(N)/dt = k_N(N)(G);$$

$$d(K)/d(N) = k(K)/k_N(N);\ \text{and}$$

$$\Delta(K) = \int_{(K)_f}^{(K)_0} d(K) \doteq \int_{(N)_f}^{(N)_0} \frac{k(K)d(N)}{k_N(N)}$$

Now the change in (K) is proportionately much smaller than the change in (N) and is never more than 18%. For the purpose of evaluating the right-hand integral, then, (K) may be considered a constant, $(K)_a$. We thus obtain

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[1] From the Ph.D. Thesis of James R. Wright, June, 1951.

[2] Olin Industries, New Haven, Conn.

[3] H. Hibbert, *J. Chem. Soc.*, **101**, 341 (1912).

[4] Hibbert used a 3:1 ratio.

TABLE I

RELATIVE REACTIVITY OF *p*-SUBSTITUTED BENZOPHENONES[a]

Substituents	Volume of methane, S.T.P. cc.[b]	%	k/k_N	k/k^0	log k/k^0	σ[c]
(Blank)[d]	4.2					
(Blank with α-naphthol)	60.7, 60.8	100[e]				
4,4'-Dichloro	36.8, 36.7	60.5	0.1921	1.485	+0.1717	+0.454[f]
4-Bromo	39.0, 39.0	64.2	.1634	1.263	+ .1014	+ .232
4-Chloro	40.2, 40.2	66.2	.1496	1.157	+ .0632	+ .227
None	42.2, 42.1	69.4	.1294	1.000	0	0
4,4'-Dimethyl	44.4, 44.3	72.9	.1096	0.847	−0.0720	−0.340[f]
4-Phenyl	45.5, 45.4	74.8	.1000	0.773	− .1117	+ .009
4,4'-Dimethoxy	48.5, 48.5	79.8	.0775	0.599	− .2228	− .536[f]
4,4'-Bis-(dimethylamino)	55.1, 54.8	90.4	.0405	0.313	− .5045	−1.38[f,g]

[a] Mole ratio of ketone to Grignard to naphthol, 4:1.27:1. [b] Results of duplicate runs, corrected for blank. [c] Ref. 5. [d] Four ml. of Grignard added to ten ml. of phenetole. [e] The average amount of methane, 60.75 cc., is taken as 100%, although the theoretical amount is 62.2 cc. [f] Twice the value for a single substituent. [g] Calculated from the data of ref. 6b.

$$\Delta(\mathrm{K}) = \frac{k(\mathrm{K})_a}{k_N}\int_{(\mathrm{N})_f}^{(\mathrm{N})_0}\frac{d(\mathrm{N})}{(\mathrm{N})} = \frac{k(\mathrm{K})_a}{k_N}\,[\ln(\mathrm{N})_0 - \ln(\mathrm{N})_f]$$

and since $(\mathrm{N})_0 = 1$

$$\Delta(\mathrm{K}) = -\frac{k(\mathrm{K})_a}{k_N}\ln(\mathrm{N})_f \text{ and } \frac{k}{k_N} = \frac{\Delta(\mathrm{K})}{(\mathrm{K})_a\ln[1/(\mathrm{N})_f]}$$

The difference between the amount of methane produced in the absence and in the presence of ketone is considered to represent the change in the amount of naphthol. The rest of the Grignard reagent was assumed to react with the ketone, since one experiment in which benzophenone was mixed with excess Grignard reagent gave an essentially quantitative yield of methyldiphenylcarbinol. The average ketone concentration, $(\mathrm{K})_a$, is closer to the initial than the final value; the value $(K)_a = (\mathrm{K})_0 - 0.4\,\Delta(\mathrm{K})$ was used in the calculations.

Hammett[5] has devised the very useful relation

$$\log k - \log k^0 = \rho\sigma$$

Fig. 1 shows the relation between log k/k^0 and substituent constant, σ, for the reaction between methylmagnesium iodide and diaryl ketones. All points but one lie close to a straight line of slope +0.362. This value is the reaction constant, ρ. The average deviation, r, is 0.018.

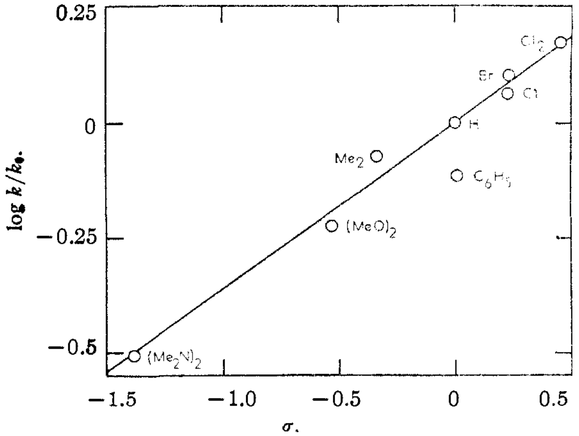

Fig. 1.—Variation of reactivity with sigma values.

The σ value −0.205 given by Hammett for the *p*-dimethylamino group does not seem to apply to reactions of benzophenone. From the kinetics of alkaline hydrolysis of ethyl benzoate in 56% acetone[6a,b,c] one can calculate a σ of −0.69 for this group.[6b] This value seemed reasonable in view of the value −0.660 for the *p*-amino group, and was therefore used in drawing Fig. 1.

The point for the *p*-phenyl group was not considered in plotting Fig. 1, because of the uncertainty of its σ; Hammett gives it as +0.009 with a probable error of 0.22. Conceivably the *p*-phenyl group could be electron-attracting in 4-aminobiphenyl, where its σ is +0.114,[7] and electron-releasing in carbonyl compounds,[6c,8] as a consideration of the appropriate resonance structures will indicate. It would then have two substituent constants like the *p*-nitro group, which has the value +1.27 in reactions of phenols and amines, and +0.778 in all other reactions. The value calculated for *p*-phenyl from this work is − 0.31 ± 0.05.

The reaction between a Grignard reagent and a ketone appears to take place in two steps[9−11]

$$\mathrm{G} + \mathrm{K} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C};\ \mathrm{G} + \mathrm{C} \xrightarrow{k_2} \mathrm{P}$$

where C is a 1:1 addition complex and P is the product, a tertiary alcoholate. If this mechanism is correct, we can assume that a steady state exists, in which the concentration of C is substantially constant during the greater part of the reaction.[12] The rate equations can thus be derived[13]

$$d(\mathrm{C})/dt = k_1(\mathrm{G})(\mathrm{K}) - k_{-1}(\mathrm{C}) - k_2(\mathrm{G})(\mathrm{C}) = 0$$

$$(\mathrm{C}) = \frac{k_1(\mathrm{G})(\mathrm{K})}{k_{-1} + k_2(\mathrm{G})}$$

$$d(\mathrm{P})/dt = k_2(\mathrm{G})(\mathrm{C}) = \frac{k_1k_2(\mathrm{G})^2(\mathrm{K})}{k_{-1} + k_2(\mathrm{G})}$$

It is evident that if k_{-1} is much smaller than $k_2(\mathrm{G})$ the rate of formation of product is propor-

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(5) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1940, pp. 184–198.

(6) (a) E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, 1801 (1938); (b) E. Tommila, *Ann. Acad. Sci. Fennicae*, Ser. **A57**, No. 13, 3 (1941); (c) E. Tommila, L. Brehmer and H. Elo, *ibid.*, Ser. **A59**, No. 9, 3 (1942); *C. A.*, **38**, 6171, 6173 (1944).

(7) N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932).

(8) E. Berliner and E. A. Blommers, *ibid.*, **73**, 2479 (1951).

(9) P. Pfeiffer and H. Blank, *J. prakt. Chem.*, **153**, 242 (1939).

(10) C. G. Swain and H. B. Boyles, THIS JOURNAL, **73**, 870 (1951).

(11) R. N. Lewis and J. R. Wright, *ibid.*, **74**, 1253 (1952).

(12) K. J. Laidler, "Chemical Kinetics," McGraw-Hill Book Company, Inc., New York, N. Y., 1950, p. 183.

(13) A similar set of rate equations is obtained if the insolubility of the Grignard–ketone complex, C, is taken into consideration.

tional to the first power of (G) and (K), so that the assumption of second-order kinetics in the rate constant calculations is reasonable.[14]

The coördination of magnesium to oxygen is an electrophilic attack, favored by electron-releasing groups in the ketone. The transfer of a negative alkyl group to the carbon in the second step is a nucleophilic attack, favored by electron-withdrawing groups such as the halogens. The experimental results show that a nucleophilic attack is the rate-determining step, as in any reaction where ρ is positive. If the electrophilic attack were not required, however, one would expect a ρ of about +2.498, which is the value for the alkaline hydrolysis of ethyl benzoates in ethanol, a reaction depending primarily on nucleophilic attack at the carbonyl group. It must be concluded that in the Grignard reaction the effects of a substituent in the two steps tend to cancel each other. A halogen, for instance, increases the reactivity of the addition complex, but reduces its rate of formation; thus the over-all effect is small. Other low reaction constants may similarly result from the second step being the rate-determining one.

Experimental

Materials.—Phenetole and the ketones were of reagent grade (Eastman Kodak Co. White Label). Methyl iodide was obtained from the General Chemical Company.

Apparatus.—A clear, colorless solution of methylmagnesium iodide in phenetole (0.8818 *M*, prepared in 67% yield), filtered through glass wool, was stored under nitrogen in a 500-cc. flask, from which it could be transferred to a 20-ml. buret by slight pressure. The buret delivered into a 100-cc. reaction-flask, which in turn was connected to a gas-buret, in which methane was collected by displacement of mercury. Pressure could be adjusted to atmospheric with a leveling bulb, final adjustment being made with the aid of a dibutyl phthalate manometer. Connections of "Tygon" tubing permitted shaking of the reaction flask.

Procedure.—The ketone (0.01110 mole) and α-naphthol (0.4000 g., 0.002775 mole) were placed in the reaction-flask and dissolved in 20 cc. of phenetole. The system was flushed with nitrogen. Exactly 4 ml. (0.003527 mole) of the Grignard reagent was admitted from the buret (ratio of ketone to Grignard to naphthol, 4:1.27:1.) The mixture was shaken for 30 seconds, and as the gas was evolved the pressure was relieved by lowering the leveling bulb. The flask was shaken after five minutes and again after ten minutes. Although all visible reaction had ceased the mixture was allowed to stand another ten minutes; then the volume, temperature and atmospheric pressure were recorded. During the reaction a second flask was charged with ketone, naphthol and phenetole, so that a duplicate run could be made immediately. All runs were made within four days, in which time no deterioration of the Grignard reagent could have occurred.[15]

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[14] Second-order kinetics were assumed in order to avoid the difficulty of integrating a third-order expression. It seems unlikely that a large error in k/k^0 would arise if the reaction were third order, as would be the case if k_{-1} were greater than $k_1(G)$. However, the ratio k/k_N would have no meaning, since the units of second- and third-order constants are different.

[15] E. P. Kohler, J. F. Stone, Jr., and R. C. Fuson, THIS JOURNAL, **49**, 3181 (1927).

NEWARK, DELAWARE RECEIVED AUGUST 20, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

The Rearrangement of Some Disubstituted Cyclic Ketones: An Unusual Dienone–Phenol Rearrangement[1]

BY ELLIOT N. MARVELL AND ADOLPH O. GEISZLER

The preparation and rearrangement of two 1-oxo-2,2-dialkyl-1,2-dihydronaphthalenes are described. Evidence for the structure of these compounds is given and the products of the rearrangements are identified as 3,4-dialkyl-1-naphthol derivatives. This rearrangement is most unusual since the same products are obtained upon rearrangement of 1-oxo-4,4-dialkyl-1,2-dihydronaphthalenes under identical conditions.

Six carbon cyclic ketones containing two double bonds, whether exo- or endocyclic, rearrange under acid catalysis into phenolic derivatives. This rearrangement, known as the dienone–phenol rearrangement, has incurred some interest recently because it is valuable in the synthesis of steroid materials.[2] A thorough knowledge of the course of the rearrangement, therefore, is desirable. If both the double bonds are endocyclic, the rearrangement to a phenol is spontaneous unless the process is blocked in some manner. Normally this blocking consists in the presence of two radicals or atoms directly attached to one carbon atom of the ring, thereby preventing aromatization. Under acid conditions one of these groups may be caused to migrate permitting the aromatization to proceed. However, all of the known examples of this type of dienone–phenol rearrangement possess the blocking groups on the carbon atom gamma to the ketone.

A mechanism for the dienone–phenol rearrangement, similar to the mechanism postulated for the retrograde pinacolinic rearrangement, has been suggested by Arnold.[3] According to this conception of the rearrangement the presence of the blocking groups on the carbon alpha to the ketone should not alter the course of the reaction. An investigation of some cases of the rearrangement involving such blocking, therefore, was undertaken and the results are described here.

Since the simple dienones of the cyclohexane series are relatively difficult to synthesize, the dihydronaphthalene system was chosen. Two examples were picked because the analogous γ-blocked systems had been studied previously[3,4] and because the expected products are known.

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[2] A list of references to work in the steroid series is given in footnote 3 of an article by R. B. Woodward and T. Singh, THIS JOURNAL, **72**, 494 (1950).

[3] R. T. Arnold, J. Buckley and J. Richter, *ibid.*, **69**, 2322 (1947).

[4] R. T. Arnold, J. S. Buckley and R. M. Dodson, *ibid.*, **72**, 3153 (1950).