Borane-Tetrahydrofuran Complex (BTHF)

1M in tetrahydrofuran

OTHER NAMES

Tetrahydrofuran borane

CAS REG. NUMBER

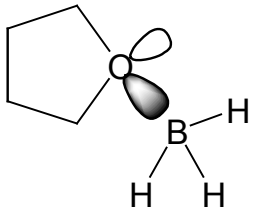
[14044-65-6]

EINECS

237-881-8 for BTHF
203-726-8 for THF

FORMULA

$(CH_2)_4OBH_3$



FORMULA WEIGHT

85.94 g/mol

RELATED REAGENTS

Dimethylsulfide borane
N,N-Diethylaniline borane

TYPICAL PROPERTIES

PHYSICAL DATA

Density at 25 °C:	0.876 g/mL
Flash point (closed cup):	-5.7 °F (-22 °C)
Boiling point:	66 °C for THF, see Stability sec.

STABILITY

BTHF is thermally unstable and must be kept cold. BTHF stabilized with <0.005 M $NaBH_4$ per mole of "BH_3". BTHF is susceptible to hydrolysis, readily reacting with water to form hydrogen and boric acid. It reacts readily with atmospheric moisture upon exposure to air resulting in a decrease in purity.

In the absence of a substrate, BTHF decomposes by cleavage of the ether ring and above 50 °C can evolve diborane.

APPEARANCE

Colorless liquid

STORAGE CONDITIONS

To maximize shelf-life, BTHF solutions should be stored below 5 °C.

PACKAGING

Packaged in cylinders

- 800 ml, containing 0.7 Kg 1M BTHF solution
- 18 liter, containing 16 Kgs 1M BTHF solution
- 90 liter, containing 79 Kgs 1M BTHF solution
- 400 liter, containing 351 Kgs 1M BTHF solution

SHIPPING INFORMATION

UN-3148, PG I

PRODUCT FEATURES

- Reduces selected functional groups
- Hydroborating agent
- Borane source for oxazaborolidine catalyzed asymmetric reductions
- High purity
- Consistent quality
- Non-corrosive to metals
- Custom packaging available

PRODUCT BENEFITS

- Excellent reagent for the reduction of amides to amines
- Preferred reagent for reduction of carboxylic acids to alcohols

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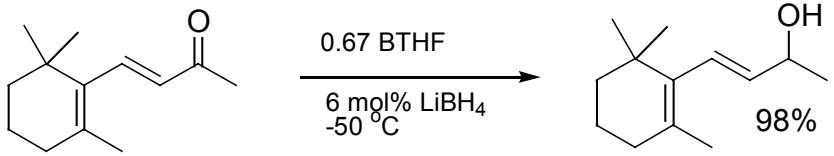
Borane-Tetrahydrofuran Complex (BTHF)

APPLICATIONS

Borane-tetrahydrofuran complex (BTHF) is a valuable reagent for the reduction of functional groups and for hydroboration reactions with carbon-carbon double and triple bonds. Functional groups that are readily reduced by BTHF include aldehyde, ketone, carboxylic acid, amide, oxime, imine, and nitrile. The carboxylic acid group is reduced at a faster rate than most groups including non-conjugated alkene.[1] Conjugated α,β-unsaturated carboxylic acids give saturated alcohols as the major products.

Ketones and the carbonyl of enones are effectively reduced with borane-tetrahydrofuran. The addition of borohydride to the reaction solution is advantageous for accelerated reduction[2] as well as higher selectivity towards carbonyl reduction in conjugated and non-conjugated enones.[3]



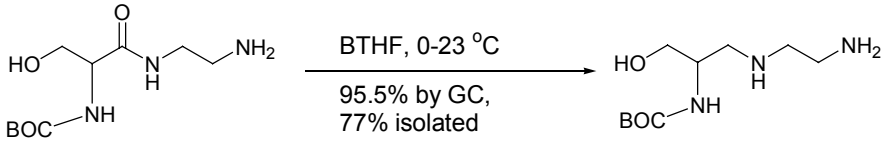
Asymmetric ketone reduction using chiral oxazaborolidine catalysts was recently reviewed.[4] Work at Callery with BTHF improved on reaction conditions to provide consistent results in the reduction.[5]

(*R*)-MeCBS reduction of acetophenone with $NaBH_4$ stabilized 1M BTHF under optimized conditions

entry	conditions	% ee[c]
1	Acetophenone and BTHF same rate[a]	95.2
2	Acetophenone 2X faster than BTHF	96.3
3	BTHF 2X faster than acetophenone	95.6
4	BF_3 Additive[b]	92.8

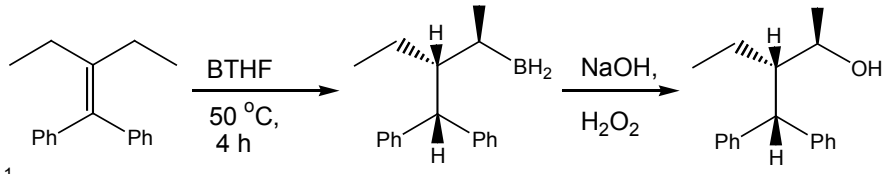
[a] Acetophenone and stabilized BTHF (~0.005M $NaBH_4$) added simultaneously to (*R*)-MeCBS. [b] Stabilized BTHF solution was added to a mixture of ketone, BF_3 and (*R*)-MeCBS. [c] Enantiomeric excess was measured with chiral column J & W 30m x 0.25 mm CDX-B.

EPIX Medical[6] has used BTHF for the reduction of an amide in the synthesis of an injectable vascular contrast agent. They optimized conditions to minimize reduction of the BOC protecting group.



Several neutral work-up methods[7] are available in addition to acidic quenching of the amine borane intermediate produced.

Alkylboranes obtained via hydroboration are thermally sensitive and are prone to undergo dehydroboration-rehydroboration until the boron group is at the terminal position.[8] This migration has been used as an approach for regio- and stereoselective control of up to three chiral centers using a new stereoselective migration of organoboranes.[9]



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[5] Matos, K.; Corella, J. A.; Burkhardt, E.R.; Nettles, S.M. U.S. 6,218,585.
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[7] Houpis, I.N.; *et al. Tetrahedron Letters* **1993,** *34,* 2593. Couturier, M.; *et al. Org. Lett.* **2001,** *3,* 465. Couturier, M.; *et al. Org. Proc. R&D* **2002**, *6,* 42-46.
[8] Laaziri, H.; Bromm, L.O.; Lhermitte, F.; Gschwind, R.M.; Knochel, P. *J. Am. Chem. Soc.* **1999**, *121,* 6940.
[9] Knochel, P. *et al. J. Am. Chem. Soc.* **2000**, *122,* 10218.