mixture was extracted with $CHCl_3$. The crude material (*ca.* 0.70 g) obtained from the dried $CHCl_3$ solution was chromatographed on neutral alumina (50 g, Merck). Elution with benzene gave unchanged diacetate (0.21 g), identified by melting point and mixture melting point. Elution with benzene–chloroform (9:1) afforded the oily monoacetate **33** (0.36 g), characterized as its *p*-nitrobenzoate, mp 119–121° (from methylcyclohexane).

Anal. Calcd for $C_{20}H_{21}O_6N$: C, 64.7; H, 5.7. Found: C, 64.3; H, 5.7.

Elution with $CHCl_3$ gave diol *22* (0.08 g), identified by melting point and mixture melting point.

The crude oily monoacetate (0.28 g) in "Analar R" acetone (20 ml) was treated with Jones solution[48] (0.6 ml) at 0°. After the solution had been stirred for 5 min, excess oxidant was destroyed by adding methanol (2 ml). After the solution had been neutralized ($NaHCO_3$) and filtered, the solvent was removed and the residue was extracted with CH_2Cl_2. The crude keto acetate (0.28 g), obtained from the dried CH_2Cl_2 solution, in dioxane (8 ml), and 40% aqueous dioxane (7.5 ml) containing KOH (9 mg/ml) was refluxed for 30 min (negative phenolphthalein reaction). The cooled solution was concentrated to dryness under high vacuum, water was added, and the mixture was extracted with $CHCl_3$. After the usual work-up, a thick oil (0.2 g) was isolated which solidified on standing. Trituration with ether and recrystallization from methylcyclohexane afforded the ketol **34**, mp 124–125°.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.1; H, 7.9. Found: C, 74.2; H, 7.9.

Registry No—**2**, 23346-32-9; **5**, 23346-30-7; **8**, 23346-31-8; **10**, 23353-38-0; **11**, 23353-39-1; **18**, 23353-40-4; *22*, 23353-41-5; *22* bis-*p*-nitrobenzoate, 23353-42-6; **23**, 23353-43-7; **23** bis-*p*-nitrobenzoate, 23353-44-8; **26**, 23359-84-4; **27**, 23353-45-9; **28**, 23353-46-0; **29**, 23359-83-3; **30**, 23353-34-6; **31**, 23353-35-7; **32**, 23353-36-8; **33** *p*-nitrobenzoate, 23353-37-9; **34**, 23353-56-2; 2,3-di(7-norcaryl)quinoxaline, 23346-33-0.

Acknowledgment—We are indebted to Dr. Y. Kashman (Tel Aviv University) for the 100-MHz nmr spectra and to Dr. O. E. Edwards (N. R. C. of Canada) for a sample of dimethylbicyclo[3.1.0]hexanone.

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(48) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

Organometallic Reaction Mechanisms. IV. The Mechanism of Ketone Reduction by Aluminum Alkyls

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A product analysis, kinetic study, and Hammett study of the reaction of triisobutylaluminum with benzophenone has been carried out in diethyl ether solvent. There is no significant participation of the second alkyl group in triisobutylaluminum reduction of benzophenone up to 94% yield of benzhydrol, which is the only product formed in the reaction. The kinetic data shows a well-behaved second-order reaction, first order in aluminum alkyl and first order in ketone. The formation of a complex between the ketone and aluminum alkyl was observed spectroscopically. Accumulation of kinetic data at several temperatures provided a linear Arrhenius plot, which allowed for calculation of activation parameters ($\Delta S^* = -10.1$ eu, $\Delta H^* = 15.8$ kcal/mol, and $\Delta G^* = 18.8$ kcal/mol). A ρ value of +0.362 was determined from a Hammett study, which indicates that the rate-determining step involves nucleophilic attack of the carbonyl group by the aluminum alkyl. All of the accumulated data is consistent with a two-step mechanism in which the first step involves a fast equilibrium to form a complex according to the equation $(i\text{-}C_4H_9)_3Al + (C_6H_5)_2C{=}O \rightleftarrows (i\text{-}C_4H_9)_3Al\cdot O{=}C(C_6H_5)_2$. The second step is rate determining and is consistent with a cyclic intramolecular β-hydrogen attack at the carbonyl group (eq 15).

Organoaluminum compounds react with carbonyl compounds in a similar way to Grignard reagents to give products of either addition, reduction, or enolization reactions or any combination of these reactions. Although the reaction of triethylaluminum with carbonyl compounds produces a mixture of addition and reduction products,[1] the primary reaction of organoaluminum compounds with branched alkyls is reduction.[2] For example, the reaction of triisobutylaluminum with carbonyl compounds is very characteristic in that no addition product is formed with most carbonyl compounds.[1b,c,3]

Recent successes in kinetic studies on the addition reaction of trimethylaluminum with benzophenone in benzene[4] and diethyl ether[5] and the reduction reaction of *t*-butylmagnesium compounds with di-*t*-butyl ketone in tetrahydrofuran[6] have encouraged the study of the mechanism of the reduction reaction of trialkylaluminum compounds with carbonyl compounds by kinetic methods. An ideal system for this study involves the reaction of triisobutylaluminum with benzophenone, since only the formation of reduction product in high yield has been reported.[1b,c] Since this reaction was reported too fast to follow kinetically in benzene,[1c] kinetic studies on this reaction were carried out in diethyl ether, a solvent which provided a convenient reaction rate for kinetic measurements. Furthermore, since triisobutylaluminum is monomeric in diethyl ether[7] and the reaction of the first alkyl group is reported to be much more rapid than that of the second alkyl group, this particular aluminum alkyl should provide the least complicated kinetic data.

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(1) (a) H. Meerwein, G. Hinz, H. Majert, and H. Sönke, *J. Prakt. Chem.*, **147**, 226 (1937); (b) K. Ziegler, K. Schneider, and J. Schneider, *Ann. Chem.*, **623**, 9 (1959); (c) T. Mole and J. R. Surtees, *Aust. J. Chem.*, **17**, 961 (1964); (d) S. Pasynkiewicz and E. J. Sliwa, *J. Organometal. Chem.*, **3**, 121 (1965).

(2) (a) K. Ziegler in "Organometallic Chemistry," H. Zeiss, Ed., Reinhold Publishing Co., New York, N. Y., 1960, Chapter 5; (b) R. Köster and P. Binger, *Advan. Inorg. Chem. Radiochem.*, **7**, 263 (1965).

(3) (a) K. Ziegler, K. Schneider, and J. Schneider, *Angew. Chem.*, **67**, 425 (1955); (b) L. I. Zakharkin, L. P. Sorokina, and I. M. Khorlina, *Zh. Obshch. Khim.*, **31**, 3311 (1961); (c) H. Haubenstock and E. B. Davidson, *J. Org. Chem.*, **28**, 2772 (1963).

(4) E. C. Ashby, J. Laemmle, and H. M. Neumann, *J. Amer. Chem. Soc.*, **90**, 5179 (1968).

(5) E. C. Ashby and J. T. Laemmle, *J. Org. Chem.*, **33**, 3398 (1968).

(6) M. S. Singer, R. M. Salinger, and H. S. Mosher, *ibid.*, **32**, 3821 (1967).

(7) (a) E. C. Ashby, J. Carter, and J. R. Sanders, unpublished results; (b) E. G. Hoffman, *Ann. Chem.*, **629**, 104 (1960); (c) K. Ziegler, W. R. Kroll, W. Larbig, and O. W. Steudle, *ibid.*, **629**, 53 (1960).

Experimental Section

Instrumentation and Apparatus.—The disappearance of benzophenone in the kinetic experiments and the determination of extinction coefficients of the ketones studied was accomplished by uv spectroscopy. A Kewaunee inert atmosphere box equipped with a recirculating system to remove moisture and oxygen[8] was used during the manipulation of air-sensitive reagents.

Temperatures were monitored with a calibrated thermometer reading to 0.1° with estimating to 0.02° possible. Reactions were timed to 0.1 sec. Calibrated syringes equipped with 8-in. stainless steel needles were used for transfer of reagents. All-glass 120-ml heavy-walled bulbs were used for all kinetic studies. The only opening to the bulb was through a three-way Teflon stopcock. The stopcock was designed so that a flow of nitrogen could be maintained on the system when samples were added or withdrawn.

Chemicals.—Triisobutylaluminum was obtained from Texas Alkyls Inc. This material was further purified by distillation in the dry box through a 1-ft packed column under vacuum (0.2 mm), taking the center cut for kinetic studies. The pot temperature was kept at 60–70° in order to minimize olefin elimination.[9] The infrared spectrum of triisobutylaluminum after distillation showed no absorption in the range of 1700–1800 cm^{-1} characteristic of the aluminum–hydrogen bond in diisobutylaluminum hydride.[10] Eastman reagent grade benzophenone was recrystallized from 95% ethanol twice and distilled under vacuum at 88° (0.05 mm), taking the center cut for kinetic studies. Glpc analysis indicated a purity of at least 99.95%. Eastman reagent grade benzhydrol, biphenyl, and the 4-substituted benzophenones (bromo, chloro, fluoro, methyl, and methoxy) were purified by recrystallation from hexane six times. Glpc analysis of these compounds indicated a minimum purity of 99%. 4-Methylmercaptobenzophenone was prepared by Friedel–Crafts acylation of thioanisole with benzoyl chloride in carbon disulfide using aluminum chloride as catalyst. The product was further purified by recrystallation until glpc showed no detectable impurity. Baker reagent grade anhydrous diethyl ether was distilled under nitrogen for lithium aluminum hydride prior to use.

Product Analysis.—Product analysis of triisobutylaluminum with benzophenone was done by glpc using 6-ft, Chromosorb W supported 10% Carbowax 20M columns. Biphenyl was used as the internal standard. Glpc analysis of a solution containing benzophenone (0.6 *M*) and biphenyl showed an area ratio of benzophenone to biphenyl of 5.41. When 1 ml of this mixture was allowed to react with 3 ml of triisobutylaluminum solution (0.452 *M*) in a rubber cap sealed bottle for 60 hr, glpc analysis after hydrolysis showed an area ratio of benzhydrol to biphenyl of 5.25 without any other detectable peak. This result indicated 97.3% conversion of benzophenone into benzhydrol.

The reaction of triisobutylaluminum with benzophenone was studied at three different ratios (3:1, 2:1, and 1:2). Two milliliters of the reaction solution were withdrawn under nitrogen at appropriate time intervals and quenched in 3 ml of 10% hydrochloric acid. Glpc analyses showed that the 3:1 and 2:1 ratio experiments produced only benzhydrol after 145-min reaction. In the 1:2 ratio experiment benzhydrol was produced in 55.7% yield after 100 min, 66.2% after 13 hr, and 66.6% after 34.3 hr.

Duplicate samples of triisobutylaluminum (0.904 mmol) and excess benzophenone (1.80 mmol) in diethyl ether (5 ml) were allowed to react. After 60 hr glpc analysis showed that 62.7 and 62.5% of the benzophenone had reacted.

Triisobutylaluminum (4.408×10^{-3} *M*) was allowed to react with excess benzophenone (9.453×10^{-3} *M*) for 397 hr. Ultraviolet spectral analysis indicated 66.2% reduction.

Ultraviolet Spectra of Ketones and Complex.—For examining the complex of triisobutylaluminum and benzophenone in diethyl ether, 35 μl of a standardized benzophenone solution was introduced into a rubber-capped 10-mm quartz ultraviolet cell containing 3 ml of 33.590×10^{-3} *M* triisobutylaluminum solution at room temperature (22°). The absorption of the mixture was recorded at appropriate time intervals from 380 to 260 mμ and compared with that of a standard benzophenone spectrum (Figure 1).

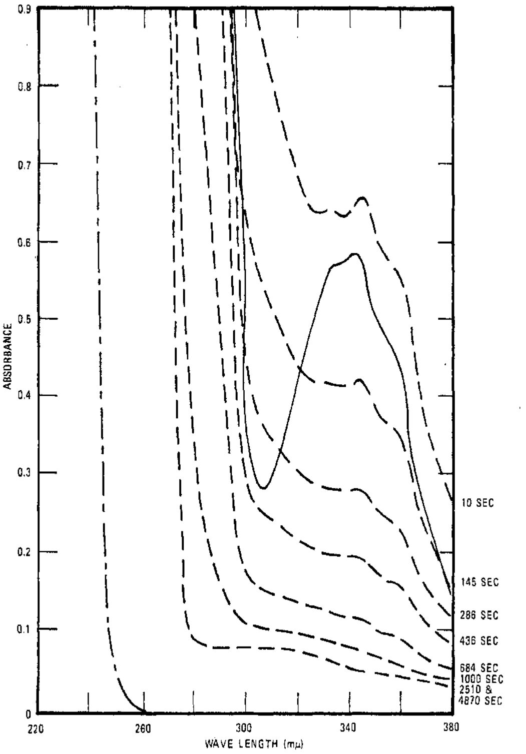

Figure 1.—Spectra of a diethyl ether solution 33.5×10^{-3} *M* in triisobutylaluminum and 5.19×10^{-3} *M* in benzophenone. Solid curve is the spectrum of a solution containing only 5.19×10^{-3} *M* benzophenone, and broken curve (— — — — —) is the spectrum of a solution containing only 33.5×10^{-3} *M* triisobutylaluminum.

The extinction coefficients and uv absorption maxima of 4-substituted benzophenones in diethyl ether are recorded in Table I.

TABLE I

ULTRAVIOLET SPECTRAL DATA FOR 4-SUBSTITUTED BENZOPHENONES

Substituent	λ_{max}, mμ	ε
H	344.5	119[a]
Br	346	166 ± 1
Cl	345	150 ± 2
F	343	130 ± 1
Me	344	151 ± 2
MeO	330	281 ± 1
MeS	308	2120 ± 30

[a] From ref 5.

Kinetic Studies.—The kinetics of the reaction of triisobutylaluminum with benzophenone in diethyl ether were determined by following the disappearance of the benzophenone band at 344.5 mμ.

All equipment was heated over a burner flame and placed hot in the entry port of a dry box which was subsequently evacuated and refilled with nitrogen twice. All transfers of solutions were performed under a flow of prepurified nitrogen through a three-way Teflon stopcock using syringes; 100 ml of distilled diethyl ether was first added to the reaction flask followed by addition of an aliquot of triisobutylaluminum standard solution. The flask was weighed and the total volume of the solution was obtained from the density of diethyl ether at the kinetic temperature. Then the flask was wrapped with aluminum foil and placed in a constant-temperature bath (25 ± 0.05°). The flask and its contents were allowed to reach temperature equilibrium before a nitrogen line was attached to one side opening of the three-way stopcock. The stopcock was then turned to

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[8] (a) T. L. Brown, D. W. Dickerhoof, D. A. Bafus, and G. L. Morgan, *Rev. Sci. Instrum.*, **33**, 491 (1962); (b) D. F. Shriver, "The Manipulation of Air Sensitive Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1969, pp 164–189.

[9] K. Ziegler, W. R. Kroll, W. Larbig, and O. W. Steudel, *Ann. Chem.*, **629**, 53 (1960).

[10] H. Reinheckel and K. Haage, *J. Prakt. Chem.*, **33**, 70 (1966).

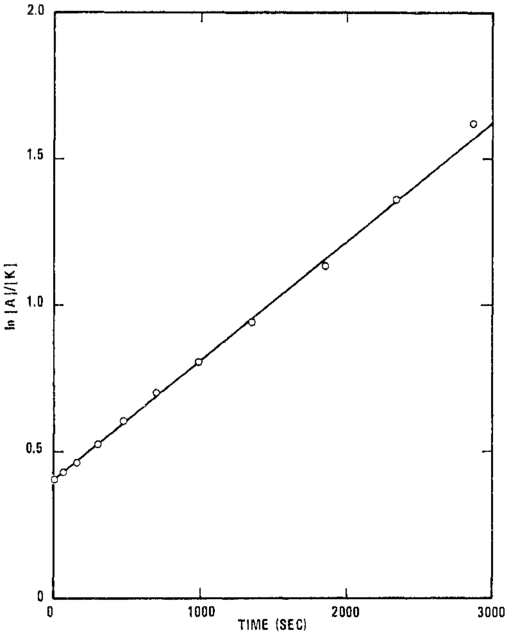

Figure 2.—Plot demonstrating second-order behavior of triisobutylaluminum and benzophenone in diethyl ether at 25° (run no. 6, Table III).

accept a syringe needle from the top with the nitrogen flow from the side, and the desired amount of benzophenone (0.25–0.65 ml) was added. A 6-ml sample was withdrawn immediately and quenched in 5 ml of ether-saturated 10% hydrochloric acid. Quenched samples were allowed to stand for 1 hr before the ether layer was transferred into a quartz cell. The amount of unreacted ketone was then determined at 344.5 mμ against a water-saturated ether sample.

The syringes (10 ml) used to withdraw the samples were flamed and purged with nitrogen by drawing gas into the barrel through the needle several times. The purging step was repeated after the syringes had cooled, after which *ca.* 5 ml of nitrogen was retained in the barrel of the syringe. This treatment was found to be necessary in order to avoid contamination of the reaction mixture during sample withdrawal. The concentration of a solution of benzophenone in diethyl ether after 14 withdrawals agreed within 0.15% of the initial concentration, and the absorbance of quenched solutions of benzophenone matched exactly the absorbance of the unquenched standard sample.

Triisobutylaluminum concentrations in diethyl ether were determined by decomposing aliquot samples with 10% hydrochloric acid, adding an excess of standard EDTA, and back titrating with standard zinc acetate solution (dithiazone indicator). The initial concentration of the triisobutylaluminum in the reaction flask was calculated from dilution. The reliability of the dilution at the kinetic concentration range was checked by diluting an aliquot of standard triisobutylaluminum solution with diethyl ether in a 200-ml volumeric flask. Some of this solution was used for kinetic runs and the remainder was weighed in order to calculate the volume from the density of diethyl ether. The solution was then hydrolyzed, decomposed, and analyzed. The analyzed concentration agreed within 0.2% of the concentration calculated by the dilution factor at the lowest concentration of triisobutylaluminum. The initial concentration of benzophenone was obtained from the extrapolation of its absorbance at 344.5 mμ *vs.* time.

Rate constants were calculated from the second-order rate equation

$$k = \frac{1}{t([\mathrm{A}]_0 - [\mathrm{B}]_0)} \ln \frac{[\mathrm{A}]\,[\mathrm{B}]_0}{[\mathrm{B}]\,[\mathrm{A}]_0}$$

where $[\mathrm{A}]_0$ and $[\mathrm{B}]_0$ are the initial concentrations of triisobutylaluminum and benzophenone and [A] and [B] represent the concentrations at time *t*. The average rate constant for each run was calculated from eight to twelve sets of benzophenone concentration–time values.

Results

The reaction of triisobutylaluminum and benzophenone in diethyl ether was found to produce on hydrolysis the reduction product benzhydrol in essentially quantitative yield without the side reactions of enolization or addition. In product-analysis studies, when triisobutylaluminum and benzophenone were allowed to react in the stoichiometric ratio of 1:2, the reaction proceeded to give benzhydrol in 66.6% yield after 34 hr. Previous workers have pointed out that only one of the isobutyl groups in triisobutylaluminum is available for reduction of benzophenone.[1b,c] Because of the importance of this point to the evaluation of kinetic data, the reaction of triisobutylaluminum and benzophenone in 1:2 ratio was repeated in duplicate. After 60 hr, the final product after hydrolysis contained 62.7 and 62.5% benzhydrol with unreacted ketone. The reaction at a ratio of 0.466:1 was further studied by following the disappearance of ketone absorbance. It showed 42% of the second group involved in the reaction after 397 hr (Table II).

Table II

Reaction of Triisobutylaluminum and Benzophenone in the Stoichiometric Ratio of 0.466:1 at 25°

Time, hr	Absorbance at 344.5 mμ	Reaction of benzophenone, %
0	1.125	0
0.36	0.779	30.7
0.97	0.618	45.1
1.92	0.538	52.2
2.94	0.495	56.0
5.86	0.465	58.7
14.0	0.448	60.2
27.5	0.423	62.4
51.2	0.410	63.6
102.0	0.396	64.8
397	0.380	66.2

The absorption spectrum of 33.59×10^{-3} *M* triisobutylaluminum in a mixture with 5.19×10^{-3} *M* benzophenone in diethyl ether was recorded at appropriate intervals of time and is illustrated in Figure 1. In diethyl ether, the ultraviolet spectrum of benzophenone has maximum absorption at 344.5 mμ (ϵ 119) and 251 mμ (ϵ 1.8×10^4) with a trough at 305 mμ.[5] Triisobutylaluminum–diethyl ether solution does not show any appreciable absorbance at wavelengths longer than 270 mμ in the concentration range studied. The spectrum of the reaction mixture indicates that the absorbance is greater for the reaction mixture than for the pure ketone at the same ketone concentration and that the absorption gradually decreases as the reaction proceeds. Neither benzophenone nor triisobutylaluminum absorb at 400 mμ. The facts, that the mixtures show some absorbance at 400 mμ, the ketone trough at 305 mμ disappears completely, and stronger absorbance at 344.5 mμ is observed, indicate that complexation between triisobutylaluminum and benzophenone occurs, although only to a small extent.

The rate of disappearance of benzophenone was followed by quenching aliquot samples of the reaction mixture at appropriate intervals with 10% hydrochloric acid and determining the absorbance of unreacted benzophenone at 344.5 mμ. The reaction be-

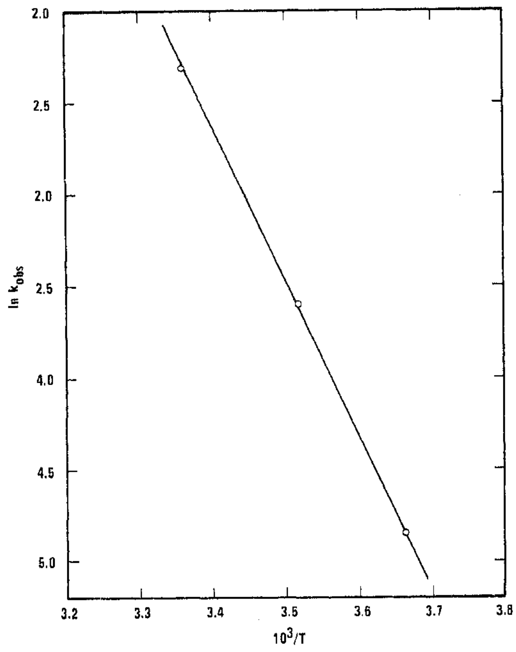

Figure 3.—Arrhenius plot of the reaction of triisobutylaluminum with benzophenone in diethyl ether over the temperature range of 0–25°.

tween triisobutylaluminum and benzophenone in diethyl ether was found to be first order in each reactant and second order overall. The average rate constant is 0.0994 ± 0.0039 l. mol^{-1} sec^{-1} at 25°. The second-order behavior was observed between 5 and 95% reaction. The rate constant was found to be independent of the reactant ratio (0.5:1 to 22:1) as well as the initial concentration of either reactant (initial benzophenone concentrations of 5.52–9.20 $\times 10^{-3}$ *M* and initial triisobutylaluminum concentrations of 4.408–160.6 $\times 10^{-3}$ *M*).

The method used for the kinetic study proved to be very satisfactory. Reaction mixtures showed no signs of hydrolysis or loss of diethyl ether owing to sample withdrawal over a period of time and the quenching procedure did not effect the actual concentration of benzophenone in solution. Data from a typical kinetic run is graphically illustrated in Figure 2 and the results of all kinetic investigations are summarized in Table III.

Measurements of reaction rates at 11.4 and 0° also showed the reaction to be second order. The Arrhenius plot is linear, as shown in Figure 3. The slope of the Arrhenius plot and the standard equations[11] were used to calculate the observed activation parameters listed in Table IV.

The second-order reaction rates of six 4-substituted benzophenones with triisobutylaluminum in diethyl ether at 25° are listed in Table V. Variation of the 4 substituents in benzophenone produced a significant but small electronic influence on the rate of reduction. The relative reactivities correlated best with Brown's substituent constant[12] σ^+ to give the Hammett equation log k/k_0 = (0.362 ± 0.070)σ^+ + 0.00 (Figure 4). The 4-thiomethyl substituent resulted in poor

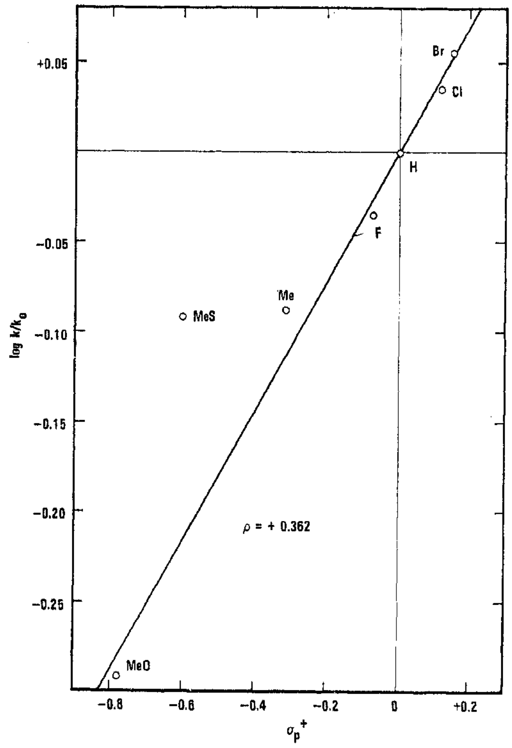

Figure 4.—Hammett plot of the reaction of triisobutylaluminum with 4-substituted benzophenones in diethyl ether at 25°.

TABLE III
RATE CONSTANTS FOR THE REACTION OF TRIISOBUTYLALUMINUM WITH BENZOPHENONE IN DIETHYL ETHER

Temp, °C	Run	$[(i\text{-}C_4H_9)_3Al]/[(C_6H_5)_2CO]$	$[(i\text{-}C_4H_9)_3Al] \times 10^3$ *M*	$[(C_6H_5)_2CO] \times 10^3$ *M*	$k_{obsd} \times 10^2$ l. mol^{-1} sec^{-1}
25	1	0.50	4.594	9.20	9.11 ± 0.42
	2	0.51	4.594	9.05	9.75 ± 0.67
	3	0.74	4.408	5.92	10.88 ± 0.50
	4	0.85	7.360	8.67	10.19 ± 0.26
	5	0.98	8.260	8.47	9.35 ± 0.12
	6	1.50	8.260	5.52	9.65 ± 0.34
	7	1.50	12.58	8.39	9.70 ± 0.22
	8	2.03	17.75	8.76	9.80 ± 0.25
	9	3.05	22.12	7.25	10.39 ± 0.21
	10	4.02	26.17	6.51	9.42 ± 0.19
	11	5.41	39.23	7.25	10.27 ± 0.11
	12	21.9	160.62	7.33	10.76 ± 0.17[a]
				Avg	9.94 ± 0.39
11.4	13	2.11	18.17	8.61	2.68 ± 0.08
	14	2.20	18.17	8.24	2.78 ± 0.07
				Avg	2.73 ± 0.05
0	15	3.26	27.15	8.32	0.785 ± 0.030
	16	3.14	27.15	8.65	0.775 ± 0.028
	17	3.38	27.15	8.04	0.791 ± 0.035
				Avg	0.784 ± 0.006

[a] Rate constant calculated from the pseudo-first-order equation $k = 1/[A]_0(1/t)\ln[B]_0/[B]$.

TABLE IV
ACTIVATION PARAMETERS FOR THE REACTION OF TRIISOBUTYLALUMINUM WITH BENZOPHENONE IN DIETHYL ETHER AT 25°

Activation energy E_a = 16.4 kcal/mol
Frequency factor A = 10^{11} l. mol^{-1} sec^{-1}
Free energy of activation ΔG^* = 18.8 kcal/mol
Enthalpy of activation ΔH^* = 15.8 kcal/mol
Entropy of activation ΔS^* = −10.1 eu

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(11) A. A. Frost and R. G. Pearson, "Kinetics and Mechanisms," John Wiley & Sons, Inc., New York, N. Y., 1961, pp 98–100.

(12) H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958).

Table V

Rate Constants for the Reaction of Triisobutylaluminum with 4-Substituted Benzophenones in Diethyl Ether at 25°

4 substituents	Run	$[(i\text{-}C_4H_9)_3Al]/[(C_6H_5)_2CO]$	$[(i\text{-}C_4H_9)_3Al] \times 10^3$ M	$[(C_6H_5)_2CO] \times 10^3$ M	$k_{obsd} \times 10^2$ l. mol^{-1} sec^{-1}
Bromo	18	5.04	19.42	3.85	11.45 ± 0.42
	19	2.52	19.22	7.62	11.14 ± 0.23
				Avg	11.29 ± 0.15
Chloro	20	4.23	21.34	5.04	10.77 ± 0.12
	21	3.30	19.20	5.81	10.78 ± 0.05
				Avg	10.78 ± 0.01
Fluoro	22	2.30	19.33	8.42	9.21 ± 0.22
	23	2.31	19.33	8.38	9.10 ± 0.28
				Avg	9.16 ± 0.06
Methyl	24	9.76	31.73	3.25	8.11 ± 0.30
	25	3.81	31.29	8.27	8.12 ± 0.08
				Avg	8.12 ± 0.01
Methoxy	26	6.86	19.48	2.84	5.07 ± 0.30
	27	4.66	19.42	4.18	5.09 ± 0.15
				Avg	5.08 ± 0.01
Thiomethyl	28	8.68	4.749	0.547	8.15 ± 0.44
	29	8.41	3.391	0.403	7.95 ± 0.20
				Avg	8.05 ± 0.10

correlation and was excluded from the calculation of the reaction constant (ρ).

Discussion

Previous workers have reported that the reactions of trimethylaluminum[1c,4,5] and triphenylaluminum[13] with ketones proceed without any occurrence of reduction products. On the other hand, triisobutylaluminum produces entirely reduction product when allowed to react with typical ketones.[1b,c,3] It has been suggested by Wittig that the mechanism of reduction involves the migration of a β hydrogen from the alkyl group of the aluminum alkyl to the carbonyl carbon. Such a mechanism already has been reasonably well demonstrated for the reduction of ketones by magnesium alkyls (Grignard reagents).[14]

The availability of the second isobutyl group in triisobutylaluminum for reduction was indicated by reaction of triisobutylaluminum with benzophenone in 1:2 ratio. A greater than 50% yield of benzhydrol indicates reaction of the second alkyl group at some reduced rate. Fortunately, however, the reactivity of the second alkyl group turned out to be kinetically unimportant. Even when the triisobutylaluminum–benzophenone ratio was 1:2, 94% of the reaction proceeded by utilization of the first alkyl group.

Spectroscopic studies indicated complex formation between the reacting species (eq 1). Similar spectral

$$(C_6H_5)_2C{=}O + (i\text{-}C_4H_9)_3Al \rightleftharpoons (C_6H_5)_2C{=}O\cdots Al(i\text{-}C_4H_9)_3 \quad (1)$$

changes have been attributed to complex formation in the addition reaction of methylmagnesium bromide[15] and trimethylaluminum[4,5] with ketones. Unfortunately, the exact extent of complexation cannot be estimated from the spectral data alone. However, the second-order kinetic results indicate that the formation of the complex occurs either quantitatively or to a very small extent. Complexation of benzophenone and trimethylaluminum in diethyl ether was found to be very small,[5] although in benzene it was quantitative.[4] These results are easily explainable on the basis that diethyl ether will compete with benzophenone as a Lewis base for the Lewis acid, trimethylaluminum, suggesting that the equilibrium constant (K) for complex formation (eq 2) is small in diethyl ether. The spectrum of benzophenone and triisobutylaluminum in diethyl ether is similar to that of benzophenone and trimethylaluminum in diethyl ether, and therefore complex formation should be even smaller with the more sterically hindered aluminum alkyl. Since the extent of complexation is relatively small, a steady-state treatment of the kinetic data is in order. In addition, the immediate change of the spectral profile in the complex study (Figure 1) suggests that the complex-formation step is fast on the time scale of conversion of reactants into products.

The second-order kinetic data obtained for the reaction of triisobutylaluminum and benzophenone in diethyl ether are similar to those of the reduction of di-*t*-butyl ketone with di-*t*-butylmagnesium in tetrahydrofuran,[6] except that the second alkyl group reacts at a competitive rate in the case of magnesium. The kinetic data are also similar to those from reaction of benzophenone and trimethylaluminum in diethyl ether,[5] where the second alkyl group is not involved at all.

The second-order kinetic data and spectroscopic observation of a complex suggests a multiple-step mechanism involving the complex as an intermediate (eq 2 and 3). If $k_2 \gg k_{-1}$ eq 5 obtains. If $k_2 \ll k_{-1}$ eq 6 obtains.

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[13] (a) G. Wittig, F. J. Meyer, and G. Gange, *Ann. Chem.*, **571**, 167 (1951); (b) T. Mole, *Aust. J. Chem.*, **16**, 807 (1963).

[14] G. E. Dunn and J. Warkentin, *Can. J. Chem.*, **34**, 75 (1956); H. S. Mosher and E. M. LaCombe, *J. Amer. Chem. Soc.*, **72**, 3994 (1950); H. S. Mosher, J. E. Stevenot, and D. O. Kimble, *ibid.*, **78**, 4374 (1956).

[15] (a) S. G. Smith, *Tetrahedron Lett.*, **7**, 409 (1963); (b) S. G. Smith and G. Su, *J. Amer. Chem. Soc.*, **86**, 2750 (1964); (c) S. G. Smith and G. Su, *ibid.*, **88**, 3995 (1966); (d) S. G. Smith and J. Billet, *ibid.*, **89**, 6948 (1967); (e) J. Billet and S. G. Smith, *ibid.*, **90**, 4108 (1968); (f) N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1962).

$$\mathrm{A} + \mathrm{B} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C} \tag{2}$$

$$\mathrm{C} \xrightarrow{k_2} \mathrm{P} \tag{3}$$

$$\frac{\mathrm{d[P]}}{\mathrm{d}t} = k_2[\mathrm{C}] = \frac{k_2k_1}{k_{-1} + k_2}[\mathrm{A}][\mathrm{B}] \tag{4}$$

$$\frac{\mathrm{d[P]}}{\mathrm{d}t} = k_1[\mathrm{A}][\mathrm{B}] \tag{5}$$

$$\frac{\mathrm{d[P]}}{\mathrm{d}t} = k_2K[\mathrm{A}][\mathrm{B}] \tag{6}$$

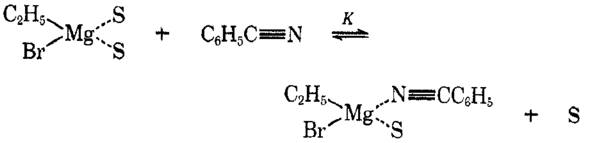
In the equations, A = triisobutylaluminum [$(i\text{-}C_4H_9)_3Al$]; B = benzophenone [$(C_6H_5)_2C{=}O$]; C = complex between reacting species; and P = product, benzhydryloxydiisobutylaluminum [$(i\text{-}C_4H_9)_2AlOCH(C_6H_5)_2$]. Equation 4 assumes a steady-state approximation. If complex formation is the rate-determining step, *i.e.*, $k_2 \gg k_{-1}$, the rate expression is given in eq 5, where $k_{\mathrm{obsd}} = k_1$. Alternatively, if product formation is the rate-determining step, *i.e.*, $k_2 \ll k_{-1}$, the rate expression reduces to eq 6, where $k_{\mathrm{obsd}} = k_2K$.

From the Hammett plot (Figure 4), the rate constants of the reduction reaction of triisobutylaluminum with 4-substituted benzophenones in diethyl ether at 25° were determined and a ρ value of $+0.362$ was calculated. The linear Hammett relationship indicates that the substituents do not shift the rate-determining step of the reaction nor produce a new reaction path to form the product. The reaction step requiring complex formation is favored by electron-releasing groups in the ketone. The transfer of the β hydrogen of the alkyl group in triisobutylaluminum to the carbon of the carbonyl group in the product formation step is aided by electron-withdrawing groups attached to the ketone. Since the overall rate of the reduction depends on both the equilibrium constant K for the complex formation (eq 2) and the rate constant k_2 for transfer of the β hydrogen atom (eq 3), the two substituent effects nearly cancel each other and thus the observed rates displayed very little variation with changing substituents. A small ρ value is also consistent with a concerted process, since substituent effects would tend to be nullified and little charge separation would be expected in the transition state.

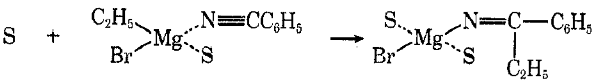
For some multiple-step mechanisms, the sign of the overall reaction constant (ρ) is not always consistent with that of the rate-determining step.[16] However, the positive ρ value, as well as spectroscopic observation of immediate complex formation, indicates that the electrophilic complex formation step is not the rate-determining step of the reaction. Therefore, the nucleophilic product formation step is considered to be the rate-determining step. The considerable negative entropy of activation ($\Delta S^{\ddagger} = -10.1$ eu) indicates that the transition state of the rate-determining step is cyclic.

A further consequence of the small ρ value is that the complex is not formed by the attack of a hydride ion at the carbon atom of the carbonyl groups, as postulated in the reaction of sodium borohydride with ketones.[17] This mechanism is analogous to that for ester hydrolysis,[18] both reactions of which possess considerably large ρ values ($+2.61$–3.06).[19]

It is important to note that the reduction rate of triisobutylaluminum[1c] and the addition rate of trimethylaluminum[4,5] with benzophenone decreases drastically when proceeding from hydrocarbon to ether solvent. Also previous studies concerning the effect of solvent in the nucleophilic addition of ethylmagnesium bromide with benzonitrile indicated that the reaction rate also decreases as the basicity of the solvent increases.[20] The explanation offered for this effect was that the formation of the product proceeds through complex formation. Since the complex is formed by displacement of one of the solvent molecules coordinated to the Grignard compound (eq 7 and 8), the more basic solvent would result in more difficult displacement of the solvent and hence a smaller concentration of complex (smaller K). Similar (but less clear cut) results have also been reported in a study of solvent effects in the reaction of ethylmagnesium bromide with benzophenone.[21]

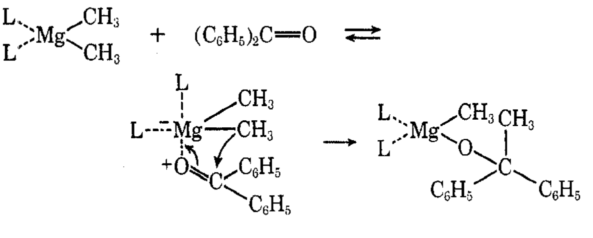


(7)



(8)

An interesting recent report on the reaction of dimethylmagnesium with benzophenone is also concerned with the effect of solvent on the mechanism of the alkylation reaction.[22] In this study the effect of donor ligands on the rate of alkylation in diethyl ether was studied. The addition of monodentate ligands had little effect on the reaction rate; however, bidendate ligands were found to either retard or accelerate the reaction. From these observations the authors postulated that the reaction involves a pentacoordinate intermediate or transition state without the displacement of a donor ligand or solvent molecule (eq 9).



(9)

Actually, one cannot distinguish with certainty between the two possible paths involving complex formation (a tetracoordinate intermediate with solvent displacement or a pentacoordinate intermediate without

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[16] W. P. Jenks, *Progr. Phys. Org. Chem.*, **2**, 63 (1964).

[17] H. C. Brown, O. H. Wheeler, and K. Ichikawa, *Tetrahedron*, **1**, 214 (1957).

[18] M. L. Bender, *Chem. Rev.*, **60**, 60 (1969).

[19] (a) G. G. Smith and R. P. Bayer, *Tetrahedron*, **18**, 323 (1962); (b) P. T. Lansbury and R. G. MacLeay, *J. Amer. Chem. Soc.*, **87**, 851 (1965); (c) J. A. Parry and K. D. Warren, *J. Chem. Soc.*, 4049 (1965); (d) K. Bowden and M. Hardy, *Tetrahedron*, **22**, 1169 (1966).

[20] A. A. Scala and E. I. Becker, *J. Org. Chem.*, **30**, 3491 (1965).

[21] R. N. Lewis and J. R. Wright, *J. Amer. Chem. Soc.*, **74**, 1253 (1952).

[22] H. C. House and J. E. Oliver, *J. Org. Chem.*, **33**, 929 (1968).

the displacement of solvent) on the basis of the data at hand. As the solvent is changed from benzene to ether, the equilibrium (eq 10) will shift to the right.

$$R_3Al + L \rightleftharpoons R_3Al\cdot L \quad (10)$$

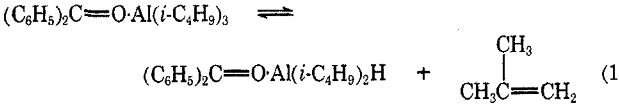
Therefore, the complexation of trialkylaluminum with ketone in ether should decrease, since solvent must be displaced, or, if solvent is not displaced, steric hindrance and decreased Lewis acidity of the metal will cause a decrease in the complexation. It would appear that the first case is more probable.

It might be suggested that, since direct spectroscopic evidence has been obtained for the occurrence of complex between the reacting species, a concerted one-step mechanism does not appear as likely. However, the question is raised whether the complex is actually an intermediate in product formation or whether it is merely involved in a nonproduct-forming equilibrium (eq 11).[15c,22] This alternative mechanism

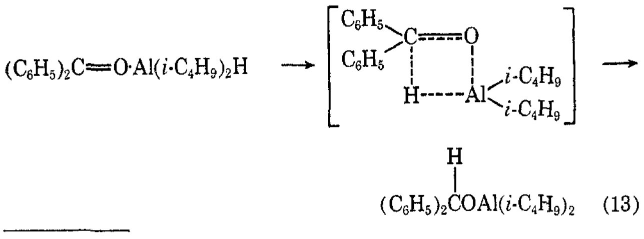
$$P \longleftarrow A + B \rightleftharpoons C \quad (11)$$

is consistent with all observations. If the complex is not involved in product formation (eq 11), then the product must be formed by a concerted attack on the carbonyl group (aluminum on oxygen and β hydrogen on carbon). However, the drastic decrease in the reaction rate from benzene to ether solvent is best explained by the fact that the concentration of complex is much greater in benzene than in ether. Therefore, it is more reasonable to believe that the product is formed *via* complex formation with the attack of β hydrogen on the carbon atom of the carbonyl group *via* a six-center transition state.

An alternative transfer of the β hydrogen of triisobutylaluminum to the carbonyl carbon, also proposed as a possibility in Grignard reduction reactions,[23] can be explained by olefin elimination as a consequence of ketone attack, followed by reduction of the ketone by diisobutylaluminum hydride (eq 12 and 13). Since diethyl ether has already been shown to be a stronger base toward aluminum alkyls than benzophenone, if the above mechanism is correct, isobutylene ahould be displaced from triisobutylaluminum in diethyl ether solvent. However, it is known that triisobutylaluminum etherate can be distilled at 80–90° without olefin displacement. Therefore, the above mechanism does not seem probable. This alternative path could be easily tested by asymmetric reduction studies, as was carried out in Grignard reduction studies.[24]



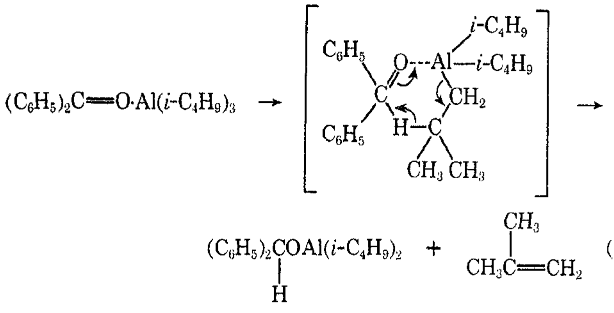
$$(C_6H_5)_2C{=}O\cdot Al(i\text{-}C_4H_9)_3 \rightleftharpoons (C_6H_5)_2C{=}O\cdot Al(i\text{-}C_4H_9)_2H + CH_3\overset{\overset{\displaystyle CH_3}{|}}{C}{=}CH_2 \quad (12)$$



(13)

Consistent with all observations, the detailed reduction mechanism proposed for the reaction of triisobutylaluminum with benzophenone in diethyl ether is given in eq 14 and 15.

$$(C_6H_5)_2C{=}O + Al(i\text{-}C_4H_9)_3 \rightleftharpoons (C_6H_5)_2C{=}O\cdot Al(i\text{-}C_4H_9)_3 \quad (14)$$



(15)

In eq 15, a rapid equilibrium step, benzophenone forms a complex with triisobutylaluminum in small concentration. In eq 16, an intramolecular rearrangement of the complex occurs in a rate-determining step to form the product *via* a cyclic six-center transition state as proposed in the Grignard reduction reaction.[25] Further work is in progress to determine with a higher degree of confidence whether the rate-determining step of this reaction proceeds through complex formation or is concerted.

Registry No.—Triisobutylaluminum, 100-99-2; benzophenone, 119-61-9; 4-bromobenzophenone, 90-90-4; 4-chlorobenzophenone, 134-85-0; 4-fluorobenzophenone 345-83-5; 4-methylbenzophenone, 134-84-9; 4-methoxybenzophenone, 611-94-9; 4-thiomethylbenzophenone, 23405-48-3.

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[23] K. Hess and H. Rheinboldt, *Chem. Ber.*, **54B**, 2043 (1921).

[24] H. D. Morrison, *Survey Progr. Chem.*, **3**, 147 (1966).

[25] F. C. Whitmore 105th National Meeting of the American Chemical Society, Atlantic City, N. J., April 1963, as quoted by H. S. Mosher and E. Lacombe, *J. Amer. Chem. Soc.*, **77**, 3994 (1950).