

SIMPLE SYNTHESIS OF MONOISOPINOCAMPEYLBORANE VIA THE BIS ADDUCT WITH TRIETHYLENEDIAMINE[†]Prabhakar K. Jadhav^{*} and Manoj C. Desai

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907 U.S.A.

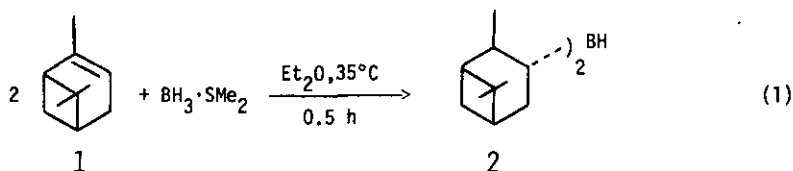
Abstract - The reaction between diisopinocampheylborane (Ipc_2BH) and triethylenediamine (TED) at 35°C occurs rapidly with displacement of α -pinene to form a solid 1:2 adduct (mp 160-161°C) of the diamine and monoisopinocampheylborane ($2\text{IpcBH}_2\cdot\text{TED}$). Generation of free monoisopinocampheylborane is readily achieved by precipitation of $\text{TED}\cdot 2\text{BF}_3$ 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 disubstituted³ 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 $\text{BH}_3\cdot\text{THF}$ or $\text{BH}_3\cdot\text{SMe}_2$ 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 equilibration⁹ of the product from a 1:1 molar ratio of α -pinene and $\text{BH}_3\cdot\text{THF}$. In this communication we record a new simple, indirect synthesis of IpcBH_2 .

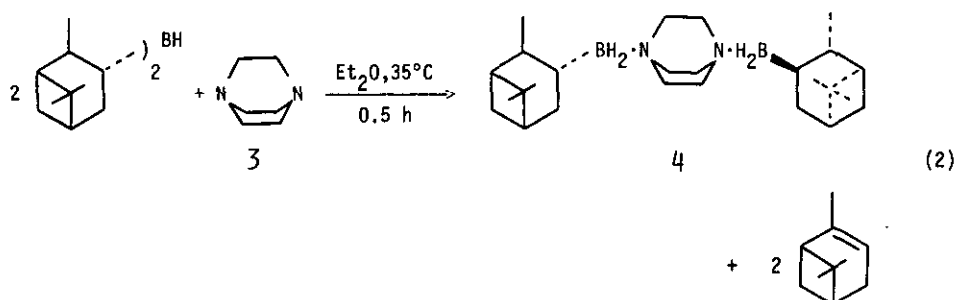
The present procedure utilizes commercially available borane-methyl sulfide (BMS) in Et_2O for the rapid preparation of diisopinocampheylborane (Ipc_2BH , 2), followed by a fast displacement of half of the α -pinene by triethylenediamine (TED, 3), forming the 1:2 adduct of the diamine and monoisopinocampheylborane ($2\text{IpcBH}_2\cdot\text{TED}$, 4). Recently it has been observed¹⁰ that TED forms both 1:1 and 1:2 adducts with $\text{BF}_3\cdot\text{OEt}_2$ and that these adducts are highly insoluble in Et_2O and THF. Therefore, generation of free IpcBH_2 by the precipitation of $2\text{BF}_3\cdot\text{TED}$ on treatment of $2\text{IpcBH}_2\cdot\text{TED}$ with $\text{BF}_3\cdot\text{OEt}_2$ 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 $\text{BH}_3\cdot\text{SMe}_2$ in Et_2O at 35°C (Eq 1).

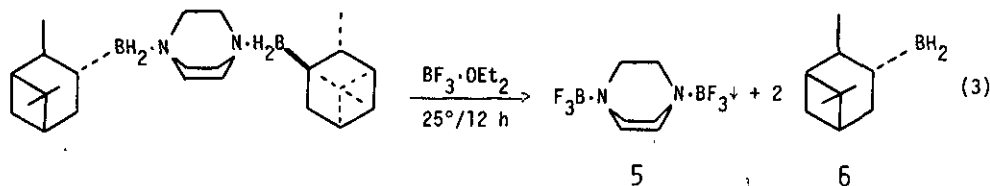


The addition of an Et_2O solution of Ipc_2BH to the flask containing half an equivalent of TED resulted in the formation of $2\text{IpcBH}_2\cdot\text{TED}$ (Eq 2).



The reaction is essentially complete in 0.5 h at 35°C (^{11}B nmr: $\delta +1.20$ relative to $\text{BF}_3\cdot\text{OEt}_2$). The reaction mixture was then cooled and the solvents removed under reduced pressure ($25^\circ/14 \text{ min}$). 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 $\text{BF}_3\cdot\text{OEt}_2$ at 25°C in THF (Eq 3). Fortunately, IpcBH_2 does not disproportionate in spite of rather slow reaction ($25^\circ/12 \text{ h}$)



in THF. Alternatively, generation of IpcBH_2 was achieved rapidly ($25^\circ/0.5 \text{ h}$) in Et_2O by the treatment of **4** with $\text{BF}_3\cdot\text{OEt}_2$ 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 $2\text{IpcBH}_2\cdot\text{TMED}$ 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 Et₂O (20 ml). It was treated with (+)- α -pinene (80.5 mmol, 12.7 ml) [α]_D²³ +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 Et₂O-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 2IpcBH₂·TED: mp 160-161°, ¹H nmr (CDCl₃-Me₄Si) δ 1.00 (d, 6H, J = 7 Hz), 1.1 (s, 6H), 1.17 (s, 6H), 3.17 (s, 6H); ¹¹B nmr (Et₂O, relative to BF₃·OEt₂) δ +1.20 (br s). To liberate free IpcBH₂, the adduct 4 (5 mmol, 2.06 g) was dissolved in THF (10 ml) and treated with BF₃·OEt₂ (10 mmol, 1.2 ml). After stirring at 25°C for 12 h, the solid 2BF₃·TED was centrifuged and the supernatant liquid was analyzed for free IpcBH₂ (9.5 mmol, 95%). Oxidation of the methanol-lyzed product provided isopinocampheol, mp 55-57°, [α]_D²³ -33.01 (c 10, benzene) in 92% enantiomeric excess.

The present method describes a rapid synthesis of a new molecular addition compound, 2IpcBH₂·TED and a simple method for the synthesis of a valuable chiral hydroborating agent.

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