absent, 565 $(M - Me)^+$, 507 $(M - Me_3Si)^+$.[7] Hydrolysis in an acetone–methanol–pyridine–water solution of ammonium chloride gave the acyl disilane silyl ether **17** in 54% yield (ir (CS_2), 6.13 (C=O) μ; NMR (C_6H_6) 4.37 (1 H, q, J = 7 Hz, MeC*H*), 2.27 (3 H, s, MeCO), 1.50 (3 H, d, J = 7 Hz, *Me*CH), 0.38 (9 H, s, $SiMe_3$), 0.37 (27 H, s, $SiMe_3$), 0.15 (9 H, s, $SiMe_3$); mass spectrum *m/e* 508 (M^+) absent, 493 $(M - Me)^+$, 435 $(M - Me_3Si^+)$), confirming the head to head coupling of the silicon ends of the silicon–carbon double bond.

The findings demonstrate that silicon–carbon double bonds can be generated under relatively mild conditions (photochemically $\lambda > 360$ nm, thermally $T \approx 70$ °C), milder than hitherto reported, and, with the substituents here employed, that new and different chemical behavior results. We are continuing this research in directions we hope will further stabilize the transient intermediate.

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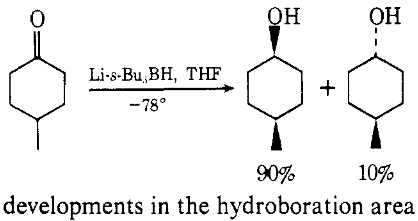
Lithium Trisiamylborohydride. A New Sterically Hindered Reagent for the Reduction of Cyclic Ketones with Exceptional Stereoselectivity

Sir:

Lithium trisiamylborohydride (LTSBH), a highly hindered trialkylborohydride, containing three β-methyl substituted secondary alkyl groups,[1] the first reagent of its kind to be reported, reduces rapidly and quantitatively unhindered cyclic and bicyclic ketones with exceptional steric control. Thus, 3-methyl- and 4-*tert*-butylcyclohexanones are quantitatively converted to *trans*-3-methylcyclohexanol and *cis*-4-*tert*-butylcyclohexanol, respectively, in greater than 99.5% isomeric purity. The stereoselectivity achieved with this new reagent is far superior to any of the reducing systems currently available. Further, the reagent exhibits certain unique characteristics quite different from all of the previously examined trialkylborohydrides attributed to the exceptionally large steric requirements resulting from the presence of the three bulky alkyl substituents on boron.

In 1972 we reported that lithium tri-*sec*-butylborohydride (L-Selectride) reduces cyclic and bicyclic ketones with remarkable stereoselectivity.[2,3] Since then numerous applications of this reagent in stereoselective organic synthesis (especially with prostaglandins) have appeared.[4] However, there is one disadvantage to this reagent. Although 2-methylcyclohexanone is reduced to *cis*-2-methylcyclohexanol in 99.3% purity, the reduction of 3- and 4-alkyl-cyclohexanones proceeds with only 90–95% stereoselectivity (eq 1). It becomes a tedious task to remove the minor component at this level. It would be desirable to have a reagent that would improve the stereoselectivity of such transformation to 99% or better.

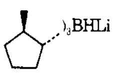


(1)

Recent developments in the hydroboration area have made available a number of hindered trialkylboranes.[5,6] Now these can be readily and cleanly converted to the corresponding trialkylborohydrides. Accordingly, we examined a number of borohydride anions derived from such prospective derivatives (*B*-cyclopentyl-9-BBN, *B*-3-pinanyl-9-BBN, *B*-thexyl-9-BBN, tricyclohexylborane, thexyllimonylborane, etc.). Each of these derivatives was tested toward 2-methylcyclohexanone and 4-*tert*-butylcyclohexanone for their stereoselectivity. Of these, the selectivity exhibited by two reagents—lithium trisiamylborohydride and lithium tris(*trans*-2-methylcyclopentyl)borohydride (LTMBH)—were especially promising, far superior to any of the reagents currently available. Both of them have three bulky β-methyl substituted secondary alkyl groups on boron. A detailed comparative study of these two reagents revealed that LTSBH exhibits significant superiority over LTMBH (Table I).

Lithium trisiamylborohydride is conveniently prepared in

Table I. Reduction of Representative Cyclic and Bicyclic Ketones with Lithium Tris(*trans*-2-methylcyclopentyl)borohydride and Lithium Trisiamylborohydride in Tetrahydrofuran[a]

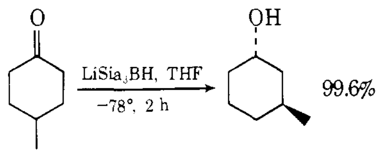
Ketone	Temp,[b] °C	Less stable isomer	Isomer, % Li-*s*-Bu_3BH		$LiSia_3BH$
2-Methylcyclopentanone	0	Cis	98.5		99.5
2-Methylcyclohexanone	0	Cis	99.3	>99.5	99.7
3-Methylcyclohexanone	−78	Trans	95.0	99.0	99.6
4-Methylcyclohexanone	−78	Cis	90.0	98.0	99.0
4-Ethylcyclohexanone	−78	Cis			99.0
4-Isopropylcyclohexanone	−78	Cis			99.0
4-*tert*-Butylcyclohexanone	−78	Cis	96.5	99.4	99.4[c]
Norcamphor	0	Endo	99.6	99.7	>99.5
Camphor	0	Exo	99.6	99.5[d]	[e]
	25		99.0		99.3[f]

[a] Reactions were carried out essentially with stoichiometric quantity of reagents; total yield of the alcohols were ⩾95% determined by GLC using a suitable internal standard. [b] Reactions at 0° were run for 1 h and those at −78° for 2 h except otherwise stated. [c] *cis*-4-*tert*-Butylcyclohexanol was isolated in 98% yield. [d] 24 h at 0°. [e] Essentially inert at 0° in 2 h. [f] 80% conversion in 72 h at 25°.

quantitative yield by the addition of 1 mole equiv of *tert*-butyllithium[7] in *n*-pentane (0°) to a tetrahydrofuran (THF) solution of trisiamylborane[8] at −78°; ^{11}B NMR (BF_3:Et_2O) exhibits two pairs of doublets at +13.28 (three parts), $J = 75$ Hz and +14.48 (one part), $J = 75$ Hz.[9] Analogously lithium tris(*trans*-2-methylcyclopentyl)borohydride is prepared in 100% yield.

Lithium trisiamylborohydride completely reduces the moderately hindered ketones, 2-methylcyclopentanone and 2-methylcyclohexanone, to the corresponding cis alcohols in ≥99.5% stereoselectivity.

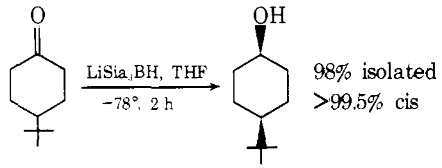
The relatively unhindered ketone, 3-methylcyclohexanone, is quantitatively reduced to *trans*-3-methylcyclohexanol in 99.6% isomeric purity (eq 2).



(2)

Under these conditions the corresponding reaction with L-Selectride proceeds with only 95% stereoselectivity.

Even more important is the reduction of 4-alkylcyclohexanones, the least hindered of the alkylcyclohexanones. Essentially all of the simple hydride reagents preferentially attack from the axial direction giving the *trans*-carbinol as the major product.[10] Application of L-Selectride increases the equatorial attack significantly (90–96%). We examined a representative series of 4-alkylcyclohexanones (alkyl = methyl, ethyl, isopropyl and *t*-butyl) with LTSBH. All of them underwent essentially quantitative conversion to *cis*-4-alkylcyclohexanols in 99% or better isomeric purity (eq 3 and 4). The unhindered bicyclic ketone, norcamphor, is reduced to the endo alcohol in 99.5% purity. Surprisingly, the highly hindered bicyclic ketone, camphor, is essentially inert to LTSBH at 0° (2 h); only 10% conversion is achieved in 24 h. However, it is possible to achieve complete conversion at higher temperature: 80% conversion, 99.3% exo, in 72 h at 25° (eq 5). The corresponding reduction with LTMBH at 0° is complete in 24 h. All of the trialkylborohydrides currently known reduce camphor completely in 1 h or less at 0°. Presumably, the exceptionally slow reaction of camphor with LTSBH is an indication of the very large steric requirements of this reagent. This is a new development in trialkylborohydride chemistry and should find use in the regioselective reduction of a particular carbonyl group in a polycarbonyl substrate.[11]



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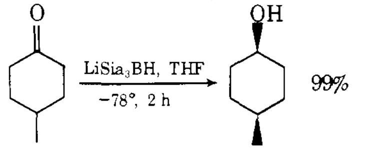

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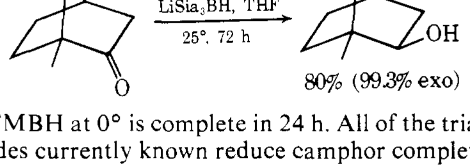

(5)

The following procedure for the reduction of 4-*tert*-butylcyclohexanone is representative. An oven-dried 250-ml flask, equipped with a sidearm fitted with a Teflon stopcock, a magnetic stirring bar, and a reflux condenser, connected to a mercury bubbler, was cooled to room temperature under a dry stream of nitrogen. Lithium trisiamylborohydride solution in THF (67 ml, 28 mmol) was introduced into the reaction flask and cooled to −78° (dry ice-acetone). Then 3.7 g (24 mmol) of 4-*tert*-butylcyclohexanone, dissolved in 25 ml of THF (maintained at 0°), was added. The resulting mixture was stirred vigorously for 2 h at −78° and then allowed to equilibrate to room temperature (1 h). The reaction mixture was hydrolyzed with 4 ml of water and 15 ml of ethanol added; the organoborane was oxidized with 10 ml of 6 M sodium hydroxide and 15 ml of 30% hydrogen peroxide. The aqueous phase was saturated with anhydrous potassium carbonate, the organic phase separated, and the aqueous phase extracted with two 20-ml portions of Et_2O-THF. The combined extracts were dried ($MgSO_4$). GLC analysis of the extract indicated the presence of *cis*-4-*tert*-butylcyclohexanol, >99.5% isomerically pure. The volatile solvents and the siamyl alcohol were removed under reduced pressure to give 3.65 g (98%) of essentially pure *cis*-4-*tert*-butylcyclohexanol as a snow-white solid, mp 80° (lit.[12] mp 82°).

In conclusion, it should be pointed out that the discovery of these new hydride reagents has provided a convenient procedure for the conversion of unhindered ketones to the corresponding thermodynamically less stable alcohols in 99% or better isomeric purity. The unusual selectivity exhibited by these reagents arising from their very high steric requirements has major potential for selective reductions, and we are actively exploring this feature.[13]

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Synthetic Methods for Sesquiterpene α-Methylene-γ-lactones

Sir:

The naturally occurring sesquiterpene α-methylene-γ-lactones such as vernolepin and aromaticin (**1**) need no introduction as targets for organic synthesis.[1] This class of biolog-