(16) P. L. Pauson, *J. Am. Chem. Soc.*, **76**, 2187 (1954).
(17) The authors are grateful to Drs. Leon Petrakis and Byron Arison for obtaining and interpreting NMR spectra and to Dr. Franz Kasler for obtaining the microanalyses.
(18) All melting points, boiling points, and refractive indices are corrected. The melting points were determined with a micro Kofler hot stage and a polarizing microscope. Ultraviolet spectra were taken on a model 14 Cary spectrometer at 25 °C and NMR spectra were obtained with a Varian Associates Model DP-60 nuclear magnetic resonance spectrometer.
(19) After sodium metal was dissolved in the appropriate alcohols, the resulting solutions were deliberately exposed to the atmosphere for about 1 min before further use. The reason for this step is that the mechanism (see ref 3) requires that a trace of aldehyde be present for reaction to occur.
(20) Y. Sprinzak, *Bull. Res. Counc. Isr.*, **3**, 104 (1953).

Stereoselective Alkylation of Cyclic Ketones by Dialkylamino- and Aryloxy(methyl)magnesium Compounds

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Reactions of dialkylamino(methyl)magnesium compounds, CH_3MgNR_2 (where NR_2 = N-*i*-Pr_2, NPh_2, and $NC_5H_8Me_2$), and aryloxy(methyl)magnesium compounds, CH_3MgOR (where OR = O-2,6-*i*-$Pr_2C_6H_3$ and O-2,6-*t*-Bu_2-4-MeC_6H_2), with cyclic ketones such as 4-*tert*-butylcyclohexanone and 2,2,6,6-tetramethyl-4-*tert*-butylcyclohexanone have been studied. These reagents exhibit excellent stereoselectivity in the alkylation of these model compounds. The selectivity of the amide or aryloxy reagent has been shown to depend on the steric requirement of the aryloxy group, the steric requirement of the ketone, and the nature of the solvent.

A recent review[1] concerning the stereochemistry of organometallic compound addition to ketones points out the paucity of stereoselective alkylating agents, especially for the case of methylation of unhindered ketones. The reaction of methyllithium, in the presence of a lithium salt such as $LiClO_4$, with 4-*tert*-butylcyclohexanone to give a 94:6 axial/equatorial alcohol ratio is probably the best example of stereoselective methylation hitherto reported.[2]

Our success with the stereoselective reduction of cyclic and bicyclic ketones with dialkylaminomagnesium hydrides[3] prompted us to apply similar reasoning to the problem of stereoselective alkylation. Namely, if such hydrides are good stereoselective reducing agents by virtue of their bulky dialkylamino groups, then similar bulkiness in an alkylating agent should produce a similar effect.

We would now like to report on the reactions of dialkylamino- and aryloxy(methyl)magnesium compounds with cyclic ketones, showing their unusual stereoselective behavior as alkylating reagents.

Experimental Section

Apparatus. Reactions were performed under nitrogen at the bench using Schlenk tube techniques.[4] GLC analyses were performed on an F and M Model 720 gas chromatograph. NMR spectra were recorded on a Jeol 100 MHz Fourier transform NMR spectrometer.

Analyses. Gas analyses were carried out by hydrolyzing samples with hydrochloric acid or methanol on a standard vacuum line equipped with a Toepler pump. Magnesium was determined by EDTA titration at pH 10 using Eriochrome Black T as an indicator.

Materials. Diisopropylamine (Aldrich), 2,6-dimethylpiperidine (Aldrich), and 2,6-diisopropylphenol (Ethyl Corp.) were dried over NaOH and fractionally distilled prior to use. Diphenylamine (Fisher), *tert*-amyl alcohol (Mallinckrodt), 2,6-di-*tert*-butyl-*p*-cresol (Eastman), and triphenylphosphine (Fisher) were used without further purification. 4-*tert*-Butylcyclohexanone (Frinton) was sublimed under vacuum prior to use.

Diethyl ether and benzene were distilled from $LiAlH_4$ and $NaAlH_4$, respectively. Diphenyl ether was fractionally distilled under vacuum. Dimethylmagnesium was prepared by the reaction of dimethylmercury with excess magnesium metal (Ventron chips) at 25 °C.[5] A solution in diethyl ether was standardized by magnesium and methane analyses (Mg/CH_4 ratio was 1.00:1.98).

Preparation of 2,2,6,6-Tetramethyl-4-*tert*-butylcyclohexanone. To a 1-L three-neck flask equipped with a reflux condenser and nitrogen bubbler was added 34.5 g of sodium (1.50 mol) and 178 mL of *tert*-amyl alcohol (excess). The mixture was stirred for 24 h under reflux until no sodium remained. Then 38.8 g of 4-*tert*-butylcyclohexanone (0.252 mol) in 158.4 g of methyl iodide (excess) was added dropwise, and the refluxing was continued for 1 week. The reaction mixture was then quenched with water and extracted with diethyl ether. The ether extract was dried over $MgSO_4$ and reduced under vacuum to give 49.6 g of an oil (93.7% crude yield). The material was crystallized twice from pentane to give 8.2 g (15.5% yield), mp 77.0–78.0 °C. The solid was sublimed at 65–85 °C at 2 mmHg. The yield was 7.1 g (mp 92.0–93.0 °C). The 2,2,6,6-tetramethyl-4-*tert*-butylcyclohexanone thus prepared was hygroscopic and was handled in a glovebox: NMR ($CDCl_3$) δ 0.95 (s, 9 H), 1.10 (s, 6 H), 1.18 (s, 6 H), 1.62 (m, 5 H); IR (Nujol) 1715 cm^{-1} (C=O); MS *m/e* 210 (M^+), 153 ($M^+ - C_4H_9$). Anal. Calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46. Found: C, 79.69; H, 12.40.

Characterization of *cis*- and *trans*-1,2,2,6,6-Pentamethyl-4-*tert*-butylcyclohexanol (Axial and Equatorial). The methylation products from the reaction of 2,2,6,6-tetramethyl-4-*tert*-butylcyclohexanone and methylmagnesium bromide were collected via GLC on a 4 ft × 0.5 in 5% Carbowax 20M on Chromosorb W column. The equatorial alcohol eluted first, as will be shown later.

***trans*-1,2,2,6,6-Pentamethyl-4-*tert*-butycyclohexanol (Equatorial).** The first material collected by GLC gave the following data: mp 44.0–45.0 °C; NMR ($CDCl_3$) δ 0.85 (s, 9 H), 0.98 (s, 3 H), 1.05 (s, 6 H), 1.13 (s, 6 H), 1.26 (m, 4 H), 1.61 (m, 1 H); IR (as melt) 3620, 3500 cm^{-1} (OH); MS *m/e* 226 (M^+), 169 ($M^+ - C_4H_9$). Anal. Calcd for $C_{15}H_{30}O$: C, 79.58; H, 13.35. Found: C, 79.39; H, 13.39.

***cis*-1,2,2,6,6-Pentamethyl-4-*tert*-butylcyclohexan-1-ol (Axial).** The second material collected by glc gave the following data: mp 35.5–36.0 °C; NMR ($CDCl_3$) δ 0.85 (s, 9 H), 0.95 (s, 3 H), 1.10 (s, 6 H), 1.15 (s, 6 H), 1.20 (m, 4 H), 1.32 (m, 1 H); IR (as melt) 3620, 3500 cm^{-1} (OH); MS *m/e* 169 ($M^+ - C_4H_9$). Anal. Calcd for $C_{15}H_{30}O$: C, 79.58; H, 13.35. Found: C, 79.40; H, 13.34.

Assignment of Stereochemistry. Preliminary assignment of stereochemistry for the isomeric alcohols was based on melting point and NMR data. The axial alcohol is expected to have a lower melting point because of less steric hindrance from association due to hydrogen bonding. Also, the α-methyl group of the axial alcohol (δ 0.95) was found at a higher field in the NMR spectrum than the corresponding signal of the α-methyl group in the equatorial alcohol (δ 0.98) since the α-methyl group is shielded more by the β-methyl groups in the axial alcohol.

In order to verify the assignment of stereochemistry, a shift reagent study was conducted. NMR samples were prepared from standard solutions of pure axial and equatorial alcohols in $CDCl_3$. Small aliquots of a standard solution of $Eu(fod)_3$ (Bio-Rad) in $CDCl_3$ were added using a microliter syringe. The NMR spectra were recorded for various shift reagent/alcohol ratios, and chemical shifts due to the

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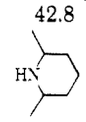
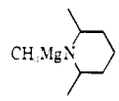
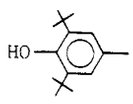
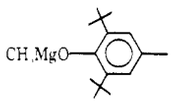
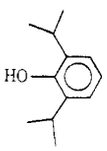
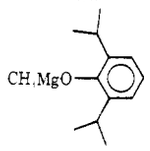
Table I. Preparation of Dialkylamino(methyl)magnesium and Methylmagnesium Aryloxide Reagents [a]

reactants					
$(CH_3)_2Mg$,[b] mmol	R_2NH or ROH, mmol	registry no.	product	registry no.	analysis (ratio) Mg/CH_3
49.9	HN-*i*-Pr_2 50.0	108-18-9	CH_3MgN-*i*-Pr_2	67209-22-7	1.00:0.99
42.9	$HNPh_2$ 42.8	122-39-4	CH_3MgNPh_2	67209-23-8	1.00:1.02
47.2	 16.1	504-03-0		67254-40-4	1.00:0.98
15.8	 47.5	2078-54-8	 (A)	67209-25-0	1.00:0.98
16.0	 15.9	128-37-0	 (B)	67209-24-9	1.00:0.99

[a] All reactions were carried out at room temperature in diethyl ether for 1 h. [b] Registry no.: $(CH_3)_2Mg$, 2999-74-8.

tert-butyl group were followed for each alcohol. The data are plotted in Figure 1. The effect of addition of the shift reagent would be expected to be larger on the axial alcohol where the *tert*-butyl and hydroxyl groups are cis; thus, the compound with the larger slope (0.854 compared to 0.283) is assigned to the axial alcohol.[6] These data are compatible with the preliminary stereochemical assignment.

Attempts to obtain a single crystal of the axial alcohol for X-ray analysis failed to yield a suitable crystal. The *p*-bromobenzoyl ester derivative was prepared but was also unsuitable.

Results and Discussion

The dialkylamino(methyl)magnesium compounds,[7] CH_3MgNR_2 (where NR_2 = N-*i*-Pr_2, NPh_2, and $NC_5H_8Me_2$), used in these studies were prepared conveniently and quantitatively by the reaction of dimethylmagnesium with an equal molar amount of the corresponding secondary amine at room temperature (eq 1). Preparation and analytical data are summarized in Table I.

$$CH_3MgCH_3 + HN\text{-}i\text{-}Pr_2 \xrightarrow{Et_2O} CH_3MgN\text{-}i\text{-}Pr_2 + CH_4 \quad (1)$$

The CH_3MgNR_2 compounds prepared by the method of eq 1 were allowed to react with two representative ketones, i.e., 4-*tert*-butylcyclohexanone (I), representing a nonsterically hindered ketone, and 2,2,6,6-tetramethyl-4-*tert*-butylcyclohexanone (II), representing a sterically hindered ketone. The results of these reactions are summarized in Tables II and III.

The least hindered methylating agents among magnesium compounds of the type CH_3MgX are methyl Grignard and dimethylmagnesium. These compounds give 60 and 64% equatorial attack, respectively, with ketone I[8] and 71 and 85% equatorial attack, respectively, with ketone II in diethyl ether. It was reasoned that increasing the steric bulk of the alkylating agent, CH_3MgX, would cause a corresponding increase in attack from the less hindered side of the ketone, namely, from the equatorial side. Hence, the effect of replacing X with the bulkier dialkylamino group $R_2'N$ was studied. In the case of ketone I, it was found that dialkyamino(methyl)magnesium compounds give essentially the same results as methyl Grignard and dimethylmagnesium in diethyl ether (expt 1–3) and benzene (expt 13 and 14). It is apparent that the bulkiness of the dialkylamino group is too far removed from the reaction center to be effective. However, the discovery was made that addition of triphenylphosphine to the reagent in a 2:1 ratio increased the steric bulk of the reagent by forming a complex between the phosphine and the magnesium. For the reagents diisopropylamino(methyl)magnesium (expt 4) and diphenylamino(methyl)magnesium (expt 5), excellent stereochemical results were obtained (95 and 100% equatorial attack, respectively). For the 2,6-dimethylpiperidine reagent (expt 6), there was only a small increase in the amount of equatorial attack with the addition of triphenylphosphine, indicating

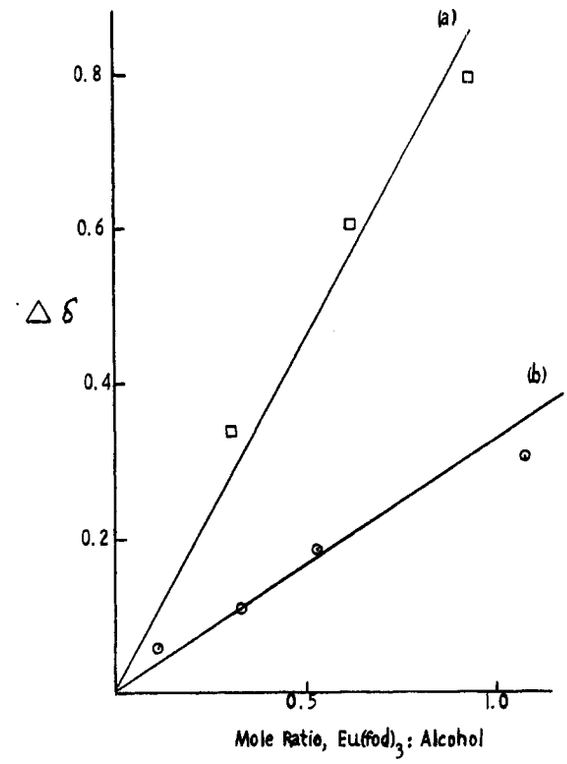
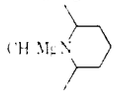
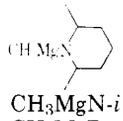
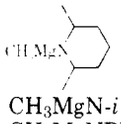
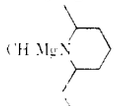
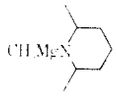


Figure 1. $Eu(fod)_3$ shift reagent study on *cis*- and *trans*-1,2,2,6,6-pentamethyl-4-*tert*-butylcyclohexanol: (a) axial alcohol and (b) equatorial alcohol.

Table II. Reactions of 4-*tert*-Butylcyclohexanone with Dialkylamino(methyl)magnesium Compounds [a]

expt.	reagent	solvent	additive	relative yield,[b] % axial OH	relative yield,[b] % equatorial OH	yield of alcohols, %	mass balance,[c] %
1	CH_3MgN-*i*-Pr_2	Et_2O		73	27	26	98
2	CH_3MgNPh_2	Et_2O		72	28	33	97
3		Et_2O		71	29	10	57
4	CH_3MgN-*i*-Pr_2	Et_2O	$2Ph_3P$	95	5	8	43
5	CH_3MgNPh_2	Et_2O	$2Ph_3P$	100	0	4	34
6		Et_2O	$2Ph_3P$	78	22	12	64
7	CH_3MgN-*i*-Pr_2	Et_2O	Ph_3P	73	27	22	12
8	CH_3MgBr	Et_2O	$2Ph_3P$	64	36	93	93
9	CH_3MgCH_3	Et_2O	$2Ph_3P$	70	31	25	52
10	CH_3MgN-*i*-Pr_2	Et_2O	$LiClO_4$	79	21	10	56
11	CH_3MgNPh_2	Et_2O	$LiClO_4$	100	0	9	87
12		Et_2O	$LiClO_4$	0	0	0	13
13	CH_3MgN-*i*-Pr_2	PhH		63	37	44	99
14	CH_3MgNPh_2	PhH		71	29	30	100
15	CH_3MgN-*i*-Pr_2	PhH	$2Ph_3P$	84	16	16	62
16	CH_3MgBr	Ph_2O		100	0	24	35
17	CH_3MgBr	Ph_2O	$2Ph_3P$	100	0	34	55
18	CH_3MgCH_3	Ph_2O		84	16	12	27
19	CH_3MgCH_3	Ph_2O	$2Ph_3P$	91	9	15.3	31.2
20	CH_3MgN-*i*-Pr_2	Ph_2O		76	24	8.6	49.3
21	CH_3MgN-*i*-Pr_2	Ph_2O	$2Ph_3P$	88	12	6.0	35.7
22	CH_3MgNPh_2	Ph_2O		100	0	3.2	50.3
23	CH_3MgNPh_2	Ph_2O	$2Ph_3P$	100	0	3.1	57.8
24		Ph_2O		0	0	0	10.3
25		Ph_2O	$2Ph_3P$	0	0	0	11.2

[a] The molar ratio of reagent to ketone was 1.0:1.0. Reactions were performed at room temperature. [b] Yields were determined by GLC using an internal standard. [c] The mass balance includes the yield of alcohols and recovered ketone.

that the steric bulk of the reagent was only slightly affected. The 2,6-dimethyl groups probably decrease the degree of bonding between magnesium and triphenylphosphine due to steric interference. When triphenylphosphine was added to the reagent in a 1:1 ratio (expt 7), there was no increase in equatorial attack. Also, the addition of triphenylphosphine to Grignard reagent in a 2:1 ratio (expt 8) or dimethylmagnesium (expt 9) had no effect on the sterochemical course of reaction. Excellent stereochemistry, however, was obtained for diphenylamino(methyl)magnesium when $LiClO_4$ was added (expt 11). The mechanism here, however, probably involves complexation of the ketone by the lithium salt.[2]

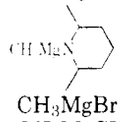
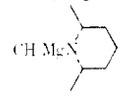
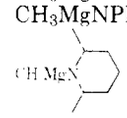
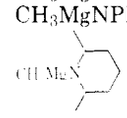
Changing solvents from diethyl ether to benzene gives no increase in equatorial attack, but a change to diphenyl ether, a less basic and more sterically hindered ether than diethyl ether, does give more equatorial attack. For example, diphenylamino(methyl)magnesium gives 100% equatorial attack in diphenyl ether (expt 22) compared to 72% in diethyl ether (expt 2). The effect is less for diisopropylamino(methyl)-magnesium (expt 20), and apparently the diphenyl ether even interferes with the ability of triphenylphosphine to complex the reagents (compare expt 21 and 4). The low yields and low mass balances obtained in all of the reactions with ketone I are due to enolization followed by Aldol condensation reactions in many cases.

Clearly then, CH_3MgNPh_2 is the most stereoselective of the CH_3MgNR_2 compounds, giving 100% equatorial attack when the solvent system is Et_2O–$2Ph_3P$ (expt 5), Et_2O–$LiClO_4$ (expt 11), or Ph_2O (expt 22); however, the yields are low (3.1–9.4%). On the other hand, CH_3MgBr in Ph_2O (expt 16) and Ph_2O–$2Ph_3P$ (expt 17) not only resulted in 100% equatorial attack, but also produced much higher yields (23.6–34.0%) than the CH_3MgNR_2 compounds. Of course, less enolization is expected with the CH_3MgBr compound than for the more basic CH_3MgNR_2 reagents.

In order to study the reagents further and circumvent the problem of enolization, alkylation studies were conducted on ketone II, a nonenolizable ketone. The results are summarized in Table III. The diisopropylamino(methyl)magnesium compound in ether gives the best stereochemical results (expt 26–28, 100% axial alcohol), even without added triphenylphosphine. The addition of triphenylphosphine increases the amount of axial alcohol for the other reagents (expt 33–35 in ether and expt 43–45 in Ph_2O), including methyl Grignard and dimethylmagnesium (expt 31 and 32 and 41 and 42), as expected. In addition, changing solvent from diethyl ether to diphenyl ether also gave increased yields of axial alcohol with all reagents (expt 36–40).

The aryloxy(methyl)magnesium compounds,[9] CH_3MgOR (where OR = O-2,6-*i*-$Pr_2C_6H_3$ and O-2,6-*t*-Bu_2-4-MeC_6H_2),

Table III. Reactions of 2,2,6,6-Tetramethyl-4-*tert*-butylcyclohexanone with Dialkylamino(methyl)magnesium Compounds [a]

expt	reagent	solvent	additive	relative yield,[b] % axial OH	relative yield,[b] % equatorial OH	yield of alcohols, %	mass balance,[c] %
26	CH_3MgBr	Et_2O		71	29	81	104
27	CH_3MgCH_3	Et_2O		86	14	109	109
28	CH_3MgN-*i*-Pr_2	Et_2O		100	0	103	106
29	CH_3MgNPh_2	Et_2O		87	13	118	118
30		Et_2O		97	3	96	103
31	CH_3MgBr	Et_2O	$2Ph_3P$	81	19	94	94
32	CH_3MgCH_3	Et_2O	$2Ph_3P$	95	5	92	92
33	CH_3MgN-*i*-Pr_2	Et_2O	$2Ph_3P$	100	0	80	89
34	CH_3MgNPh_2	Et_2O	$2Ph_3P$	88	12	108	108
35		Et_2O	$2Ph_3P$	100	0	82	83
36	CH_3MgBr	Ph_2O		79	21	106	106
37	CH_3MgCH_3	Ph_2O		89	11	92	92
38	CH_3MgN-*i*-Pr_2	Ph_2O		100	0	99	99
39	CH_3MgNPh_2	Ph_2O		79	21	80	80
40		Ph_2O		100	0	95	103
41	CH_3MgBr	Ph_2O	$2Ph_3P$	90	10	104	104
42	CH_3MgCH_3	Ph_2O	$2Ph_3P$	80	20	104	104
43	CH_3MgN-*i*-Pr_2	Ph_2O	$2Ph_3P$	100	0	91	91
44	CH_3MgNPh_2	Ph_2O	$2Ph_3P$	100	0	28	100
45		Ph_2O	$2Ph_3P$	100	0	89	96

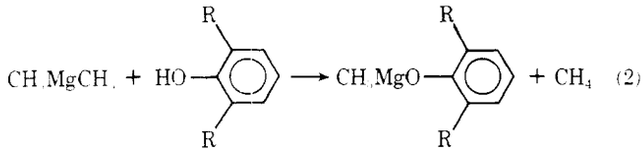
[a] The molar ratio of reagent to ketone was 2.0:1.0. Reactions were performed at room temperature. [b] Yields were determined by GLC using an internal standard. [c] The mass balance includes the yield of alcohols and recovered ketone.

Table IV. Reactions of 4-*tert*-Butylcyclohexanone with Methylmagnesium Aryloxides [a]

expt	reagent	solvent	additive	relative yield,[d] axial OH	relative yield,[d] equatorial OH	yield of alcohols, %	mass balance,[e] %
46	A[b]	Et_2O		56	44	15	68
47	B[c]	Et_2O		87	13	33	74
48	A	Et_2O	$2Ph_3P$	57	43	14	67
49	B	Et_2O	$2Ph_3P$	77	23	39	73
50	A	Ph_2O		0	0	0	0
51	B	Ph_2O		0	0	0	39
52	A	Ph_2O	$2Ph_3P$	0	0	0	0
53	B	Ph_2O	$2Ph_3P$	0	0	0	77

[a] The molar ratio of reagent to ketone was 1.0:1.0. Reactions were performed at room temperature. [b] Reagent A is CH_3MgO-2,6-*t*-Bu_2-4-MeC_6H_2; analysis is provided in Table I. [c] Reagent B is CH_3MgO-2,6-*i*-$Pr_2C_6H_3$; analysis is provided in Table II. [d] Yields were determined by GLC using an internal standard. [e] The mass balance includes the yield of alcohols and recovered ketone.

used in these studies were prepared conveniently and quantitatively by the reaction of dimethylmagnesium with an equal molar amount of the corresponding phenol at room temperature (eq 2, where R = *i*-Pr and *t*-Bu). Preparation and analytical data are summarized in Table I.



(2)

The CH_3MgOR compounds prepared from eq 2 were allowed to react with the two representative ketones, 4-*tert*-butylcyclohexanone (I) and 2,2,6,6-tetramethyl-4-*tert*-butylcyclohexanone (II). The results of these reactions are summarized in Tables IV and V.

The effect of replacing X in the general formula CH_3MgX with the bulkier aryloxy group (OPh) was studied. In the case of ketone I, it was found that reagent A (CH_3MgO-2,6-*t*-Bu_2-4-MeC_6H_2) gave similar results to the methyl Grignard and reagent B (CH_3MgO-2,6-*i*-$Pr_2C_6H_3$) gave a modest increase in the amount of equatorial attack (expt 46 and 47). For both reagents the addition of triphenylphosphine to the reagent in a 2:1 ratio produced little change in the results. Previously, the addition of triphenylphosphine to dialkylamino(methyl)magnesium compounds led to a substantial increase in the amount of equatorial attack, presumably because the steric bulk of the reagent was increased by complexation of the magnesium by Ph_3P (expt 48 and 49). Changing solvent

Table V. Reactions of 2,2,6,6-Tetramethyl-4-*tert*-butylcyclohexanone with Methylmagnesium Alkoxides[a]

expt	reagent	solvent	additive	relative yield,[d] % axial OH	relative yield,[d] % equatorial OH	yield of alcohols, %	mass balance,[e] %
54	A[b]	Et_2O		94	6	95	95
55	B[c]	Et_2O		100	0	89	96
56	A	Et_2O	$2Ph_3P$	89	11	107	107
57	B	Et_2O	$2Ph_3P$	100	0	99	99
58	A	Ph_2O		100	0	89	111
59	B	Ph_2O		100	0	71	89
60	A	Ph_2O	$2Ph_3P$	100	0	32	91
61	B	Ph_2O	$2Ph_3P$	100	0	19	72

[a] The molar ratio of reagent to ketone was 2.0:1.0. Reactions were performed at room temperature. [b] Same as footnote *b* in Table IV. [c] Same as footnote *c* in Table IV. [d] Yields were determined by GLC using an internal standard. [e] The mass balance includes the yield of alcohols and recovered ketone.

from diethyl ether to diphenyl ether (expt 50 and 51) resulted in the loss of all alcohol products, unlike the advantageous effect found with the CH_3MgNR_2 compounds. Enolization, followed by Aldol condensation reactions, was responsible for the low yields and low mass balances.

The problem of enolization was removed by employing a nonenolizable substrate, ketone II. Excellent stereochemical results (100% axial alcohol) were obtained for reagent B in diethyl ether even without added triphenylphosphine (expt 55). Changing solvents from diethyl ether to diphenyl ether gave an increase in equatorial attack for reagent A (from 94 to 100% axial alcohol), and so both reagents A and B give 100% equatorial attack in Ph_2O. As in the case of alkylation with CH_3MgNR_2 compounds, the addition of Ph_3P (expt 60 and 61) to ketones I and II in Ph_2O has a detrimental effect on the yield.

It is evident from the data that the stereoselectivity of dialkylamino- and aryloxy(methyl)magnesium compounds as alkylating agents depends on several factors. However, the steric requirement of the reagent seems to be the most important factor. Of course, the effectiveness of a reagent can be increased if the ketone contains a group close enough to the carbonyl group to supply some steric hindrance at the carbonyl site. Presumably, for steric reasons the choice of solvent also has an influence. Diphenyl ether is a more effective solvent than diethyl ether, perhaps because the association of the reagent changes, being more associated in diphenyl ether than in diethyl ether. If indeed the degree of association of the reagent is nearly the same in both solvents or if only the monomer reacts regardless of the concentration of associated species, Ph_2O solvated to the magnesium compounds would be expected to provide significantly greater steric hindrance than the reagent solvated to diethyl ether if the degree of solvation is the same. Past experience would indicate that it is the monomer that is reacting, and these results indicate that the degree of solvation of the magnesium compounds with Ph_2O and Et_2O is approximately the same.

The ease of preparation of these alkylating reagents in addition to the excellent stereochemistry observed indicates that these dialkylamino- and aryloxy(methyl)magnesium reagents may have considerable potential as stereoselective alkylating agents, especially for nonenolizable substrates.

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Registry No.—CH_3Br, 74-83-9; 4-*tert*-butylcyclohexanone, 98-53-3; 2,2,6,6-tetramethyl-4-*tert*-butylcyclohexanone, 49714-25-2; *cis*-1,2,2,6,6-pentamethyl-4-*tert*-butylcyclohexan-1-ol, 67209-26-1; *trans*-1,2,2,6,6-pentamethyl-4-*tert*-butylcyclohexan-1-ol, 67209-27-2.

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