An Improved Synthesis of Monoisopinocampheylborane

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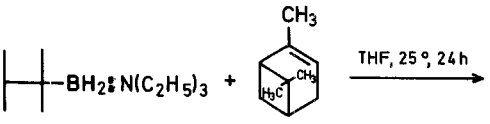
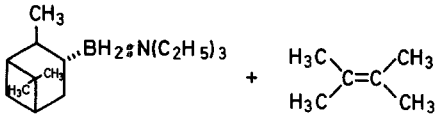
Neat thexylborane:triethylamine [thexylBH$_2$:N(C$_2$H$_5$)$_3$], synthesized in the reaction of neat 2,3-dimethyl-2-butene and neat borane:dimethyl sulfide at 25° followed by removal of dimethyl sulfide and addition of triethylamine, reacts with α-pinene at 25° within 2–3 h to provide, after removal of volatiles (2,3-dimethyl-2-butene and excess triethylamine), neat monoisopinocampheylborane:triethylamine (**1**) in ≥94% yield. Reagent **1** in pentane undergoes a facile reaction with boron trifluoride etherate [BF$_3$:O(C$_2$H$_5$)$_2$] at 25° to yield free monoisopinocampheylborane (**2**) (solution), readily separated at 0° to −5° from precipitated BF$_3$:N(C$_2$H$_5$)$_3$.

The reaction of thexylborane:triethylamine[2] with α-pinene prepared from 2,3-dimethyl-2-butene, BH$_3$:THF, and triethylamine is slow, requiring 24 h at 25° for the quantitative formation of **1**[3,4].





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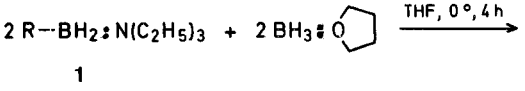
The procedure requires a relatively long reaction time and utilizes BH$_3$:THF, which is less convenient to handle than borane:dimethyl sulfide[5]. The reagent is a highly promising one for asymmetric hydroboration[4] and reductions[6]. It appeared desirable, therefore, to develop a more simple, more convenient synthesis of monoisopinocampheylborane (**2**).

The present procedure utilizes neat borane:dimethyl sulfide for the rapid preparation of thexylborane, a fast displacement of 2,3-dimethyl-2-butene by α-pinene, and a convenient removal of triethylamine from the product with boron trifluoride etherate. With these changes, the synthesis of **2** becomes a simple, rapid process.

Neat thexylborane was prepared in 20 minutes by the reaction of neat 2,3-dimethyl-2-butene with borane:dimethyl sulfide at 25°. Dimethyl sulfide was removed by evacuation and a slight excess (20%) of triethylamine was added. At 25° the addition of α-pinene results in the displacement of 2,3-dimethyl-2-butene and the formation of **1**. The reaction is essentially complete in 2–3 h. The volatiles, 2,3-dimethyl-2-butene and excess triethylamine, were pumped off (14 torr), leaving essentially pure **1** as a colorless viscous liquid in a yield of ≥94%. Methanolysis followed by oxidation provided ~94% isopinocampheol and 5–6% of thexyl alcohol.

The product **1** reacts only slowly with olefin at 0° or 25°[4]. This, therefore, necessitates the removal of triethylamine from **1** to facilitate the reaction. Removal of triethylamine with boron trifluoride in tetrahydrofuran was disappointingly slow[2]. However, borane in tetrahydrofuran served as an effective means for removal of the triethylamine, leaving the borane presumably as the dimer **2**, for ready hydroboration of olefins[4].



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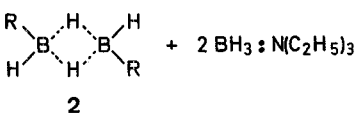

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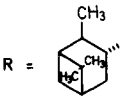

Borane:triethylamine is inert for hydroboration, except at elevated temperature. Hence, its removal is not needed for further hydroboration. However, following oxidation, the presence of borane:triethylamine interferes with the isolation

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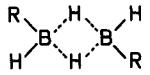
of the products. Consequently, the alkaline reaction mixture was refluxed for 12 h to achieve complete hydrolysis and destruction of borane:triethylamine. Such conditions are not desirable in reactions involving asymmetric syntheses, since they could result in significant racemization. An alternate procedure to remove triethylamine was desired. In fact, triethylamine can easily be removed from **1** in pentane by treating the solution with an equivalent amount of boron trifluoride etherate at 25° for 15 min. On cooling to −5°, $BF_3:N(C_2H_5)_3$ crystallizes out of solution. The pentane solution of the product (presumably as **2**) can then be recovered by decantation in nearly quantitative yield.

$$2\ R{-}BH_2:N(C_2H_5)_3 + 2\ BF_3:O(C_2H_5)_2$$

1

pentane, 25°, 15 min →



$$+\ 2\ BF_3:N(C_2H_5)_3$$

2

The new procedure thus describes a short and efficient synthesis of both **1** and **2**. It also makes available a convenient synthesis of neat thexylborane from 2,3-dimethyl-2-butene and commercially available borane:dimethyl sulfide, a modification of our earlier reported procedure[5]. Finally, the boron trifluoride etherate procedure is generally useful for the separation of triethylamine from the monoalkylborane:triethylamine derivatives, which are now readily available[3].

Preparation of Monoisopinocampheylborane (2):

With the usual experimental setup[7], all operations are carried out under nitrogen in a 200-ml flask. The flask is charged with borane:dimethyl sulfide[8] (10.0 ml, 100 mmol). 2,3-Dimethyl-2-butene (12.0 ml, 100 mmol) is added to it dropwise, keeping the flask in a water bath at 25°. After 20 min, dimethyl sulfide is removed under aspirator vacuum (14 torr) for 10–15 min yielding thereby neat thexylborane (100 mmol). To this product is added triethylamine (16.8 ml, 120 mmol) at 25°, forming the addition compound[2]. (+)-α-Pinene (16.0 ml, 100 mmol, $[\alpha]_D$: +48.07°[9], 94% optical purity) is then added over the stirred reaction mixture. After stirring of the reaction mixture for 3 h at 25°, 2,3-dimethyl-2-butene and excess triethylamine are removed under aspirator vacuum (14 torr) for 3–4 h providing **1** (~100 mmol), as a viscous liquid. The product is then dissolved in pentane (30 ml).

To **1** in pentane (12.8 ml of 1.56 molar solution, 20 mmol) there is added at 25°, boron trifluoride etherate (2.5 ml, 20 mmol). The reaction mixture is stirred at 25° over a period of 15 min in which time two layers separate. On cooling the reaction flask in an ice-salt bath, the lower layer of boron trifluoride:triethylamine crystallizes out. The free product **2** in pentane is then decanted off to another flask using a double-ended needle[7]. The crystalline boron trifluoride:triethylamine is thoroughly washed with pentane (15 ml) and pentane washings are transferred to the main solution.

Methanolysis with methanol (3.2 ml, 80 mmol) causes evolution of hydrogen (~36 mmol). The product after removal of pentane and excess methanol is distilled to yield pure isopinocampheylboronate; yield: 2.671 g (67%, assuming 94% **1** in the reaction mixture); b.p. 56–57°/0.05 torr. Oxidation of the boronate with alkaline hydrogen peroxide yields isopinocampheol ($[\alpha]_D^{24}$: −34.2°, c=1.35 in benzene) in about 97% optical purity[10].

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[6] Research in progress with Dr. A. K. Mandal.

[7] H. C. Brown, G. W. Kramer, A. B. Levy, M. M. Midland, *Organic Syntheses via Boranes*, Wiley-Interscience, New York, 1975.

[8] Available from the Aldrich Chemical Company.

[9] We are indebted to Dr. E. Klein of the Dragoco Co., Holzminden, West Germany, for a generous gift of (+)-α-pinene of high rotation.

[10] Based on the maximum rotation of $[\alpha]_D^{27.5}$: −35.1° reported for isopinocampheol, H. C. Brown, N. M. Yoon, *Israel J. Chem.* **15**, 12 (1977).

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