Silane Reductions in Acidic Media. IV. Reductions of Alkyl-Substituted Cyclohexanones by Mono-, Di, and Trialkylsilanes. Stereochemistry of Alcohol and Ether Formation^{1a,b}

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Stereochemical results from the reduction of 4-*tert*-butyl-, 4-methyl-, 3-methyl-, 2-methyl-, and 3,3,5-trimethylcyclohexanones by mono-, di-, and tri-*n*-alkylsilanes and by α -, β -, and γ -branched trialkylsilanes in aqueous sulfuric acid-ethyl ether and trifluoroacetic acid media are reported. Alcohols are formed by silane reductions in aqueous sulfuric acid-ethyl ether. Both trifluoroacetates and symmetrical ethers are produced in trifluoroacetic acid media; alkyl branching at the α positions of alkylsilanes or of cyclohexanones and increasing the number of *n*-alkyl groups bonded to silicon dramatically decreases the relative yield of ether products. Steric factors govern the stereochemical outcome of silane reductions of ketones to alcohols and alcohol derivatives. Increasing the number, but not the length, of linear carbon chains and increasing the branching at the α and β positions of alkylsilanes increases the relative yield of the thermodynamically less stable alcohol. Factors influencing the stereoselectivity of hydride transfer to *O*-alkyloxonium ions resulting in symmetrical ethers have also been determined. The stereoselectivities in organosilane reductions are compared to those from other hydride reducing agents, and the relative importance of conformational equilibria on the stereoselectivity in reductions of methylcyclohexanones is discussed.

Stereoselective control of reaction products in the reduction of cyclic ketones has been the subject of numerous investigations.² Hydride reducing agents, such as lithium aluminum hydride, sodium borohydride, and their alkoxy derivatives, undergo predominant axial attack on the relatively unhindered carbonyl group of cyclic ketones, such as 4-*tert*-butylcyclohexanone, to give predominantly the more stable alcohol;³ diborane and aluminum hydride similarly produce a preponderance of the more stable equatorial alcohol.⁴ Mixtures of isomeric alcohols are usually obtained in these reductions. However, nearly exclusive production of the more stable alcohol (>95%) from cyclic ketones has been achieved in dissolving metal reductions using lithium in ammonia.⁵

Few reducing agents are capable of effecting stereoselective control in ketone reductions that result in a preponderance of the less stable alcohol. The general approach that has been successfully applied to reductions of cyclic ketones to the less stable axial alcohol has been to increase the steric bulk of the reducing agent. Trialkyl- and diarylborohydrides,⁶ for example, have shown marked success in reversing the usual tendency for hydride transfer to the carbonyl group from the axial direction.⁷

Like the more commonly used aluminum and boron hydrides, silicon hydrides are effective reducing agents for the carbonyl group of ketones.^{1a} However, except for the lightinduced hydrosilation of cyclic ketones with trichlorosilane,⁸ there has been no report on the stereoselectivity of ketone reductions by silanes. Alkylsilanes are conveniently prepared by substitution reactions at silicon using chlorosilanes and organometallic compounds; in these reactions the steric bulk of alkyl substituents can be varied widely. Consequently, the effect of increasing the steric bulk of silane reducing agents on the stereoselectivity of ketone reductions can be examined systematically. Such a study of the structural variations of alkyl-substituted organosilanes on the stereoselectivity of product formation is expected to provide information essential to the proper design of truly highly selective reducing agents.

Unlike the more commonly used aluminum and boron hydrides, ketone reductions by the silicon hydrides are catalyzed by Bronsted acids. Activation of the carbonyl carbon by an acid is required before hydride transfer can occur. In order to determine the stereoselectivity in ketone reductions by organosilanes we have examined the reductions in protonic acid media of alkyl-substituted cyclohexanones by mono-, di-, and trialkylsilanes having different steric requirements.

Results

Reductions in Aqueous Sulfuric Acid-Ethyl Ether Mixtures. Aldehydes and ketones are conveniently reduced to alcohols without structural rearrangement by alkylsilanes in aqueous sulfuric acid using ethyl ether as the solvent.^{1a} The alkylsilanes are, in turn, oxidized to the corresponding alkylsilanols. The relative yields of the thermodynamically less stable alcohol from the reductions of selected alkyl-substituted cyclohexanones by mono-, di-, and trialkylsilanes in aqueous sulfuric acid-ethyl ether media (eq 1) are presented in Table I. With the exception of re-





ductions by triethylsilane, the rapidly stirred reaction mixtures were heterogeneous. Ketone reductions under the reaction conditions reported in Table I were generally complete within 24 hr at room temperature.

n-Butylsilane is capable of three individual hydride transfer reactions. However, only two of the three hydrogens are rapidly transferred in reductions of carbonyl compounds. When 1 molar equiv of n-butylsilane was used to reduce the ketones listed in Table I, nearly 0.3 equiv of nbutylsilane remained unreacted. When 0.36 molar equiv of n-butylsilane (1.1 molar equiv of hydride) was employed

 Table I

 Stereoselectivities of Organosilane Reductions of Alkyl-Substituted Cyclohexanones in Aqueous Sulfuric Acid—Ethyl Ether Mixtures^a

					Relative y	vield, % cyc	lohexanol ^b	, <i>c</i>
Registry no.	Silane (mmol)	mmol of ketone	mmol of acid	<i>cis</i> -4- <i>tert</i> - Butyl-d	cis-4- Methyl-	<i>trans</i> -3- Methyl-	<i>cis-2-</i> Methyl-	<i>trans</i> -3,3,5- Trimethyl-
1600-29-9	n-BuSiH ₃ (5.5)	5.0	3.5	10	18	19	31	74
	(1.8)	5.0	3.5	13				
542 - 91 - 6	$Et_{2}SiH_{2}(5.0)$	5.0	3.5	20	26	29	41	85
617-86-7	$Et_{3}SiH(6.0)$	5.0	3.5	32	35	39	54	(90) ^e
998-41-4	n-Bu ₃ SiH (5.5)	5.0	3.5	22	25	35	51	(89) ^e
2929 - 52 - 4	n-Hex ₃ SiH (10)	5.0	3.5	21		32		

^a Reactions were run at room temperature $(28 \pm 3^{\circ})$. Aqueous sulfuric acid $(0.5 \text{ g of a } 73 \text{ g \% solution of aqueous sulfuric acid prepared from 0.5 mol of 96% H₂SO₄ and 1.0 mol of water) was added to the silane and ketone in 0.6 ml of ethyl ether. ^b Unless indicated otherwise the yield of alcohol products was essentially quantitative. Recovered yields of alcohol products after work-up approaching 90% could be attained in these small-scale reactions. ^c The precision of analysis is within <math>\pm 1\%$ from duplicate runs. ^d The yield of *cis*-4-tert-butylcyclohexanol from the reduction of 4-tert-butylcyclohexanone with phenylsilane was 9% and with tetramethyldisiloxane was 21% using similar reaction conditions. ^e Observed relative yield of alcohol products are also obtained.

 Table II

 Stereoselectivities of Organosilane Reductions of Alkyl-Substituted Cyclohexanones in Trifluoroacetic Acida

			mmol of CF ₃ CO ₂ H	Relative yield, % cyclohexanol ^{b,c}					
Registry no.	Silane (mmol)	mmol of ketone		<i>cis</i> -4- <i>tert</i> - Butyl-	cis-4- Methyl-	trans-3- Methyl-	<i>cis</i> -2- Methyl-	trans- 3,3,5-Tri- methyl-	
	n-BuSiH ₂ d (5.0)	5.0	34	16					
	3 ()	5.0	34	21					
13154-66-0	n-PrSiH ₂ $e(2.5)$	2.4	5.0	20			37		
	$Et_3SiHf(6.0)$	5.0	34	32	36	42	48g	84	
	n-Hex, SiH (6.0)	5.0	10				44		
17922 - 08 - 1	i-Pent SiH (4.0)	3.0	20	30	33	38	48	83	
33729 - 87 - 2	$c-Pent_{3}SiH(4.0)$	3.0	21	44	48	51	59	95	
6485-81-0	$i-Bu_3SIH(3,0)$	2.5	17.5	55	56	61	62^{g}	93	
6531-11-9	sec - $\mathbf{Bu}_{3}\mathbf{SiH}^{h}(2.5)$	2.2	5.1	56			64		
	(2.5)	3.0	21	(55) ⁱ	(58) ⁱ	$(67)^{i}$	(64) <i>j</i>	96	
30736-07-3	$t-Bu_{3}SiH_{2}(2.5)$	2.5	18	$(68)^i$	(67 <i>)</i> i	(73) ⁱ	(66) ^k	89	

^a Reactions were run at room temperature $(28 \pm 3^{\circ})$. The ketone in trifluoroacetic acid was added to the silane. ^b Relative yield of alcohol products; symmetrical ethers are also formed (see Tables III and IV). ^c The precision of analysis is within $\pm 1\%$ from duplicate runs. ^a At -20° the relative yield of *cis*-4-*tert*-butylcyclohexanol was only 3% (44 hr reaction time). ^e Using a 14-fold excess of CF₃CO₃H the yield of *cis*-4-*tert*-butylcyclohexanol was 17%. With PMHS the yield of *cis*-4-*tert*-butylcyclohexanol was 19%. ^f Identical results from 4-*tert*-butylcyclohexanone were observed when only 1 equiv of acid was observed. ^g Less than 1% methylcyclohexanol was 58% when 5 mmol of ketone and silane were used with 34 mmol of acid. ⁱ 3 mol % olefin product(s) obtained. ^j 4 mol % methylcyclohexane. ^k 30 mol % methylcyclohexane.

for the reduction of 4-tert-butylcyclohexanone (Table I), 72% of the ketone was reduced within 4 hr; an additional 40 hr was required to reduce the remaining 28% of 4-tertbutylcyclohexanone. The silane compound formed from nbutylsilane after two hydride transfer reactions was a relatively unreactive solid polymeric siloxane from which the reduction products were conveniently isolated. Since unreacted n-butylsilane (bp 54-56°) can be easily separated from alcohol products by fractional distillation, the use of n-butylsilane provides a simple, convenient method for producing the more stable alcohol isomer predominantly in reductions of relatively unhindered cyclic ketones.

With trisubstituted branched-chain alkylsilanes, such as tri-sec-butylsilane, and trialkylsilanes possessing more than 12 carbon atoms, such as tri-n-hexylsilane, reaction times for reductions of cyclic ketones are greater than 24 hr. In addition, in these reductions acid-catalyzed dehydration of the alcohol products becomes important. Such difficulties can be circumvented if reductions with these more bulky silanes are carried out in trifluoroacetic acid media.

Reductions in Trifluoroacetic Acid Media. The relative yields of the thermodynamically less stable alcohol from the reductions of alkyl-substituted cyclohexanones by mono-, di-, and trialkylsilanes in trifluoroacetic acid (eq 2)



are presented in Table II. The reaction solutions were homogeneous, and the reactions were, with the exception of those using di-*tert*-butylsilane and tri-*sec*-butylsilane, noticeably exothermic. The trifluoroacetate derivatives formed in these reductions^{1a} were usually converted by a mild hydrolysis procedure to the corresponding alcohols. Analysis of the trifluoroacetate products prior to hydrolysis, and of the alcohol products after hydrolysis, showed

			Symr	netrical ethers
	Trifluo	roacetates	%	% axial/
Ketone	% yield	% V/% IV	Yield	% equatorial ^b
Ia	83	0.47	17	1.04
Ib	83	0.56	17	с
Ic	87	0.72	13	с
Id	>99	0.92	<1	с
Ie	84	8.1	16	3.65

^a Reductions were run at room temperature using 1.0 mmol of ketone, 0.8 mol of triethylsilane, and 6.5 mmol of trifluoroacetic acid. Reaction time was 24 hr. ^b Ratio of axial to equatorial alkyl substitution of oxygen determined by ¹H NMR spectroscopy or by GLC analysis. ^c Could not be determined. J. Org. Chem., Vol. 40, No. 26, 1975 3823

amount of ether formation is dependent on the structures of both the ketone and silane. Organosilane reductions of cyclohexanones with alkyl substituents in remote positions with respect to the carbonyl group, 4-tert-butyl-, 4-methyl-, 3-methyl-, and 3,3,5-trimethylcyclohexanones, give a substantially higher proportion of symmetrical ethers than 2-methylcyclohexanone, a ketone having an alkyl group that can effectively shield the carbonyl group. Reduction of 2-methylcyclohexanone by n-butylsilane in trifluoroacetic acid, for example, gives 46% symmetrical ethers, compared to 74% symmetrical ethers from the reduction of 4-tertbutylcyclohexanone by n-butylsilane under similar reaction conditions. The relative yield of symmetrical ethers is also dependent on the nature of alkyl substitution of the organosilane; the greater the number of alkyl groups and the greater the branching of the alkyl groups, especially at the α position, the less is the relative proportion of symmetrical ethers formed during reduction. Significant con-

			Table IV		
Symmetrical	Ether	and	Trifluoroacetate Product	Distributions in	Reductions of
•	4-t	ert.	Butvlcvclohexanone by (Organosilanes ^a	

						Syı	mmetrical e	$thers^c$	
			Triflue	oroacetates ^{b,c}		trans -			
Silane (mmol)	mmol of ketone	mmol of CF ₃ CO ₂ H	% yieldd	% cis/% trans	% yield ^d	trans, %f,i	cis,trans %f,j	cis,cis %f,k	% cis/ % trans ^e
$\overline{n \cdot \mathrm{BuSiH}}$, (5.0)	5.0	34	37	0.19	63	44	46	10	0.49
(1.8)	5.0	34	40	0.27	60	50	43	7	0.40
(50)	50	125	26	0.031s	74	67	29	4	0.23s
n-PrSiH. (2.5)	2.4	5.0	50	0.25	50	53	40	7	0.37
PMHS (4.0)	5.0	34	66	0.23	34	30	55	15	0.76
Et.SiH (18)	18	135	83	0.49	17	25	48	27	1.04
(22)	$\tilde{20}$	20	93	0.53	7	19	45	36	1.41
c-Pent, SiH (4.0)	3.0	21	89	0.79	11	13	35	52	2.28
i-Bu,SiH (2.7)	2.5	17.5	86	1.08	14	18	43	39	1.53
sec-Bu, SiH (2.5)	3.0	21	94	1.22	6	3	24	73	5.67
$t - Bu_2 SiH_2$ (5.2)	5.2	35	97h	2.12	Ō				

^a See footnote a, Table II. ^b Analyzed as the alcohol unless indicated otherwise. ^c See footnote c, Table II. ^d Unless indicated otherwise, trifluoroacetates and symmetrical ethers were formed in nearly quantitative yields. ^e 2(% cis, cis-) + %cis, trans-/2(% trans, trans-) + % cis, trans-. f Relative yield of isomeric ether; duplicate runs show that the precision of analysis is within $\pm 2\%$ of the reported value. ^g Reaction was run at -20° for 44 hr; isolated yield of ethers was 74\%. ^h 3\% cycloalkene. ⁱ Registry no., 56889-95-3. ^j Registry no., 56942-33-7. ^k Registry no., 56942-34-8.

that no change in the isomeric ratio of products occurred during the hydrolysis procedure. The primary silane products were the corresponding silyl trifluoroacetates which formed mixtures of silanols and disiloxanes upon hydrolysis.

Organosilane reductions of Ia-e were generally complete within 2-4 hr when 7 molar equiv of trifluoroacetic acid was used. However, more than 2 days were required for complete reduction of 3- and 4-methylcyclohexanones by di-tert-butylsilane (1 molar equiv of silane), and reaction times of more than 12 days were necessary for complete reduction of 2-methyl- and 3,3,5-trimethylcyclohexanones by the same reducing agent. In ketone reductions di-tert-butylsilane was approximately 100 times less reactive than tri-sec-butylsilane. When 2 hydride equiv of di-tert-butylsilane per ketone were employed, the silane products consisted of di-tert-butylsilyl trifluoroacetate (4%) and either di-tert-butylsilanediol or its trifluoroacetate derivative (96%). After hydrolysis of the reaction mixture di-tertbutylsilanediol was isolated in 91% yield. Thus the second hydride transfer is more rapid than the first, and both hydrides per molecule of di-tert-butylsilane are effective in reducing ketones.

In trifluoroacetic acid media symmetrical ether formation is a major competing reaction in ketone reductions (eq 3).^{1a} As shown by the data in Tables III and IV, the relative trol over reaction products can be achieved in these reductions by proper choice of silane, temperature (low temperatures favor the ether), and acid concentration (high concentrations favor the ether) so that ether or alcohol products can be produced selectively.

$$(m + 2n) \operatorname{R}_2 \operatorname{C=O} \xrightarrow{\operatorname{R'_3SiH}}_{\operatorname{CF_3COOH}} m \operatorname{R}_2 \operatorname{CHOOCCF_3} +$$

$$nR_2CHOCHR_2$$
 (3)

With the exception of those ethers formed in reductions of 2-methylcyclohexanone, symmetrical ethers were not noticeably converted to trifluoroacetates under the reaction conditions employed, and the trifluoroacetates did not form symmetrical ethers. Symmetrical ethers were not formed in the reductions of alkyl-substituted cyclohexanones in aqueous sulfuric acid-ethyl ether.

When the 2-methylcyclohexyl ethers having an isomeric cis to trans ratio of 1.02 were treated with 6.0 equiv of trifluoroacetic acid at room temperature for 24 hr, only 61% of the ethers (cis/trans = 0.73) was recovered. Both *cis*- and *trans*-2-methylcyclohexyl trifluoroacetates were produced (39% yield) in an isomeric ratio (cis/trans = 0.98) nearly identical with that of the reactant ethers, and 1-methylcyclohexyl trifluoroacetate was also formed in 39% yield. These results indicate that cleavage of the 2-methylcyclohexyl ethers occurs by elimination, that only the cis-substituted 2-methylcyclohexyl ring of the symmetrical ethers undergoes elimination, and that the unique ether cleavage reaction occurs with both *cis,cis*- and *cis,trans*-2-methylcyclohexyl ethers but not with the trans,trans isomer (eq 4).



Table IV reports the relative yields of the three isomeric symmetrical ethers formed in the organosilane reductions of 4-tert-butylcyclohexanone. Like the relative yield of symmetrical ethers in these reductions, the cis to trans ratio for the ether products reflects the nature of alkyl substitution of the organosilane. The cis to trans ratio for the ethers magnifies the corresponding ratio for trifluoroacetate products. Within experimental limits no changes in the relative yields of the isomeric ether products were observed when the reduction of 4-tert-butylcyclohexanone was monitored at intervals over a 27-hr period.

Except in reductions by tri-sec-butylsilane or di-tertbutylsilane and of 2-methylcyclohexanone, elimination products were not observed during the reductions of alkylsubstituted cyclohexanones by organosilanes. Approximately 3 mol % of cycloalkene was observed in reductions of 4-tert-butyl-, 4-methyl-, and 3-methylcyclohexanones by tri-sec-butylsilane and di-tert-butylsilane when 7 molar equiv of trifluoroacetic acid was used. The olefin or olefins produced in each of these reductions were relatively stable toward addition of trifluoroacetic acid under the reaction conditions employed; no change in the yield of olefin was observed over a 20-hr period after complete reduction of each of the 3- and 4-substituted cyclohexanones.¹⁰ From the results in Table II for the tri-sec-butylsilane reduction of Ia in which only 2 equiv of acid was used, and in which no elimination-addition occurs, an estimate of a maximum of 3-4% olefin formation in reductions of Ia-c is reasonable. Cycloalkene products were not obtained from the reductions of 3,3,5-trimethylcyclohexanone by any of the organosilanes listed in Table II.¹¹

The preferred orientation in elimination reactions of 2methylcyclohexanol derivatives results in the formation of 1-methylcyclohexene.¹² Subsequent reduction of 1-methylcyclohexene by organosilanes¹³ forms methylcyclohexane under the reaction conditions employed for reduction of 2methylcyclohexanone (eq 5). The yields of methylcyclohex-

$$R_{3}SiH + OCH_{3} + CF_{3}COOH \rightarrow OCH_{3} + R_{3}SiOOCCF_{3}$$
(5)

ane from organosilane (given in parentheses) reductions of 2-methylcyclohexanone were <1% (Et₃SiH), <1% (*i*-Bu₃SiH), 4% (*sec*-Bu₃SiH), and 30% (*t*-Bu₂SiH₂). No 1-methylcyclohexyl trifluoroacetate, the expected addition product from 1-methylcyclohexene and trifluoroacetic acid, was observed.

Discussion

Stereoselectivity of Alcohol Formation. The results reported in Tables I and II describe the importance of steric factors from both the ketone and the silane reducing agent in determining the stereochemical outcome of organosilane reductions of alkyl-substituted cyclohexanones. Increasing the steric bulk of the organosilane reducing agent increases the relative yield of the thermodynamically less stable alcohol or alcohol derivative.

The relative yield of the less stable isomer, IIIa-e or Va-e, increases with increasing substitution of n-alkyl groups at silicon. An increase of approximately 10% in the proportion of hydride transfer that results in the production of axial alcohol occurs with each successive n-alkyl substitution at silicon when silane reductions are performed in aqueous sulfuric acid-ethyl ether; smaller increases are observed when the corresponding reductions occur in trifluoroacetic acid. In general, the effect of increasing n-alkyl substitution is additive, suggesting that steric interference to hydride transfer is dependent on the composite steric bulk of the organosilane and that hydride transfer does not occur preferentially from fixed geometries, such as A and B, in which the larger alkyl substituents, especially of mono- and dialkylsilanes, are positioned to avoid steric crowding with the ketone during hydride transfer.14



Branching at the α and β positions of trialkylsilanes increases the relative yield of the less stable alcohol product in ketone reductions. Only small differences in product yields from reductions of Ia-e in trifluoroacetic acid were observed with triisobutylsilane and tri-sec-butylsilane (Table II). However, when the relatively free rotation of each of the alkyl groups of an α -branched trialkylsilane is restricted, as in tricyclopentylsilane, the increase in the relative yields of Va-e is significantly less than the corresponding yields in reductions by tri-sec-butylsilane. As with the effect of increasing the chain length of tri-n-alkylsilanes, the effect of tricyclopentylsilane compared to trisec-butylsilane (α branching) on the stereoselectivity of ketone reductions is most evident with 3- and 4-alkylcyclohexanones. Branching at the γ position of trialkylsilanes is not effective in altering the relative yields of Va-e from those obtained using triethylsilane.

n-Butylsilane and di-tert-butylsilane rapidly undergo two hydride transfer reactions; the third hydride transfer from *n*-butylsilane is relatively slow. A comparison of the results from Tables I and II for reduction of Ia by 1.1 and 0.36 molar equiv of *n*-butylsilane show a 3-5% increase in the relative yield of IIIa or Va due to the transfer of the third hydride. Although the exact stereochemical outcome from the transfer of the first hydride is unknown, these results are predictably similar to those observed by Rickborn and Wuesthoff for reductions of sodium borohydride:^{3b} in successive hydride transfer reactions from polyhydride reducing agents, the transfer of the first hydride results in the higher yield of the more stable alcohol isomer.

The stereochemical outcome of reductions of alkyl-substituted cyclohexanones by n-alkylsilanes in aqueous sulfuric acid-ethyl ether or in trifluoroacetic acid is comparable to similar results from reductions with boron and aluminum hydrides (Table V). Equatorial attack is preferred in reductions of 3,3,5-trimethylcyclohexanone because of the steric interference toward attack from the axial side due to

Table V	
Comparative Stereoselectivities of Boron,	Aluminum, and Silicon Hydrides

	Relative yield, % cyclohexanol							
Reducing agent	cis-4-tert-Butyl-	cis-4-Methyl- ^{c,d}	trans-3- Methyl- ^{c, e}	cis-2-Methyl-	trans-3,3,5- Trimethyl-			
LiAlH ₄ , Et ₂ O	11 ^{3d}	17 ⁶ a (16)	16^{6a} (16)	24 ^{3d}	55			
NaBH, <i>i</i> -PrOH, 0% reaction ^{3b}		11 1	13 ` ´	25	58			
NaBH, <i>i</i> -PrOH, 100% reaction ^{3b}	2016	24 (25)	24(25)	40	62			
B ₂ H ₅ ^{46,c}	10	15`´	12(17)	25	66			
<i>n</i> -BuSiH ₃ <i>a</i>	10	18	19 (16)	31	74			
AlH,	13.46⁴e			26	8817			
$LiAlH(O-t-Bu)_{3}^{3e}$	10	14	17 (18)	37	$88,94^{3f}$			
Et,SiH,a	20	26	29 (27)	41	85			
Et ₃ SiH ^a	32	35	39 (38)	54	90			
Et ₃ SiH ^b	32	36	42 (37)	48	84			
LiĂlH(OMe)₃	4118		. /	69³d	7319			

^a Data taken from Table I. ^b Data taken from Table II. ^c Values in parentheses are calculated using the conformational energies for conformers of methylcyclohexanones²¹ with the values from reductions of 4-*tert*-butylcyclohexanone as the model for the equatorial conformer and 5 α -cholestan-3-one²⁰ or 3,3,5-trimethylcyclohexanone as the model for the axial conformer. ^d Calculated yield = 0.94 (% cis-4-tert-butyl-) + 0.06 (% β -3-cholestanol). ^e Calculated yield = 0.90 (% cis-4-tert-butyl-) + 0.10 (% trans-3,3,5-trimethyl-).

the axial methyl group in the 3 position.² Hydride transfer which avoids torsional strain^{2,15} is generally predominant in reductions of Ia-d.

The relative yields of the less stable alcohol from reductions of 4-methyl- and 3-methylcyclohexanones are consistently greater than those from 4-tert-butylcyclohexanone. Unlike the conformationally biased 4-tert-butylcyclohexanone, conformations of methylcyclohexanones in which the alkyl substituent is in the axial position are not negligible.²¹ For example, in the equilibrium mixture at room temperature the equatorial-methyl chair conformer of 3methylcyclohexanone is present to the extent of only 90%; the axial-methyl chair conformer accounts for more than 9% of 3-methylcyclohexanone. If the assumption is made that hydride transfer to the equatorial-methyl conformer of 3-methylcyclohexanone occurs with the same ratio of axial to equatorial attack as 4-tert-butylcyclohexanone and that the model for the axial-3-methyl conformer is 3,3,5trimethylcyclohexanone, the relative yields of alcohol products from reductions of 3-methylcyclohexanone can be predicted within $\pm 1\%$ for the majority of the reducing agents in Table V.22 Using suitable model compounds the same procedure can be applied to estimate the product yields from reductions of 4-methylcyclohexanone.

The relative yields of the less stable cis isomer from reductions of 2-methylcyclohexanone are uniformly 10-30% greater than those from the corresponding reductions of 4*tert*-butylcyclohexanone. In the equatorial conformation the 2-methyl substituent has an additional axial β hydrogen (C) which increases the steric requirement for axial at-



tack. Stereochemical results from reductions of a model compound, *cis*-2-methyl-4-*tert*-butylcyclohexanone,²³ in which the 2-methyl substituent is fixed in the equatorial position indicate, however, that the effect of the additional axial β hydrogen cannot completely account for the higher yields of the less stable isomer found in reductions of 2-methylcyclohexanone. Nor can the conformational equilibrium of the reactant ketone completely account for the ob-

served higher yields of cis alcohol. Ashby has shown that complexation with the carbonyl group in reductions of 2methylcyclohexanone by complex metal hydrides causes an increase in the relative yield of *cis*-2-methylcyclohexanol. This increase has been explained as being due to a change in the relative proportion of the metal ion complexed axial-2-methylcyclohexanone conformer with the increasing bulk of the complexing agent.²³ In silane reductions utilizing Bronsted acids, protonation of the ketone carbonyl group may also change the conformational equilibrium of the reactant 2-methylcyclohexanone.

Strikingly different stereochemical results are obtained in reductions of alkyl-substituted cyclohexanones by bulky boron and silicon hydrides. The boron hydrides are especially sensitive toward 3,3,5-trimethylcyclohexanone and 2-methylcyclohexanone, yielding the thermodynamically less stable isomer in high stereochemical purity. In contrast, the silicon hydrides show no such differentiation and, in fact, exhibit less ability to discriminate stereochemically between alkyl-substituted cyclohexanones as the steric requirement of the silane is increased. Unlike boron hydrides, such as lithium tri-sec-butylborohydride and lithium perhydro-9b-boraphenalylhydride (LiPBPH), whose approach to the carbonyl group of 4-tert-butylcyclohexanone appears to be influenced by remote alkyl substituents, silicon hydrides show no similar steric influence in reductions of 4-tert-butylcyclohexanone. The differences in the stereoselectivities of the bulky boron and silicon hydrides is explained by the differences in the mechanisms for borohydride and silane reductions and will be discussed in a subsequent paper.²⁵

Stereoselectivity of Ether Formation. The yields of symmetrical ethers and trifluoroacetates reported in Table III indicate the relative importance of steric effects on ether formation in the triethylsilane reduction of alkyl-substituted cyclohexanones. The relative yields of ethers formed in reductions of cyclohexanones having alkyl substituents in the 3 and 4 positions are nearly identical (13-17%). In contrast, reduction of 2-methylcyclohexanone by triethylsilane gives less than 1% of symmetrical ethers.²⁶

We have previously described ether formation as occurring by hydride transfer to the oxonium ion, VI, formed from the nucleophilic addition of an alcohol to the protonated carbonyl group, followed by elimination of a molecule of water (Scheme I).^{1a,27} Ether formation competes with trifluoroacetolysis of the alcohol. The decreased yield of ethers from the reduction of 2-methylcyclohexanone (Id)

Scheme I

$$R_2C = O + H^+ \implies R_2C = \stackrel{+}{O}H \xrightarrow{Et_3SiH} R_2CHOH$$
 (6)

~ 1 **•**

$$R_2C = 0 + R_2CHOH \xrightarrow{H} R_2C \swarrow_{OCHR_2}$$
 (7)

 $R_2C \swarrow OH + H^+ \rightleftharpoons R_2C = OCHR_2 + H_2O$ (8)

$$R_2 C = \overset{+}{O} C H R_2 \xrightarrow{Et_3 S i H} R_2 C H O C H R_2$$
(9)

Scheme II

Ia + IIa $\overset{H^+}{\underset{-H_2O}{\overset{H^+}{\longrightarrow}}}$ trans-VIa $\overset{trans, trans-4-tert}{\underset{k_{lc}}{\overset{k_{lc}}{\longrightarrow}}}$ butylcyclohexyl ether Ia + IIIa $\overset{H^+}{\underset{-H_2O}{\overset{K_{cVI}}{\longrightarrow}}}$ cis-VIa $\overset{cis.trans-4-tert}{\underset{k_{cc}}{\longrightarrow}}$ butylcyclohexyl ether is trans.trans-tert-butylcyclohexyl ether

compared to that from 4-tert-butylcyclohexanone indicates either (1) that steric factors in reactions leading to VI decrease the effective concentration of VI, (2) that there is steric hindrance to hydride transfer from triethylsilane to VI, or (3) that the decreased yield of ethers is due to a combination of 1 and 2. Since reduction of Id by *n*-butylsilane gives a 46% yield of symmetrical ethers, the lower yield of ethers in silane reductions of Id indicates that there is indeed steric hindrance to hydride transfer from alkylsilanes to VI.

As seen from the data in Tables III and IV, the isomeric ratio of symmetrical ether products is also governed by the steric requirement of the organosilane. With the exception of the triethylsilane reduction of 3,3,5-trimethylcyclohexanone, the cis to trans ratio for ethers magnifies the cis to trans alcohol ratio. Among the trialkylsilanes in reductions of 4-tert-butylcyclohexanone this magnification is on the order of two to three. The cis to trans ratio of ethers in reductions of Ia by triisobutylsilane, however, is only a factor of 1.5 times that of the alcohol, possibly reflecting different steric requirements for hydride transfer to protonated ketone and VI in this case.

Since two isomeric alcohols are formed in silane reductions of alkyl-substituted cyclohexanones, two isomeric oxonium ion intermediates are formed in the reaction scheme leading to ether formation. Reduction of the two isomeric oxonium ions gives three isomeric ethers (Scheme II). If there is no discrimination in oxonium ion formation ($K_{t-\text{VIa}} = K_{c-\text{VIa}}$) the yields of symmetrical ethers will reflect the relative concentrations of alcohol products formed by silane reduction, and the relative rates of hydride transfer to each oxonium ion (k_{tc}/k_{tt} and k_{cc}/k_{ct}) can be determined. Table VI lists the selectivity ratios, k_{tc}/k_{tt} and k_{cc}/k_{ct} , which were calculated by assuming that [IIIa]/[IIa] = [cis-VIa]/[trans-VIa].²⁸

Comparison of the isomeric ratios in Table VI shows that hydride transfer to VIa is much more sensitive to the steric bulk of the organosilane reducing agent than is hydride transfer to the corresponding protonated ketone, and that reduction of *cis*-VIa gives a higher yield of the less stable isomer than does the reduction of *trans*-VIa.²⁹ Thus changing the steric bulk of the acid required to activate the carbonyl group in silane reductions dramatically af-

Table VI Stereoselectivities of Organosilane Reductions of trans-VIa and cis-VIa in Reductions of 4-tert-Butylcyclohexanone

The second design of the second secon	THE REAL PROPERTY AND ADDRESS OF THE REAL PROPERTY ADDR				
Silane (mmol)	mmol of ketone	mmol of CF₃- COOH	IIIa ^a / IIa	$rac{k_{tc}}{k_{tt}}^{b}$	k _{cc} / k _{ct} c
n-BuSiH ₃ (5.0)	5.0	34	0.19	0.91	1.7
(1.8)	5.0	34	0.27	0.58	2.0
(50)	50	125	0.031	0.45	d
n-PrSiH ₃ (2.5)	2.4	5.0	0.25	0.51	0.54
PMHS (4.0)	5.0	34	0.23	1.4	3.8
$Et_3SiH(18)$	18	135	0.49	1.7	4.5
(22)	20	20	0.53	2.6	d
$c-Pent_3SiH(4.0)$	3.0	21	0.79	3.3	d
$-Bu_{3}SiH(2.7)$	2.5	17.6	1.08	1.4	2.3
ec-Bu,SiH (2.5)	3.0	21	1.22	14	d

^a Data taken from Table IV. ^b $k_{tc}/k_{tt} = (\% \text{ IIa} - \% \text{ trans}, \text{trans ether})/\% \text{ trans, trans ether}$. ^c $k_{cc}/k_{ct} = (\% \text{ IIIa} - \% \text{ cis, cis ether})/\% \text{ cis, cis ether}$. ^d % cis, cis ether > % IIIa; does not necessarily imply that the reducing agent discriminated in favor of *cis*-VIa; in nearly every case either the yield of the cis, cis isomer was relatively low or the total yield of ethers was low and the experimental yields obtained relatively uncertain.

fects the stereoselectivity of hydride transfer. Similar effects are becoming increasingly evident in reductions by metal hydrides^{6b,23,30} and by metal alkoxides.³¹

Experimental Section

Instrumentation. Infrared spectra were obtained on a Perkin-Elmer Model 621 grating spectrophotometer. Mass spectra were obtained using a Finnigan Model 1015 gas chromatograph-mass spectrometer operated at 70 eV. Proton magnetic resonance spectra were obtained with a Varian Model A-60A spectrometer; chemical shifts are reported in δ units using tetramethylsilane as the internal reference. Analytical GLC analyses were performed on Varian Aerograph Models 1864 and 2720 gas chromatographs using thermal conductivity detectors. Use was made of 5-ft columns of 10% SE-30, 25% glycerol, and 20% Carbowax 20M and 10-ft columns of 20% Carbowax 20M, all on Chromosorb P. Melting points were obtained on a Thomas-Hoover apparatus and were uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Materials. Commercial samples of 3- and 4-methylcyclohexanones were used without further purification. 2-Methylcyclohexanone and 4-tert-butylcyclohexanone were purified by distillation prior to use. A sample of 3,3,5-trimethylcyclohexanone was prepared by a standard Jones oxidation procedure from commercially available 3,3,5-trimethylcyclohexanol. Isomeric mixtures of each of the methylcyclohexanols and 4-tert-butylcyclohexanol were commercially available and used without further purification. A mixture of 3,3,5-trimethylcyclohexanols (52% cis, 48% trans) was prepared by a lithium aluminum hydride-ether reduction of 3,3,5-trimethylcyclohexanone. Diethyl-, triethyl-, tri-n-butyl-, and tri-nhexylsilanes, polymethylhydrogensiloxane (PMHS), and tetramethyldisiloxane were commercially available and used without further purification. Phenyl-, n-butyl-, and n-propylsilanes were prepared by standard lithium aluminum hydride reductions of the corresponding organotrichlorosilanes.^{1a} Triisobutyl- and triisopentylsilanes were prepared by standard methods from the corresponding Grignard reagents and trichlorosilane. Tri-sec-butyl- and tricyclopentylsilanes were prepared by standard methods from organolithium reagents and trichlorosilane. The preparation of ditert-butylsilane has been described.³² The physical constants and spectra of organosilanes prepared by these methods were consistent with their structure and with the reported literature values.

2-Methylcyclohexyl Ether. To a solution of 5.60 g (50.0 mmol) of 2-methylcyclohexanone and 1.76 g (20.0 mmol) of *n*-butylsilane cooled at 0° was added dropwise 9.2 ml (125 mmol) of trifluoroacetic acid over a 40-min period. The flask containing the homogeneous reaction solution was then stoppered and stored in a freezer at -40° for 144 hr, at which time ¹H NMR analysis indicated that all of the ketone had been reduced. Excess sodium hydroxide (50 ml of 3 N NaOH) was added, and the reaction mixture was stirred rapidly for 5 hr. The organic materials were extracted five

			Chemical shift, δ	a	
Allerel errol o	Grade	Trifluoro	Dacetates ^b	Symme	etrical ethers ^b
Aikyicycio- hexanone	alkene	IV	v	Axial ^c	Equatorial ^d
Ia	5.71	5.37	4.97	4.05	3.62
Ib	5.70	5.37	5.04	4.1	-3.8 ^e
Ic	5.67	5,47	5.08	4.15	3.8
Id	f	5.31	4.74	3.79	3.18
Ie	5.53	5.46	5.2	4.08	g

 Table VII

 ¹H NMR Absorptions of Reaction Products from Silane Reductions of Ia—e in Trifluoroacetic Acid

^a Relative to internal Me₄Si in trifluoroacetic acid; temperature 37°. ^b Multiplet absorptions; peak width ±0.1 ppm for axial-substituted isomers, ±0.2 ppm for equatorial-substituted isomers. ^c Contribution from axial-axial and axial-equatorial substituted isomers. ^d Contribution from axial-equatorial and equatorial-equatorial substituted isomers. ^f Broad unresolvable absorptions. ^f Not observed in trifluoroacetic acid owing to formation of 1-methylcyclohexyl trifluoroacetate. ^g Not observed owing to broad linewidth and low concentration of this isomer.

times with 10-ml portions of pentane, and the combined pentane extract was stirred over solid potassium hydroxide for 3 hr. The potassium hydroxide was filtered, and the pentane solution was concentrated under reduced pressure. Vacuum distillation gave 2.41 g (11.5 mmol, 46% yield) of 2-methylcyclohexyl ether: bp 76.5-78.0° (0.3 Torr); ir (film) 1075 cm⁻¹ (C-O-C); ¹H NMR (CCl₄) multiplets centered at δ 3.43 and 2.79 (1 H) and complex absorptions between δ 0.7 and 2.1 (12 H); mass spectrum m/e (rel intensity) 211 (0.033, P + 1), 210 (0.20, parent ion), 114 (3.9), 97 (27), 55 (100).

Anal. Calcd for C₁₄H₂₆O: C, 79.94; H, 12.46. Found: C, 79.72; H, 12.35.

4-tert-Butylcyclohexyl Ether. To a stirred solid-liquid mixture of 7.70 g (50.0 mmol) of 4-tert-butylcyclohexanone and 4.40 g (50.0 mmol) of n-butylsilane at 0° was added 0.2 ml (125 mmol) of trifluoroacetic acid dropwise over a 60-min period. The heterogeneous mixture slowly became homogeneous during the addition of trifluoroacetic acid. After complete addition of trifluoroacetic acid the reaction mixture was cooled to -40° for 44 hr, at which time ¹H NMR analysis indicated complete reduction of 4-tert-butylcyclohexanone. Vacuum distillation of the reaction mixture at 30 Torr removed trifluoroacetic acid, water, and unreacted n-butylsilane. Continued distillation at 0.3 Torr gave 5.34 g (18.5 mmol, 74% yield) of 4-tert-butylcyclohexyl ether, bp 147-160° (0.3 Torr). GLC analysis on a 2-ft 20% Carbowax 20M column at 205° gave three peaks with retention times of 2.9, 4.9, and 7.4 min and having relative peak areas of 4, 29, and 67%, respectively. Each of these compounds was collected and analyzed separately.

cis, cis-4-tert-Butylcyclohexyl ether was a viscous liquid: 2.9 min retention time; ir (film) 1398, 1370, 1240 (tert-butyl), and 1050 cm⁻¹ (C-O-C); ¹H NMR (CCl₄) δ 3.58 (m, 2 H), 1.9 (m, 4 H), 1.75-1.1 (m, 14 H), and 0.87 (s, 18 H); mass spectrum *m/e* (rel intensity) 295 (0.04, P + 1), 294 (0.17, parent ion), 156 (2.0), 139 (5.8), 123 (6.0), 99 (14), 83 (30), and 57 (100).

Anal. Calcd for C₂₀H₃₈O: C, 81.56; H, 13.00. Found: C, 81.70; H, 13.04.

cis,trans-4-tert-Butylcyclohexyl ether was a white solid: mp 61.0-62.2°; 4.9 min retention time; ir (film) 1399, 1370, 1240, 1230 (tert-butyl), and 1085 cm⁻¹ (C-O-C); ¹H NMR (CCl₄) δ 3.62 (m, 1 H), 3.10 (m, 1 H), 1.9 (m, 4 H), 1.67-0.9 (m, 14 H), and 0.87 (s, 18 H); mass spectrum m/e (rel intensity) 295 (0.025, P + 1), 294 (0.09, parent ion), 156 (0.83), 139 (5.5), 123 (6.0), 99 (11.5), 83 (28.5), 57 (100).

Anal. Calcd for C₂₀H₃₈O: C, 81.56; H, 13.00. Found: C, 81.77; H, 13.00.

trans,trans-4-tert-Butylcyclohexyl ether was a white solid: mp 85.2-86.0°; 7.4 min retention time; ir (KBr) 1395, 1370, 1240, 1225 (tert-butyl) and 1090 cm⁻¹ (C-O-C); ¹H NMR (CCl₄) δ 3.55 (m, 2 H), 1.83 (m, 8 H), 1.6-0.9 (m, 10 H), and 0.85 (s, 18 H); mass spectrum *m/e* (rel intensity) 295 (0.01, P + 1), 294 (0.048, parent ion), 156 (0.42), 139 (4.7), 123 (6.2), 99 (9.5), 83 (35), 57 (100).

Anal. Calcd for C₂₀H₃₈O: C, 81.56; H, 13.00. Found: C, 81.43; H, 12.96.

4-tert-Butylcyclohexyl Trifluoroacetate. To 7.80 g (50.0 mmol) of 4-tert-butylcyclohexanol (mixture of isomers) was added 11.40 g (100.0 mmol) of trifluoroacetic acid. The homogeneous reaction solution was allowed to remain at room temperature for 24 hr and was then quenched with an excess of a saturated sodium bicarbonate solution. The organic materials were extracted twice with 25-ml portions of ether. The combined ether extract was

dried over anhydrous magnesium sulfate, and the ether was removed under reduced pressure after filtering the magnesium sulfate. Vacuum distillation gave 7.10 g (28.0 mmol, 56% yield) of 4-*tert*-butylcyclohexyl trifluoroacetate (36% cis and 64% trans by GLC analysis): bp 97-102 (18 Torr); ir (film) 1785 cm⁻¹ (C=O); ¹H NMR (CCl₄) δ 5.24 and 4.83 (m, 1 H), 2.35-1.0 (m, 9 H), and 0.90 (s, 9 H). Trifluoroacetate esters of other alkyl-substituted cy-clohexanols were prepared by a similar procedure.

General Reduction Procedure in Aqueous Sulfuric Acid-Ethyl Ether. The reduction of 4-tert-butylcyclohexanone by triethylsilane illustrates the general reduction procedure. To a rapidly stirred solution of 0.78 g (5.0 mmol) of 4-tert-butylcyclohexanone and 0.70 g (6.0 mmol) of triethylsilane in 0.6 ml of ether was added 0.5 g of aqueous H_2SO_4 (prepared by adding 0.5 mol of 96% sulfuric acid to 1.0 mol of H₂O) at room temperature. The exothermic, initially heterogeneous reaction mixture became homogenous after several minutes. The reaction solution was quenched with 25 ml of a saturated sodium bicarbonate solution 15 min after the addition of aqueous sulfuric acid and was extracted three times with 16-ml portions of ether. The combined ether extract was dried over and filtered from anhydrous magnesium sulfate, and the magnesium sulfate filter cake was rinsed several times with small portions of ether. The combined ether washes and extract was concentrated under reduced pressure. GLC analysis of the product mixture indicated the presence of unreacted triethylsilane, triethylsilanol, and a 90% recovered yield of 4-tert-butylcyclohexanol (32% cis, 68% trans); no other compounds were evident.

The optimum acid concentration used in these reductions was selected as 3.5 mmol of sulfuric acid (0.50 g of 73 g % aqueous H_2SO_4) per 5.0 mmol of I, when 0.6 ml of ethyl ether was used, based on reaction times for the reduction of 4-*tert*-butylcyclohexanone by triethylsilane. When 1.75 mmol of sulfuric acid was used, complete reduction was observed only after 20 hr at room temperature. With 3.5 mmol of sulfuric acid reduction was complete within 1 hr; and when 5.25 mmol of sulfuric acid was employed, less than 15 min reaction times were required. No change in the ratio of *cis*-to *trans*-4-*tert*-butylcyclohexanol was observed over the period of time required for each of these reductions.

General Reduction Procedure in Trifluoroacetic Acid. The reduction of 3,3,5-trimethylcyclohexanone with tri-sec-butylsilane illustrates the general reduction procedure. To a stirred solution of 0.70 g (5.0 mmol) of 3,3,5-trimethylcyclohexanone and 1.10 g (5.5 mmol) of tri-sec-butylsilane was added 2.5 ml (34 mmol) of trifluoroacetic acid at room temperature. The mildly exothermic, initially heterogeneous reaction mixture became homogeneous within 5 min. Reduction was complete in 2 hr by ¹H NMR analysis. Analysis by ¹H NMR spectroscopy indicated 98% 3,3,5-trimethylcyclohexyl trifluoroacetate (only the trans isomer was observed) and 2% ether products.³³ Excess 3 N sodium hydroxide was added to the reaction solution and the mixture was rapidly stirred for 12 hr. The organic materials were extracted three times with 15-ml portions of ether. The combined ether extract was dried over and filtered from anhydrous magnesium sulfate, and the magnesium sulfate filter cake was rinsed several times with small portions of ether. The combined ether washes and extract was concentrated under reduced pressure. Analysis by GLC gave a 90% recovered yield of 3,3,5-trimethylcyclohexanol (4% cis, 96% trans). An alternate procedure, adding the silane to a stirred solution of ketone and trifluoroacetic acid, gave identical results.

Product Analyses. Reaction solutions from reductions in triflu-

oroacetic acid were analyzed by ¹H NMR spectroscopy prior to quenching. Reaction products were identified from the chemical shifts and characteristic splittings of absorptions in the δ 3-6 spectral region (Table VII). Structural assignments were verified by GLC analysis followed by GLC collection and identification of products in those cases where particular standards were not available.

Product yields were determined by GLC analyses for the vast majority of reactions reported in this study. Isomeric alcohols from 2-, 3-, and 4-methylcyclohexanone reductions were separated and analyzed on 5-ft, 25% glycerol columns at 100°. Isomeric alcohols from 4-tert-butylcyclohexanone reductions were separated and analyzed on a 5-ft 20% Carbowax 20M column programmed from 135 to 180° at 4°/min. Isomeric alcohols from 3,3,5-trimethylcyclohexanone reductions were separated and analyzed on a 10-ft 20% Carbowax 20M column at 180°. In each separation the axial isomer eluted first, as determined by the agreement between ¹H NMR and GLC analyses and by ¹H NMR analyses of the separate isomers of 4-methylcyclohexanol and 2-methylcyclohexanol from GLC collections. The individual thermal conductivities of alcohol, symmetrical ether, and trifluoroacetate products were determined and used to obtain absolute yields. The thermal conductivities of the geometrical isomers of each alcohol were assumed to be identical;³⁴ those of symmetrical ether and trifluoroacetate geometrical isomers were identical within experimental error. GLC results were reproducible within $\pm 1\%$ on duplicate runs.

Yields of olefinic products were determined by ¹H NMR spectroscopy through comparison with the known absolute yields of alcohol products. For many reactions product yields were determined both by GLC analysis and by ¹H NMR spectroscopy. Yields from ¹H NMR spectral analyses were calculated from averaged integrations of proton absorptions by comparison to an internal standard. Excellent agreement between ¹H NMR and GLC yields was observed; for example, compared to the results from GLC analyses, the relative percent of alcohol isomers from ¹H NMR analyses agreed within 2% for 2-methyl- and 4-tert-butylcyclohexanone reductions.

Control experiments and specific product analyses are included as supplementary material. $^{35}\,$

Reduction of 4-tert-Butylcyclohexanone by Di-tert-butylsilane. Silane Products. Di-tert-butylsilane (3.0 mmol) and 4tert-butylcyclohexanone (2.5 mmol) were added to 17.5 mmol of trifluoroacetic acid, and the reaction mixture was kept at roomtemperature for 91 hr. A product identified as di-tert-butylsilyl trifluoroacetate by ¹H NMR analysis of the reaction mixture (Si-H, s, δ 4.63) was observed in low yield (3.5% of reacted silane). Ditert-butylsilanediol was isolated in 91% yield from the reaction mixture after quenching with aqueous sodium bicarbonate and extraction with ether as a white, crystalline solid, mp 151.5-152.0° (lit.³⁶ mp 152°).

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Registry No.-Ia, 98-53-3; Ib, 589-92-4; Ic, 591-24-2; Id, 583-60-8; Ie, 873-94-9; IIa, 21862-63-5; IIc, 7443-55-2; IIe, 767-54-4; IIIa, 937-05-3; IIIb, 7731-28-4; IIId, 7443-70-1; IVa, 7600-15-9; IVb, 31003-54-0; IVc, 31003-46-0; IVd, 31003-41-5; IVe, 56889-89-5; Va, 7556-86-7; Vb, 31003-53-9; Vc, 31123-86-1; Vd, 31003-40-4; Ve, 56889-88-4; trans-IIa, 56889-93-1; cis-VIa, 56889-94-2; trifluoroacetic acid, 76-05-1; cis, cis-3,3,5-trimethylcyclohexyl ether, 56889-96-4; cis, trans-3,3,5-trimethylcyclohexyl ether, 56942-35-9; trans.trans-3,3,5-trimethylcyclohexyl ether 56942-36-0; 2-methylcyclohexyl ether, 56889-97-5.

Supplementary Material Available. Control experiments for reactions performed in aqueous sulfuric acid-ethyl ether and specific product analyses for reductions in trifluoroacetic acid will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche $(105 \times 148 \text{ mm}, 24 \times \text{reduction}, \text{nega-})$ tives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for \$4.00 for photocopy or \$2.50 for microfiche, referring to code number JOC-75-3821.

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- (9) Reaction times for complete reduction in trifluoroacetic acid were de-pendent on the relative amount of acid employed. Longer reaction times vere required when less acid was used. However, there was little effect on the relative yields of isomeric cyclohexanol derivatives by changing the acid concentration.
- (10) However, cyclohexene and 4-tert-butylcyclohexene do undergo addition of trifluoroacetic acid under the reaction conditions usually employed for organosilane reductions (5-7 equiv of CF₃COOH); after 22 hr at room temperature cyclobexene produced cyclohexyl trifluoroacetate in 80% yield and 4-*tert*-butylcyclohexene gave 3- and 4-*tert*-butylcyclohexyl tri-fluoroacetates in 89% yield. The unreacted cycloalkenes accounted for the remainder of the material in each case. The production of these trifluoroacetates indicates that similar addition reactions of trifluoroacetic acid with alkylcyclohexenes can occur.
- Although no cycloalkene products were observed from the reduction of (11)3,3,5-trimethylcyclohexanone by either di-*tert*-butylsilane or tri-sec-but-ylsilane, elimination products would be expected by analogy to the corresponding reductions of 3-methylcyclohexanone. Because of the longer reaction times required for reductions of le, addition of trifluoroacetic acid to 3,3,5-trimethylcyclohexene may have occurred undetected to give a mixture of cis- and trans-3,3,5-trimethylcyclohexyl trifluoroacetates, the expected addition products.
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none was reduced by triethylsilane in the presence of a 6 molar equiv excess of 4-*tert*-butylcyclohexanol (26% cis, 75% trans) under reaction conditions similar to those reported in Table VI. Analysis of the reaction products after complete reduction (Ila, 73%, Illa, 27%) showed that, within experimental error, no discrimination between Ila and Illa had occurred in the formation of *cis*-VIa and *trans*-VIa. The observed relative yields of ether products, 24% *trans*, trans-, 52% *cis*, *trans*-, and 24% *cis*, *cis*-4-*tert*-butylcyclohexyl ethers, could be predicted within experimental error from the data for triethylsilane (6.7 equiv CF₃COOH reaction) in Table VI.

(29) The reduction of 3,3,5-trimethylcyclohexanone by triethylsilane provides the only exception to these generalizations. The symmetrical ethers, 67% trans,trans-, 23% cis,trans-, and 10% cis,cis-3,3,5-trimethylcyclohexyl ethers, constituted 16% of the reduction products. Using the observed isomeric ratio, Ille/Ile = 6.2, the relative rates for hydride transfer were k_{tt}/k_{tc} = 3.5 and k_{ct}/k_{cc} = 0.40, significantly less than the ratio of Ille to Ile.

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Silane Reductions in Acidic Media. V. Reductions of Alkyl-Substituted Cyclohexanones by Di- and Tri-*tert*-butylsilanes. Steric Hindrance to Nucleophilic Attack at Silicon in the Trifluoroacetolysis of Silyl Alkyl Ethers^{1a,b}

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Results are reported for the reductions of alkyl-substituted cyclohexanones by di-tert-butylsilane, di-tertbutylmethylsilane, and tri-tert-butylsilane in trifluoroacetic acid. The reactivities of di- and tri-tert-butylsilanes reflect the steric bulk of the tert-butyl groups. However, the inductive effect of alkyl substituents is pronounced; tri-tert-butylsilane reacts faster than di-tert-butylsilane in reductions of cyclohexanones. The thermodynamically less stable isomers are formed predominantly in tert-butylsilane reductions of cyclic ketones with remote substituents. However, silyl alkyl ethers formed in these reductions undergo trans elimination of silanol in competition with nucleophilic displacement at silicon. The relative rate for elimination increases with the increased steric bulk of alkyl groups bonded to silicon.

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The reactivities of organosilicon compounds are strongly influenced by the steric bulk of *tert*-butyl substituents.²⁻⁴ The *tert*-butyl group shields silicon from nucleophilic reagents that normally attack silicon.^{4a} This steric effect should also be evident in the relative rates for reduction of ketones by *tert*-butylsilanes and in the stereoselectivities of these reductions. Indeed, in reductions of alkyl-substituted cyclohexanones di-*tert*-butylsilane is observed to be approximately 100 times less reactive than tri-*sec*-butylsilane.^{1a}

Silvl alkyl ethers have been observed previously in organosilane reductions of carbonyl compounds when limited amounts of Bronsted acids are employed, and are presumed intermediates in these reactions.⁵ Such compounds, which have proven to be highly useful in protecting the alcohol functional group in synthetic transformations,⁶ are quantitatively solvolyzed in acidic media to alcohols. Alkoxy-tert-butyldimethylsilanes,6c although significantly more stable toward solvolysis, also react quantitatively with nucleophilic reagents to form alcohols. Nucleophilic attack at silicon in silvl alkyl ethers occurs in preference to attack at carbon. However, when silicon is shielded by more than one bulky tert-butyl group the rate of nucleophilic substitution at silicon may be sufficiently low so as to allow alternate pathways to become dominant.

In this paper we wish to report that highly hindered diand tri-*tert*-butylsilanes do undergo selective hydride transfer reactions with alkyl-substituted cyclohexanones but that these reactions are complex owing to reactions caused by the shielding of silicon by *tert*-butyl groups. A novel elimination reaction of di- and tri-*tert*-butylsilyl alkyl ethers occurs in these reactions in competition with nucleophilic substitution at silicon. **Di-tert-butylmethylsilane.** The reactions of alkyl-substituted cyclohexanones with di-tert-butylmethylsilane are significantly and unexpectedly faster than those with ditert-butylsilane. Using 6.6 equiv of trifluoroacetic acid, reductions of 4-tert-butyl, 4-methyl-, 2-methyl-, and even 3,3,5-trimethylcyclohexanone are complete within 20 hr at room temperature. Di-tert-butylmethylsilane is 20 to 40 times more reactive than di-tert-butylsilane in these reactions.

Results

In Table I product yields from reductions of alkyl-substituted cyclohexanones by di-tert-butylmethylsilane are presented and compared to those from reductions by di-tertbutylsilane under the same reaction conditions. Only cycloalkene and cyclohexyl trifluoroacetate products are observed at 20 hr in reductions of alkylcyclohexanones by ditert-butylmethylsilane when 6.6 equiv of trifluoroacetic acid is used. Cycloalkene formation is significant when ditert-butylmethylsilane is employed under these reaction conditions and occurs to a greater extent than in reductions by di-tert-butylsilane. The relatively high yield of olefinic products in these reactions is surprising since under the same reaction conditions elimination processes are minimal (<1%) when less bulky silane reducing agents are used.^{1a}

To determine the source of elimination processes in ketone reductions, lower acid concentrations were employed in order to decrease the rate of reduction and of solvolysis of the presumed silyl ether intermediates. Prior determinations had shown that alcohol, alkyl ether, and trifluoroacetate reaction products could not be the source of the alkenes formed in reductions by *tert*-butylsilanes. 4-*tert*-Butylcyclohexanone was treated with di-*tert*-butylmeth-