Available online at www.sciencedirect.com

ScienceDirect

Tetrahedron Letters 48 (2007) 3531–3534

Tetrahedron Letters

Novel Grignard reaction of chelated boric esters derived from diethyl (2*R*,3*R*)-tartrate: a one-step access to a bulky γ,γ,γ-trisubstituted γ-hydroxy-β-ketoester via selective arylation and sequent deboronation☆

Yan Zhou and Zixing Shan*

Department of Chemistry, Wuhan University, Wuhan 430072, China

Received 3 March 2007; accepted 19 March 2007
Available online 21 March 2007

Abstract—Reaction of the tetracoordinated spiroborate esters derived from diethyl (2*R*,3*R*)-tartrate with Grignard reagents was further examined and found that sterically hindered MesMgBr has different reaction behavior from PhMgBr to the spiroborate esters. It has been proved that in the case of PhMgBr reaction, the formation of the chiral bicyclodiboronic ester (*R*,*R*)-**2** was accomplished step by step via two 1,3-cyclizations of the hydrolytic products of the resulting boron compound. However, in the case of MesMgBr reaction, only one esteral group of the tartrate moiety was diarylated, and a bulky γ,γ,γ-trisubstituted γ-hydroxy-β-ketoester and mesitylboronic anhydride were provided after the resultant was worked up. The composition and structure of the products were authorized by the spectral and single crystal X-ray analysis. A formation mechanism of γ-hydroxy-β-ketoester and mesitylboronic anhydride was also suggested.

Boron compounds have rich reaction chemistry.[1] Alkyl borate is one of the most important classes of boron compounds, and they have been widely applied to the preparation of organic boron compounds and synthesis of other useful materials.[2] However, tricoordinate boric ester generally is sensitive toward moisture. Recently, we synthesized a series of chiral spiroborate ester possessing an O_3BN framework through convenient procedures,[3] which show high stability to hydrolysis and thermolysis due to the presence of the N→B bond. It has been observed that some of the chiral spiroborate esters are good chiral promoter for asymmetric borane reduction of prochiral ketones,[4] imines[5] and oxime ethers,[6] and asymmetric aldol addition.[7] To widen the application scope of the spiroborate esters in asymmetric synthesis, we examined the reaction of the spiroborate esters with an O_3BN framework derived from diethyl (2*R*,3*R*)-tartrate with PhMgBr, and unexpectedly, a hydrolytically stable tricoordinated chiral bicyclo[4.4.0]diboronic ester (*R*,*R*)-**2** was obtained in medium yield.[8] It has been estimated that (*R*,*R*)-**2** was formed via a selective intermolecular dehydration and 1,3-cyclization between 1,4-bis(diphenyl)-1,2,3,4-tetraol and $PhB(OH)_2$, which were generated from hydrolysis of the reaction product by aq NH_4Cl. The current investigation further administrated that the selective bicyclization was completed in two steps. At the first stage, the tetraol reacted with one mole of $PhB(OH)_2$ to furnish a semi-esterified 1,3-cyclization product (4*R*,5*R*)-4-diphenylhydroxymethyl-5-hydroxy-2,6,6-triphenyl-1,3,2-dioxaboro-cyclohexane (*R*,*R*)-**1**,[9] which has been confirmed by the single crystal X-ray analysis[10] (Fig. 1), and this monocyclization product can further react with second $PhB(OH)_2$ molecule to give (*R*,*R*)-**2** (Scheme 1). Systematic examination on the reaction of this class of chiral spiroborate ester with Grignard reagent found that the reaction product of the spiroborate esters were in close relationship with the composition of the chiral spiroborate ester and Grignard reagent. As far as the reactions toward the spiroborate esters derived from diethyl (2*R*,3*R*)-tartrate are concerned, sterically hindered MesMgBr (Mes, mesityl group, i.e., 2,4,6-trimethylphenyl) showed different reaction behavior from PhMgBr to the spiroborate esters.

Keywords: Spiroborate ester; Grignard reaction; Selective arylation; γ-Hydroxy-β-keto ester.

☆ Chiral Borate Esters in Asymmetric Synthesis: 7.

* Corresponding author. Tel.: +86 27 87219074; fax: +86 27 68754067; e-mail: zxshan@whu.edu.cn

0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2007.03.098

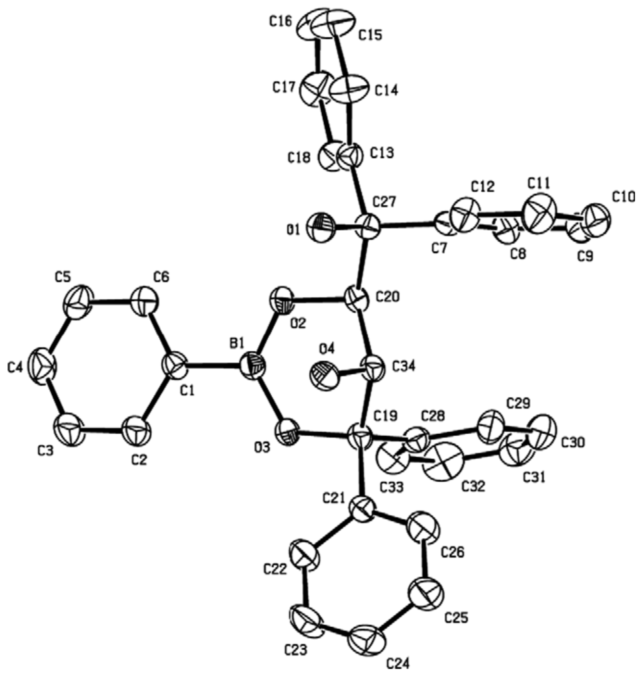


Figure 1. Molecular structure of (*R*,*R*)-**1** with 50% probability ellipsoids (hydrogen atoms and the solvent EtOH are omitted for clarity).

Chiral spiroborate ester, for example (*R*,*R*,*S*)-**1**, which was prepared from diethyl (2*R*,3*R*)-tartrate, boric acid and L-proline according to the lit.,[8] was added to the Grignard reagent MesMgBr in THF cooled with ice-bath in several portions with vigorous stirring. After complete addition, the reaction mixture was continued to stir in ice-bath for 1 h, and then warmed up to reflux for additional 1.5 h, cooled, and quenched with saturated aq NH_4Cl. The organic phase was separated, dried over anhydrous Na_2SO_4, evaporated and purified via column chromatography, white solid product **3** was obtained. No boron was detected. The IR spectra of **3** show adsorption of hydroxyl group (at 3471 s), esteral group (at 1745 s), carbonyl group in a strong H bonding environment (at 1608 m) as well as mesityl group, indicating that it could be a deboration product bearing mesityl group derived from the tartaric moiety of (*R*,*R*,*S*)-**1**. The ^{1}H NMR spectra of **3** indicate that in the compound, there are two misityl groups, one ethyl group, one hydroxyl group (6.36, s, disappeared after adding D_2O) as well as a methylene group (3.94, s, 2H); but, there is no signal of pyrrolidine ring. The ^{13}C NMR spectra and FBA-MS of **3** are in conformity with the above comment. It can be concluded based on the above facts that **3** is 4,4-dimesityl-4-hydroxy-3-oxobutanoic ester **3** (Scheme 2).[11] Composition and structure of **3** were further affirmed by the single crystal X-ray structural analysis (Fig. 2),[10] and it clearly exhibits that there is a hydrogen bond between the β-oxygen and γ-OH in this molecule. On the other hand, mesitylboronic anhydride **4** was successfully separated from the organic phase. It goes without saying that selective

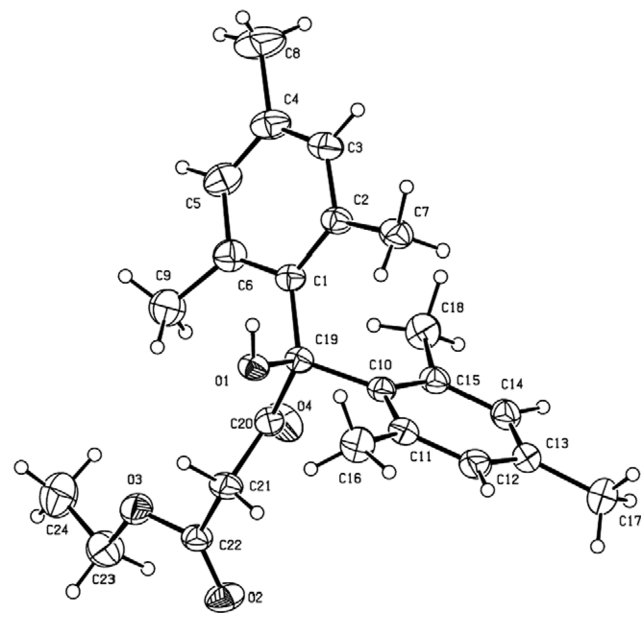
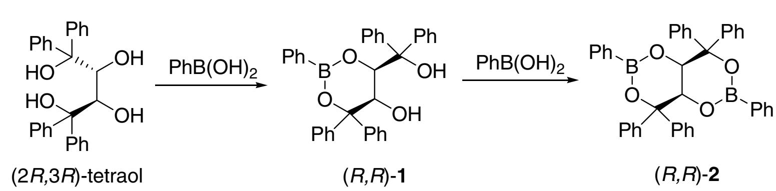
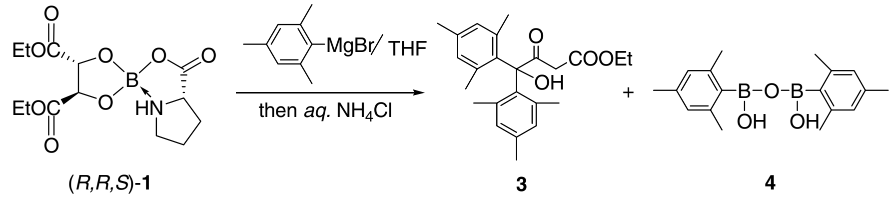


Figure 2. Molecular structure of **3** with 50% probability ellipsoids.



Scheme 1. Formation of (*R*,*R*)-**2** from (2*R*,3*R*)-tetraol and $PhB(OH)_2$ step by step.



Scheme 2. Reaction of (*R*,*R*,*S*)-**1** derived from diethyl (2*R*,3*R*)-tartrate with MesMgBr.