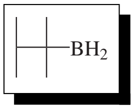
Thexylborane[1]



[3688-24-2] $C_6H_{15}B$ (MW 98.02)

InChI = 1/C6H15B/c1-5(2)6(3,4)7/h5H,7H2,1-4H3

InChIKey = DFZFZKDSPYJVRQ-UHFFFAOYAV

(readily available monoalkylborane useful for regioselective hydroboration of alkenes and dienes; thexylalkylboranes and thexyldialkylboranes are useful intermediates for the synthesis of unsymmetrical ketones, cyclic ketones, *trans* disubstituted alkenes, conjugated dienes, and diols[1])

Alternate Name: (1,1,2-trimethylpropyl)borane.

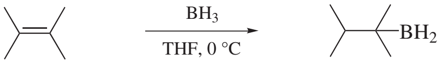
Physical Data: generally prepared in situ; dimeric in THF. It can be isolated as a liquid, mp −34.7 to −32.3 °C.[2]

Solubility: sol ether, hydrocarbon, and halocarbon solvents; THF is generally the solvent of choice; reacts rapidly with protic solvents.[1a]

Form Supplied in: not commercially available.

Analysis of Reagent Purity: analyzed by NMR and IR spectroscopy and by hydrogen evolution upon reaction with methanol.[1a,3]

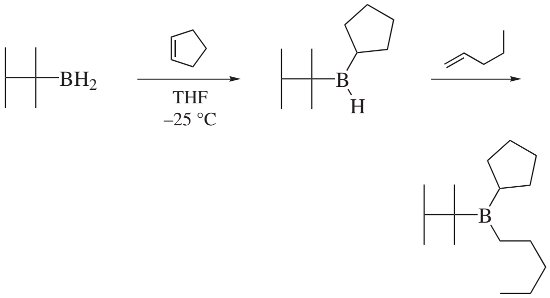
Preparative Method: most conveniently prepared from ***Borane–Tetrahydrofuran*** and 2,3-dimethyl-2-butene in THF (eq 1).[1a,2]



(1)

Handling, Storage, and Precautions: very reactive with oxygen and moisture; must be handled using standard techniques for handling air-sensitive materials.[3] The reagent is reported to be stable for at least a week when stored at 0 °C in THF solution under N_2.[1a] However, at rt the boron atom slowly migrates from the tertiary position to the primary (3% in 8 days).[4] Use in a fume hood.

Hydroboration of Alkenes. Reactions of alkenes with thexylborane have been extensively studied and several reviews have appeared.[1] Thexylborane ($ThxBH_2$) in THF reacts with 2 equiv of relatively unhindered alkenes to form thexyldialkylboranes. The regioselectivity in the hydroboration of alkenes with thexylborane is similar to that of borane in THF. For example, hydroboration of 2 equiv of 1-hexene with thexylborane followed by oxidation produces a 95:5 mixture of 1-hexanol and 2-hexanol. Hydroboration of a terminal monosubstituted alkene with thexylborane in a 1:1 ratio gives a mixture of both the thexylmonoalkylborane and thexyldialkylborane. (Preparation of thexylmonoalkylboranes from monosubstituted alkenes can be accomplished using ***Chloro(thexyl)borane–Dimethyl Sulfide***). With most disubstituted and some trisubstituted alkenes, it is possible to prepare the corresponding thexylmonoalkylborane by treating 1 equiv of the alkene with thexylborane at −20 to −25 °C.[5] Thexylmonoalkylboranes can hydroborate relatively unhindered alkenes to form thexyldialkylboranes containing two different alkyl groups (eq 2).[6]



(2)

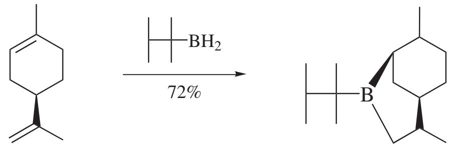
Hydroboration of a hindered alkene with either thexylborane or thexylmonoalkylborane is slow and is accompanied by dehydroboration of the thexylmonoalkylborane, producing a monoalkylborane and 2,3-dimethyl-2-butene. Lower reaction temperatures and the presence of excess 2,3-dimethyl-2-butene in the reaction may reduce the amount of dehydroboration.[6] Sterically hindered alkenes can be hydroborated under high pressure (6000 atm) to produce highly hindered trialkylboranes, such as trithexylborane,[7] but this procedure does not appear to be practical for synthetic purposes.

Mixed thexyldialkylboranes have also been prepared by treating thexylborane consecutively with different halomagnesium or lithium dialkylcuprates.[8] This procedure offers the advantage of being able to introduce methyl or aryl groups onto the boron atom.

The hydroboration of either terminal or internal alkynes with thexylborane in a 2:1 ratio gives good yields of the expected thexyldialkenylboranes, but the reaction of thexylborane with 1 equiv of a terminal alkyne is reported to give at most 20% of the thexylalkenylborane.[1a,4]

Complete dehydroboration of the thexyl group in thexylmonoalkylboranes can be achieved by treating thexylmonoalkylboranes with a fourfold excess of ***Triethylamine***.[5] This reaction provides a general method for the synthesis of monoalkylboranes as the triethylamine complexes. More recently, it has been found that thexylborane–triethylamine or thexylborane–***N,N,N′,N′-Tetramethylethylenediamine*** adducts can be used to hydroborate hindered alkenes directly (with concomitant loss of the thexyl group as 2,3-dimethyl-2-butene) to give the monoalkylborane–amine adducts.[9] ***Monoisopinocampheylborane***, a useful chiral hydroborating reagent, can be prepared by this reaction.[10]

Thexylborane is the reagent of choice for the hydroboration of dienes to form *B*-thexylboracyclanes (eq 3)[11] since the reaction of borane with dienes tends to give polymeric products.[12] Stereoselective cyclic hydroboration of dienes by thexylborane has been employed to prepare acyclic diols with 1,3-, 1,4-, and 1,5-asymmetric induction (eq 4).[13] In the cyclic hydroboration of appropriately substituted 1,5-dienes to yield 1,5-diols, 1,2-asymmetric induction was employed as a key step (eq 5) in the synthesis of the Prelog–Djerassi lactone.[14]



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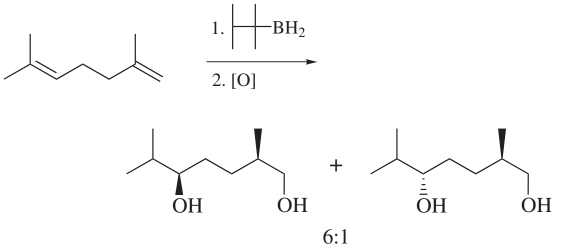

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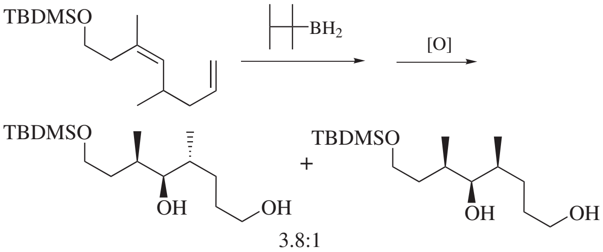
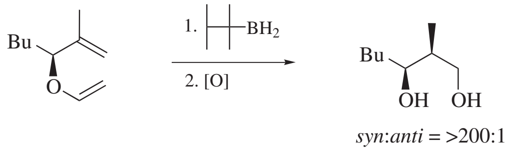


(5)

Cyclic hydroboration of allyl vinyl ethers provides a highly stereoselective synthesis of 1,3-diols with *syn* stereochemistry (eq 6).[15] The *syn* stereoselectivity observed in the cyclic hydroboration of allyl vinyl ethers is opposite to the stereoselectivity observed in the acyclic hydroboration of allylic alcohols (see eq 9).[18] Remote stereocontrol in the hydroboration–reduction of enones with thexylborane has also been reported (eq 7).[16] This reaction is proposed to occur by a rapid hydroboration of the carbon–carbon double bond followed by an intramolecular reduction of the carbonyl group by the intermediate dialkylborane.



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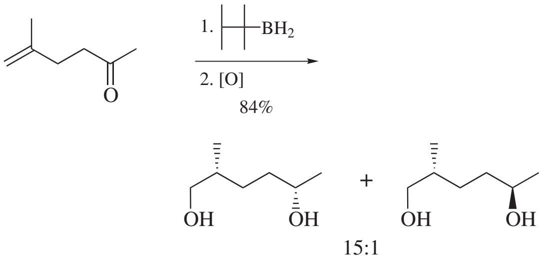
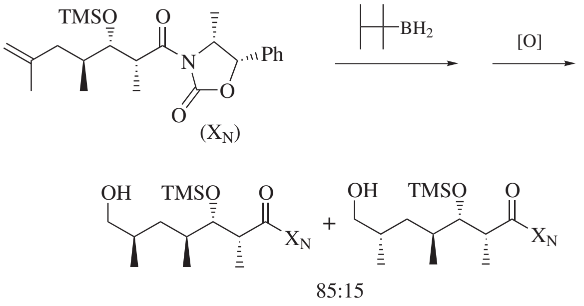


(7)

Acyclic diastereoselection in the hydroboration of alkenes has been reported by several groups. Evans and co-workers[17] observed high levels of 1,3-asymmetric induction in the hydroboration of a number of terminal alkenes bearing substituents at the 2-position of the alkene and a proximal chiral center, as illustrated in eq 8. These workers concluded that the diastereoselection is directed primarily by the nearest chiral center in each of the substrates, and they proposed a transition state model to account for the observed diastereoselectivity. The hydroboration of acyclic secondary allylic alcohols with thexylborane, yielding 1,3-diols with high *anti* (or *threo*) diastereoselection, has also been reported (eq 9).[18] The diastereoselection observed in this reaction does not require the use of a protecting group on the allylic alcohol. Thexylborane proves to be the hydroboration reagent of choice for reaction with trisubstituted alkenes, but terminal alkenes give higher diastereoselection with the more sterically demanding reagents ***9-Borabicyclo[3.3.1]nonane*** or ***Dicyclohexylborane***.



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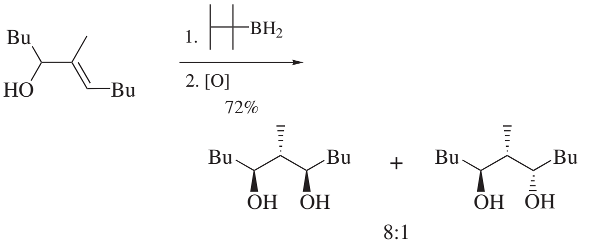
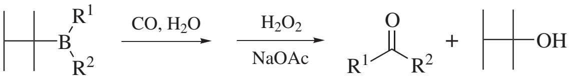


(9)

Selective Functional Group Reductions. The selective reduction of functional groups by thexylborane has been reported,[19a] and the relative reactivity of thexylborane with common functional groups has been compared to that of other borane reagents (***Diborane***, ***Disiamylborane***, and thexylchloroborane–dimethyl sulfide).[19] Acidic hydrogens in –OH, –CO_2H, and –SO_3H groups react at moderate to rapid rates with thexylborane with the evolution of hydrogen. Aldehydes generally react rapidly with thexylborane yielding alcohols after hydrolysis. However, ketones and most other carbonyl groups react only slowly with thexylborane. Carboxylic acids can be reduced to aldehydes by 2.5 equiv of thexylborane, but ***Chloro(thexyl)borane–Dimethyl Sulfide*** is the borane reagent of choice for this transformation. Nitriles, oximes, epoxides, and aromatic nitro compounds are reduced only slowly, and alkyl nitro compounds, disulfides, sulfones, and tosylates do not react with thexylborane.

Use of Thexyldialkylboranes in Synthesis. Thexyldialkylboranes are particularly useful in synthetic reaction sequences due to the availability of a variety of these compounds and the low migratory aptitude of the tertiary thexyl group in most rearrangement reactions. Several reviews of the role of boron in synthesis have appeared.[1,2,20]

Synthesis of Ketones. Reaction of thexyldialkylboranes with ***Carbon Monoxide*** in the presence of water followed by oxidation provides a novel route to the synthesis of ketones (eq 10).[21] Yields in this reaction are generally in the 50–80% range. The observed migratory aptitude for the alkyl groups is: primary > secondary > tertiary. Cyclic ketones can be prepared from dienes by cyclic hydroboration with thexylborane followed by carbonylation and oxidation (eq 11).[22] This annulation procedure stereoselectively provides the *trans*-ring fusion in both the indanone and decalone systems. This methodology has been successfully employed in the stereospecific annulation of 1,5-diene substrates to form the *trans*-hydroazulene nucleus.[23]



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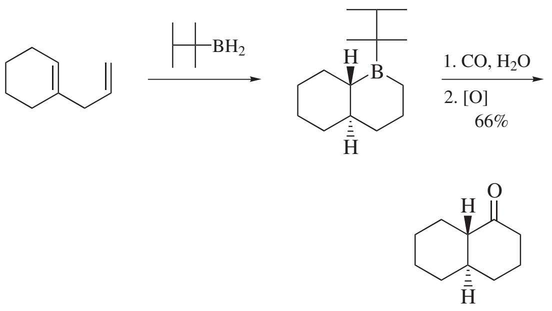
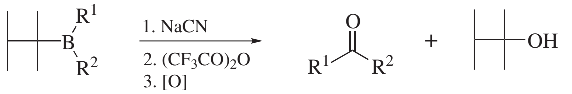


(11)

An alternate procedure to convert thexyldialkylboranes into ketones via an intermediate cyanoborate has been reported (eq 12)[24] which avoids the use of carbon monoxide under high pressure. Yields are quite good, generally >75%, and no special equipment is required for the reaction. This procedure has been employed in the synthesis of the heterocyclic ring system of δ-coniceine (**1**) (eq 13).[25]



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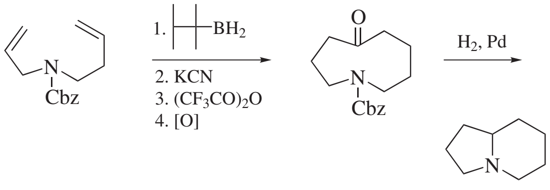
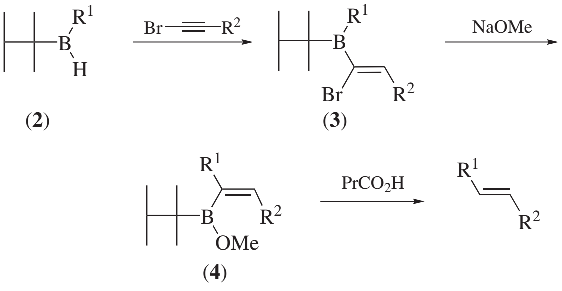


(13)

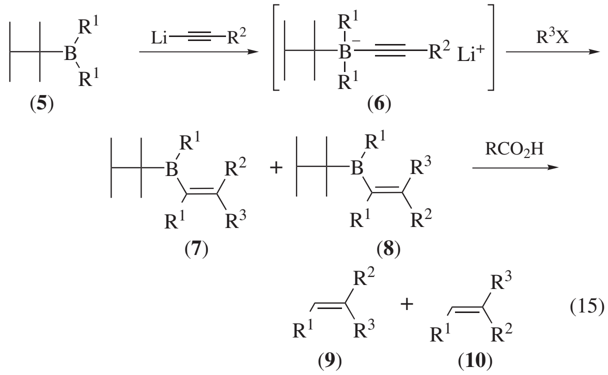
(**1**)

Synthesis of Alkenes. The stereoselective synthesis of (*E*)-disubstituted alkenes[26] can be carried out by treating a thexylmonoalkylborane (**2**) with a 1-bromo-1-alkyne to yield the intermediate thexylalkyl(1-bromo-1-alkenyl)borane (**3**), which is then treated with ***Sodium Methoxide*** to induce a stereospecific rearrangement of the alkyl group (R^1) from boron to carbon. Stereospecific protonolysis of the resulting intermediate (**4**) provides the (*E*)-alkene in high isomeric purity and good to excellent yield (eq 14).



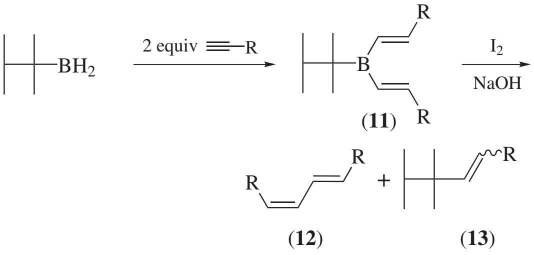
(14)

Trisubstituted alkenes can be synthesized[27] by first treating a thexyldialkylborane (**5**) with an alkynyllithium to yield a thexyldialkylalkynylborate (**6**), which is then alkylated with migration of an alkyl group from boron to carbon to give the thexylalkylvinylboranes (**7** and **8**) (eq 15). After acid hydrolysis, the trisubstituted alkenes (**9** and **10**) are obtained in >70% yield in a ratio of about 9:1. The major product (**9**) in all cases is the isomer in which the migrating group (R^1) and the group introduced by alkylation (R^3) are *cis* to each other. Various alkylating agents are effective in this reaction including primary alkyl iodides, benzyl and allyl bromides, ***Dimethyl Sulfate***, and ***Triethyloxonium Tetrafluoroborate***.

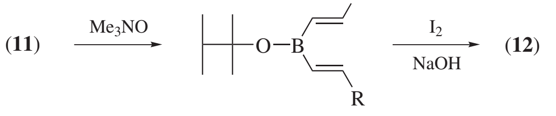


(15)

Synthesis of Dienes. Thexylborane reacts with 2 equiv of 1-alkyne to give the corresponding thexyldialkenylborane (**11**) in good yield (eq 16).[4] However, when (**11**) is treated with ***Sodium Hydroxide*** and ***Iodine*** to induce rearrangement, an almost equal mixture of the desired (*E,Z*)-diene (**12**) and alkene (**13**) results where either the alkenyl group or the thexyl group migrates with approximately equal facility.[28] This problem can be surmounted by selectively oxidizing the thexyl group in the thexyldialkenylborane (**11**) with ***Trimethylamine N-Oxide*** before the reaction with iodine and sodium methoxide.[28] This procedure appears to be useful only for the synthesis of symmetrical (*E,Z*)-dienes (**12**) due to the difficulty in preparing unsymmetrical thexyldialkenylboranes in a stepwise hydroboration sequence from two different 1-alkynes.

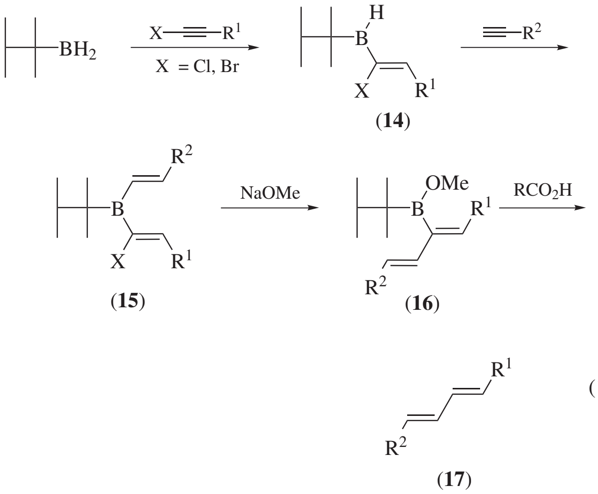


(16)



(17)

However, thexylborane will react with 1-chloro-1-alkynes and 1-bromo-1-alkynes (but not with 1-iodo-1-alkynes) to give thexyl(1-haloalkenyl)boranes (**14**) in high yield (eq 18).[29] This observation enabled the development of a general and highly stereospecific synthesis of conjugated (*E,E*)-dienes. The borane (**14**) reacts stereoselectively with a 1-alkyne to give the thexyldialkenylborane (**15**), which is then treated with sodium methoxide to produce (**16**) Compound (**16**) is protonolyzed with refluxing isobutyric acid to give the (*E,E*)-diene (**17**) in 53–63% yield and >98% isomeric purity.[29] The intermediate (**16**) is also transformed into the (*E*)-enone (**18**) in 50% yield by oxidation with ***Hydrogen Peroxide*** and NaOAc (eq 19).[29]



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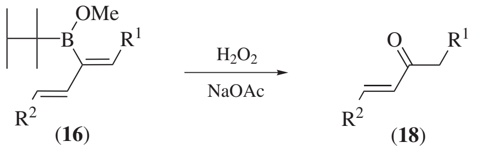
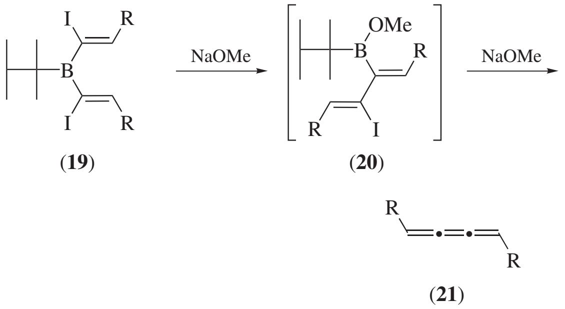


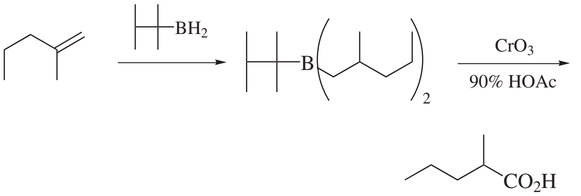
(19)

A stereoselective synthesis of 1,2,3-butatrienes was also developed based on the reaction of thexylborane with 1-halo-1-alkynes. In this synthesis, 2 equiv of a 1-iodo-1-alkyne react with thexylborane to give the thexyldialkenylborane (**19**) that rearranges to the 1,2,3-butatriene (**21**) upon treatment with 2 equiv of sodium methoxide (eq 20).[29b,30] Although the yields of (**21**) are only moderate (47%, R = butyl; 29%, R = cyclohexyl), the products are of high isomeric purity.



(20)

Synthesis of Carboxylic Acids. A convenient procedure for the direct oxidation of organoboranes from terminal alkenes to carboxylic acids has been reported.[31] The oxidation gives high yields with a number of different organoboranes derived from a variety of borane reagents including thexylborane. Several different oxidizing agents (***Pyridinium Dichromate***, ***Sodium Dichromate*** in aqueous H_2SO_4, and ***Chromium(VI) Oxide*** in 90% aqueous acetic acid) are effective for the reaction. For example, 2-methyl-1-pentene is converted to 2-methylpentanoic acid in 86% yield (eq 21).



(21)

Related Reagents. 9-Borabicyclo[3.3.1]nonane Borane–Tetrahydrofuran; Chloro(thexyl)borane–Dimethyl Sulfide; Dicyclohexylborane; Disiamylborane.

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