


# Ti-Catalyzed Reaction of $\beta$ -Pinene with $\text{BF}_3 \cdot \text{THF}$ <sup>†</sup>

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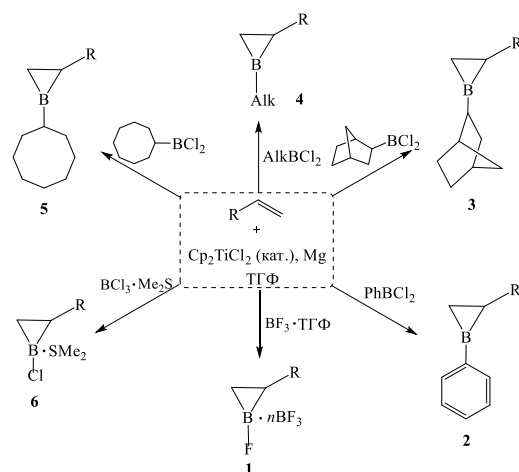
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**Abstract:** The reaction between  $\beta$ -pinene and  $\text{BF}_3 \cdot \text{THF}$  in the presence of the catalytic system  $\text{Cp}_2\text{TiCl}_2/\text{Mg}$  was carried out for the first time to obtain a 1-fluoro-substituted boraspirane, undescribed previously. The reaction proceeds stereoselectively, but is complicated by the rearrangement of the  $\beta$ -pinene under the Ti-catalyzed reaction conditions.

**Keywords:** cycloboration; organoborane compounds;  $\beta$ -pinene;  $\text{Cp}_2\text{TiCl}_2$

## 1. Introduction

The  $\text{Cp}_2\text{TiCl}_2$ -catalyzed cycloboration of  $\alpha$ -olefins with boron halides  $\text{BX}_3$  ( $\text{X} = \text{F}$  and  $\text{Cl}$ ) or  $\text{RBCl}_2$  ( $\text{R} = \text{Alk}$ ,  $\text{Ar}$ ) provides a convenient one-pot procedure for the conversion of olefinic structures into a rare class of organoboron compounds—boriranes **1–6** (Scheme 1) [1–5].  $\alpha,\omega$ -Dienes can also be used as monomers to obtain 1,2-disubstituted boriranes [6].



**Scheme 1.** Synthesis of 1,2-disubstituted boriranes **1–6** via  $\text{Cp}_2\text{TiCl}_2$ -catalyzed reaction of  $\alpha$ -olefins with boron halides or dihaloboranes.

Methylenecycloalkanes were used as monomers to expand the scope of this method to prepare three-membered cyclic organoboron compounds, which allowed one to obtain spiroboriranes. As an example, 1-Phenyl-substituted spiroboracarabocycles were formed with a yield of 70–80% after the  $\text{Cp}_2\text{TiCl}_2$ -catalyzed cycloboration of methylenecycloalkanes with  $\text{PhBCl}_2$  [7], and when  $\text{BF}_3 \cdot \text{THF}$  was used as a boron reagent, target 1-fluoro-substituted spiroboracarabocycles were formed in a mixture with isomerization products of a starting monomer (1-methylcycloalk-1-enes) [8].



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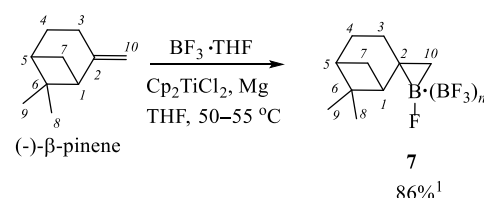
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We explored the cycloboration reaction of  $\beta$ -pinene used as the starting material to continue these studies. Pinane terpenoids are attractive monomers in organic synthesis, which is due to their availability in nature and wide practical use as raw materials to produce organic polymers [9,10], insecticides, fragrant and medicinal substances [11,12]. The studies of new transformations of natural terpenoids to obtain known and new pharmacologically active low molecular bioregulators, therefore, are relevant and in demand.

As a part of an ongoing program in our laboratories aimed at the metall-catalyzed synthesis of new organoborane compounds we, for the first time, carried out the Ti-catalyzed reaction of  $\beta$ -pinene with  $\text{BF}_3 \cdot \text{THF}$ .

## 2. Results and Discussion

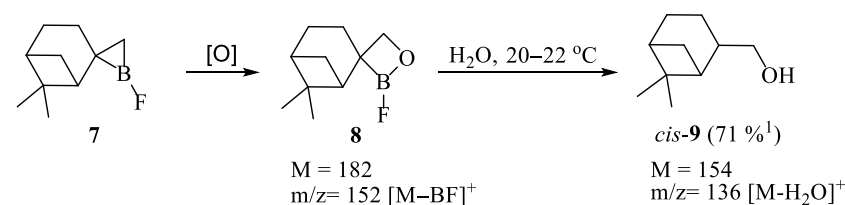
We found that the reaction between  $\beta$ -pinene and  $\text{BF}_3 \cdot \text{THF}$  in the presence of catalytic system  $\text{Cp}_2\text{TiCl}_2/\text{Mg}$  under the developed conditions (20 mol%  $\text{Cp}_2\text{TiCl}_2$ , 40 mol%  $\text{Mg}$ , THF, 4–6 h, 50–55 °C) gives the 1'-fluoro-substituted spiro[bicyclo [3.1.1]heptane-2,2'-borirane] **7** in an 86% yield (Scheme 2).



**Scheme 2.** Reaction between  $\beta$ -pinene and  $\text{BF}_3 \cdot \text{THF}$  under the action of  $\text{Cp}_2\text{TiCl}_2/\text{Mg}$  catalytic system. (<sup>1</sup> Yield determined by <sup>1</sup>H NMR).

No signals of a double bond of the methylene group  $\text{C}^2=\text{C}^{10}\text{H}_2$  were observed in <sup>1</sup>H and <sup>13</sup>C NMR spectra of the reaction mixture after the reaction termination. The signal of a  $\text{C}^7$  bridge carbon atom was detected in a more high-frequency field (up to 33.01 ppm) of a <sup>13</sup>C NMR spectrum in comparison with that of a starting  $\beta$ -pinene (27.8 ppm), which indicated its complete consumption. In addition, the difference in <sup>1</sup>H NMR chemical shifts of  $\text{C}^7\text{H}^A$  and  $\text{C}^7\text{H}^B$  diastereotopic protons of the reaction product **7** was 1.46 ppm, whereas it was 0.89 ppm in the starting  $\beta$ -pinene. The signals of carbon and hydrogen atoms of the  $\text{C}^{10}\text{H}_2\text{--B--C}^2(\text{C}^1\text{H})(\text{C}^3\text{H}_2)(\text{C}^9\text{H})$  group directly bound to a quadrupole boron atom or 2–3 chemical bonds away were expectedly not detected in <sup>1</sup>H and <sup>13</sup>C NMR time scales [13], which is typical for three-membered cyclic systems (a series of boriranes [1–6], [14] and borirenes [15,16]). The <sup>11</sup>B NMR spectrum of the compound **7** contains a broadened signal at  $\delta_B -0.97$  ppm, and <sup>19</sup>F NMR spectrum shows a signal at  $\delta_F -151.09$  ppm. Additional signals at  $\delta_B -0.01$  and  $\delta_F -155.78$  ppm in the <sup>11</sup>B and <sup>19</sup>F NMR spectra, respectively, are assigned to  $\text{BF}_3$  that forms a complex with the boraspirane **7**. The reaction product characterized with multinuclear NMR spectroscopy, therefore, was 1'-fluoro-substituted spiro[bicyclo[3.1.1]heptane-2,2'-borirane] **7** formed under the reaction conditions as a complex with boron trifluoride.

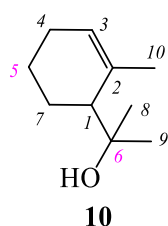
In the mass spectrum of the compound **7**, the molecular ion peak is absent, but the oxidation product **8** yields a fragmentary ion peak with  $m/z$  152  $[\text{M--BF}]^+$  by loss of BF group (Scheme 3).



**Scheme 3.** Oxidation of 1-fluoro-substituted boraspirane **7** by oxygen with subsequent hydrolysis. (<sup>1</sup> Isolated yields given).

The fact that mirtanol **9** with its exclusively *cis* configuration is formed indicates that the reaction is stereoselective.

The *o*-ment-6-en-8-ol **10** was isolated as a byproduct in a 20% yield after the hydrolysis (Figure 1). It is known that  $\beta$ -pinene undergoes the skeletal rearrangements of a pinane backbone in the presence of acid catalysts (such as boron trifluoride or Ti compounds) to form monocyclic and acyclic products (derivatives of  $\alpha$ -pinene, limonene, myrcene, etc.). It is obvious that the monocyclic *o*-ment-6-en-8-ol **10** is a product of double bond isomerization and C<sup>5</sup>–C<sup>6</sup> bond cleavage of a four-membered fragment of  $\beta$ -pinene under the reaction conditions. We observed previously the isomerization of  $\alpha$ -olefins to isomeric alk-2-enes [2] and methylenecycloalkanes to 1-methylcycloalk-1-enes [8] under the conditions of Ti-catalyzed cycloboration with boron trifluoride.



**Figure 1.** Structure of *o*-ment-6-en-8-ol **10**.

### 3. Conclusions

In summary, we performed the cycloboration of  $\beta$ -pinene for the first time using  $\text{BF}_3 \cdot \text{THF}$  reagent in the presence of a  $\text{Cp}_2\text{TiCl}_2/\text{Mg}$  two-component catalytic system to obtain 1'-fluoro-substituted spiro[bicyclo[3.1.1]heptane-2,2'-borirane **7**, undescribed previously. Skeletal rearrangements of the bicyclic backbone of  $\beta$ -pinene are possible under the conditions of Ti-catalyzed reaction. The development of new methods and approaches to prepare boron-containing derivatives is of great practical interest from the point of view of creating new molecules with potential biological activity.

### 4. Experimental Part

All reactions with organometallic and organoboron compounds were performed using standard Schlenk techniques.  $\beta$ -Pinene,  $\text{BF}_3 \cdot \text{THF}$  and  $\text{Cp}_2\text{TiCl}_2$  were obtained from commercial sources and used without further purification. THF was dried by distillation over sodium/benzophenone and stored under an argon atmosphere. The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{11}\text{B}$ ,  $^{19}\text{F}$  and 2D homo- (COSY) and heteronuclear (HSQC, HMBC, DOSY) NMR spectra were measured in  $\text{CDCl}_3$  on a Bruker Avance-400 spectrometer [400.13 ( $^1\text{H}$ ), 100.62 ( $^{13}\text{C}$ ), 128.33 ( $^{11}\text{B}$ ), 376.37 ( $^{19}\text{F}$ ) MHz]. The chemical shifts ( $\delta$ ) are given in parts per million (ppm) relative to  $\text{Me}_4\text{Si}$  (for  $^1\text{H}$  and  $^{13}\text{C}$  NMR chemical shifts),  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  ( $^{11}\text{B}$  NMR) and  $\text{CCl}_3\text{F}$  ( $^{19}\text{F}$  NMR) standards. Multiplicity is given in br, s, d and m for broad, singlet, doublet and multiplet, respectively. Coupling constants (*J*) are given in Hz. Mass spectra were recorded on Shimadzu GCMS-QP2010 Ultra, capillary column Supelco PTE-5 (60 m  $\times$  0.25 mm, carrier gas helium, ramp from 40 to 280  $^\circ\text{C}$  at a rate 8 deg/min, ionizing electrons energy 70 eV, injector temperature 260  $^\circ\text{C}$ , ion source temperature 200  $^\circ\text{C}$ ).

Chromatographic analysis was performed on a chromatograph using a 2000  $\times$  2 mm column (SE-30 (5%) stationary phase on Chromaton N-AW-HMDS (0.125–0.160 mm), helium carrier gas (30 mL/min), and temperature programming from 50 to 300  $^\circ\text{C}$  at an 8  $^\circ\text{C}/\text{min}$  rate).

$\text{Cp}_2\text{TiCl}_2$ -catalyzed reaction of  $\beta$ -Pinene with  $\text{BF}_3 \cdot \text{THF}$ . A glass reactor (20 mL) under a dry argon atmosphere at 0  $^\circ\text{C}$  was charged under stirring with  $\text{Cp}_2\text{TiCl}_2$  (0.4 mmol, 0.10 g), magnesium (powder) (1.6 mmol, 0.04 g), THF (10 mL),  $\beta$ -pinene (2 mmol) and  $\text{BF}_3 \cdot \text{THF}$  (8 mmol, 1.12 g). The temperature was raised to ~50–55  $^\circ\text{C}$  and the mixture was stirred about 4–6 h. Then the reaction mixture was cooled to room temperature and centrifuged, the excess of magnesium was filtered off, the solvent was evaporated, and boraspirane **7** was analyzed by NMR spectroscopy in an argon atmosphere in  $\text{CDCl}_3$ .

1'-Fluoro-spiro[bicyclo[3.1.1]heptane-2,2'-borirane] (7): Yield 86% (determined by  $^1\text{H}$  NMR),  $^1\text{H}$  NMR:  $\delta$  2.35–2.41 (m, 1H,  $\text{CH}^A$ ), 2.00–2.05 (m, 1H, CH), 1.88–1.97 (m, 2H, CH,  $\text{CH}^A$ ), 1.42–1.50 (m, 1H,  $\text{CH}^B$ ), 1.21 (br s, 3H), 1.00 (br s, 3H), 0.91–0.96 (m, 1H,  $\text{CH}^B$ ) ppm.  $^{13}\text{C}$  NMR:  $\delta$  42.7, 41.3, 33.0, 28.0, 23.1, 18.5 ppm.  $^{11}\text{B}$  NMR:  $\delta$  –0.97, –0.01 ( $\text{BF}_3$ ) ppm.  $^{19}\text{F}$  NMR:  $\delta$  –151.09, –155.78 ( $\text{BF}_3$ ) ppm. GC-MS:  $m/z$  152  $[\text{M}-\text{BF}]^+$ .

$\text{Cp}_2\text{TiCl}_2$ -catalyzed reaction of  $\beta$ -Pinene with  $\text{BF}_3\cdot\text{THF}$  after addition water. To a solution of boraspirane 7, synthesized according to above described procedures, water (2 mL) was added under oxygen atmosphere and the mixture was stirred for 1 h. The organic layer was separated, the aqueous layer was extracted with diethyl ether ( $2 \times 10$  mL), extracts were combined with the organic phase. The solvent was evaporated and the residue was distilled under reduced pressure.

*cis*-Myrtanol (9): Yield 63% (0.194 g), colorless oil,  $[\alpha]_{\text{D}}^{21} = -8.6$  ( $\text{CHCl}_3$ ,  $c = 0.081$ ), bp  $85^\circ\text{C}$  (4 mm).  $^1\text{H}$  NMR:  $\delta$  3.55–3.63 (m, 2H), 2.36–2.42 (m, 1H), 2.23–2.30 (m, 1H), 2.02–2.07 (m, 1H), 1.87–2.01 (m, 4H), 1.42–1.52 (m, 1H), 1.21 (s, 3H), 0.99 (s, 3H), 0.96 (d,  $J = 9.5$  Hz, 1H) ppm.  $^{13}\text{C}$  NMR:  $\delta$  76.8, 44.4, 42.8, 41.4, 38.6, 33.1, 27.9, 25.9, 23.3, 18.7 ppm. GC-MS:  $m/z$  136 (10%)  $[\text{M}-\text{H}_2\text{O}]^+$ .

*o*-Menth-6-en-8-ol (10): Yield 25% (0.077 g), colorless oil,  $[\alpha]_{\text{D}}^{21} = -78.1$  ( $\text{CHCl}_3$ ,  $c = 0.44$ ), bp  $70^\circ\text{C}$  (1 mm).  $^1\text{H}$  NMR:  $\delta$  5.38–5.43 (m, 1H), 1.97–2.11 (m, 3H), 1.86–1.94 (m, 1H), 1.77–1.85 (m, 1H), 1.67 (s, 3H), 1.52 (m, 1H), 1.24–1.32 (m, 1H), 1.21 (s, 3H), 1.19 (s, 3H) ppm.  $^{13}\text{C}$  NMR:  $\delta$  134.0, 120.52, 72.7, 44.9, 30.9, 27.4, 26.8, 26.2, 23.9, 23.3 ppm. GC-MS:  $m/z$  136 (4%)  $[\text{M}-\text{H}_2\text{O}]^+$ .

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**Conflicts of Interest:** The authors declare no conflict of interest.

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