# SIMPLE SYNTHESIS OF MONOISOPINOCAMPHEYLBORANE VIA THE BIS ADDUCT WITH TRIETHYLENEDIAMINE†

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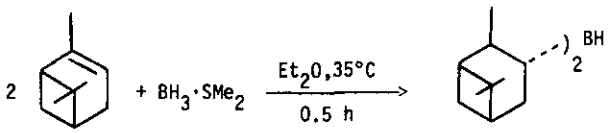
Abstract - The reaction between diisopinocampheylborane ($Ipc_2BH$) and triethylenediamine (TED) at 35°C occurs rapidly with displacement of α-pinene to form a solid 1:2 adduct (mp 160-161°C) of the diamine and monoisopinocampheylborane ($2IpcBH_2 \cdot TED$). Generation of free monoisopinocampheylborane is readily achieved by precipitation of $TED \cdot 2BF_3$ by simple treatment of the adduct with boron trifluoride etherate.

Monoisopinocampheylborane ($IpcBH_2$, 6) has emerged as a useful chiral hydroborating agent in the recent past. It achieves asymmetric hydroboration of trisubstituted[1,2] alkenes to provide the corresponding alcohols, upon oxidation, in 52-100% enantiomeric purities. More recently it has been observed that $IpcBH_2$ is also very effective for the asymmetric hydroboration of trans disubstituted[3] olefins giving optically active alcohols in the range of 70-92% e.e. The synthesis of $IpcBH_2$ by direct hydroboration of α-pinene (1) with borane is difficult. The limiting factor is failure of the hydroboration reaction to stop at the monoalkylborane stage. Hydroboration of olefins, such as α-pinene, with $BH_3 \cdot THF$ or $BH_3 \cdot SMe_2$ generally proceeds rapidly past the monoalkylborane stage.[4,5] Consequently, $IpcBH_2$ has been prepared by indirect approaches.[1,6-8] More recently, it has been synthesized by the equilibration[9] of the product from a 1:1 molar ratio of α-pinene and $BH_3 \cdot THF$. In this communication we record a new simple, indirect synthesis of $IpcBH_2$.

The present procedure utilizes commercially available borane-methyl sulfide (BMS) in $Et_2O$ for the rapid preparation of diisopinocampheylborane ($Ipc_2BH$, 2), followed by a fast displacement of half of the α-pinene by triethylenediamine (TED, 3), forming the 1:2 adduct of the diamine and monoisopinocampheylborane ($2IpcBH_2 \cdot TED$, 4). Recently it has been observed[10] that TED forms both 1:1 and 1:2 adducts with $BF_3 \cdot OEt_2$ and that these adducts are highly insoluble in $Et_2O$ and THF. Therefore, generation of free $IpcBH_2$ by the precipitation of $2BF_3 \cdot TED$ on treatment of $2IpcBH_2 \cdot TED$ with $BF_3 \cdot OEt_2$ becomes a convenient process.

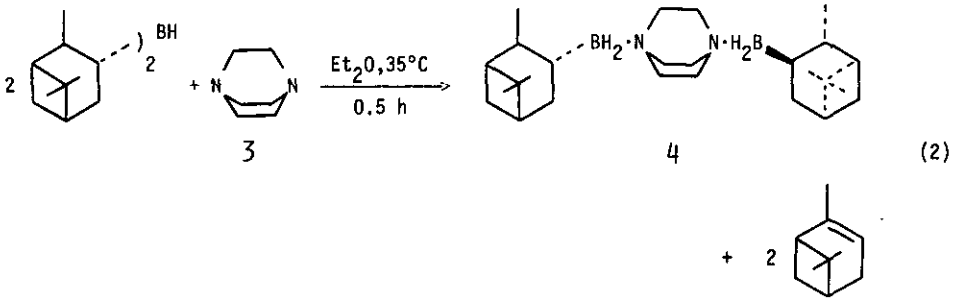
† Dedicated to Professor Herbert C. Brown on the occasion of his 70th birthday.

Thus, $Ipc_2BH$, 2, was prepared by the reaction of α-pinene with $BH_3 \cdot SMe_2$ in $Et_2O$ at 35°C (Eq 1).




1 2 (1)

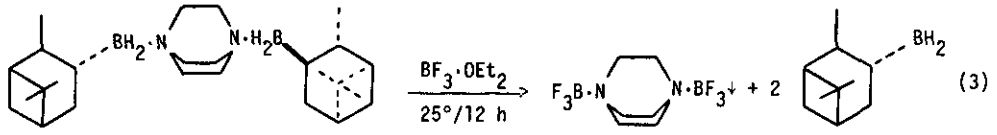
The addition of an $Et_2O$ solution of $Ipc_2BH$ to the flask containing half an equivalent of TED resulted in the formation of $2IpcBH_2 \cdot TED$ (Eq 2).




3 4 (2)

The reaction is essentially complete in 0.5 h at 35°C ($^{11}B$ nmr: δ +1.20 relative to $BF_3 \cdot OEt_2$). The reaction mixture was then cooled and the solvents removed under reduced pressure (25°/14 min). At that point, the bis adduct 4 was thrown out as a white solid. It was crystallized through a $Et_2O$:pentane mixture to provide 4 in 79% isolated yield. $^1H$ nmr and $^{11}B$ nmr data revealed that the bis adduct 4 was very pure. Methanolysis provided pure $IpcB(OMe)_2$ by $^{11}B$ nmr. The adduct 4 is readily soluble in $Et_2O$, THF, and chloroform, but is insoluble in pentane.

Free $IpcBH_2$ was generated by the treatment of 4 with two equivalents of $BF_3 \cdot OEt_2$ at 25°C in THF (Eq 3). Fortunately, $IpcBH_2$ does not disproportionate in spite of rather slow reaction (25°/12 h)




5 6 (3)

in THF. Alternatively, generation of $IpcBH_2$ was achieved rapidly (25°/0.5 h) in $Et_2O$ by the treatment of 4 with $BF_3 \cdot OEt_2$ providing $IpcBH_2$ in $Et_2O$. Methanolysis of 6, followed by oxidation, provided isopinocampheol in 92% e.e. It is interesting to note that the displacement of α-pinene from $Ipc_2BH$ with TED proceeds rapidly and smoothly, comparable to the displacement with TMED.[7] However, the latter reaction proceeds to yield $2IpcBH_2 \cdot TMED$ of 100% e.e. On the other hand, TED gave a product with the same optical purity as that of the α-pinene used.

The experimental procedure follows. All operations were carried out under nitrogen.[4] In a 100-ml flask with septum inlet, magnetic stirring bar and reflux condenser connected to a mercury bubbler was placed borane-methyl sulfide (35 mmol; 3.53 ml, 9.89 *M*) and anhydrous $Et_2O$ (20 ml). It was treated with (+)-α-pinene (80.5 mmol, 12.7 ml) $[\alpha]_D^{23}$ +47.1 (neat), 92% e.e., and heated under reflux for 0.5 h. The reaction mixture was then transferred with the help of a double-ended needle to a flask containing TED (17.5 mmol, 1.97 g) and further refluxed for 0.5 h. With flask in the water bath (25°C), solvents were removed under reduced pressure (14 mm) to provide a white solid. It was dissolved in refluxing $Et_2O$-Pentane mixture, transferred to a centrifuge tube, and allowed to cool slowly. At that point, the adduct crystallizes out as small white needles. The solvent was removed by centrifugation and the solid washed with cold pentane and then dried under vacuum to provide 5.75 g (79%) of $2IpcBH_2 \cdot TED$: mp 160-161°, $^1H$ nmr ($CDCl_3Me_4Si$) δ 1.00 (d, 6H, J = 7 Hz), 1.1 (s, 6H), 1.17 (s, 6H), 3.17 (s, 6H); $^{11}B$ nmr ($Et_2O$, relative to $BF_3 \cdot OEt_2$) δ +1.20 (br s). To liberate free $IpcBH_2$, the adduct 4 (5 mmol, 2.06 g) was dissolved in THF (10 ml) and treated with $BF_3 \cdot OEt_2$ (10 mmol, 1.2 ml). After stirring at 25°C for 12 h, the solid $2BF_3 \cdot TED$ was centrifuged and the supernatant liquid was analyzed for free $IpcBH_2$ (9.5 mmol, 95%). Oxidation of the methanolyzed product provided isopinocampheol, mp 55-57°, $[\alpha]_D^{23}$ -33.01 (c 10, benzene) in 92% enantiomeric excess.

The present method describes a rapid synthesis of a new molecular addition compound, $2IpcBH_2 \cdot TED$ and a simple method for the synthesis of a valuable chiral hydroborating agent.

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