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Working with Hazardous Chemicals

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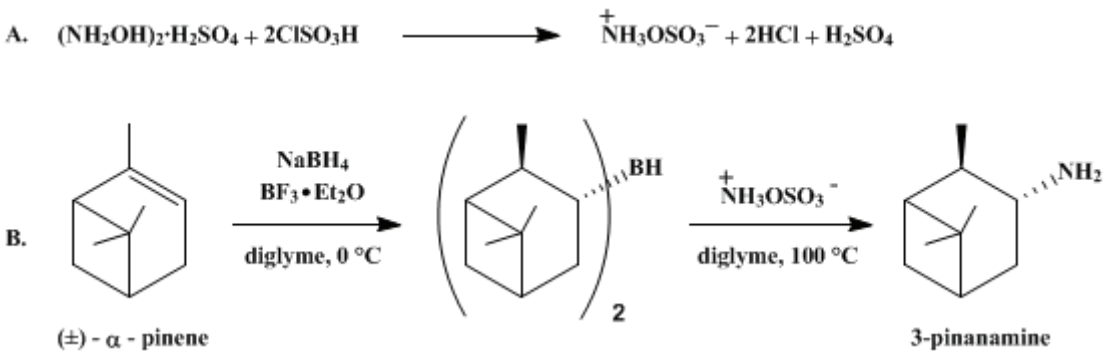
BORANES IN FUNCTIONALIZATION OF OLEFINS TO AMINES: 3-PINANAMINE

[Bicyclo[3.1.1]heptan-3-amine, 2,6,6-trimethyl-]



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1. Procedure

A. *Hydroxylamine-O-sulfonic acid* (**1**). A 500-ml., three-necked, round-bottomed flask is fitted with a mechanical stirrer, dropping funnel, and calcium chloride drying tube. Finely powdered hydroxylamine sulfate (26.0 g., 0.158 mole) (Note 1) is placed in the flask, and 60 ml. (107 g., 0.92 mole) of chlorosulfonic acid (Note 1) is added dropwise over 20 minutes with vigorous stirring (Note 2). After the addition is complete, the flask, with stirring, is placed in a 100° oil bath for 5 minutes. The pasty mixture is cooled to room temperature, and the flask is placed in an ice bath. To the stirred mixture 200 ml. of diethyl ether is slowly added over 20–30 minutes (Note 3). During the ether addition, the pasty contents change to a colorless powder which is collected by suction on a Büchner funnel. The powder is washed with 300 ml. of tetrahydrofuran, then with 200 ml. of ether. The product **1**, after drying, weighs 34–35 g. (95–97%). Iodometric titration shows the product is 96–99% pure (Note 4) and adequate for the following reaction.

B. 3-*Pinanamine* (**3**). A 1000-ml., three-necked, round-bottomed flask is fitted with a gas-inlet tube, a reflux condenser connected to a mineral oil bubbler, and a sealed mechanical stirrer. The system is flamed with a Bunsen burner while being flushed with dry nitrogen. The reaction vessel is then cooled under a nitrogen stream in an ice bath while a slight positive pressure of nitrogen is maintained. A solution of 3.12 g. (0.0824 mole) of sodium borohydride (Note 5) in 100 ml. of diglyme (Note 6) is added to the flask, followed by 27.25 g. (0.2004 mole) of (±)-α-pinene (Note 7). Hydroboration is achieved by dropwise addition of 15.6 g. (0.110 mole) of boron trifluoride diethyl etherate (Note 8) over a 15-minute period. Di-3-pinanylborane (**2**) precipitates as a white solid. The ice bath is removed, and the reaction mixture is stirred at room temperature for 1 hour. Hydroxylamine-*O*-sulfonic acid (**1**) (24.9 g., 0.220 mole) in 100 ml. of diglyme is added dropwise to the mixture over a 5-minute period (Note 9). The mixture is then heated in a 100° oil bath for 3 hours. The mixture is cooled to room temperature, and 80 ml. of concentrated hydrochloric acid is added over a 5-minute period. The mixture is poured into 800 ml. of water and extracted with two 100-ml. portions of ether. The ether layers are discarded, and the aqueous layer is made alkaline with sodium hydroxide pellets (60–65 g. is needed). The aqueous layer is extracted with two 100-ml. portions of ether, the combined ether extracts are dried over anhydrous sodium sulfate, and the drying agent is removed by filtration. The filtrate is transferred to a 500-ml. ice-cooled flask fitted with a magnetic stirring bar. A solution of 85–88% phosphoric acid (12 g., 0.10 mole) in 100 ml. of ethanol is added to the flask over 10 minutes with stirring. The precipitated colorless crystals are collected with suction on a Büchner funnel, and the salt is suspended in 300 ml. of hot water contained in a 1-l. flask. The mixture is heated and magnetically stirred in a 120–130° oil bath

until all the salt has dissolved (*ca.* 20–30 minutes) then quickly filtered with suction. Pure phosphate salt immediately precipitates as colorless plates, which are collected on a Büchner funnel and dried in a desiccator. The yield is 16.6 g. (33.1%). A second crop of 4.4 g. can be obtained by concentrating the mother liquor to about half its original volume. The total yield of pure phosphate salt is 21.0 g. (41.8%), m.p. 275–280° (dec.) (Note 10). The salt is easily converted to free amine **3** by the following procedure: 10 g. (0.040 mole) of the salt is dissolved in 40 ml. of aqueous 3 *M* sodium hydroxide and extracted with two 50-ml. portions of ether. The combined extracts are dried over anhydrous sodium sulfate, the drying agent is removed by filtration, and the solvent is removed under reduced pressure with a rotary evaporator. The residual oil is distilled, giving 5.9 g. (93% from phosphate salt) of amine **3** as a colorless liquid, b.p. 83° (13 mm.) (Note 11).

2. Notes

1. Commercial hydroxylamine sulfate and chlorosulfonic acid, obtained from Eastman Kodak Company, were used directly. The checkers found that commercially available hydroxylamine-*O*-sulfonic acid is sometimes of low purity; therefore, the use of freshly prepared reagent is recommended.
2. Hydrogen chloride gas is evolved during the addition. The reaction should be carried out in a hood, and an aqueous base scrubber is recommended.
3. Rapid addition of the ether must be avoided because of its high reactivity with chlorosulfonic acid.
4. Iodometric titration was carried out as follows: About 100 mg. of hydroxylamine-*O*-sulfonic acid was exactly weighed and dissolved in 20 ml. of distilled water. Sulfuric acid (10 ml. of 10% solution) and 1 ml. of saturated potassium iodide solution were then added. After the solution was allowed to stand for 1 hour, liberated iodine was titrated with 0.1 *N* sodium thiosulfate solution until the iodine color disappeared. The following stoichiometric relation was used: 0.1 *N* $Na_2S_2O_3$ (1 ml.) = 5.66 mg.

. Hydroxylamine-*O*-sulfonic acid should be stored in tightly sealed bottles in a refrigerator.
5. Commercial sodium borohydride was obtained from Ventron Corporation and used directly.
6. Commercial diglyme (dimethyl ether of diethylene glycol) was obtained from Ansul Chemical Company, Marinette, Wisconsin, and purified by distillation from lithium aluminum hydride at 62–63° (15 mm.) [*Org. Synth.*, **Coll. Vol. 6**, 719 (1988)].
7. (±)-α-Pinene, b.p. 54° (22 mm.), was obtained from Aldrich Chemical Company, Inc., and distilled before use.
8. Commercial boron trifluoride etherate, b.p. 46° (10 mm.), available from Matheson, Coleman and Bell, was distilled from calcium hydride before use.
9. *Caution! Since (±)-α-pinene is hydroborated to the dialkylborane state (R_2BH), a large amount of hydrogen is evolved on addition of hydroxylamine-O-sulfonic acid. Consequently, the addition should be carried out dropwise and adequate ventilation should be provided.*
10. The phosphate salt has the empirical formula $C_{10}H_{19}N{\cdot}H_3PO_4$.
11. The product showed one peak on GC (3% SE-30, 70°C).

3. Discussion

Hydroxylamine-*O*-sulfonic acid can also be prepared from hydroxylamine sulfate and 30% fuming sulfuric acid (oleum).[2] The present procedure is essentially that of F. Sommer *et al.*[3]

The hydroboration–amination sequence in diglyme is a general procedure for the conversion of olefins to primary amines without rearrangement and with predictable stereochemistry.[4] An alternative procedure, using tetrahydrofuran as solvent and either hydroxylamine-*O*-sulfonic acid or chloramine, can be applied to terminal olefins and relatively unhindered internal and alicyclic olefins.[5] *O*-Mesitylenesulfonylhydroxylamine also gave desired amines in comparable yield.[6] Alternative procedures for the hydroboration of olefins use commercially available solutions of diborane in tetrahydrofuran[7] or dimethylsulfide.[8]

Olefins may be converted to primary amines by the Ritter reaction[9] or by reaction with mercury(II) nitrate in acetonitrile.[10] In both cases regiospecificity for the formal addition of ammonia across the

double bond is opposite to that observed in the hydroboration–amination sequence.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 7, 254

References and Notes

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

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrogen chloride,
hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

ether,
diethyl ether (60-29-7)

hydrogen (1333-74-0)

acetonitrile (75-05-8)

sodium hydroxide (1310-73-2)

chlorosulfonic acid (7790-94-5)

sodium sulfate (7757-82-6)

potassium iodide (7681-11-0)

sodium thiosulfate (7772-98-7)

nitrogen (7727-37-9)

iodine (7553-56-2)

phosphoric acid (7664-38-2)

hydroxylamine sulfate (10046-00-1)

mercury(II) nitrate

dimethylsulfide (75-18-3)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

chloramine (10599-90-3)

boron trifluoride etherate,
boron trifluoride diethyl etherate (109-63-7)

calcium hydride (7789-78-8)

diglyme,
dimethyl ether of diethylene glycol (111-96-6)

sodium borohydride (16940-66-2)

Hydroxylamine-O-sulfonic acid (2950-43-8)

3-Pinanamine,
Bicyclo[3.1.1]heptan-3-amine, 2,6,6-trimethyl- (17371-27-6)

(±)-α-pinene (7785-70-8)

Di-3-pinanylborane (21947-87-5)

O-Mesitylenesulfonylhydroxylamine