

intensity was observed which may have been the desired 1-butyl-2-methyl-6-phenyl-4(1H)-pyridone (15). None of the triketone 4 was detected. Similarly, tlc of the crude reaction product showed three spots.

In two other experiments in which diketoenamine 13d was treated with a much larger excess of PPA (ten times the amount used above), the pyrone 16 (once recrystallized) was isolated in yields of 50–60%. A further purified sample was analyzed.

Anal. Calcd for C₁₂H₁₀O₂: C, 77.40; H, 5.41. Found: C, 77.18; H, 5.49.

Registry No.—4, 1469-95-0; 6, 7294-90-8; 7, 7294-91-9; 13a, 14337-92-9; 13b, 14337-93-0; 13c, 14337-94-1, 13d, 14337-95-2; chelate of 13d, 14481-59-5; 14a, 14337-87-2; 14b, 7143-75-1; 14c, 14337-85-0; 16, 1013-99-6.

A Kinetic Study of the Reduction of Di-*t*-butyl Ketone with *t*-Butylmagnesium Compounds¹

MALCOLM S. SINGER,² RUDOLF M. SALINGER, AND HARRY S. MOSHER

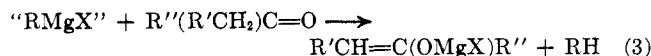
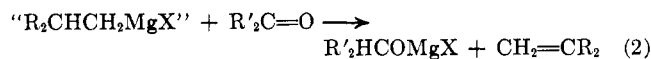
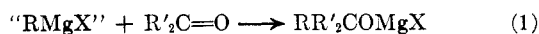
Department of Chemistry, Stanford University, Stanford, California 94305

Received July 28, 1967

The rates of the reduction of di-*t*-butyl ketone with di-*t*-butylmagnesium and with the Grignard reagent from *t*-butyl chloride in tetrahydrofuran solvent have been studied and the reactions found to obey competitive consecutive second-order kinetics with $k_1 = 10k_2$ for the di-*t*-butylmagnesium reagent and $k_1' = 3.3k_2'$ for the Grignard reagent. The rates of the reductions by these two reagents under comparable conditions were very nearly the same. Mechanistic interpretations of these results, especially those from the Grignard reagent, are complicated by several factors which are discussed.

The recent publication by Ashby, Duke, and Neuman³ on the kinetics of the Grignard *addition* reaction has prompted us to publish results on a kinetic study of the Grignard *reduction* reaction.

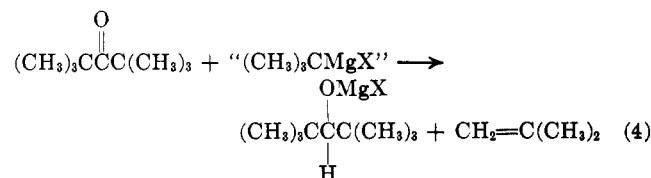
The products of the reaction of Grignard reagents or dialkylmagnesium compounds with ketones arise from either addition (eq 1), reduction (eq 2), or enolization (eq 3), or a combination of these reactions. Here



“RMgX” is used to represent the Grignard reagent from RX without purporting to suggest any specific structure and without designating the associated solvent. These equations can also be used to represent the reactions of dialkylmagnesium compounds if X is replaced by R. This second R group may (or may not) react further with another molecule of ketone. The *relative* rates of addition, reduction, and enolization have been studied^{4,5,6} as well as the kinetics of the addition reaction alone.^{3,7} We are unaware of any kinetic study aimed specifically at the reduction reaction of Grignard reagents and/or dialkylmagnesium compounds.

The system chosen for study was the reaction of di-*t*-butyl ketone (2,2,4,4-tetramethyl-3-pentanone) with a

t-butyl Grignard reagent and with di-*t*-butylmagnesium. Hereafter in this paper R will be used exclusively to represent the *t*-butyl group.



The choice of di-*t*-butyl ketone precludes the enolization reaction (eq 3) and the use of the sterically hindered ketone and bulky Grignard reagent not only prevents the addition reaction⁸ (eq 1) but also causes the reduction reaction to proceed at a conveniently slow rate.

Results

The rate of appearance of product was followed by quenching aliquots or individual samples of the reaction mixture at appropriate intervals with 1 *M* ammonium chloride solution and determining the relative amounts of starting material (di-*t*-butyl ketone) and product (di-*t*-butylcarbinol) by gas chromatography. The original experiments were in ether solvent but the gradual formation of a precipitate in the reaction mixture as it progressed forced a change to tetrahydrofuran (THF) solvent in which the reaction was completely homogeneous. The results of the kinetic investigations are summarized in Table I for the di-*t*-butylmagnesium reagent and in Table II for the Grignard reagent from *t*-butyl chloride. Figure 1 is representative of the second-order rate plots for the data from the Grignard reagent experiments. The plots for the di-*t*-butylmagnesium experiments were entirely analogous. In those experiments in which the *t*-butyl Grignard reagent or di-*t*-butylmagnesium reagent were in excess, the ketone was completely used and the rate followed second-order kinetics (as indicated in Figure 1)

(1) We gratefully acknowledge support by the National Science Foundation (RG955 and GP-6738) for these investigations.

(2) Taken in part from the M. S. Thesis of M. S. Singer, Stanford University, Stanford, Calif., 1963. Complete presentation of the data on the *t*-butyl Grignard reductions can be found in this source.

(3) E. C. Ashby, R. B. Duke, and H. M. Neuman, *J. Am. Chem. Soc.*, **89**, 1964 (1967).

(4) J. Miller, G. Gregoriou, and H. S. Mosher, *ibid.*, **83**, 3966 (1961).

(5) D. O. Cowan, Ph.D. Thesis, Stanford University, Stanford, Calif., 1962.

(6) H. O. House and D. D. Traficante, *J. Org. Chem.*, **28**, 355 (1963).

(7) (a) N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1963). (b) M. Anteunis, *J. Org. Chem.*, **26**, 4214 (1961); **27**, 596 (1962). (c) C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, **73**, 870 (1951). (d) J. G. Aston and S. A. Bernhard, *Nature*, **165**, 485 (1950). (e) S. G. Smith and G. Su, *J. Am. Chem. Soc.*, **86**, 2750 (1964). (f) M. Oki, *Tetrahedron Letters*, 1785 (1967).

(8) F. C. Whitmore and R. S. George, *J. Am. Chem. Soc.*, **64**, 1239 (1942).

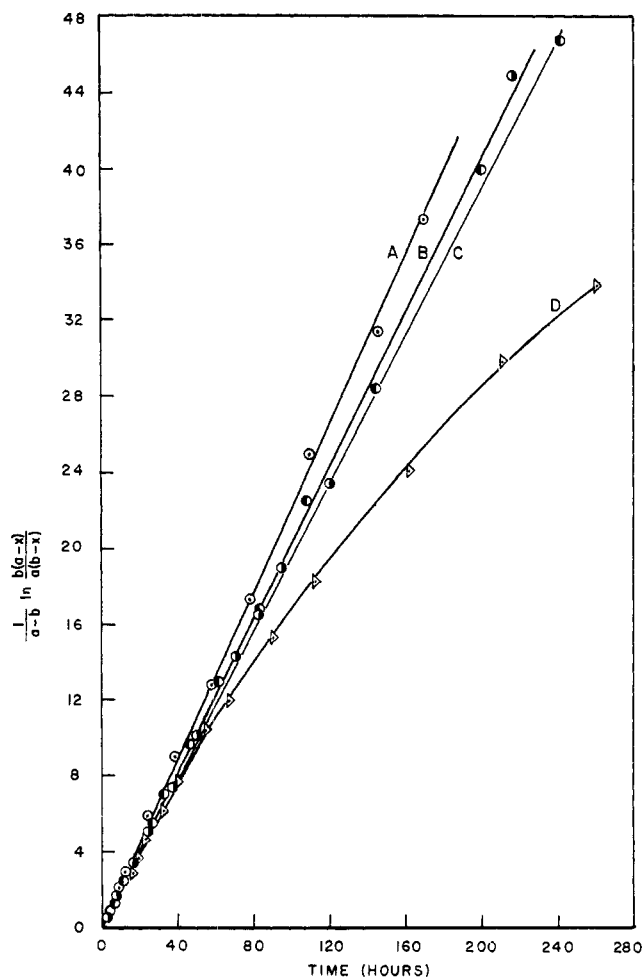


Figure 1.—Second-order plots for the reaction of the Grignard reagent from *t*-butyl chloride with di-*t*-butyl ketone in tetrahydrofuran at 45.2°: A, 0.114 *N* Grignard reagent, 0.0285 *N* ketone; B, 0.114 *N* Grignard reagent, 0.057 *N* ketone; C, 0.228 *N* Grignard reagent, 0.114 *N* ketone; D, 0.228 *N* Grignard reagent, 0.228 *N* ketone. In this case the plot is $x/[a(a-x)]$ vs. time. The last plotted points in A, B, C, and D represent, respectively, 96.7, 99.7, 96.4, and 79.4% completion of the reaction.

throughout 95% of the reaction. The rate constants for simple second-order kinetics in Tables I and II were obtained from the slope of the usual second-order rate plots as indicated in Figure 1. In these reactions no evidence for any product other than di-*t*-butylcarbinol was observed either by gas chromatography or preparative work-up of reaction mixtures.

When the organomagnesium compound and ketone were in equivalent amounts (*i.e.*, one magnesium-bound *t*-butyl group per ketone molecule), about 85–90% of the ketone was converted to carbinol and 10–15% of ketone was recovered from the hydrolyzed reaction mixture. The reason for this incomplete conversion is not known. A small amount of thermal decomposition of the Grignard reagent or di-*t*-butylmagnesium may occur upon heating to 45.2° (the temperature used for most of the kinetic runs), since traces of isobutylene were detected in the vapor above a sample of di-*t*-butylmagnesium stored for 5 weeks at room temperature, but specific studies aimed at observing this decomposition showed less than 10% decomposition at 66° over 2 weeks. Thus this by itself cannot be the cause of the incomplete utilization of ketone in

TABLE I
RATES OF REACTION OF DI-*t*-BUTYLMAGNESIUM
WITH DI-*t*-BUTYL KETONE
 $R_2Mg + R_2CO \xrightarrow[k_2]{k_1} (R_2CHO)_2Mg + 2CH_2=C(CH_3)_2$
THF solvent, 45.2°

Concn of R_2Mg , ^a moles/l.	Concn of R_2CO , ^a moles/l.	Rate constant, ^c l./moles sec $\times 10^4$
0.114	0.114	k_1 1.8
0.114	0.228	k_1 1.8
		k_2 0.1
0.114	0.456	k_1 1.9
0.057	0.057	k_1 1.7
0.057	0.114	k_1 1.5
		k_2 0.2
<i>b</i>	0.114	k^b 0.4

^a The *t*-butyl group is represented by R. The concentration was determined by titration for basic magnesium. This solution was less than 0.001 *N* in chloride. ^b In this experiment, additional ketone was added to the reaction mixture of 0.114 *M* R_2Mg and 0.114 *M* R_2CO , from the first example in the above table, after the reaction mixture had been allowed to stand for 384 hr. The initial reaction (half-life of 13.5 hr) as symbolized by k_1 was 98% complete after 170 hr. The calculation of k^b was then carried out for the second-order rate at which the reaction resumed after additional ketone was added. ^c When a single k_1 is recorded this was calculated as a simple second-order rate constant. When both k_1 and k_2 are recorded, these were calculated according to the method of A. A. Frost and W. C. Schwemer, *J. Am. Chem. Soc.*, **74**, 1268 (1952), for a competitive second-order process.

TABLE II
RATES OF REACTION OF GRIGNARD REAGENT^a FROM *t*-BUTYL
CHLORIDE WITH DI-*t*-BUTYL KETONE IN THF AT 45.2°

Concn of $RMgCl$, ^b moles/l.	Concn of R_2CO , ^b moles/l.	Rate constant, ^c l./mole sec $\times 10^4$
0.228	0.228	k_1' 5.8
		k_2' 1.9
0.228	0.114	k_1' 5.8
0.228	0.057	k_1' 6.5
0.114	0.0285	k_1' 6.4
0.114	0.057	k_1' 5.9
0.114	0.114	k_1' 5.8
		k_2' 1.8
0.228 ^d	0.228	k_1' 4.7
		k_2' 1.8

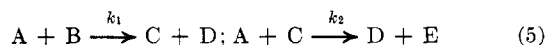
^a The concentration of the Grignard reagent from *t*-butyl chloride is calculated as $RMgCl$ and experimentally is the concentration of basic magnesium by titration of aliquots after hydrolysis with dilute hydrochloric acid to a phenolphthalein end point. This Grignard solution had a chloride concentration by Volhard titration of 0.239 *N*. ^b R represents the *t*-butyl group. ^c These rate constants are calculated from the data in Table III. If the rates had been calculated on the basis of $R_2Mg_2Cl_2$ the molar concentration would be 0.5 and the rate constants doubled. The second-order rate constants k_1' when Grignard is in excess are obtained from the slope of the usual second-order rate plot. When the Grignard reagent and ketone were present in equivalent amounts, k_1' and k_2' were obtained for a competitive consecutive second-order process as given in ref 10 and 11. ^d The Grignard reagent from *t*-butyl bromide instead of chloride.

these experiments. It is possible that a small amount (10 to 15% at most) of the organomagnesium *t*-butyl groups are being removed by some simultaneous competitive but unknown reaction. Oxygen was rigorously excluded, and it seems unlikely that this result can be ascribed to the reaction of Grignard reagent with traces of oxygen. It is possible that a small percentage of the *t*-butyl groups on magnesium are "tied-up" by some unreactive complex with oxygen-containing products such as $RMgX \cdot (R'OMgX)_n$ (where X may also be OR'). Anteunis^{7b} has made this

latter suggestion in another context. Nesmeyanov⁹ as well as Bikales and Becker^{7a} have demonstrated that the previously claimed cases of relatively stable complexes between Grignard reagents and *carbonyl compounds* can be explained successfully in other ways. Thus, if such an unreactive complex with RMgX is involved, it must be with the magnesium alcoholate products. For a reaction starting with equivalent amounts of ketone and magnesium-bound *t*-butyl groups which utilizes 90% of these *t*-butyl groups this would mean not more than one out of ten groups were "tied-up" in such a complex. It is therefore likely that, if this is the explanation, the complex has several alkoxy groups associated with each RMgX.

Discussion

When the *molar* ratio of di-*t*-butylmagnesium to ketone was 1:2 (*i.e.*, one *t*-butyl group from the organomagnesium compound per ketone molecule) the rate of the reaction followed simple second-order kinetics *only for the first third of the reaction*. A plot of $x/a[(a-x)]$ vs. time showed no significant deviation from linearity in the very early stages of the reaction; zero intercept was within experimental error. The rate for the latter part of the reaction decreased markedly from that expected of a simple second-order process. The rate data for such experiments do not fit first-order dependence upon R_2Mg nor second-order dependence upon R_2Mg with random utilization of R groups. Second-order plots of the data for reactions using *equivalent* amounts of R_2Mg and R_2CO became seriously nonlinear after the first third of the reaction. The best agreement for a kinetic scheme was found for a competitive consecutive second-order reaction sequence.

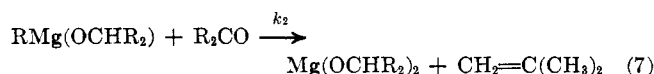


A relatively simple mathematical solution to competitive, consecutive second-order kinetics is available when the concentration of one reactant is twice that of the other.¹⁰ A computer program has been devised for such systems,¹¹ but numerical values for the rate constants k_1 and k_2 shown in Tables I and II were obtained by using the extended numerical data already published.^{10,11}

From the calculated rate constants given in Table I it is seen that k_1 , the rate of this initial reaction, is *ca.* ten times as large as k_2 for the di-*t*-butylmagnesium reagent. One can only speculate concerning the nature of the species involved in the slow second stage of the reduction reaction represented by k_2 . The simplest postulate is that the initial reaction proceeds by rate k_1 (eq 6) to give the *t*-butylmagnesium alkoxide



species $RMg(OCHR_2)$. This intermediate then can react with ketone at rate k_2 (eq 7). Magnesium alk-

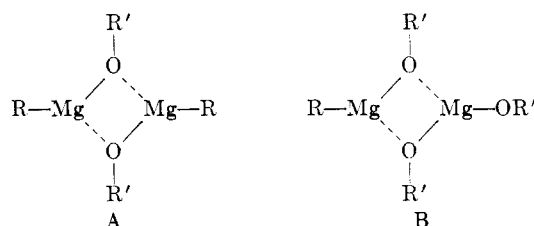


(9) A. N. Nesmeyanov, "Selected Works in Organic Chemistry," The Macmillan Co., New York, N. Y., 1963, pp 259-262.

(10) A. A. Frost and W. C. Schwemer, *J. Am. Chem. Soc.*, **74**, 1268 (1952); W. C. Schwemer and A. A. Frost, *ibid.*, **73**, 4541 (1951).

(11) C. A. Burkhard, *Ind. Eng. Chem.*, **52**, 678 (1960).

oxides are apparently associated in ether solution.¹² Therefore, one might expect that the initial product in eq 6 would complex strongly with other organometallic reagents in solution. Thus the actual process may not be as simple as eq 6 and 7 would indicate. For instance, two of the alkylmagnesium alkoxide species might complex in a rapid process to give a dimer which could have structure A with associated solvent



molecules. The R groups in A logically might be expected to have a lowered reactivity in the later stages of the reduction reaction as observed. This alternative suggests that there would be a third rate constant k_3 corresponding to the reactivity of the final R group in B. Since this would become most important in the rate process during the last part of the reaction, this alternative might be indistinguishable experimentally from the simple postulate of eq 6 and 7 especially if k_3 did not differ greatly from k_2 .

In theory this type of alternative could be complicated by the equilibrium represented by eq 8. The

$$2RMg(OCHR_2) \rightleftharpoons R_2Mg_2(OCHR_2)_2 \rightleftharpoons R_2Mg + Mg(OCHR_2)_2 \quad (8)$$

present data are incompatible with a facile equilibrium such as eq 8 *which is shifted predominantly to the right*. If this were the case, the reaction should not show the competitive consecutive second-order kinetics observed. Furthermore, these data are probably not compatible with a kinetically important complexing of the intermediate $RMgOCHR_2$ with the initial R_2Mg . Assuming that the rate of reduction of the ketone by a complex such as $R_2Mg \cdot RMgOCHR_2$ was appreciably different from that of R_2Mg alone, one would expect the deviation from second-order kinetics to be apparent earlier in the reaction than actually observed. Nevertheless, such equilibria could be involved to a minor extent without being detected kinetically.

In order to gain more information concerning the slow second stage, one of the reaction mixtures (Table I, line 1) with di-*t*-butylmagnesium initially present in twice the stoichiometric amount (*i.e.*, two magnesium-bound *t*-butyl groups for each ketone molecule) was allowed to react for 30 half-lives (384 hr). Additional ketone was then added in order to react with the remaining organomagnesium alkyl groups (Table I, line 8). If equilibration of the initially formed

(12) (a) H. O. House, A. Latham, and G. M. Whitesides, have determined that the i value for 0.112 *M* solution of methylmagnesium 3-methyl-3-pentoxide is 2.8. We wish to thank Professor House for the opportunity of seeing a preprint of this work prior to publication. (b) The sensitivity of Grignard association measurements to the presence of oxygen is evidently caused by association of alkylmagnesium alkoxy species: A. D. Vreugdenhil and C. Blomberg, *Rec. Trav. Chim.*, **82**, 453, 461 (1963); **83**, 1096 (1964); **84**, 39 (1965). (c) For further studies on alkylmagnesium alkoxides see D. Bryce-Smith and B. J. Wakefield, *Proc. Chem. Soc.*, 376 (1963); 2483 (1964). (d) Experiments implicating alkylmagnesium alkoxy species as intermediates in Grignard reactions have been described: H. O. House and D. D. Traficante, *J. Org. Chem.*, **28**, 355 (1963); H. O. House and W. L. Respass, *ibid.*, **30**, 301 (1965).

TABLE III^a
 REACTIONS OF THE GRIGNARD REAGENT FROM *t*-BUTYL HALIDE WITH DI-*t*-BUTYL KETONE IN TETRAHYDROFURAN AT 45.2°

	(1) 0.228 N " <i>t</i> -Bu-MgCl" + 0.228 M <i>t</i> -Bu ₂ C=O										
Time, hr	2.0	4.0	6.0	9.0	12.0	23.5	31.0	39.0	63.0	121	193
% reaction	10.8	18.2	24.9	31.5	36.3	52.5	59.2	65.0	71.0	77	81
	(2) 0.228 N " <i>t</i> -BuMgCl" + 0.114 M <i>t</i> -Bu ₂ C=O										
Time, hr	2.0	4.0	6.0	8.0	12.0	16.0	21.0	33.0	50.1	81.0	216
% reaction	11.6	18.3	24.0	31.2	41.5	49.6	57.0	70.8	81.4	91.8	99.7
	(3) 0.228 N " <i>t</i> -BuMgCl" + 0.057 M <i>t</i> -Bu ₂ C=O										
Time, hr	1.75	3.0	4.5	6.0	8.0	12.0	17.0	27.0	48.5	84.0	170
% reaction	8.3	15.0	20.6	27.8	34.1	47.0	57.2	73.1	89.1	97.3	99.8
	(4) 0.114 N " <i>t</i> -BuMgCl" + 0.0285 M <i>t</i> -Bu ₂ C=O										
Time, hr	2.0	4.0	6.0	9.0	15.0	23.0	38.0	58.0	97.0	121	268
% reaction	6.25	11.6	17.4	22.8	31.2	52.9	60.7	75.6	89.1	92.6	99.1
	(5) 0.114 N " <i>t</i> -BuMgCl" + 0.057 M <i>t</i> -Bu ₂ C=O										
Time, hr	3.5	6.0	10.0	14.0	22.5	33.0	46.0	71.0	118	168	300
% reaction	9.8	12.5	20.2	28.4	39.3	49.8	60.0	72.2	85.6	92.0	98.1
	(6) 0.114 N " <i>t</i> -BuMgCl" + 0.114 M <i>t</i> -Bu ₂ C=O										
Time, hr	4.0	8.0	16.5	27.0	40.0	55.0	77.0	162.0	210	260	366
% reaction	9.2	16.5	28.5	38.8	47.3	54.3	61.6	73.4	77.4	79.4	81.3
	(7) 0.228 N " <i>t</i> -BuMgBr" + 0.228 M <i>t</i> -Bu ₂ C=O										
Time, hr	2.0	5.0	7.5	9.0	12.8	24.0	32.0	38.8	62.1	97.0	
% reaction	7.6	14.0	20.6	25.1	31.6	45.1	52.8	57.8	65.7	74.2	

^a These are selected values from much more extensive data.²

alkylmagnesium alkoxide had occurred and was substantially to the right as represented in eq 8, the subsequent reaction with the liberated R₂Mg would have started again at a rate represented by rate constant k_1 . If no equilibration had occurred or if it occurred very slowly and was displaced to the left, as written in eq 8, the reaction should resume at a rate characterized by k_2 . Actually the observed new rate, k^b , was about twice that predicted for nonequilibration and one-fifth that expected for an equilibrium displaced to the right, *i.e.*, $k^b = 2k_2 = 0.2k_1$. These results are therefore not definitive but are certainly incompatible with a rapid equilibrium (eq 8) displaced toward the di-*t*-butylmagnesium.

All of these results cannot positively reveal the nature of the intermediate between reactions represented by k_1 and k_2 ; the conclusion is firm, however, that the first R group in di-*t*-butylmagnesium reacts approximately ten times faster than the second R group.

When the di-*t*-butylmagnesium was in excess of the ketone only k_1 was calculated using the approximation that only the first *t*-butyl group would react since k_1 was shown to be ten times k_2 . Graphical analysis of the data from such experiments where there were two *t*-butyl groups for each ketone molecule indicated that simple second-order kinetics were followed for the first 60% of the reaction; where there were four magnesium-bound *t*-butyl groups per each ketone molecule such second-order kinetics were followed through 80 to 95% of the reaction. It is important to note that this competitive consecutive second-order aspect of the R₂Mg reaction will be clearly demonstrated only when near equivalent amounts of reagents are being employed and when the reaction is followed beyond 50% reaction.

The kinetics of the reduction reaction of the Grignard reagent from *t*-butyl chloride with di-*t*-butyl ketone in tetrahydrofuran (Table III) were qualitatively similar to the kinetics found for the di-*t*-butylmagnesium reductions (Table IV). When the Grignard reagent was

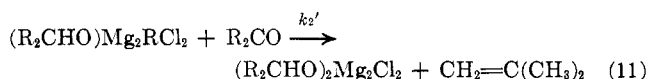
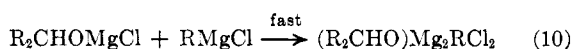
in fourfold excess (4 equiv, as measured by basic magnesium titration, per ketone molecule), a standard second-order plot was linear to 95% reaction (Figure 1). With twofold excess of Grignard reagent, second-order plots were linear to 80% reaction or better, but when equivalent amounts of Grignard reagent and ketone were allowed to react there was serious deviation from linearity for second-order plots starting at about 40% reaction. This deviation could be rationalized by application of the competitive, consecutive second-order analysis^{10,11} assuming that the first reaction stage goes with a rate k_1' which is 3.3 times faster than rate k_2' for the second stage of the reaction, whatever it may be. The differences in rates (3.3:1) between the first and second stages in these *t*-butyl Grignard reduction reactions is not so great as that observed (10:1) between the comparable stages of the di-*t*-butylmagnesium reductions. The rate constants are given in Table II where the concentration of Grignard reagent is based on the equivalents of basic magnesium by titration. The necessary information concerning the molecularity of *t*-butyl Grignard solutions in THF in this concentration range is not available. The recent work of Ashby and Walker¹³ shows an *i* value of approximately 2 for the Grignard reagent from *t*-butyl chloride in ether over the concentration range 0.2 to 2.0 M. Since the Grignard reagent from ethyl chloride in ether shows a higher *i* value than this and since the *i* value for the Grignard reagent from ethyl chloride in THF in the same concentration range is approximately 1, it is at least reasonable to assume that the *i* value for the *t*-butyl reagent in THF will also be about 1. The conclusion of competitive consecutive second-order kinetics in this reaction is in no way dependent upon the assumed structure of the Grignard reagent as either *t*-BuMgCl, *t*-Bu₂Mg₂Cl₂, or *t*-Bu₂Mg+MgCl₂. The numerical value of the rate constants will, of course,

(13) E. C. Ashby and F. Walker, *J. Organometal. Chem. (Amsterdam)*, **7**, 17 (1967).

TABLE IV
REACTIONS OF DI-*t*-BUTYLMAGNESIUM WITH DI-*t*-BUTYL KETONE IN TETRAHYDROFURAN AT 45.2°

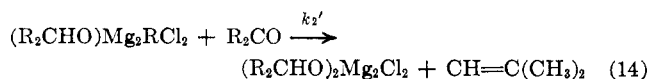
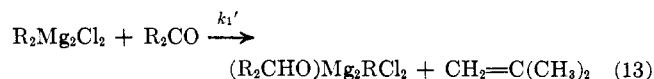
	(1) 0.114 M <i>t</i> -Bu ₂ Mg + 0.114 M <i>t</i> -Bu ₂ C=O									
Time, hr	2.0	4.0	6.0	8.0	12.6	24.0	29.0	35.5	60.1	170
% reaction	11.4	21.9	30.8	36.7	48.6	66.4	70.4	76.4	82.2	98.0
	(2) 0.114 M <i>t</i> -Bu ₂ Mg + 0.228 M <i>t</i> -Bu ₂ C=O									
Time, hr	2.0	4.0	6.0	8.0	12.0	24.0	37.3	56.5	76.3	120.5
% reaction	11.3	19.8	26.5	32.4	40.7	50.6	55.3	59.8	63.2	71.4
	(3) 0.114 M <i>t</i> -Bu ₂ Mg + 0.456 M <i>t</i> -Bu ₂ C=O									
Time, hr	1.0	2.0	4.0	6.0	8.0	24.0	32.0	48.0	78.0	
% reaction	12.8	22.4	33.4	40.8	47.2	65.4	69.2	71.6	79.4	
	(4) 0.057 M <i>t</i> -Bu ₂ Mg + 0.057 M <i>t</i> -Bu ₂ C=O									
Time, hr	2.0	4.0	8.0	12.0	24.5	30.0	32.0	49.0	74.0	80.0
% reaction	5.4	11.6	23.0	29.4	46.7	52.2	51.4	65.4	73.6	76.8
	(5) 0.057 M <i>t</i> -Bu ₂ Mg + 0.114 M <i>t</i> -Bu ₂ C=O									
Time, hr	2.0	4.0	7.0	11.0	24.3	36.5	48.0	72.0	98.0	148
% reaction	7.1	11.7	17.2	24.0	38.1	45.5	49.1	56.8	61.3	70.0
	(6) 0.114 M <i>t</i> -Bu ₂ C=O added to reaction 1, 214 hr after (1) was 98% complete (384 hr after start of reaction 1)									
Time, hr	5.0	7.5	24.0	29.0	48.5					
% reaction	21.6	24.8	36.8	39.6	48.4					

depend upon concentration term used. In any event, the values for k_1' and k_2' in Table II have been arrived at on the basis of an RMgCl formulation of the Grignard reagent using the basic magnesium concentration equivalent to the Grignard concentration. The mechanistic interpretation of these results are more obscure than those from the case of the di-*t*-butylmagnesium reagent because of the variety of schemes which might account for the observed results. One possible but by no means unique scheme which would account for the kinetics would be the initial reaction of Grignard and ketone according to eq 9 by rate k_1' followed by a



fast complexing of the initial product with the initial Grignard reagent (eq 10) which would then be followed by a slower reaction of the complex and ketone by rate k_2' (eq 11) to give product. Such a scheme is not illogical since the magnesium alcoholate would be a stronger base than the ether solvent and should thereby displace the complexed ether of the Grignard reagent.

Alternatively the kinetic behavior alone can be explained by an initial fast reaction to form an associated species (eq 12) which is more reactive in the reduction



reaction than RMgCl. This fast equilibrium is then followed by a process in which the two R groups react successively with ketone molecules according to eq 13 and 14 by rates k_1' and k_2' . There are obvious complications possible in such a scheme including the dissociation of the product in eq 13, the reverse of eq 10.

It has been postulated^{4,5,7b,14,15} that this equilibrium, which is also related to that of eq 8, is catalyzed by magnesium halide. If this is a facile equilibrium¹⁶ in the *t*-butyl case it must be displaced to the left; otherwise, the rate in later stages of the reaction would not fall off as observed.

Still another complication which could conceivably accommodate the kinetics is the extension of eq 12 to include dissociation of the complex $\text{R}_2\text{Mg}_2\text{Cl}_2$ to give R_2Mg and MgCl_2 (*i.e.*, the Schlenk equilibrium). According to this scheme the Schlenk equilibrium would need to be fast with respect to the reduction reaction so that regardless of the position of the Schlenk equilibrium the concentration of R_2Mg , even though very small, would be proportional to that of RMgCl. A second requirement of this scheme would be that the species R_2Mg would of necessity need to be many times more reactive than RMgCl (or $\text{R}_2\text{Mg}_2\text{Cl}_2$). Under these circumstances the R_2Mg could then react as previously discussed according to eq 6 and 7. It is obvious that the possible complications in the *t*-butyl Grignard case, as contrasted with the di-*t*-butylmagnesium case, are so numerous that definite mechanistic conclusions cannot be made beyond the fact that the kinetic data fit competitive consecutive second-order kinetics in which the second stage is slower by a factor of 0.333 than the first stage.

It is noteworthy that the relative rates of this reduction reaction using either the di-*t*-butylmagnesium reagent or the Grignard reagent from *t*-butyl chloride are very nearly the same. For instance, the half-life of the reaction of 0.228 M ketone with 0.228 M Grignard reagent at 42.5° in THF was 21 hr while the half-life of the 0.114 M dialkylmagnesium reagent with the same ketone concentration was 24 hr. This similarity in rates for the reduction reaction for these two reagents is in contrast to the reports that the rate of the addition of dimethylmagnesium to acetone is many times greater

(14) M. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1962).

(15) D. O. Cowan and H. S. Mosher, *J. Org. Chem.*, **28**, 204 (1963).

(16) Professor H. O. House, in a personal communication, indicates that nmr studies have established that in other cases this is a fast reaction on an nmr time scale which is shifted far to the left. NOTE ADDED IN PROOF.—This work has now been published: H. O. House, R. A. Latham, and G. M. Whitesides, *J. Org. Chem.*, **32**, 2481 (1967). We wish to thank Professor House for communicating these results before publication.

than that of the corresponding Grignard reagent¹⁷ and twice as fast^{7a} in its addition to benzophenone.

Other cases where there is an unusual decrease in reactivity of organomagnesium compounds as the reaction progresses have been observed in the reaction of diethylmagnesium and ethylmagnesium bromide with benzonitrile in THF,¹⁸ methylmagnesium bromide with benzophenone in THF,^{7a} ethylmagnesium bromide with benzalaniline in ether,¹⁹ diethylmagnesium (but not ethylmagnesium bromide) with hexyne-1 in ether,²⁰ and dimethylmagnesium with benzophenone in ether-benzene.^{7b}

The progress of the reduction of di-*t*-butyl ketone with the Grignard reagent *in ether* could be followed, but the slow formation of a precipitate as the reaction progressed renders any mechanistic conclusions rather tenuous.² It was observed, however, that the reduction by the Grignard reagent from *t*-butyl chloride in ether was about eight times faster than in THF. It was also apparent that the rate in ether² decreased in a fashion consistent with the competitive consecutive second-order kinetics found in THF solvent with k_1/k_2 very roughly equal to 20.

Experimental Section

Reagents.—Tetrahydrofuran, ethyl ether, and dioxane were distilled under nitrogen from lithium aluminum hydride or from a Grignard reagent. *t*-Butyl chloride was fractionated through an efficient column immediately before use. Because vapor phase chromatography showed the presence of isobutylene, indicating some thermal decomposition during distillation, the distillate was collected over anhydrous potassium carbonate to remove the hydrogen chloride which must also be formed. Di-*t*-butyl ketone (2,2,4,4-tetramethyl-3-pentanone) was prepared by the method of Percival, Wagner, and Cook.²¹ The yield of material of about 98% purity was 75%. Impurities of neopentyl alcohol, neopentyl trimethylacetate, and di-*t*-butylcarbinol were removed by purification on a Megachrom preparative vapor phase chromatograph, using 10% UCON Polar on firebrick packing. It was subjected to a final distillation under nitrogen to remove any traces of UCON Polar which might have been carried over from the gas chromatography.

The Grignard reagent from *t*-butyl chloride was prepared in an all glass apparatus similar to that used by Miller, *et al.*,³ which was modified by removal of the reactant mixing flasks and mixing chamber and substitution of a single reaction vessel.² Analysis of the Grignard reagent in tetrahydrofuran used in most of the studies reported here showed 0.454 *N* basic magnesium and 0.479 *N* chloride.

Di-*t*-butylmagnesium.—A solution of *t*-butylmagnesium chloride in ethyl ether was prepared in the usual manner, under

nitrogen, from 7.0 g (0.29 mole) of sublimed magnesium²² and 26.3 ml (0.24 mole) of freshly distilled *t*-butyl chloride in 275 ml of ethyl ether. The solution was boiled for 1 hr after all the chloride was added and allowed to cool. Dioxane (21.4 ml, 0.25 mole) in 50 ml of ether was added dropwise with stirring; the mixture stirred for an additional 24 hr, then was allowed to settle for 18 hr. The supernatant was forced through a sintered-glass filter by nitrogen pressure. The cloudy filtrate was allowed to settle 24 hr and filtered again, giving a clear, colorless solution. Tetrahydrofuran (27 ml) was added, the solvent removed under the vacuum of a mechanical pump, and the residue baked at 40–45° for 4 hr and then redissolved in 100 ml of tetrahydrofuran. Analysis showed 0.644 *N* basic magnesium and less than 0.001 *N* chloride.

Kinetics.—For reactions of the Grignard reagent from *t*-butyl chloride in tetrahydrofuran, di-*t*-butyl ketone and Grignard solution were mixed in a reaction vessel in the all-glass apparatus.² The vessel was then isolated by closing the connecting Teflon stopcock and removed from the apparatus. A rubber septum was placed on the side arm above the Teflon stopcock. The reaction flask was placed in a thermostatted bath at 45.2° and samples for analysis were removed by a hypodermic syringe through the rubber septum and stopcock. For reactions in ethyl ether, separate ampoules were filled, sealed (under nitrogen), and quenched at various times. For the reactions with di-*t*-butylmagnesium and with the Grignard reagent from *t*-butyl bromide in THF, appropriate amounts of the reagent and tetrahydrofuran were mixed in the reaction flask (using a nitrogen-filled drybox for transfers) which was then placed in the thermostatted bath. The requisite amount of di-*t*-butyl ketone was then added, and samples taken with hypodermic syringes.

The samples were quenched with 1 *M* aqueous ammonium chloride solution and the light organic layer was separated, dried over potassium carbonate, and analyzed by vapor phase chromatography using Apiezon M or 10% UCON Polar columns on an Aerograph instrument. The areas under the peaks corresponding to unreacted di-*t*-butyl ketone and to the reaction product, di-*t*-butylcarbinol, were measured using a planimeter. The combined areas of the ketone and carbinol peaks were taken as proportional to the total starting material and product. The area of the carbinol peak, divided by the combined areas, gave the fraction reacted. Calibration with known mixtures showed that this method was accurate to ±1%. Both analytical and preparative control experiments found no product other than di-*t*-butylcarbinol for this reaction.

Calculations.—To calculate rate constants for consecutive competitive second-order reactions, the methods given by Frost and Schwemer^{10,11} were used. When the approximation was made that only one alkyl group from the di-*t*-butylmagnesium reacts, equations for simple second-order kinetics were used. For equimolar concentrations, $1/(1 - R)$ was plotted as a function of time. *R* represents the fraction reacted; the rate constant was obtained by dividing the slope of the line by the initial molar concentration of either reactant. For reactions with an excess of reactant A over reactant B, $\ln \{ [B]_0/[A]_0 + ([A]_0 - [B]_0)/[A]_0(1 - R) \}$ was plotted against time. The rate constant was obtained by dividing the slope of this line by $([A]_0 - [B]_0)$.

Registry No.—Di-*t*-butylketene, 815-24-7; di-*t*-butylmagnesium, 14627-81-7; *t*-butylmagnesium chloride, 677-22-5; *t*-butylmagnesium bromide, 2259-30-5.

(22) We wish to thank the Dow Chemical Co. for a generous amount of this magnesium.

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

(18) S. J. Storfer and E. I. Becker, *J. Org. Chem.*, **27**, 1868 (1962).

(19) R. E. Dessy and R. M. Salinger, *J. Am. Chem. Soc.*, **83**, 3530 (1961).

(20) R. E. Dessy, J. H. Wotiz, and C. A. Hollingsworth, *ibid.*, **79**, 358 (1957).

(21) W. C. Percival, R. B. Wagner, and N. C. Cook, *ibid.*, **75**, 3731 (1953).