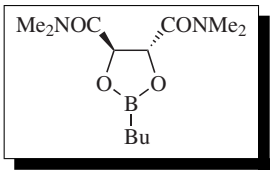
(*R,R*)-2-Butyl-4,5-bis(dimethylaminocarbonyl)-1,3-dioxaborolane[1]



[161344-85-0] $C_{12}H_{23}BN_2O_4$ (MW 270.13)

InChI = 1/C12H23BN2O4/c1-6-7-8-13-18-9(11(16)14(2)3)10
(19-13)12(17)15(4)5/h9-10H,6-8H2,1-5H3/t9-,10-/m1/s1
InChIKey = AFQWQRBBIZKYTE-NXEZZACHBH

(enantioselective cyclopropanation[1])

Solubility: soluble in CH_2Cl_2, $ClCH_2CH_2Cl$, toluene, benzene and most organic solvents.

Form Supplied in: colorless oil, not commercially available.

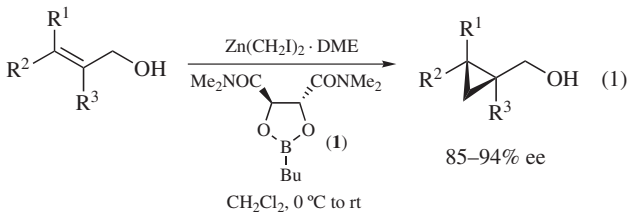
Analysis of Reagent Purity: NMR (^1H, ^{11}B).

Preparative Methods: the reagent is easily prepared from commercially available butylboronic acid (or its more stable diethanolamine complex) and (*R,R*)-(+)-*N,N,N′,N′*-tetramethyltartaric acid diamide.[2] The other enantiomer is also readily available from (*S,S*)-(+)-*N,N,N′,N′*-tetramethyltartaric acid diamide.

Purity: not easily purified since the reagent hydrolyzes slowly in the presence of moisture and oxidizes slowly in the presence of oxygen. The formation of crystals over time is an indication of decomposition.

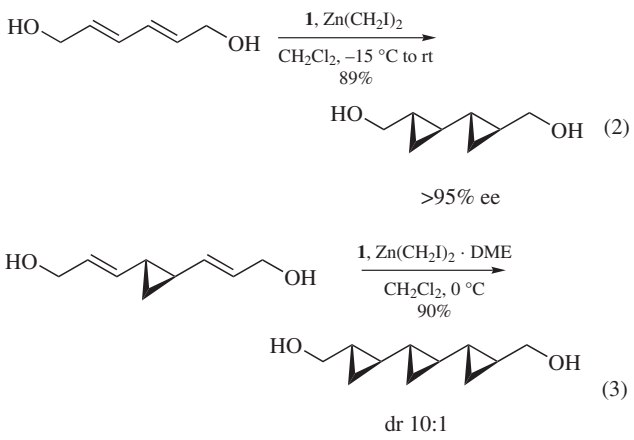
Handling, Storage, and Precaution: the reagent is stable indefinitely when stored under an inert atmosphere.

Enantioselective Cyclopropanation of Allylic Alcohols. (*R,R*)-2-Butyl-4,5-bis(dimethylaminocarbonyl)-1,3-dioxaborolane (**1**) is one of the most effective chiral additives for the enantioselective cyclopropanation of allylic alcohols.[3] The synthesis of a wide range of substituted cyclopropylmethanols proceeds with excellent enantiocontrol (85–93% ee) when a solution of the alcohol and the dioxaborolane ligand is added to bis(iodomethyl)zinc. The use of the DME complex of bis(iodomethyl)zinc is preferable on large scale (eq 1).[4]



(1)

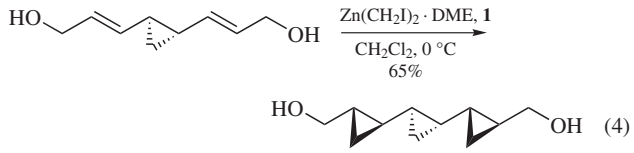
The reaction can also be used in bidirectional chain synthesis to generate bis(cyclopropyl) derivatives simultaneously (eq 2 and 3).[5] This reaction was used as the key step for elaboration of the polycyclopropane natural products FR-900848 and U-106305.



(2)

(3)

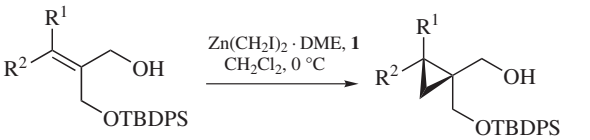
Extremely high diastereoselectivities are also observed when the antipode of the starting material is used, providing efficient access to the other diastereomer (eq 4).



(4)

The reaction has also been extended to the enantioselective cyclopropanation of 3-tributylstannylprop-2-en-1-ol,[5a] to 3-iodo-[3a] and 3-chloroprop-2-en-1-ol.[6] The first two are useful precursors in palladium-catalyzed cross-coupling reactions[7] while the last was used in the total synthesis of callipeltoside A.

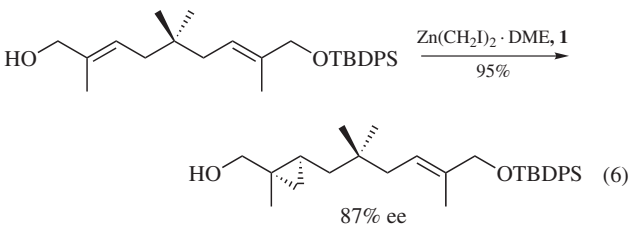
The enantioselective cyclopropanation reaction is quite general and practical. For example, the cyclopropanation reaction has been used to synthesize 3-methylcyclopropylmethanol, a precursor to curacin A.[8] Tri- and tetrasubstituted allylic alcohols are also converted into their corresponding cyclopropanes with high enantiocontrol (eq 5).



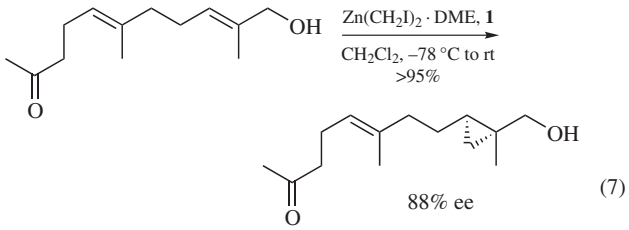
R^1 = H, R^2 = Et >98% (89% ee)
R^1 = Me, R^2 = Me 85% (88% ee)

(5)

Polyenes can also be cyclopropanated at the allylic alcohol position with high chemo- and enantioselectivities due to the strong directing ability of the chiral ligand. This reaction has been used to generate key precursors of bicyclohumulenone (eq 6)[9] and noranthoplone (eq 7).[3a]

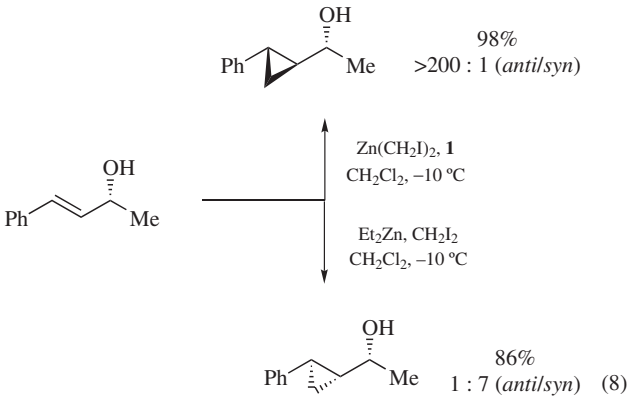


(6)



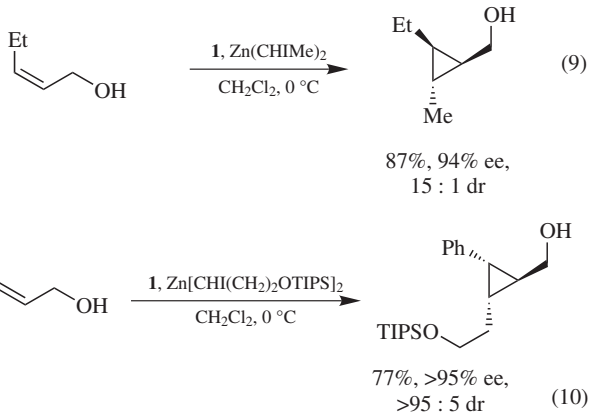
(7)

Unprecedented high *anti*-selectivities are obtained when *E*-substituted chiral allylic alcohols are treated with bis(iodomethyl)zinc and the dioxaborolane ligand (eq 8).[10] In contrast, the *syn*-isomer is obtained if the substrate is treated with the zinc reagent in the absence of the chiral ligand.[11] The method complements that involving the direct reduction of cyclopropylketones with $LiAlH_4$ or DIBAL-H.[12]



(8)

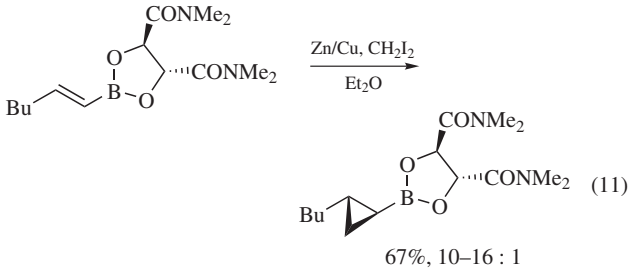
Enantioselective Synthesis of 1,2,3-Trisubstituted Cyclopropanes. The chiral dioxaborolane ligand can also be used to generate 1,2,3-substituted cyclopropyl units when the appropriate 1,1-diiodoalkane is used in the preparation of the zinc reagent (eq 9).[13] The reaction affords 1,2,3-trisubstituted cyclopropanes with excellent enantio- and diastereocontrol, including those obtained from functionalized zinc reagents (eq 10).



(9)

(10)

Use as a Chiral Auxiliary: Synthesis of Cyclopropylboronic Acids. The chiral dioxaborolane unit can also be used as an effective chiral auxiliary in the synthesis of enantiomerically enriched cyclopropylboronic acids. For example, 1-alkenylboronic esters bearing the tetramethyltartramide group undergo diastereoselective cyclopropanations to afford the cyclopropylboronic acid (eq 11).[14] These products can be used for *in situ* Suzuki coupling reactions[15] or can be oxidized to produce 2-substituted cyclopropanols.



(11)

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