

SYNLETT Spotlight 194

CBS Oxazaborolidines – Versatile Catalysts for Asymmetric Synthesis

Compiled by René T. Stemmler



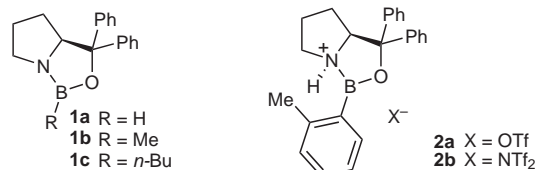
This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

René T. Stemmler was born in Frankfurt/Main, Germany, in 1976. He studied chemistry at the University of Freiburg, Germany and the University of North Carolina at Chapel Hill, NC, USA. Currently, he is pursuing his PhD under the supervision of Professor Carsten Bolm at the RWTH Aachen University, Germany. His research is focused on the design and synthesis of novel, chiral organometallic catalysts and the development of new reactions for asymmetric catalysis.

Institut für Organische Chemie der RWTH Aachen, Landoltweg 1,
52074 Aachen, Germany
E-mail: rene.stemmler@oc.rwth-aachen.de

Introduction

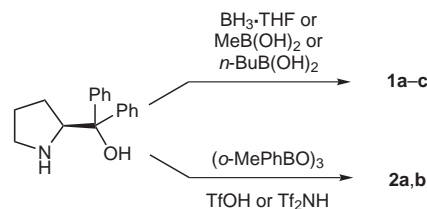
CBS Oxazaborolidines **1a–c** are well-established catalysts, which mediate the enantio- and diastereoselective reduction of highly functionalized ketones.^{1,2} Recently, the substrate scope has been extended to include oxime ethers³ and ketimines.⁴ Accordingly, these reagents have been extensively applied in natural product synthesis, for instance in the recently published total syntheses of (–)-laulimalide,⁵ brevetoxin-B,⁶ (+)-tanikolide,⁷ and bistramide A.⁸ Additionally, oxazaborolidines **1** were used in the kinetic resolution⁹ and the dynamic kinetic resolution of atropisomeric lactones.^{9b,10}



More recently, the protonated oxazaborolidinium salts **2a** and **2b** were used as chiral Lewis acids¹¹ in catalytic enantioselective Diels–Alder reactions,¹² the cyanosilylation

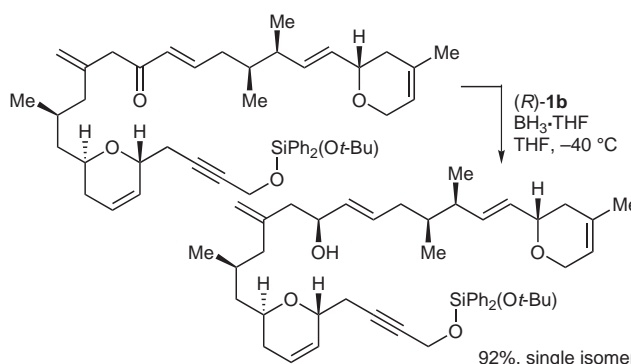
of aldehydes,¹³ Michael additions,¹⁴ and a vinylogous Mukaiyama aldol reaction.¹⁵

Compound **1a** is typically generated in situ by reaction of (*S*)- or (*R*)-2,2-diphenylhydroxymethylpyrrolidine with BH₃·THF,² while oxazaborolidines **1b,c** may be prepared using the corresponding boronic acids.^{1c,16} In a similar fashion, reaction of the same chiral pyrrolidine substrate with *o*-tolylboroxine furnishes *o*-tolyl-CBS-oxazaborolidine,¹⁶ which, when protonated with triflic acid or triflimide, affords the oxazaborolidinium salts **2a** and **2b**, respectively.^{12b,d} The facile preparation and modification of the oxazaborolidines, along with their high reactivity and selectivity, render members of this class of molecules as important candidates for future applications in asymmetric catalysis.

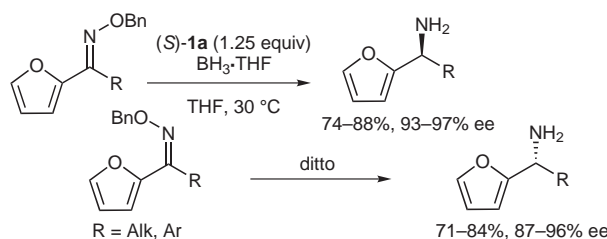


Abstracts

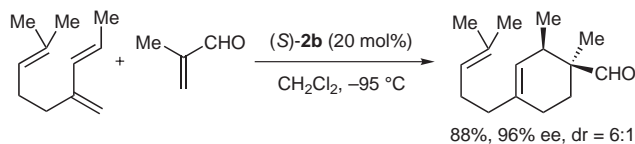
(A) One representative example of the value of the CBS reagents of type **1** in natural product synthesis was recently demonstrated in the total synthesis of (–)-laulimalide A by Uenishi, in which a highly functionalized and complex 1,2-enone was diastereoselectively reduced to the corresponding allylic alcohol in high yield. A single isomer was obtained.⁵



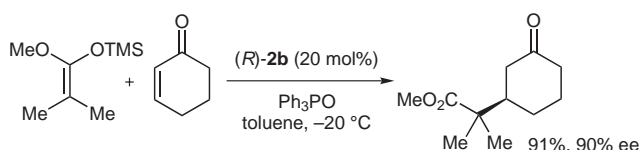
(B) Demir et al. described the stereospecific reduction of benzyl oxime ethers to the corresponding free amines. In the presence of oxazaborolidine (*S*)-**1a** the *E*-isomer was reduced to the *S*-enantiomer, whereas reduction of the *Z*-isomer with the same reagent leads to the *R*-isomer with high enantioselectivity. Ozonolysis of the furan ring of each isomer allowed enantioselective access to the corresponding amino acids in high yields.^{3a}



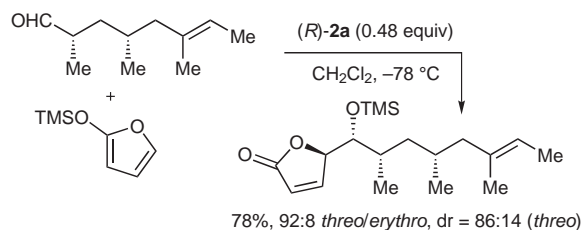
(C) The total syntheses of the odorants georgyone, arborone, and structural congeners were reported by Corey and co-workers. The key steps in each synthesis involved an intermolecular Diels–Alder reaction catalyzed by the oxazaborolidinium salt (*S*)-**2b**. For instance, the intermediate in the synthesis of (–)-georgyone, which is shown here, was prepared with 96% ee and a diastereomeric ratio of 6:1.^{12a}



(D) A catalytic, enantioselective Michael addition using 20 mol% of catalyst (*R*)-**2b** was recently accomplished by Corey, in which, for instance, the reaction of a silyl ketene acetal with cyclohexenone furnished the 1,4-addition product in 91% yield with 90% ee.¹⁴



(E) Very recently, Boeckman et al. reported the first application of chiral oxazaborolidinium salts in an asymmetric vinylogous Mukaiyama aldol reaction. The assembly of a butenolide was accomplished with good diastereoselectivity by the addition of trimethylsilyloxyfuran to an aldehyde in the presence of catalyst (*R*)-**2a**. Additional methyl substituents on the diphenyl moiety of the oxazaborolidinium salt improved the diastereoselectivity to 95:5 (*threo/erythro*), with a diastereomeric ratio (*threo*) of >95:5.¹⁵



References and Notes

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- (2) CBS represents the initials of the researchers who discovered the reagents **1a–c**, namely Corey, Bakshi, and Shibata: (a) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551. (b) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C.-P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925.
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- (16) Compounds (*S*)-**1b**, (*R*)-**1b**, and (*S*)-*o*-tolyl-CBS-oxazaborolidine are commercially available.