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X-RAY CRYSTAL STRUCTURE OF A CHIRAL OXAZABOROLIDINE CATALYST FOR ENANTIOSELECTIVE CARBONYL REDUCTION

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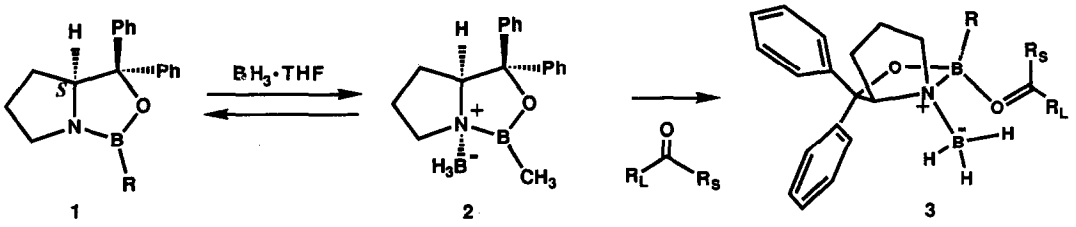
Summary: *The three dimensional structure of the chiral complex* **2**, *which is an effective reagent for the enantioselective reduction of ketones, has been determined by X-ray crystallography to be as shown in Figure 1.*

Chiral oxazaborolidines **1**, with R = H, CH_3 or alkyl, (or enantiomers) catalyze the reduction of ketones by borane or catecholborane as stoichiometric reductant to produce secondary alcohols with high enantiofacial selectivity.[1] This process is extremely useful in synthesis because only 5-10 mole % of **1** generally suffices to ensure >20/1 enantioselectivity and because the catalyst precursor (*S*)- or (*R*)-2-[diphenylhydroxymethyl]-pyrrolidine can be recovered efficiently for reuse. The reductions using borane and **1**, R = CH_3 for example, proceed by way of complexation of BH_3 and **1**, R = CH_3, to give adduct **2** which has been characterized previously by ^1H, ^{13}C and ^{11}B NMR spectroscopy.[1] Reaction of **2** with the ketonic substrate is considered to occur by way of transition state assembly **3**, a model which correctly predicts the absolute configuration of the product for a very large number of examples.[1] This [illegible] catalyzed reduction of [illegible]

epoxides,[1c] PAF antagonists,[2] ginkgolide B,[3] bilobalide,[4] forskolin,[5] fluoxetine,[6] 1-deuterated primary alcohols,[7] isoproteranol,[8] α-hydroxy acids,[1e] denopamine,[9] 2-hydroxymethylpyrrolidines (precursors for their own catalytic enantioselective synthesis),[10] and α-amino acids.[11] The structure of the reactive complex **2** has now been verified by a single-crystal X-ray diffraction study which revealed interesting three-dimensional detail and which is described herein.

Reaction of (*S*)-2-[diphenylhydroxymethyl]-pyrrolidine with methylboronic acid was carried out as previously described[1b,1c] to give **1**, R = CH_3, which was converted to the borane adduct **2**[12] by treatment in toluene with gaseous B_2H_6[13] and filtration of the resulting crystalline precipitate. Slow recrystallization of these colorless crystals from a CH_2Cl_2–hexane bilayer at -20 °C gave clear, colorless cubes of **2**.[14] One such crystal (0.36 x 0.32 x 0.4 mm), orthorhombic, space group $P2_12_12_1$, 4 molecules per unit cell, was subjected to X-ray diffraction analysis and yielded the structure shown in Figure 1,[15] which is in complete agreement with previous



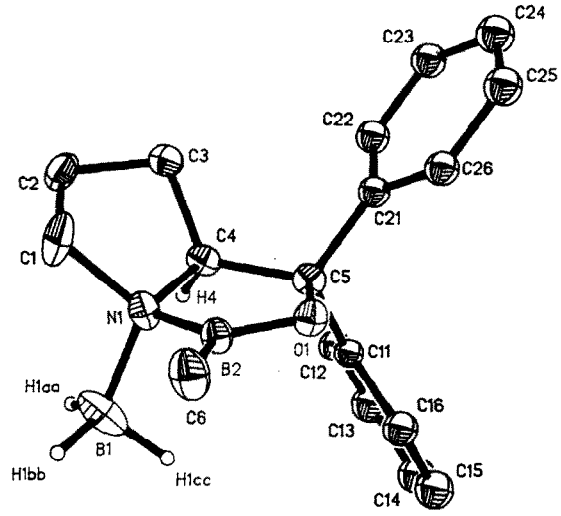


Figure 1. X-Ray structure of borane complex 2.

proposals.[1] The N_1B_1 bond distance (1.62 Å) is close to that reported for ammonia borane (1.604 Å) and N_1B_2 is considerably shorter (1.486 Å). The O_1B_2 distance (1.335) is definitely shorter than the OB distance in the phenylboronate ester of catechol (1.394) indicating substantial O_1B_2 π-bonding in **2**. The results of the present study provide additional evidence for transition state assembly **3** for the catalytic CBS reduction.[1,16]

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12. All operations were carried out in an argon atmosphere because of sensitivity to H_2O and O_2.
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14. ^1H NMR (400 MHz, CD_2Cl_2) δ 7.56 (m, 2H), 7.3 - 7.1 (m, 8H), 4.58 (m, 1H), 3.14 (m, 1H), 1.89 (m, 2H), 1.58 (m, 1H), 1.6 - 1.8 (br.), 1.25 (m, 1H), 0.69 (s, 3H); ^{11}B NMR (96 MHz, CD_2Cl_2) δ 40.47, -12.87 (quartet, J_{BH} = 98.2 Hz).
15. A total of 3364 reflections were collected at -70 °C; unit cell dimensions a = 9.010(4) Å, b = 12.987(3) Å, c = 14.386(3) Å, Z= 4. Least squares refinement of the data using 1987 reflections converged on the structure shown in Fig. 1 with R = 0.0846 and a goodness of fit 0.91.
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