Stereoselective Organometallic Alkylation Reactions. II. Organomagnesium and Organoaluminum Addition to Ketones Having Varied Steric Requirements. A New Concept of Stereochemical Control[1]

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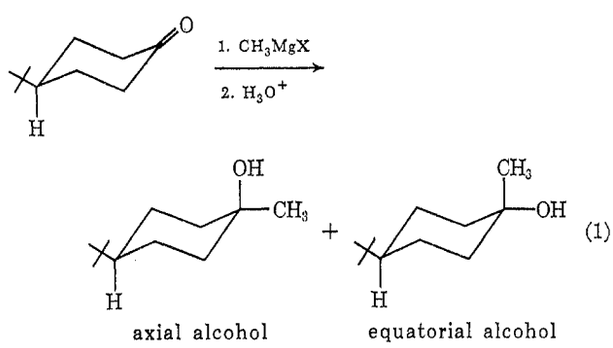
The stereochemistry of organoaluminum and organomagnesium addition to several ketones has been investigated. Alkylation occurred from the least hindered side of the molecule in all cases studied with organoaluminum and organomagnesium compounds in diethyl ether as well as with organoaluminum compounds in a 1:1 reactant ratio in benzene. However, when the organoaluminum compound to ketone ratio was 2:1 or greater in benzene solvent, a significant and often predominant percentage of the product resulted *via* alkylation from the most hindered side of 2-methylcyclopentanone, 4-*tert*-butylcyclohexanone, and 3,3,5-trimethylcyclohexanone. We conclude that the reversal of stereochemistry in these cases is due neither to the fundamental nature of four- and six-center transition states nor to a conformational change in the complexed ketone but to a compression of the complexed carbonyl group in a six-center transition state against the 2,6-diequatorial hydrogens in the cyclohexanone cases and against the 2-methyl group in the 2-methylcyclopentanone case. In those ketones in which product ratios are dependent on reactant ratios, the "compression effect" opposes the "steric approach factor." When the organoaluminum compound to ketone ratio is 2:1 or greater in benzene solvent, results with norcamphor, 3-methylcyclopentanone, and *cis*-3,4-dimethylcyclopentanone are nearly identical with those found with a 1:1 reactant ratio. In these ketones the "compression effect" is either nonexistant owing to equivalent substituents on carbon atoms adjacent to the carbonyl or reinforces the "steric approach factor." Further evidence against a conformational change from the chair form of 4-*tert*-butylcyclohexanone to the half-chair of the ketone–aluminum alkyl complex to explain the change in stereochemistry is provided by a nmr analysis of the spectra of 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3 and the corresponding complex with $AlCl_3$. Both spectra indicate clearly the presence of axial and equatorial hydrogens in the 2,6 positions indicating that the complex is not in the half-chair conformation. The concepts of "steric approach control" and "torsional strain" do not provide a satisfactory explanation for the observed stereochemistry; however, the proposed "compression effect" does provide a satisfactory explanation of the observed stereochemistry in this study as well as all other studies involving organometallic alkylation reactions with which we are familiar.

Early concepts concerning factors involved in the stereochemistry of reduction of cyclic ketones were formulated by Dauben.[2] "Steric approach control" assumed an early, reactant-like transition state in which the entering group approached the least hindered side of the ketone. "Product development control" assumed a late, product-like transition state in which the observed stereochemistry reflected the stability of the products. In the absence of significant steric factors involving the attacking reagent on the substrate, "product development control" determined the observed stereochemistry.

Competitive rate experiments involving reduction of several cyclohexanones have demonstrated that the rate of axial attack is greatly reduced when the axial hydrogen at C-3 and/or C-5 is replaced by an axial methyl group, whereas the rate of equatorial attack remains essentially constant.[3] Thus, factors other than "product development control" appear to influence stereochemistry.

One of the first comprehensive studies concerning the steric course of alkylation of cyclic ketones by organometallic compounds was reported by Houlihan.[4] Methyl Grignard reagents were allowed to react with 4-*tert*-butylcyclohexanone in diethyl ether to yield the 4-*tert*-butyl-1-methylcyclohexanols (eq 1). With all reagents studied the axial alcohol was always formed in 50% or greater yield. Thus, attack was found to occur predominantly at the least hindered side of the carbonyl group, the equatorial side.



(1)

Chérest and Felkin[5] considered the stereoselectivity of alkylation of cyclohexanones (chair conformation) to be influenced by two factors: (1) the steric strain of the incoming group with the 3,5-axial substituents and (2) the torsional strain (single bond repulsion) of the incoming group with the 2,6-axial substituents. The two effects oppose each other; steric strain hinders axial attack whereas torsional strain hinders equatorial attack. The actual stereochemistry of alkylation depends upon which effect is greater in a particular case. They suggest that for a cyclohexanone derivative with no axial substituent larger than hydrogen small entering groups (hydride) are opposed more strongly by torsional strain and therefore attack occurs predominantly from the axial side, whereas larger groups (methyl, ethyl, etc.) are opposed more strongly by steric strain and attack occurs predominantly from the equatorial side.[6] If the cyclohexanone contains one or more large axial substituents (methyl, ethyl, etc.) at the 3 or 5 positions, steric strain is highly important regardless of the size of the incoming group.

(1) We are indebted to the National Science Foundation (Grant No. GP-31550X) for partial support of this work.

(2) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Amer. Chem. Soc.*, **78**, 2579 (1956).

(3) E. Eliel and Y. Senda, *Tetrahedron*, **26**, 2411 (1960).

(4) W. J. Houlihan, *J. Org. Chem.*, **27**, 3860 (1962).

(5) M. Chérest and H. Felkin, *Tetrahedron Lett.*, 2205 (1968).

(6) (a) M. Chérest, H. Felkin, and C. Frajerman, *ibid.*, 379 (1971); (b) M. Chérest and H. Felkin, *ibid.*, 383 (1971).

An apparent exception to the Chérest and Felkin concept[5,6] occurs when trimethylaluminum is allowed to alkylate 4-*tert*-butylcyclohexanone in 2:1 ratio in hydrocarbon solvent.[7] Reaction of 4-*tert*-butylcyclohexanone with 1 equiv of $(CH_3)_3Al$ in benzene solvent gives predominantly equatorial attack (~70%) as predicted, but reaction with 2 or more equiv of trimethylaluminum gives predominantly axial attack (~90%).

Earlier we reported[8] that the reaction of $(CH_3)_3Al$ and benzophenone in a 1:1 ratio results in a transition state describing the rate-determining step as containing one molecule of $(CH_3)_3Al$ and one molecule of ketone. The reaction occurs through the formation of a complex followed by formation of a four-center transition state. On the other hand, when $(CH_3)_3Al$ and benzophenone were allowed to react in a 2:1 or greater ratio, it was found that the transition state describing the rate-determining step contains two molecules of $(CH_3)_3Al$ and one molecule of ketone. The mechanism of this reaction is envisioned as attack of a molecule of $(CH_3)_3Al$ on the 1:1 complex, possibly *via* a six-center transition state, to form the product. In light of the fact that two different mechanisms are operating in these two cases,[8] it is not surprising to find a difference in the stereochemistry; however, such a dramatic change in the stereochemistry was surprising.

Close scrutiny of molecular models depicting four- and six-center transition states do not readily reveal the reason for the unusual stereochemistry found in the reaction of $(CH_3)_3Al$ and 4-*tert*-butylcyclohexanone in hydrocarbon solvent. From a steric point of view, axial attack on a chair conformation should be hindered by the 3 and 5 axial substituents regardless of whether the transition state is four or six center. It is conceivable that cyclohexanones complexed to aluminum alkyls exist in conformations other than chairs, or other factors, not yet considered, might be important. In order to resolve the speculation surrounding this unusual stereochemical observation, a comprehensive study of the reaction of aluminum alkyls and aryls with several ketones was undertaken. In most cases the organomagnesium compounds with corresponding alkyl or aryl groups were also studied for comparison purposes. In addition, an nmr study of 4-*tert*-butylcyclohexanone and 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3 (axial 3-D) and their aluminum chloride complexes was undertaken in order to obtain evidence for the preferred conformation of these species in solution.

Experimental Section

Materials.—Trimethylaluminum and triethylaluminum were obtained from Texas Alkyls, Inc., and distilled through a 1-ft glass helix packed column prior to use. Triphenylaluminum was prepared and purified by the method of Eisch,[9] mp 240–241° (lit.[9] mp 240–242°). Grignard reagents were prepared by methods reported in detail elsewhere.[10]

2-Methylcyclopentanone, 3-methylcyclopentanone, and *cis*-3,4-dimethylcyclopentanone, obtained from Chemical Samples Co., were dried over activated 4-A molecular sieve prior to use. 3,3,5-Trimethylcyclohexanone, obtained from Chemical Samples Co., was distilled under nitrogen prior to use. Norcamphor (Aldrich Chemical Co.) and 4-*tert*-butylcyclohexanone (Frinton Lab.) were sublimed prior to use. Analysis of all ketones by glpc showed each of them to be at least 98% pure.

Fisher reagent grade anhydrous aluminum chloride was sublimed under nitrogen at 200°.

4-*tert*-Butylcyclohexanone-*cis*-3,5,5-d_3 (axial 3-D) was obtained from 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3 oxime[11] by cleavage with sodium bisulfite followed by hydrolysis with dilute HCl.[12] The reaction progress was followed by glpc.

Fisher certified anhydrous diethyl ether was distilled from $LiAlH_4$ prior to use. Fisher certified thiophene-free benzene was distilled from $NaAlH_4$ prior to use.

Apparatus and Procedure.—A Varian A-60D, 60 MHz spectrometer was used for recording nuclear magnetic resonance spectra. An F & M Model 720 gas chromatograph was used to identify all reaction products. Transfers of materials used in this study were performed in a glove box described elsewhere[13] or were transferred in Schlenk tubes under a blanket of high-purity nitrogen.

Calibrated syringes equipped with stainless steel needles were usef for transfer of reagents. Deliveries could be reproduced to better than ±0.5%.

Solutions of ketones were prepared by weighing out a known amount of ketone in a calibrated volumetric flask and diluting to the mark with an appropriate solvent.

Solutions of organoaluminum compounds and Grignard reagents were prepared by diluting known amounts of the standard reagents with an appropriate solvent. In the case of Grignard reagents, magnesium analysis was carried out by EDTA titration of a hydrolyzed aliquot at pH 10 using Eriochrome Black T as an indicator. The concentrations of organoaluminum solutions were determined by hydrolysis of an aliquot followed by aluminum analysis which was carried out by EDTA–zinc acetate titration at pH 4 using dithizone as an indicator.

Reactions.—All reactions were carried out on a vacuum manifold equipped with three-way glass stopcocks attached to 24/40 inner joints. Round-bottom flasks equipped with 24/40 outer joints were attached to the manifold and the system was evacuated, flamed, and refilled with nitrogen three times prior to use.

In the case where a 1:1 ratio of organoaluminum compound to ketone in benzene was desired, an appropriate amount of ketone was added to the flask under nitrogen flush followed by injection of the correct amount of organoaluminum reagent. This mode of addition ensured that at no time was the organoaluminum compound in excess. In all other cases, ketone was added to the organometallic compounds. Mixing was accomplished *via* rapid stirring with a Teflon stirring bar.

Product Analysis.—Products were analyzed by glpc where separations were possible and by nmr spectroscopy in other cases. In those cases where glpc was employed, reaction mixtures were hydrolyzed with distilled water. After an appropriate internal standard was added and the metallic salts had separated from the organic layer, a sample of the supernatant layer was withdrawn for analysis. The following conditions were employed for product analysis by glpc. For trimethylaluminum addition to 4-*tert*-butylcyclohexanone, a 10 ft × 0.25 in. column of 20% SAIB on Chromosorb W at 182° (flow 60 ml/min) gave the following retention times for ketone, axial alcohol, and equatorial alcohol: 11.3, 8.7, and 10.7 min. For trimethylaluminum addition to 3,3,5-trimethylcyclohexanone, the same column and conditions gave retention times of 5.0, 4.3, and 6.0 min for the ketone, axial alcohol, and equatorial alcohol, respectively. For trimethylaluminum addition to 2-methylcyclopentanone, a 15-ft column of 10% diglycerol on Chromosorb W at 80° gave 5.4, 7, and 12.4 min for ketone, *trans*-1,2-dimethylcyclopentanol, and *cis*-1,2-dimethylcyclopentanol, respectively. For triethylaluminum addition to 4-*tert*-butylcyclohexanone, a column of 20% SAIB on 5 Chromosorb W at 150° (flow 60 ml/min) gave the following retention times for ketone, axial alcohol (alkyla-

(7) (a) E. C. Ashby and S. H. Yu, *J. Chem. Soc. D*, 351 (1971); (b) E. C. Ashby, S. H. Yu, and P. V. Roling, *J. Org. Chem.*, **37**, 1918 (1972); (c) J. L. Namy and H. Normant, *C. R. Acad. Sci. Ser. C*, **272**, 1334 (1971).

(8) E. C. Ashby, J. Laemmle, and H. M. Neumann, *J. Amer. Chem. Soc.*, **90**, 5183 (1968).

(9) J. J. Eisch and W. Kaska, *ibid.*, **88**, 2976 (1966).

(10) (a) F. W. Walker and E. C. Ashby, *ibid.*, **91**, 3845 (1969); (b) E. C. Ashby, J. Laemmle, and H. M. Neumann, *ibid.*, **94**, 5421 (1972).

(11) We are indebted to Professor A. C. Huitric, College of Pharmacy, University of Washington, for a generous gift of 0.8 g of 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3 oxime.

(12) S. H. Pines, J. M. Chemerda, and M. A. Kozlowski, *J. Org. Chem.*, **31**, 3446 (1966).

(13) T. L. Brown, D. W. Dickerhoof, D. A. Bafus, and G. L. Morgan, *Rev. Sci. Instrum.*, **33**, 491 (1962).

tion), equatorial alcohol (alkylation), axial alcohol (reduction), and equatorial alcohol (reduction): 30, 39, 45, 27.7, and 32.2 min. For triethylaluminum addition to 3,3,5-trimethylcyclohexanone, the same column at 155° gave retention times of 9.6, 13.3, 18, 10.4, and 12.3 min for ketone, axial alcohol (alkylation), equatorial alcohol (alkylation), axial alcohol (reduction), and equatorial alcohol (reduction), respectively.

The isomeric alcohols resulting from the methylation of norcamphor, 3-methylcyclopentanone, and *cis*-3,4-dimethylcyclopentanone could not be separated by glpc. In addition, the isomeric alcohols resulting from the phenylation of all ketones studied could not be determined by glpc owing to dehydration. Thus, the isomer ratios in these cases were determined by nmr analysis.

Several known mixtures of authentic samples of the methylnorborneols were prepared. The peak heights of the methyl singlets of the exo alcohol (73 Hz) and endo alcohol (74 Hz) in benzene were related to their concentrations. Reaction mixtures involving norcamphor were analyzed by comparing the nmr spectra in benzene to those of the authentic mixtures.

The isomer ratios in the case of the methylation of 3-methylcyclopentanone and *cis*-3,4-dimethylcyclopentanone and in the phenylation of all ketones was determined by nmr spectroscopy utilizing the peak areas of the hydroxyl protons of the alcohols in DMSO-d_6. In these cases work-up of reaction mixtures was carried out as follows. When benzene was employed as a solvent, the reaction solution was subjected to vacuum until all benzene had been removed. Wet ether was then added to the carbinolate in order to effect hydrolysis. The solution was then transferred to a separatory funnel and the aluminum salts were removed by repeated washings with distilled water. The ether layer was separated and allowed to evaporate and DMSO-d_6 was added to the sample. The sample was then dried over Linde 4A molecular sieve and transferred to a nmr tube. The purpose of this treatment was twofold. First, no acids were used in the work-up in order to minimize dehydration and equilibration and no evidence of either was found. Secondly, only the carbinolate was subjected to vacuum to remove solvent, thus lessening the possibility of stripping out a portion of the desired alcohols. Addition of benzaldehyde to the sample as an internal nmr standard demonstrated that this method was satisfactory with all ketones and 100% recovery was realized. In those cases where ether was employed as a solvent, the work-up was identical except that the solution was hydrolyzed directly with distilled water.

The assignment of each alcohol hydroxyl peak to a particular isomer was based on numerous reports in the literature concerning their chemical shifts in DMSO and in DMSO-d_6.[14] For the reaction of trimethylaluminum and 3-methylcyclopentanone the chemical shifts for the hydroxyl protons are τ 5.82 for *trans*-1,3-dimethylcyclopentanol and 5.90 for *cis*-1,3-dimethylcyclopentanol. For the methylation of *cis*-3,4-dimethylcyclohexanone, the chemical shifts are τ 5.8 for *trans*-1-methyl-*cis*-3,4-dimethylcyclopentanol and 5.97 for *cis*-1,3,4-trimethylcyclopentanol. In the case of the phenylation of 4-*tert*-butylcyclohexanone, the chemical shifts are τ 5.44 and 5.27 for the axial and equatorial hydroxyl protons, respectively. In the case of phenylation of 3,3,5-trimethylcyclohexanone, a single hydroxyl resonance was observed at τ 5.5 for the axial alcohol. No other hydroxyl peak was observed in any run. In the case of the phenylation of 2-methylcyclopentanone, the chemical shifts of the hydroxyl protons are τ 5.52 for *trans*-1-phenyl-2-methylcyclopentanol and 5.23 for *cis*-1-phenyl-2-methylcyclopentanol. In the case of the phenylation of 3-methylcyclopentanone, the chemical shifts of the hydroxyl protons are τ 5.23 for *trans*-1-phenyl-3-methylcyclopentanol and 5.25 for *cis*-1-phenyl-3-methylcyclopentanol. In the case of the phenylation of *cis*-3,4-dimethylcyclopentanone, the chemical shifts for the hydroxyl protons are τ 5.14 for *trans*-1-phenyl-*cis*-3,4-dimethylcyclopentanol and 5.22 for *cis*-1-phenyl-3,4-dimethylcyclopentanol.

In all cases involving reaction of trimethyl- and triphenylaluminum in a 2:1 ratio in benzene and the corresponding Grignard reagents with ketones in all ratios in ether, 100% yield of alcohols formed by addition was realized. In the cases involving triethylaluminum reaction with ketones, both alkylation and reduction were observed. When organoaluminum compounds were allowed to react with ketones in 1:1 ratio in benzene or in diethyl ether, reaction rates were much slower, resulting in conversion to alcohol product from 50 to 100% depending on the individual cases with the remaining material being unreacted ketone. Thus, no products other than those arising from normal alkylation were observed except in the case of triethylaluminum–ketone reaction, which produced some reduction product.

Ketone–$AlCl_3$ Complexes.—Solutions of 4-*tert*-butylcyclohexanone–aluminum chloride complex and 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3 (axial 3-D)–aluminum chloride complex were prepared by adding an appropriate amount of ketone solution in benzene to a weighed amount of $AlCl_3$ in a 1-ml volumetric flask and diluting to the mark with benzene. All the $AlCl_3$ dissolved to give solutions 1 *M* in complex. The formation of complex was verified by the fact that solubility of $AlCl_3$ in the benzene–ketone solution greatly exceeded the solubility of $AlCl_3$ in benzene as determined in this study and reported elsewhere.[15] Solutions of 4-*tert*-butylcyclohexanone–aluminum chloride in benzene were initially colorless but turned yellow over a period of time. This color is possibly due to formation of small amounts of condensation products.[16] However, a 1.2 *M* solution of 4-*tert*-butylcyclohexanone–aluminum chloride in benzene at room temperature was sampled over a period of time by glpc. The peak area of the ketone remained the same for equal sample injections after 1 week and no other peaks were detected. Thus the concentration of condensation products formed must be very small. Nevertheless, as an added precaution, samples employed in the nmr study were stored in sealed nmr tubes and were kept frozen at all times except when actual spectra were being taken.

Results and Discussion

Table I illustrates the reaction of several organoaluminum compounds with 4-*tert*-butylcyclohexanone.

TABLE I

REACTION OF ORGANOALUMINUM COMPOUNDS WITH 4-*tert*-BUTYLCYCLOHEXANONE

AlR_3	Solvent	Initial [AlR_3], *M*	Ratio of AlR_3/ ketone	% axial[a] alcohol	% equatorial[a] alcohol
$(CH_3)_3Al$	Benzene	0.28	0.5	80	20
		0.37	1.0	76	24
		0.41	1.5	53	47
		0.45	2.0	17	83
		0.48	3.0	12	88
$(C_2H_5)_3Al$[b]	Benzene	0.43	1.0	88	12
		0.54	2.0	17	83
		0.62	4.0	14	86
$(C_6H_5)_3Al$	Benzene	0.074	1.0	51	49
		0.077	2.0	27	73
		0.078	4.0	8	92
$(CH_3)_3Al$	Diethyl ether	0.33	1.0	85	15
		0.42	3.0	87	13
$(C_2H_5)_3Al$[b]	Diethyl ether	0.27	1.0	88	12
		0.33	3.0	88	12
$(C_6H_5)_3Al$	Diethyl ether	0.17	1.0	44	56
		0.19	3.0	44	56

[a] Normalized as per cent axial alcohol + per cent equatorial alcohol = 100%. [b] Reaction gives some reduction product with the equatorial alcohol predominating (~78%) in all cases.

It may be noted that in the reaction of $(CH_3)_3Al$ and $(C_2H_5)_3Al$ in benzene solvent the predominant isomer formed is the axial alcohol when the organoaluminum compound to ketone ratio is 1:1 or less. The same

(14) (a) O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **86**, 1256 (1964); (b) R. J. Ouellette, *ibid.*, **86**, 4378 (1964); (c) G. D. Meakins, R. K. Percy, E. E. Richards, and R. N. Young, *J. Chem. Soc. C*, 1106 (1968); (d) J. Battioni, W. Chodkiewicz, and P. Cadiot, *C. R. Acad. Sci., Ser. C*, **264**, 991 (1967); (e) J. Battioni, M. Chapman, and W. Chodkiewicz, *Bull. Soc. Chim. Fr.*, 976 (1969); (f) J. Battioni and W. Chodkiewicz, *ibid.*, 981 (1969); (g) *ibid.*, 1824 (1971).

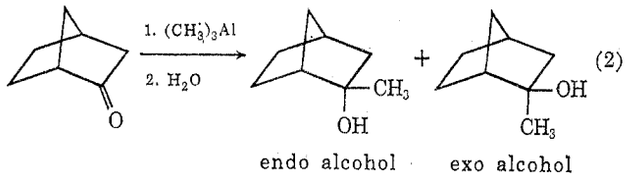
(15) (a) B. Menschutkin, *J. Russ. Phys. Chem. Soc.*, **41**, 1089 (1909); (b) L. Bruner, *Z. Phys. Chem.*, **41**, 333 (1902).

(16) (a) J. G. Pereira, *Chemiker 2*, **33**, R406 (1909); (b) E. Louis, *C. R. Acad. Sci.*, **95**, 602 (1882); (c) C. Courtot and V. Ouperoff, *ibid.*, **191**, 416 (1930).

is true for these compounds in diethyl ether at all reactant ratios. These reactions are believed to involve four-center transition states[8,17] and a reasonable explanation of the stereochemistry of the products is that the organometallic reagent attacks at the least hindered (equatorial) side of the chair conformation of the ketone. When the ratio of $(CH_3)_3Al$ or $(C_2H_5)_3Al$ to ketone is 2:1 or greater in benzene solvent, the predominant product is the equatorial alcohol arising from attack at the more hindered (axial) side of the chair conformation of the molecule. On the other hand, triphenylaluminum presents a slightly different picture. As in the case of $(CH_3)_3Al$ and $(C_2H_5)_3Al$ the ratio of product alcohol from triphenylaluminum is essentially the same in 1:1 reactant ratio in benzene and all ratios in ether. However, the initial ratio of alcohols is about 50:50 when the $(C_6H_5)_3Al$ to ketone ratio is 1:1 followed by the usual change involving predominant axial attack. Thus the reaction of $(C_6H_5)_3Al$ with ketone in benzene in 1:1 ratio and in ether in all ratios appears to have little preference for attack at either the axial or equatorial position. However, the significant point is that the ratio changes in favor of axial attack as the $(C_6H_5)_3Al$ to ketone ratio in benzene is increased from 1:1 to 2:1 or greater.

Considerations Involving an Early Transition State. Steric Approach Control *vs.* Compression Effect.—Assuming an early transition state, three possibilities were considered as explanations of the unusual stereochemistry observed in the reactions of excess organoaluminum compounds with 4-*tert*-butylcyclohexanone in benzene solvent. First, it was considered that the reversal in stereochemistry may be inherent in the change from a four- to a six-center transition state. That is, a six-center transition state may always lead to alkylation of a substrate from the opposite side when compared to a four-centered transition state. Alternatively, it was considered possible that the 4-*tert*-butylcyclohexanone–AlR_3 complex might exist in a conformation other than a chair (*e.g.*, boat or half chair), thus rendering the axial side the least hindered side in a six-center transition state. Finally, it was considered possible that some other, heretofore unknown factor might have given the observed result.

In order to obtain information as to whether a change in product isomer ratio will always occur when a ketone is subjected to alkylation *via* a four- or six-center transition state, the reaction of trimethylaluminum with norcamphor in benzene was examined (eq 2). Since



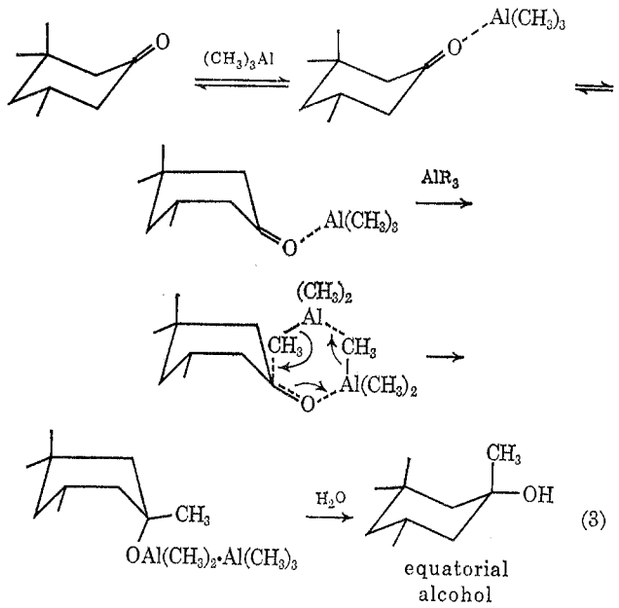
norcamphor is a rigid bicyclic ketone, the possibility of a conformational change in which the endo side becomes the least hindered side is eliminated. The results show that alkylation of norcamphor in benzene by trimethylaluminum over a $(CH_3)_3Al$:ketone ratio of 0.5–4 produced on hydrolysis 95% of the endo alcohol regardless of the R_3Al:ketone ratio. These results can be easily explained by noting that attack occurs primarily from the least hindered side of the molecule, *i.e.*, the exo side. They also show that a reversal in stereochemistry does not occur in all systems when the mechanism of alkylation changes from a four-center to a six-center transition state.

The results with the rigid norcamphor molecule suggested further study concerning the possibility that the reversal in stereochemistry found with 4-*tert*-butylcyclohexanone and excess $(CH_3)_3Al$ in benzene may be due to the fact that the complexed ketone exists in a nonchair conformation (boat or half chair). A boat conformation transition state has been used to explain the large percentage of axial attack on 3,3,5-trimethylcyclohexanone by various aluminohydrides.[18] If the 4-*tert*-butylcyclohexanone–AlR_3 complex exists in a boat conformation, the side of the molecule which is most hindered in the chair conformation becomes the least hindered in the boat conformation. Although attack on the boat conformation of the complex is from the least hindered side, after alkylation the boat flips back to the chair conformation, exhibiting the methyl group axial as if the chair conformation of the complex had been attacked from the most hindered side. Two factors that argue against this conformational change are the following: (1) the boat conformation is a higher energy conformation than the chair (thus the rate of reaction of the boat conformation would have to be hundreds of times faster than that of the chair conformation) and (2) if the transition state resembles the product to any extent, it should be of higher energy owing to the bulk of the resulting $-OAl(CH_3)_2 \cdot Al(CH_3)_3$ groups interacting with the endo hydrogens and the flagpole hydrogen. In order to obtain more evidence concerning this point, the stereochemistry of the reactions of trimethyl- and triphenylaluminum with 3,3,5-trimethylcyclohexanone was studied. It has been pointed out that the 3-axial methyl group destabilizes the chair conformation such that 3,3,5-trimethylcyclohexanone and its AlR_3 complex should exist in flexible conformations to a greater extent than 4-*tert*-butylcyclohexanone.[18] It should be noted that, owing to the steric requirement of the 3-axial methyl group, if attack in the 2:1 case occurs *via* the chair conformation of the complex, the extent of axial attack should be much less than in a similar reaction with 4-*tert*-butylcyclohexanone. However, if attack occurs through the boat conformation of the complexed ketone, then the percentage of axial attack for 4-*tert*-butylcyclohexanone and 3,3,5-trimethylcyclohexanone should be comparable since the steric factors would be nearly equal (eq 3).

The results, shown in Table II, demonstrate that the percentage of axial attack is much smaller than that found with 4-*tert*-butylcyclohexanone. For example, in all cases involving the reaction of excess $(CH_3)_3Al$ or $(C_2H_5)_3Al$ with 4-*tert*-butylcyclohexanone in benzene, the equatorial alcohol is the major product whereas in the case of 3,3,5-trimethylcyclohexanone it is never the major product. In the case of arylation involving triphenylaluminum, 4-*tert*-butylcyclohexanone gives 92% axial attack at 4:1 ratio whereas the results with 3,3,5-trimethylcyclohexanone show no axial attack at any ratio. In addition, the reaction

(17) E. C. Ashby and J. Laemmle, *J. Org. Chem.*, **33**, 3389 (1968).

(18) S. R. Landor and J. P. Regan, *J. Chem. Soc. C*, 1159 (1967).



(3)

TABLE II

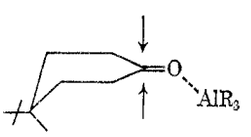
REACTION OF ORGANOALUMINUM COMPOUNDS WITH 3,3,5-TRIMETHYLCYCLOHEXANONE IN BENZENE

AlR_3	Initial $[AlR_3]$, M	Ratio of AlR_3/ ketone	% axial[a] alcohol	% equatorial[a] alcohol
$(CH_3)_3Al$	0.60	1.0	100	0
	0.74	2.0	81	19
	1.55	4.0	60	40
$(C_2H_5)_3Al$[b]	0.42	1.0	100	0
	0.53	2.0	89	11
	0.62	4.0	78	22
$(C_6H_5)_3Al$	0.073	1.0	100	0
	0.076	2.0	100	0
	0.078	4.0	100	0

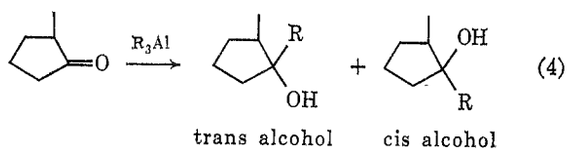
[a] Normalized as per cent axial alcohol + per cent equatorial alcohol = 100%. [b] Reaction gives some reduction product with the axial alcohol predominating (~70–75%) in all cases.

of $(CH_3)_3Al$, $(C_2H_5)_3Al$, and $(C_6H_5)_3Al$ with 3,3,5-trimethylcyclohexanone in diethyl ether gave 100% equatorial attack regardless of the ratio of R_3Al to ketone. Thus, in order for the steric requirement of the 3 axial methyl group to be important, it is unlikely that attack on 3,3,5-trimethylcyclohexanone would occur through the boat conformation of the ketone–AlR_3 complex.

Although reaction of excess $(CH_3)_3Al$ with cyclohexanones does not appear to occur through the boat conformation of the complexed ketone, other conformations with lower energy requirements cannot be immediately overruled. For example, it is possible that a significant percentage of the 4-*tert*-butylcyclohexanone–AlR_3 complex might exist in a half-chair conformation. Top-side attack on the complex in this



conformation by a second organoaluminum molecule would be somewhat favored owing to the steric effect of the flagpole hydrogen on C-4, although it does not seem reasonable that attack from this direction is so favorable as to result in 90% attack from this side. Top-side attack would, of course, produce equatorial alcohol. In order to pursue this possibility further, the reaction of 2-methylcyclopentanone with Grignard reagents and aluminum alkyls were investigated (eq 4). The alkylation of this ketone was reported



(4)

to result in 60–70% trans attack (giving cis alcohol) in the case of Grignard reagent alkylation,[14d,g] thereby demonstrating a much smaller steric requirement than for norcamphor. Although the 2-methylcyclopentanone ring can pucker to some extent, it cannot undergo conformational distortions so servere that the side of the ring possessing the methyl group (cis side) is the least hindered Therefore, if the reason for the reversal of stereochemistry observed with the cyclohexanone systems is due to conformational changes which render the axial side of the chair conformation of the complexed ketone the least hindered side, then little or no change in stereochemistry with reactant ratio in the case of organoaluminum alkylation of 2-methylcyclopentanone in benzene should be observed since such a conformational change is not possible. The results are shown in Table III.

TABLE III

REACTION OF ORGANOALUMINUM COMPOUNDS AND GRIGNARD REAGENTS WITH 2-METHYLCYCLOPENTANONE

RM	Solvent	Initial [RM], M	Ratio of RM/ ketone	% cis[a] alcohol	% trans[a] alcohol
$(CH_3)_3Al$	Benzene	0.1	1.0	60	40
		0.2	2.0	23	77
		0.4	4.0	22	78
$(C_6H_5)_3Al$		0.076	1.0	100	0
		0.076	2.0	94	6
		0.076	4.1	84	16
CH_3MgBr	Diethyl ether	0.88	8.8	60	40
C_6H_5MgBr	Diethyl ether	0.34	4.0	100	0

[a] Normalized as per cent cis alcohol + per cent trans alcohol = 100%.

It should be noted that, when Grignard reagents and trimethylaluminum react with 2-methylcyclohexanone in 1:1 ratio, attack trans to the 2-methyl group takes place, producing the cis alcohols as the predominant product. These reagents are known to alkylate ketones *via* a four-center transition state[8,10b] and the stereochemistry observed can readily be explained by noting that attack occurs preferentially at the least hindered side of the molecule. In the case of $(CH_3)_3Al$ alkylation in a 2:1 or greater ratio in benzene, a much larger percentage of cis attack is observed, producing the trans alcohol. Even in the case of $(C_6H_5)_3Al$, more cis attack is observed when the R_3Al:ketone ratio is varied from 1:1 to 4:1. Thus a significant increase in the amount of attack from the most hindered side of the molecule is ob-

served when the R_3Al:ketone ratio is 2:1 compared to when the ratio is 1:1.

The results presented thus far indicate that the reversal in stereochemistry observed in the organoaluminum ketone systems in benzene is due neither to a fundamental occurrence inherent in the nature of a six-center transition state nor to conformational changes in the complexed ketone but to a factor not previously described. The concept of "steric approach control" satisfactorily explains the results of the AlR_3–ketone reactions in 1:1 ratio in benzene as well as Grignard reagent and AlR_3 reactions in ether in all ratios owing to the fact that simple bimolecular reactions should be controlled by steric factors. However, both the concepts of "steric approach control" and "torsional strain" are inadequate to explain the results of the AlR_3–ketone reaction in benzene in 2:1 or greater ratios.

The following explanation satisfies the stereochemistry observed with each ketone. Figure 1 represents the various orientations of the carbonyl oxygen to substituents on adjacent carbon atoms for each ketone studied. (It should be noted that Figure 1 indicates the cyclohexanones to be in perfect chair conformations and the cyclopentanones to be planar. While this may not be exactly the case, it is a reasonable approximation.) Calculations by Allinger[19a] and Fournier[19b] give the dihedral angle H_{eq}–C–C–O in cyclohexanones as 3.3 and 5.6°, respectively. The dihedral angle H_{eq}–C–C–O···AlR_3 in the cyclohexanone–AlR_3 complex would be expected to be as large as or larger than in the uncomplexed ketone owing to the steric interaction of the complexed carbonyl with the 2,6-diequatorial hydrogens Figure 1A illustrates the angle between the carbonyl oxygen and the hydrogens on adjacent carbons for the 4-*tert*-butylcyclohexanone–AlR_3 complex. It can be seen that equatorial attack by a second molecule of R_3Al compresses the complexed carbonyl against the equatorial hydrogens in the transition state. On the other hand, axial attack leads to a staggered arrangement between the complexed carbonyl and hydrogens on adjacent carbon atoms. Thus, in the case of the cyclohexanones, this "compression effect" favors attack from the more hindered side of the molecule in the 2:1 R_3Al:ketone ratio. This same effect explains the stereochemistry observed with the other ketones. In the case of 2-methylcyclopentanone, Figure 1B shows the orientation between the carbonyl oxygen and the substituents on the 2 carbon atom and Figure 1C shows the orientation between the carbonyl oxygen and the substituents on the 5 carbon atom. Trans attack by a second organoaluminum molecule compresses the complexed carbonyl into a methyl group and a hydrogen in the transition state, whereas cis attack compresses the complexed carbonyl between two hydrogens. Thus, the "compression effect" favors attack by a second molecule of organoaluminum compound from the most hindered side of the ketone, the cis side.

In the above cases the "compression effect" and the "steric approach factor" oppose each other. Thus, a reversal of stereochemistry is anticipated where the ratio of organoaluminum compound to ketone is increased from 1:1 to 2:1. Norcamphor represents a different case. Figure 1C represents the orientation of the carbonyl group of norcamphor with the hydrogens on the 3 carbon atom. It can be seen that the complexed carbonyl will be compressed against the exo or endo hydrogens equally regardless of whether exo or endo attack occurs. Endo attack on norcamphor will compess the complexed carbonyl against the hydrogen on the 1 carbon atom, however, whereas exo attack does not (Figure 1D). Thus, in the case of norcamphor, the "steric approach factor" and the "compression effect" operate in the same direction. Thus, it is anticipated that exo attack to give endo alcohol will be highly favored regardless of the R_3Al:ketone ratio, and a reversal in stereochemistry will not be observed. This prediction was justified when 95% endo alcohol was observed in the reaction of $(CH_3)_3Al$ with norcamphor in benzene in ratios varying from 0.5 to 4.

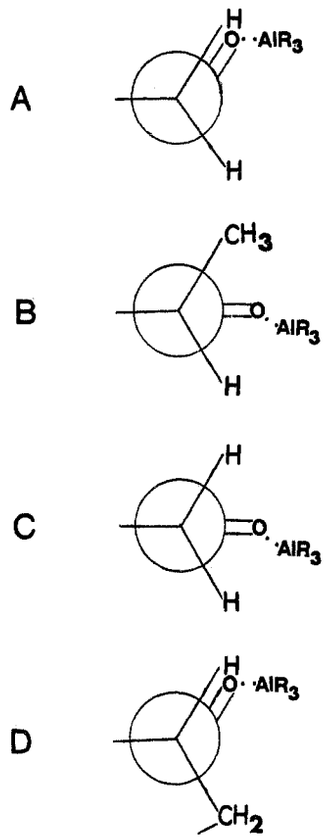
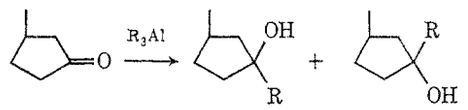


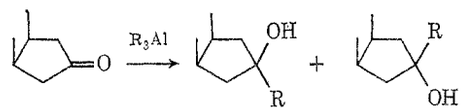
Figure 1.—Orientation of the complexed carbonyl oxygen to substituents on adjacent carbon atoms for (A) 4-*tert*-butylcyclohexanone, 3,3,5-trimethylcyclohexanone; (B) 2-methylcyclopentanone; (C) norcamphor, 2-methylcyclopentanone, 3-methylcyclopentanone, *cis*-3,4-dimethylcyclopentanone; (D) norcamphor.

Further evidence supporting our conclusions was obtained from a study of organoaluminum compounds and Grignard reagents with 3-methylcyclopentanone and *cis*-3,4-dimethylcyclopentanone (eq 5, 6). Figure 1C represents the orientation between the complexed carbonyl oxygen and the hydrogens on adjacent carbons for these ketones. Attack on these molecules from either side by a second organoaluminum molecule compresses the complexed carbonyl oxygen against nearly equivalent hydrogens. Thus, unlike previous

(19) (a) N. L. Allinger, M. T. Tribble, and M. A. Miller, *Tetrahedron*, **28**, 1173 (1972); (b) J. Fournier and B. Waegell, *ibid.*, **26**, 3195 (1970).



cis alcohol trans alcohol (5)



cis alcohol trans alcohol (6)

examples, complexes involving these ketones exhibit little net "compression effect" and the stereochemistry will be controlled by other factors. The results are illustrated in Tables IV and V. It should be noted

TABLE IV

REACTION OF ORGANOALUMINUM COMPOUNDS AND GRIGNARD REAGENTS WITH 3-METHYLCYCLOPENTANONE

RM	Solvent	Initial [RM], M	Ratio of RM/ ketone	% cis[a] alcohol	% trans[a] alcohol
$(CH_3)_3Al$	Benzene	0.40	1.0	61	39
		0.20	2.0	57	43
		0.40	4.0	56	44
$(C_6H_5)_3Al$	Benzene	0.076	1.0	58	42
		0.076	2.0	63	37
CH_3MgBr	Diethyl ether	0.88	8.8	58	42
C_6H_5MgBr	Diethyl ether	0.34	4.0	58	42

[a] Normalized as per cent cis alcohol + per cent trans alcohol = 100%.

TABLE V

REACTION OF ORGANOALUMINUM COMPOUNDS AND GRIGNARD REAGENTS WITH *cis*-3,4-DIMETHYLCYCLOPENTANONE

RM	Solvent	Initial [RM], M	Ratio of RM/ ketone	% cis[a] alcohol	% trans[a] alcohol
$(CH_3)_3Al$	Benzene	0.40	1.0	92	8
		0.20	2.0	91	9
		0.40	4.0	90	10
$(C_6H_5)_3Al$	Benzene	0.078	1.0	91	9
		0.078	2.0	100	0
CH_3MgBr	Diethyl ether	0.88	8.8	92	8
C_6H_5MgBr	Diethyl ether	0.34	4.0	92	8

[a] Normalized as per cent cis alcohol + per cent trans alcohol = 100%.

that the product isomer ratio remains essentially the same with both ketones regardless of the ratio of organoaluminum compound to ketone. These results are consistent with our arguments concerning the existence of a "compression effect" and also reinforce our previous suggestion that a change in transition state (four- to six-center) in itself does not result in such a change in stereochemistry.

The "compression effect" proposed here is similar to effects proposed by other workers to explain the fact that diborane attacks 4-*tert*-butylcyclohexanone preferentially from the axial side.[20] However, this viewpoint is not held by most workers, for the following reasons. Microwave and nmr studies have shown that in the case of acetaldehyde the preferred conformation is one in which a hydrogen atom eclipses the carbonyl group and that propionaldehyde exists mainly in the conformation in which a methyl group is eclipsed by the double bond.[21] In 4-*tert*-butylcyclohexanone the carbonyl group is almost eclipsed by the 2,6-equatorial hydrogens (Figure 1A) and complete eclipsing in an early transition state may even be favorable. "Torsional strain" and "eclipsing" in the sense used by Chérest and Felkin imply a repulsion between single bonds.[5] As noted above,[21] the forces between single and double bonds appear to be attractive. *Since ultraviolet studies of benzophenone–$Al(CH_3)_3$ complex indicate that the double bond remains intact, we believe that the effect described in this paper is a steric effect. The effective bulk of the carbonyl group is increased to such an extent by complexation with an organoaluminum compound that severe interactions with groups on adjacent carbons can occur in the transition state. Hence we choose to call this effect a "compression effect" as opposed to an "eclipsing effect" or "torsional effect" which, as previously stated, denotes single bond repulsion.*

One interesting factor concerning the addition of organoaluminum compounds to ketones in a 2:1 or greater reactant ratio should be pointed out. In those cases where a reversal of stereochemistry occurs, ketones exhibiting relatively small steric requirements (4-*tert*-butylcyclohexanone, 2-methylcyclopentanone), show no tendency to yield a further significant change in isomer ratio as the reactant ratio is increased from 2:1 to higher ratios, if the organoaluminum compound also possesses a small entering group (methyl, ethyl). However, the isomer ratio continues to change with reactant ratio beyond 2:1 with these same ketones when the organoaluminum compound possesses a large entering group (phenyl) (Tables I, III). On the other hand, the product ratio continues to change with reactant ratio beyond 2:1 for those ketones exhibiting a relatively large steric requirement (3,3,5-trimethylcyclohexanone) regardless of the size of the entering group (Table II). The reason for this difference is found in the relative rates at which organoaluminum compounds react with ketones by the two mechanisms. In the one case, the rate-controlling step is the rearrangement of an organoaluminum–ketone complex (eq 7) and the other is the reaction of complex with a

$$C \longrightarrow P \quad (7)$$

second molecule of organoaluminum compound (eq 8).[8] It should be noted that rearrangement of com-

$$C + A \longrightarrow P \quad (8)$$

plex (eq 7) is a first-order process and is independent of the reactant ratio beyond 1:1. Attack on the complex by a second organoaluminum molecule is a second-order process in which the rate of reaction increases as the ratio of organoaluminum compound to ketone increases.

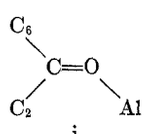
In those cases in which the isomer ratio does not increase significantly beyond a 2:1 reactant ratio, almost all reactions proceed through an attack on the complex at a 2:1 reactant ratio. Thus, the isomer ratio observed is that produced solely by reaction *via* eq 8 at 2:1 and greater reactant ratios. On the

(20) J. Klein and D. Lichtenberg, *J. Org. Chem.*, **35**, 2654 (1970).

(21) (a) R. W. Klib, C. C. Lin, and E. B. Wilson, *J. Chem. Phys.*, **26**, 1695 (1957); (b) R. J. Abraham and J. A. Pople, *Mol. Phys.*, **3**, 609 (1960).

other hand, in those cases where the isomer ratio changes significantly with reactant ratio beyond 2:1, the relative rates of reaction *via* both paths are comparable. Thus, the isomer ratio observed is that due to reaction *via* both mechanisms. As the ratio of organoaluminum compound to ketone is increased beyond 2:1, the rate of product formation through rearrangement of complex remains unchanged but the rate of product formation *via* attack on complex is increased. Hence more product resulting from attack at the most hindered side of the ketone is observed. It should be noted that this effect occurs with ketones having large steric requirements or organoaluminum compounds having large entering groups. This is due to the fact that, as noted before, the "steric approach factor" and the "compression effect" oppose each other. Thus, in those cases with a large "steric approach factor," reaction *via* attack on complexes where the "compression effect" operates will be slowed down relative to rearrangement of complex.

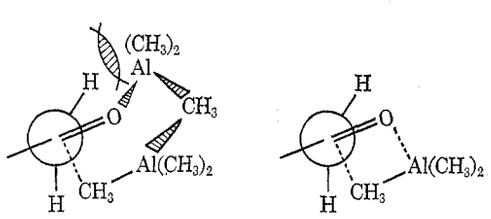
The reason a "compression effect" is observed in the case of a six-center transition state but not in the case of a four-center transition state is the spatial arrangement of the atoms in each case.[22] In the 4-*tert*-butylcyclohexanone–$Al(CH_3)_3$ complex, for example, the unit i lies in a plane. Attack on this complex by



i

another molecule of $(CH_3)_3Al$ leads to a six-center transition state in which the attacking species is perpendicular to the plane of the carbonyl group. Compression then occurs between the complexed carbonyl and the groups on C_2 and C_6 which lie on the opposite side of the carbonyl from the entering $(CH_3)_3Al$. The compression effect is then due to the $Al(CH_3)_3$ originally complexed to the carbonyl and not to the attacking $(CH_3)_3Al$ (transition state A).

In a four-center transition state, the $(CH_3)_3Al$ molecule lies perpendicular to the plane of the carbonyl group. Since the $(CH_3)_3Al$ is on the opposite



transition state A transition state B

side of the carbonyl group from the groups on C-2 and C-6 which the carbonyl must eclipse in the transition state, no compression involving the $Al(CH_3)_2$ unit will occur in an early transition state (transition state B). Steric approach control should then determine the isomer ratio.

Considerations Involving a Late Transition State. Product Development Control.—The discussion to this point has assumed an early, reactant-like transition state in the reaction of $(CH_3)_3Al$ with ketones in 2:1 ratio. The possibility of a late, product-like transition state should also be considered. If a late transition state occurs, the stereochemistry could be determined by the position of the large $OAlR_2 \cdot AlR_3$ group in the product. This group will tend to occupy the least hindered position in the product, *i.e.*, equatorial in the case of alkylation of 4-*tert*-butylcyclohexanone and 3,3,5-trimethylcyclohexanone, exo in alkylation of norcamphor, and trans in alkylation of 2-methylcyclopentanone, 3-methylcyclopentanone, and *cis*-3,4-dimethylcyclopentanone. The entering group would then occupy the remaining position, *i.e.*, axial in alkylation of 4-*tert*-butylcyclohexanone and 3,3,5-trimethylhexanone, endo in alkylation of norcamphor, and cis in alkylation of 2-methylcyclopentanone, 3-methylcyclopentanone, and *cis*-3,4-dimethylcyclopentanone.

If product development control determined the observed isomer ratio in the reaction of $(CH_3)_3Al$ with ketones in 2:1 ratio, then all ketones would show an increase in attack from the more hindered side when compared to 1:1 reactant ratio. While a change in isomer ratio with reactant ratio does occur in R_3Al alkylation involving 4-*tert*-butylcyclohexanone, 3,3,5-trimethylcyclohexanone, and 2-methylcyclopentanone, it does not occur in R_3Al alkylation involving norcamphor, 3-methylcyclopentanone, and *cis*-3,4-dimethylcyclopentanone. Therefore the final position of the $OAlR_2 \cdot AlR_3$ group is not a factor in the determination of the isomer ratio of the reactions reported herein and thus product development control cannot explain the observed stereochemistry in these reactions.

Nmr Evidence for the Chair Conformation of the Complex.—The importance of knowing the preferred conformation of cyclohexanones and their aluminum alkyl complexes in stereoalkylation has already been

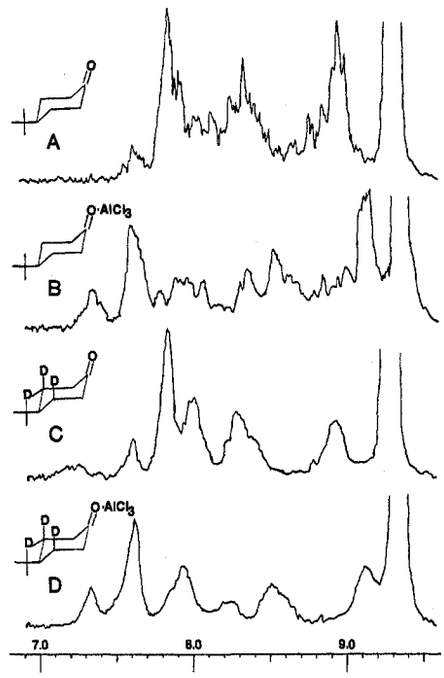


Figure 2.—60-MHz nuclear magnetic resonance spectra for 1 *M* benzene solutions of (A) 4-*tert*-butylcyclohexanone, (B) 4-*tert*-butylcyclohexanone–$AlCl_3$ complex; (C) 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3; (D) 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3–$AlCl_3$ complex.

(22) For a detailed discussion of the nature of the transition state in $(CH_3)_3Al$ alkylation of benzophenone see H. M. Neuman, J. Laemmle, and E. C. Ashby, *J. Amer. Chem. Soc.*, **95**, 2597 (1973).

pointed out. In this connection an nmr study involving 4-*tert*-butylcyclohexanone and 4-*tert*-butylcyclohexanone-*cis*-3,5,5-d_3 (axial 3D) and their $AlCl_3$ complexes was undertaken. Figure 2 illustrates the 60-MHz nmr spectra of the ketones and their $AlCl_3$ complexes as 1 *M* solutions in benzene (τ 2.73). The low-field doublets of the trideuterated ketone (τ 7.69, J_{gem} = −13.4 Hz) and complex (τ 7.42, J_{gem} = −17.0 Hz) are assigned to equatorial protons on C-2 and C-6. The assignments are based on the following facts: (1) the signals integrate to two protons in each case, (2) the signals appear basically as doublets in the nondeuterated compounds,[23a] (3) the widths of the signals are relatively narrow owing to axial–equatorial H–D vicinal coupling constants,[23b] and (4) the relatively large shift of these protons in going from ketone to complex. The high-field doublets of the trideuterated ketone (τ 8.14, J_{gem} = −13.4 Hz)[24] and complex (τ 8.10, J_{gem} = −17.0 Hz) are assigned to the axial protons on C-2 and C-6. These assignments are based on the following facts: (1) the signals intergrate to two protons in each case, (2) the signals give a complex splitting pattern in the nondeuterated compounds,[23a] (3) the widths of the signals are relatively broad owing to axial–axial H–D vicinal coupling constants,[23b] and (4) the relatively slight shift of these protons in going from ketone to complex.

The nmr spectra of ketone and ketone–$AlCl_3$ show nonflexible conformations displaying axial and equatorial protons on C-2 and C-6. The spectra are consistent with a very high population of the chair form of the ketone and ketone–$AlCl_3$. The spectra do not rule out the possibility of an equilibrium between the chair conformation and certain nonchair conformations, where the equilibrium is in the direction of a high predominance of the chair form. Unfortunately, the spectra do not allow predictions regarding detectable limits of nonchair conformers.

(23) (a) W. F. Trager and A. C. Huitric, *Tetrahedron Lett.*, 825 (1966); (b) A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964).

(24) A JEOL H4 100 spectrometer was used to obtain 100-MHz nmr spectra for all samples. In this case a distinct doublet at τ 8.14 was observed.

Registry No.—$(CH_3)_3Al$, 75-24-1; $(C_2H_5)_3Al$, 97-93-8; $(C_6H_5)_3Al$, 841-76-9; CH_3MgBr, 75-16-1; C_6H_5MgBr, 100-58-3; 4-*tert*-butylcyclohexanone, 98-53-3; 3,3,5-trimethylcyclohexanone, 873-94-9; 2-methylcyclopentanone, 1120-72-5; 3-methylcyclopentanone, 1757-42-2; *cis*-3,4-dimethylcyclopentanone, 19550-72-2.

Acknowledgment.—We are grateful to Dr. A. C. Huitric for helpful comments concerning the interpretation of the nmr spectra shown in Figure 2.

Reaction of Alkali Metal Diphenylmethides with 1,1-Dichloroalkanes. Conjugate Addition to 1,1-Diphenylalkenes

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Received February 8, 1973

The reaction of sodium diphenylmethide (1′) with methylene chloride was previously considered to proceed by a twofold alkylation to give 1,1,3,3-tetraphenylpropane (**3**). The reaction is shown to proceed by a single alkylation to give diphenylethyl chloride, which is dehydrohalogenated to diphenylethylene. Conjugate addition of 1′ to the latter olefin, followed by neutralization, gives **3**. Conjugate addition of 1′ to other 1,1-diphenylalkenes is not observed. Alkali triphenylmethides react similarly with methylene chloride, except that elimination is not possible, and the monoalkylation product does not react further.

Previously, sodium diphenylmethide in liquid ammonia was shown to react with α,ω-dihaloalkanes including methylene chloride and ethylene chloride, to give the tetraphenylalkanes corresponding to twofold alkylation of the halide by the anion, although the triphenylmethide ion reacted but once with methylene chloride to give triphenylethyl chloride.[2]

Subsequently, sodium and potassium diphenylmethide were shown to undergo quite different reactions with chloroform (proton abstraction) and carbon tetrachloride (displacement on halogen).[3] Also, methylene iodide was shown to iodinate certain organometallic compounds,[4] and ethylene bromide and iodide were shown to react with 1′ differently than did the chloride.[5] It thus seemed important to reexamine the reaction of the alkali diphenylmethides with the methylene halides.

When potassium diphenylmethide (1′) was treated with 0.5 molar equiv of methylene chloride, the orange color, as previously noted,[2] was not discharged, but a substantial excess of halide did discharge the color. Work-up of this reaction mixture gave almost none of the expected tetraphenylpropane (**3**), but gave 1-chloro-2,2,4,4-tetraphenylbutane (**4**), in 40% conversion. Gas chromatography indicated a small amount of tetraphenylpropane (about 15%), but showed a 35% recovery of diphenylmethane (**1**). Three mechanisms were considered to explain these results; path C, Scheme I, was shown to be correct.

When hydrocarbon **3** was treated with ammoniacal potassium amide, a red color indicative of an anion was observed, but, when the color was discharged by methylene chloride, starting material was largely recovered, indicating a slight extent of ionization. This rules out path A, Scheme I, since diphenylmethide must be an even weaker base than amide ion. Path B, Scheme I,

(1) NSF Undergraduate Research Participant, summer, 1971.

(2) C. R. Hauser, C. F. Hauser, and P. J. Hamrick, *J. Org. Chem.*, **24**, 397 (1959).

(3) C. R. Hauser, W. G. Kofron, W. R. Dunnavant, and W. F. Owens, *J. Org. Chem.*, **26**, 2627 (1961).

(4) R. L. Gay, T. F. Crimmins, and C. R. Hauser, *Chem. Ind. (London)*, 1635 (1966).

(5) W. G. Kofron and C. R. Hauser, *J. Amer. Chem. Soc.*, **90**, 4126 (1968).