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Concerning the Mechanism of Trimethylaluminum Addition to Benzophenone

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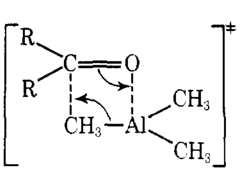
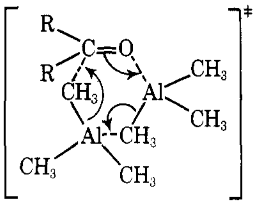
Because of the stereochemical significance of the reaction of $(CH_3)_3Al$ with substituted cyclohexanones in 2:1 ratio in benzene, an attempt was made to more clearly define the nature of the transition state involved in this reaction. In this connection, molecular weight and NMR studies were carried out on the systems $(CH_3)_3Al–O(C_2H_5)_2$, $(CH_3)_3Al–Ph_2C{=}O$, and $(CH_3)_2AlCl–Ph_2C{=}O$ in an attempt to distinguish among three suggested reaction pathways. One pathway involving the intermediate formation of two molecules of monomeric $(CH_3)_3Al$ bound to one molecule of $Ph_2C{=}O$ was eliminated by the data. All of the available data more strongly support a pathway involving cyclic six-center transition state.

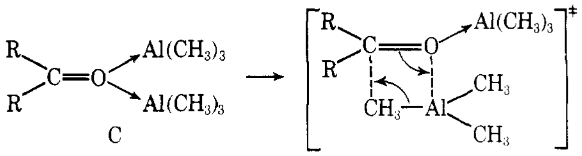
The reaction between $(CH_3)_3Al$ and benzophenone in benzene is known to proceed by two distinct mechanistic pathways depending on the stoichiometric ratio of reactants.[1] At 1:1 ratio the reaction is first order in $(CH_3)_3Al$ and first order in ketone and is presumed to proceed via a four-center transition state (A) whereas in 2:1 ratio the reaction is second order in $(CH_3)_3Al$ and first order in ketone and is presumed to proceed via a six-center transition state (B). When the reaction is carried out in diethyl ether the kinetic order (first order in $(CH_3)_3Al$ and first order in ketone) is independent of the stoichiometric ratio of reactants and the mechanism has been represented as proceeding through transition state A.[2]


A


B

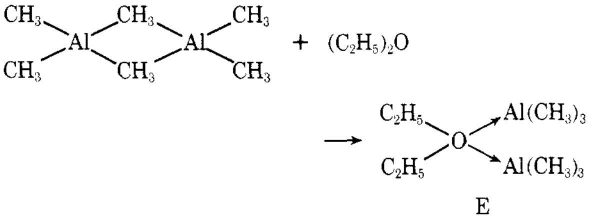
Since this reaction proceeds via two distinct mechanistic pathways in benzene and hence via two distinct transition states, it was presumed that the stereochemistry of the reaction at $(CH_3)_3Al$:ketone ratios of 1:1 and 2:1 would be different. In this connection, it was found that the reaction of $(CH_3)_3Al$ with 4-*tert*-butylcyclohexanone in 1:1 ratio in benzene resulted in 75% equatorial attack whereas the reaction in 2:1 ratio resulted in 90% axial attack. This is a rather dramatic and unprecedented stereochemical result and we have expended considerable effort in attempts to arrive at a satisfactory explanation.[3,4]

Recently, Kawasaki[5] has rationalized stereochemical data assuming transition state B and Starowieyski[6] has provided evidence for B by noting the stability of an acetophenone–$(AlCl_3)_2$ adduct. On the other hand, Mole[7] has suggested that the reaction in 2:1 ratio proceeds via the intermediate C leading to transition D. Because an understanding of the unusual stereochemical results of this reaction involving cyclohexanones necessitates an accurate picture of the transition state, we have set out to study the nature of the transition state involved in this reaction.

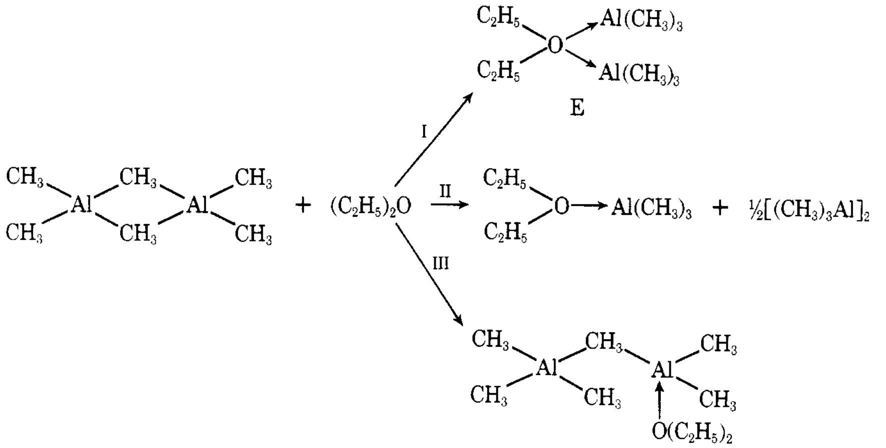

C D

Results and Discussion

If Mole is correct about the intermediacy of C, then it should be possible to detect such an intermediate spectroscopically (NMR) or by observing the colligative properties of the solutions on mixing $(CH_3)_3Al$ and $Ph_2C{=}O$ in 2:1 ratio in hydrocarbon solvent. We have approached this study in two ways. (1) substituting diethyl ether for $Ph_2C{=}O$ (we have shown comparable basicities of diethyl ether and $Ph_2C{=}O$ toward $(CH_3)_3Al$[3]), we should observe a structure comparable to C (e.g., E) when $(CH_3)_3Al$ and diethyl ether are allowed to react in 2:1 ratio provided that such a structure is present. Then (2) it should be possible to make a direct observation of C, provided that it is present in solution, by reaction of $(CH_3)_3Al$ and benzophenone in 2:1 ratio at sufficiently low temperatures where the addition reaction is very slow or nonexistent. Since the basicity of diethyl ether and benzophenone are approximately the same toward $(CH_3)_3Al$,[3] an analogy between the behavior of $(CH_3)_3Al$ and diethyl ether in 2:1 ratio and $(CH_3)_3Al$ and benzophenone in 2:1 ratio should


(1)

E



(2)

(3)

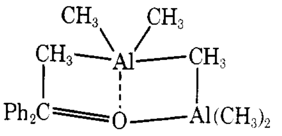
(4)

exist. The advantage of course, in studying the reaction of $(CH_3)_3Al$ with ether is that after complexation, no further reaction can take place (unlike the case with $Ph_2C{=}O$) thus making the system easier to study than the system involving benzophenone.

Reaction of $(CH_3)_3Al$ and Diethyl Ether in 2:1 Ratio. When $(CH_3)_3Al$ and diethyl ether are allowed to react in 2:1 ratio in toluene, three different reaction pathways are possible (I, II, and III). The product from pathway I (E) is easily distinguishable from the product of pathway II by both molecular weight measurements and NMR spectroscopy and from product III by NMR spectroscopy. The molecular weight in benzene of the 2:1 $(CH_3)_3Al–O(C_2H_5)_2$ mixture gave on four additions (0.04–0.15 M) the values 145.8, 143.1, 143.3, and 144.4. The molecular weight of the product expected for pathway II is 145 and for pathways I and III is 218. The molecular weight data then indicate that one-half of the $(CH_3)_3Al$ dimer is completely cleaved to the monoetherate when the $(CH_3)_3Al{:}O(C_2H_5)_2$ ratio is 2:1 and the other half remains in solution as unsolvated $(CH_3)_3Al$ dimer. These results were verified by 100-MHz FT ^1H NMR at −80 °C in toluene. The NMR data are consistent with a 2:1 mixture of $(CH_3)_3Al{\cdot}O(C_2H_5)_2$ and $(CH_3)_3Al$ dimer (ratio of methyl groups $3[(CH_3)_3Al{\cdot}O(C_2H_5)_2]{:}2$(terminal methyls in $\frac{1}{2}[(CH_3)_3Al]$): 1(bridging methyls in $\frac{1}{2}[(CH_3)_3Al]_2$).

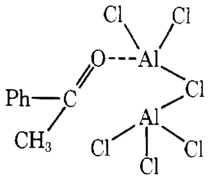
Reaction of $(CH_3)_3Al$ and Benzophenone in 2:1 Ratio. The above data indicate that diethyl ether coordinates so strongly with $(CH_3)_3Al$ dimer that it breaks all of the bridging methyl bonds in a molecule to which ether is attached (pathway II). If the analogy between the basicity of ether and benzophenone toward $(CH_3)_3Al$ is correct, then similar results should be observed with $Ph_2C{=}O$ as were observed with diethyl ether. Addition of $(CH_3)_3Al$ to benzophenone at −78 °C was found to be negligible over the period of time needed to obtain the NMR spectra. Integration of the spectrum for $(CH_3)_3Al$ dimer in toluene at −78 °C showed a 1:2 ratio of bridging to terminal methyl groups. When benzophenone was added to $(CH_3)_3Al$ in 1:2 ratio, the ratio of methyl groups now was 2:1. The low-field signal is due not only to the bridging methyl of the $\frac{1}{2}[Al(CH_3)_3]_2$ dimer remaining in solution, but also to the terminal methyl groups of $(CH_3)_3Al{\cdot}O{=}CPh_2$. Substantiation of this assignment was made by noting that the same low-field signal was observed for $(CH_3)_3Al{\cdot}O{=}CPh_2$ prepared by the reaction of $(CH_3)_3Al$ and $Ph_2C{=}O$ in 1:1 ratio. Thus it is clear that C is not an intermediate in the reaction, but that benzophenone (like diethyl ether) cleaves the $(CH_3)_3Al$ dimer completely when allowed to react in 1:2 ratio to form the monosolvate $(CH_3)_3Al{\cdot}O{=}CPh_2$ and $[(CH_3)_3Al]_2$ according to pathway II.

The question still remains, however, as to whether the initially formed $(CH_3)_3Al{\cdot}O{=}CPh_2$ is attacked by the second molecule of $(CH_3)_3Al$ via transition state B or D. As we have pointed out earlier,[3] there is not a great deal of difference between the two transition states if the transition state is represented by F. The major difference between B and D is that the $(CH_3)_3Al$ in D is free to rotate while in B rigidity is imposed by a bridging methyl group. The important question from a stereochemical standpoint (nature of the transition state) is whether or not a methyl bridge bond is formed as the free monomeric $(CH_3)_3Al$ attacks the $Ph_2C{=}O{\cdot}Al(CH_3)_3$ complex. The formation of such a bond (B) would be energetically favored over D by 6 kcal. In addition, the large negative entropy of activation ($\Delta S^{\ddagger}$) for this reaction (−21.1 eu) supports a cyclic transition state.[3] Because evidence for pathway III involving ether or benzophenone was not found and since only a small concentration of the intermediate would be necessary to effect reaction, further effort was made to indicate the validity of this pathway.



F

Reaction of $(CH_3)_2AlCl$ with $Ph_2C{=}O$ in 2:1 Ratio. Starowieyski and co-workers[6] have presented evidence for a complex (G) in which one chlorine bridge remains intact when $AlCl_3$ is admixed with acetophenone in 2:1 ratio. We had shown earlier[8] that $(CH_3)_2AlCl$ shows similar stereochemistry to $(CH_3)_3Al$ when allowed to react with 4-*tert*-butylcyclohexanone (91% axial attack in 2:1 ratio). By carrying out a study with $(CH_3)_2AlCl$ similar to that we have just described for $(CH_3)_3Al$, we felt that we should be able to observe pathway III (if indeed it exists) since Cl–Al bridge bonds are stronger than CH_3–Al bridge bonds. Also $(CH_3)_2AlCl$ would better resemble the actual situation with $(CH_3)_3Al$ than would $AlCl_3$ used in the study by Starowieyski. Since $(CH_3)_2AlCl$ shows the same unusual stereochemistry as $(CH_3)_3Al$ when allowed to react with 4-*tert*-butylcyclohexanone in benzene, the reaction is presumed to take place via the same transition state.



G

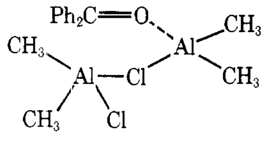
The 60-MHz ^1H NMR spectra for 1:1 and 2:1 ratios of $(CH_3)_2AlCl{:}O{=}CPh_2$ show clearly (Table I) that $(CH_3)_2AlCl$ and $Ph_2C{=}O$ in 2:1 ratio form the complex (H) containing two different methyl groups in 1:1 ratio since neither methyl group

Table I. ^{1}H NMR Data for Aluminum Alkyls and Complexes with Ether and Benzophenone in Toluene

Ratio (Al:O)	$(CH_3)_3Al$: $O(C_2H_5)_2$ [a,c]	$(CH_3)_3Al$: $O{=}CPh_2$ [b,c]	$(CH_3)_2AlCl$: $O{=}CPh_2$ [b,c]
1:0	−2.09, −2.66 (1:2)	−2.08, −2.65 (1:2)	−2.42
1:1	−2.41	−2.07	−2.08
2:1	−2.07, −2.42, −2.65 (1:3:2)	−2.08, −2.65 (2:1)	−2.07, −2.2 (1:1)

[a] Solutions 1 M in $(CH_3)_3Al$. [b] Solutions 0.2 M in $Ph_2C{=}O$. [c] Measured from toluene methyl singlet.

corresponds to that of free $(CH_3)_2AlCl$ or $(CH_3)_2AlCl\cdot O{=}CPh_2$.



H

It is of course very difficult to obtain information concerning the exact structure of a transition state. However, in this study, it was possible to eliminate the intermediacy of complex C and to provide a modest amount of circumstantial evidence to support a six-center transition state in the reaction of $(CH_3)_3Al$ or $(CH_3)_2AlCl$ with benzophenone in 2:1 ratio in benzene. Because of the importance of the stereochemical outcome of organometallic addition reactions, a better understanding of the transition states in such reactions as discussed here should be of considerable value.

Experimental Section

Materials. Trimethylaluminum (Ethyl Corp.) was distilled under N_2 in a glove box. Diethyl ether was distilled under N_2 from $LiAlH_4$. Benzophenone was doubly distilled and stored in a desiccator over P_2O_5. Aluminum chloride was purified by sublimation under N_2 at 180 °C and transferred in a glove box. Benzene was distilled from $NaAlH_4$ under N_2 and toluene was distilled under N_2 from sodium.

Aluminum Alkyl Solutions. All aluminum alkyl solutions were standardized by total aluminum analysis (EDTA) and total methane after hydrolysis. The purity of each aluminum alkyl was further checked by NMR for the presence of aluminum alkoxides. The solutions were handled at the bench using standard Schlenk tube techniques.

Molecular Weight. Molecular weight measurements were carried out according to a procedure previously reported.[9] The k_f for benzene was determined experimentally using Me_3Al; $k_f = 5.163$. All solutions were prepared by weight and all additions were by weight.

NMR Samples. NMR samples for 100-MHz ^{1}H NMR were prepared in a glove box using 10% by volume of toluene-d_8 (Aldrich Chemical Co.) and then vacuum sealed. The NMR samples for 60-MHz ^{1}H NMR were prepared by addition of reagents to an NMR tube fitted with a serum cap and filled with nitrogen. The NMR tube was immersed in a dry ice–acetone bath before addition of Me_3Al or Me_2AlCl to the $Ph_2C{=}O$ which was added at room temperature.

NMR. ^{1}H NMR spectra (100 MHz) were recorded on a JEOL 100-MHz Fourier transform instrument. A Varian A-60D equipped with a low-temperature probe was used for obtaining 60-MHz NMR spectra. The $(CH_3)_3Al\cdot O{=}CPh_2$ (2:1) sample was checked for product formation by raising the probe temperature to where coalescence of the complex peaks would allow observation of product peaks.

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Registry No.—$(CH_3)_3Al$, 75-24-1; $(CH_3)_2AlCl$, 1184-58-3; $O(C_2H_5)_2$, 60-29-7; $O{=}CPh_2$, 119-61-9; $(CH_3)_3Al{:}O(C_2H_5)_2$, 14878-85-4; $(CH_3)_3Al{:}O{=}CPh_2$, 60706-08-3; $(CH_3)_2AlCl{:}O{=}CPh_2$(1:1 ratio), 60706-09-4; $(CH_3)_2AlCl{:}O{=}CPh_2$(1:2 ratio), 60706-10-7.

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