



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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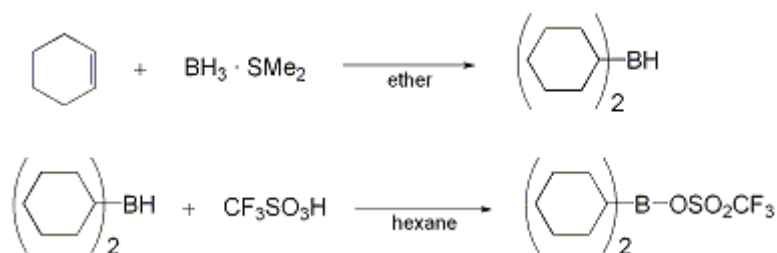
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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DICYCLOHEXYLBORON TRIFLUOROMETHANESULFONATE

[Methanesulfonic acid, trifluoro-, anhydride with dicyclohexylborinic acid]



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1. Procedure

Caution! Borane-dimethyl sulfide complex is foul smelling. All operations using dimethyl sulfide must be carried out in a well-ventilated hood.

*Dicyclohexylboron trifluoromethanesulfonate.*² An oven-dried, 250-mL, round-bottomed flask containing a stir bar and capped with a rubber septum is charged with cyclohexene (33.4 mL, 0.33 mol) (Note 1) and dry diethyl ether (100 mL) (Note 2), and kept at 0°C under nitrogen. Borane-dimethyl sulfide complex (16.6 mL, 0.16 mol) (Note 1) is added dropwise during 30 min with stirring. The reaction mixture is stirred for 3 hr at 0°C, then the solid is allowed to settle without stirring. The supernatant organic solution is removed as much as possible by syringe (Notes 3, 4), and the residual solid is dried under reduced pressure (Note 5) to give dicyclohexylborane (26.3-28.3 g, 92-99% yield) (Note 6), which is used without purification for the preparation of the triflate.

The solid is suspended in 100 mL of dry hexane (Note 2) and trifluoromethanesulfonic acid (24.0 g, 0.16 mol) (Note 1) is added dropwise via a glass syringe (Notes 7, 8) over 30 min with constant stirring, during which time vigorous gas evolution occurs; the solid gradually dissolves, and the solution develops a yellow-orange color (Note 9). Stirring is continued at room temperature for 1 hr, then the reaction mixture is left for 1-2 hr without stirring. A semi-solid phase separates and the top layer is transferred via cannula into a dry, 250 mL round-bottomed flask (Note 10). The flask is placed in a -20°C freezer for 36 hr. Large crystals form and the mother liquor is transferred via cannula to another dry, 100-mL, round-bottomed flask. The crystals are dried under reduced pressure at 0°C for 5 hr giving 40.8 g (78%) of dicyclohexylboron trifluoromethanesulfonate. The mother liquors are concentrated to dryness under nitrogen (N_2) using a rotary evaporator (Note 11). The residue is redissolved in 20 mL of dry hexane and crystallized in a -20°C freezer as described above to give an additional 7 g of product. The total yield of dicyclohexylboron trifluoromethanesulfonate is 47.8 g (92%) (Notes 12, 13). The isolated crystals are dissolved in hexane in a graduated cylinder equipped with a ground glass joint and a stopcock-equipped syringe inlet to make a 1 M stock solution (Notes 14, 15).

2. Notes

1. Cyclohexene was purchased from Wako Pure Chemical Ltd. Japan, or Aldrich Chemical Company, Inc., and used after distillation from lithium aluminum hydride. Borane-dimethyl sulfide complex was obtained from Aldrich Chemical Company, Inc., and was used as received.³ Trifluoromethanesulfonic acid was purchased from Wako Pure Chemical Ltd. Japan or Aldrich Chemical Company, Inc., and used without purification. The checkers used a freshly opened ampule of trifluoromethanesulfonic acid for each run.

2. Diethyl ether was freshly distilled from benzophenone ketyl. Hexane was distilled from lithium

aluminum hydride .

3. The supernatant organic solution might contain active borane . The solution that was removed was treated with methanol to destroy any active borane . The waste containing dimethyl sulfide must be treated appropriately before being discarded.

4. Care must be taken to avoid loss of product that is easily taken up in the syringe. The checkers found it more convenient to perform the reaction in a tared, round-bottomed Schlenk flask. Solvent was then removed from the solid dicyclohexylborane by filtration using a positive nitrogen flow.

5. Dicyclohexylborane bumps during the drying step, and the checkers found that it is advantageous to use a vacuum adapter containing a glass frit and an auxiliary cold trap to prevent contamination of the vacuum line with the product.

6. The submitter obtained 27.2-30.0 g (96-105% yield) of dicyclohexylborane .

7. Trifluoromethanesulfonic acid is highly corrosive, and a glass syringe must be used for this operation. Plastic syringes are rapidly destroyed by trifluoromethanesulfonic acid , leading to safety hazards if used for this procedure.

8. The reaction of dicyclohexylborane and trifluoromethanesulfonic acid is highly exothermic. On one occasion, the checkers cooled the reaction in an ice bath during the addition period, with no effect on product yield. The submitter reports that he once experienced a sudden vigorous reaction under cooling conditions, probably due to accumulation of unreacted triflic acid. It thus appears safer to add the acid at room temperature, slowly, so that it reacts immediately.

9. The submitter obtained a colorless solution of boron triflate, but the checkers observed development of a yellow-orange color upon addition of triflic acid. Regardless of the color, the triflate solution could be used without a decrease in yields.

10. The small semi-solid yellow layer (about 2 mL) was left behind.

11. The rotary evaporator was back-flushed with dry N₂, and it is recommended that a drying column be inserted between the evaporator and the water aspirator.

12. Dicyclohexylboron trifluoromethanesulfonate exhibited the following spectroscopic properties: ¹H NMR (400 MHz, CDCl₃) δ: 67 (m, 10 H), 1.19 (m, 12 H) ; ¹³C NMR (100 MHz, CDCl₃) δ: 118.3 (q, J = 316), 30.5, 26.9, 26.6, 26.5 ; ¹¹B NMR (115 MHz, hexane/C₆D₆: δ relative to BF₃:Et₂O) δ 59.2 (br s) ; lit.^{2b} ¹¹B NMR δ 59.6 (br s) .

13. The submitter obtained the product in 89% yield (one crop) by using this crystallization procedure.

14. An alternative isolation procedure follows. When the reaction between dicyclohexylborane and trifluoromethanesulfonic acid was complete, the liquid layer was transferred via cannula to a tared, graduated cylinder, the top of which had been modified with a stopcock-equipped syringe inlet and a ground glass joint. This flask was directly attached to a rotary evaporator (Note 10) for removal of solvent. The resulting orange-yellow oil was dried under high vacuum with an auxiliary cold trap in order to obtain an accurate weight of the product, which solidified into a solid mass (23.2 g, 81% yield). This material was dissolved in hexane to give a 1 M solution that was stored in a refrigerator. Upon cold storage, dicyclohexylboron trifluoromethanesulfonate crystallizes from solution, but the crystals easily redissolve when the solution is stirred at room temperature before use. Reagent solutions prepared in this way gave excellent results in the aldol reaction, p. 116.

15. A stock solution of dicyclohexylboron trifluoromethanesulfonate in hexane is reasonably stable, if stored at ≈4°C under nitrogen. It may be purified by storing the hexane solution at -20°C, collecting the crystals that form, and redissolving this material in a calculated amount of dry hexane to give a 1 M solution.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory," National Academy Press; Washington, DC, 1995.

3. Discussion

Dialkylboron trifluoromethanesulfonates (triflates) are particularly useful reagents for the preparation of boron enolates from carbonyl compounds, including ketones, thioesters and acyloxazolidinones.⁴ Recently, the combination of dicyclohexylboron trifluoromethanesulfonate and triethylamine was found to effect the enolization of carboxylic esters.⁵ The boron-mediated asymmetric aldol reaction of carboxylic esters is particularly useful for the construction of anti β-hydroxy-α-methyl

carbonyl units.⁶ The present procedure is a slight modification of that reported by Brown, et al.²

References and Notes

1. Venture Laboratory, Kyoto Institute of Technology, Matsugasaki, Kyoto, 606-8585, Japan.
 2. (a) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975, p 28; (b) Brown, H. C.; Ganesan, K.; Dhar, R. K. *J. Org. Chem.* **1993**, *58*, 147.
 3. Soderquist, J. A.; Negron, A. *Org.Synth., Col. Vol. IX* **1998**, 95.
 4. See, eg. (a) Kim, B. M.; Williams, S. F.; Masamune, S. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 2 (Heathcock, C. H., Ed.), Chapter 1.7, p 239; (b) Cowden, C. J.; Paterson, I. *Org. React.* **1997**, *51*, 1.
 5. Abiko, A.; Liu, J.-F.; Masamune, S. *J. Org. Chem.* **1996**, *61*, 2590.
 6. Abiko, A.; Liu, J.-F.; Masamune, S. *J. Am. Chem. Soc.* **1997**, *119*, 2586. See the procedure for the anti-selective asymmetric aldol reaction of carboxylic esters, p. 116.
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Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Dicyclohexylboron trifluoromethanesulfonate:
Methanesulfonic acid, trifluoro-, anhydride with
dicyclohexylborinic acid (13); (145412-54-0)

Borane- dimethyl sulfide complex:
Methyl sulfide, compd. with
borane (1:1);
Borane, compd. with
thiobis[methane] (1:1); (13292-87-0)

Cyclohexene (8,9); (110-83-8)

Dicyclohexylborane:
Borane, dicyclohexyl- (8,9); (1568-65-6)

Trifluoromethanesulfonic acid: HIGHLY CORROSIVE:
Methanesulfonic acid, trifluoro- (8,9); (1493-13-6)