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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

**KETONES AND ALCOHOLS FROM ORGANOBORANES: PHENYL HEPTYL KETONE, 1-HEXANOL, AND 1-OCTANOL**

[1-Octanone, 1-phenyl-]

A. \( n-C_6H_9CH\equivCH + BH_3 \rightarrow (C_6H_{13})_3B \)

B. \( (C_6H_{13})_3B + N_2\rightarrow PhCH=CH + H_2O_2, \Delta \rightarrow \)

C. \( (C_6H_{13})_3B \rightarrow NaOH \rightarrow n-C_6H_{12}OH \)

D. \( \text{BH}_3, \text{THF} \rightarrow \)

E. \( [\text{CH}_3]_2\text{CHCH(CH}_3)_2\text{BH} \rightarrow [\text{CH}_3]_2\text{CHCH(CH}_3)_2\text{B} \rightarrow n-C_8H_{17} \)

F. \( [\text{CH}_3]_2\text{CHCH(CH}_3)_2\text{B} \rightarrow n-C_8H_{17} \rightarrow \text{NaOH}, H_2O_2 \rightarrow \rightarrow n-C_8H_{17}OH \)

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1. Procedure

A. **Trihexylborane.** A dry, 1-l., three-necked flask is equipped with a magnetic stirring bar, a reflux condenser fitted with a drying tube, a pressure-equalizing dropping funnel to which is attached a rubber septum cap, and a three-way, parallel sidearm connecting tube fitted with a thermometer and an inlet tube (containing a stopcock), permitting introduction of a dry nitrogen atmosphere. The apparatus is flushed with nitrogen and charged with 27.8 g. (0.331 mole) of 1-hexene (Note 1) and 150 ml. of anhydrous tetrahydrofuran (Note 2) with a hypodermic syringe, and 103 ml. (0.110 mole) of a 1.07 \( M \) solution of borane in tetrahydrofuran (Note 3) is added dropwise over a 20-minute period to the stirred solution, while the reaction temperature is maintained below ca. 20° with an ice bath. After the addition, the reaction mixture is stirred for an additional one hour at room temperature. The resulting solution of trihexylborane (Note 4) is ready for use in the next step.

B. **Phenyl heptyl ketone.** To the solution prepared in Section A. is added 18 ml. (1.0 mole) of water. The nitrogen flow is ceased, and the drying tube is quickly replaced with a stopcock attached with
Tygon tubing, to a gas-measuring tube. A solution of 14.6 g. (0.100 mole) of diazoacetophenone (Note 5) in 125 ml. of tetrahydrofuran is added to the stirred solution over a period of one hour. After the addition is complete, the mixture is stirred vigorously for one hour at room temperature, then heated to reflux for one hour. The resulting mixture is cooled to approximately 25° with an ice bath (Note 6), (Note 7), and (Note 8). A solution of 73 ml. (0.2 mole) of 3 N sodium acetate solution is added, followed by the dropwise addition of 23 ml. (0.22 mole) of 30% hydrogen peroxide, maintaining the reaction temperature below ca. 20° (ice-cooling). The cooling bath is then removed, and the mixture is stirred at room temperature for one hour.

The resulting mixture is saturated with sodium chloride. The organic phase is separated, washed with three 50-ml. portions of saturated brine solution, dried over sodium sulfate, and concentrated on a rotary evaporator. Distillation of the residue through a 7-cm. Vigreux column separates 15.34–15.99 g. (75–80%) of phenyl heptyl ketone, b.p. 118–120° (0.60 mm.) \( \eta^D_{20} 1.5034 \) (Note 9).

C. 1-Hexanol. To a solution of trihexylborane in a 500-ml. three-necked flask [prepared from 25.3 g. (0.301 mole) of 1-hexane in 150 ml. of tetrahydrofuran and 84 ml. of a 1.20 M solution of borane in tetrahydrofuran, as described in Section A] is added 34 ml. (0.1 mole) of a 3 N solution of sodium hydroxide. This is followed by the dropwise addition of 36 ml. (0.35 mole) of 30% hydrogen peroxide at a rate such that the reaction temperature is maintained at approximately 35° (water bath). After being stirred at room temperature for one hour, the mixture is poured into 100 ml. of water. The organic phase is separated, and the aqueous phase is extracted with 50 ml. of diethyl ether. The combined organic extracts are washed with three 50-ml. portions of saturated brine solution and dried over Drierite. After the bulk of the solvent is removed by distillation, the residue is fractionated with a 24-in., Teflon spinning band column (Note 10), yielding 7.7–8.2 g. (25.1–26.7%) of 1-hexanol of 95% purity, b.p. 145–153° and 10.1–15.4 g. (33.3–50.3%) of pure 1-hexanol, b.p. 153–155° (Note 11). The total yield of material with >95% purity is 58.4–77%.

D. Bis(3-methyl-2-butyl)borane (disiamylborane). A dry, 500-ml., three-necked flask is equipped as described in Section A. The apparatus is flushed with nitrogen, and the flask is charged with 92 ml. (0.11 mole) of a 1.2 M solution of borane in tetrahydrofuran. The flask is cooled with an ice bath before a solution of 15.4 g. (0.220 mole) of 2-methyl-2-butene (Note 12) in 40 ml. of anhydrous tetrahydrofuran is added to the stirred solution over a 30-minute period. After the addition is complete, the reaction mixture is kept below ca. 10° for 2 hours. The resulting solution is used directly in the next step.

E. Addition of disiamylborane to 1-octene. To the solution prepared in Section D is added a solution of 11.2 g. (0.100 mole) of 1-octene (Note 13) in 20 ml. of anhydrous tetrahydrofuran over a 30-minute period, while the reaction temperature is maintained below ca. 20°. The ice bath is removed and stirring is continued for one hour at room temperature.

F. 1-Octanol. The stirred solution prepared in Section E is cooled below ca. 10° with an ice bath, and a solution of 34 ml. (0.1 mole) of 3 N sodium hydroxide is introduced. This is followed by the dropwise addition of 36 ml. (0.35 mole) of 30% hydrogen peroxide, added at a rate such that the reaction temperature is maintained between 30–35°. After the addition is complete, the mixture is stirred at room temperature for 1.5 hours. The reaction mixture is then extracted with 100 ml. of ether. The ether extract is washed with four 100-ml. portions of water and dried over Drierite. After removal of solvent on a rotary evaporator, the residue is distilled through a 3-cm. Vigreux column, giving, as a forerun, 9.6–10.5 g. of 3-methyl-2-butanol, b.p. 110–115°, followed by 8.5–9.1 g. (65–70%) of 1-octanol, b.p. 182–186° (Note 14).

2. Notes

1. 1-Hexene (99%), purchased from Aldrich Chemical Company, Inc., was stored over molecular sieves and distilled prior to use.
2. Commercial tetrahydrofuran, purchased from British Drug House (Canada) Ltd. or Fisher Scientific Company, was refluxed over sodium metal, distilled from sodium metal, then redistilled from lithium aluminum hydride under a nitrogen atmosphere. [See Org. Synth., Coll. Vol. 5, 976 (1973) for warning regarding the purification of tetrahydrofuran.]
3. A commercial one molar solution of borane in tetrahydrofuran, obtained from Alfa Inorganics, Inc., was standardized by measuring the amount of hydrogen evolved on titration with 40% aqueous ethylene glycol.

4. The trihexylborane solution contains approximately 94% primary and 6% secondary boron-bound alkyl groups.3,4

5. Diazocetophenone was prepared as described in Org. Synth., Coll. Vol. 6, 386 (1988).

6. Approximately 95% of the theoretical amount of nitrogen is evolved.

7. GC indicates a 92% yield of product. Using a 10 ft. by 0.25 in. column packed with 20% NPGSE (Neopentyl Glycol Sebacate Ester) suspended on Chromosorb W heated to 235° and a helium flow rate of 60 ml per minute, the submitters found a retention time of 21 minutes for phenyl heptyl ketone.

8. Distillation of the product from the crude reaction mixture at this stage gives somewhat lower yields. Therefore, residual organoboranes are oxidized prior to isolation of product.

9. 1-Hexanol, 18.5–20.3 g. (78–86%), boiling at approximately 35° (0.75 mm.), is obtained as a forerun. The checkers found that two distillations were required to give a product of >95% purity.

10. A forerun of approximately 1.0 g., b.p. 135–145°, comprised largely of 2-hexanol (75%), is discarded. The submitters used a stainless-steel spinning band column with equivalent results.

11. The product may be analyzed by use of a GC column packed with 20% SF-96 suspended on Chromosorb WAW, 5 ft. by 0.25 in., operated at 105°. Using a helium flow rate of 60 ml per minute, the submitters found a retention time of 4 minutes.

12. Commercial 2-methyl-2-butene (99%), purchased from Chemical Samples Company, 4692 Kenny Road, Columbus, Ohio 43220, was used as received.

13. 1-Octene (97%), b.p. 122–123°, purchased from the Aldrich Chemical Company, Inc., was stored over molecular sieves and distilled prior to use.

14. The product may be analyzed by using a GC column packed with 20% SF-96 suspended on Chromosorb WAW, 5 ft. by 0.25 in., operated at 140°. Using a helium flow rate of 60 ml per minute the submitters found a retention time of 3.5 minutes.

3. Discussion

Phenyl heptyl ketone has been prepared by the Friedel-Crafts acylation of benzene with octanoyl chloride.5 It is also a product of the thermal decomposition of the mixed iron(II) salts of benzoic and octanoic acids.6

The present preparation of phenyl heptyl ketone illustrates the formation of a homologated ketone from the reaction of a trialkylborane with an α-diazoketone. It is representative of a fairly general reaction between an organoborane and a stabilized diazo compound, as illustrated in the accompanying equation, yielding the corresponding ketone,7 diketone,8 nitrile,9 ester,9 or aldehyde.10

\[
\text{R}_3\text{B} + \text{N}_2\text{CH}_3 \xrightarrow{\text{H}_2\text{O}} \text{RCH}_2\text{A}
\]

\[\text{A=COCH}_3, \text{COC}_6\text{H}_5, \text{CO(CH}_2)_2\text{H}_5, \text{CHO}\]

The extent of reaction is conveniently monitored by measuring the quantity of nitrogen evolved. Organoboranes derived from terminal olefins react readily (>90% gas evolution) at room temperature or below, whereas more highly hindered organoboranes react more sluggishly (ca. 3–6 hours of reflux) to complete the liberation of nitrogen.

The enol borinate intermediates are rapidly hydrolyzed to product in the presence of water.10,11 Since neither the organoborane nor diazo compound reacts with water appreciably under the experimental conditions, hydrolysis is conveniently accomplished in situ by adding water to the organoborane solution prior to the addition of diazo substrate. Although the product may be isolated from the crude mixture by extraction and distillation, an oxidation step (to convert residual organic boron-containing material to boric acid) is employed, since it gives somewhat higher isolated yields.

An adaptation of the procedure, employing deuterium oxide as the hydrolytic medium, permits the synthesis of α-deuterio ketones and esters in high isotopic purity. a,a-Dideuterio ketones and esters are also produced in high purity using the appropriate α-deuteriodiazocarbonyl precursor.12
A useful extension of the facile, in situ hydrolysis is the alkylation of cyclic α-diazo ketones\(^{13}\) \((n = 3,4,5,6)\). This adaptation obviates the necessity of the several separate (yield-lowering) steps required for the removal of activating or blocking groups by other alkylation methods.\(^{14}\)

The principal disadvantage of this procedure is that only one alkyl group of the trialkylborane is constructively utilized. The reaction is also sensitive to steric factors. Although yields are excellent for terminal olefins, the reaction becomes more sluggish and yields of ketone decrease progressively as steric effects in the trialkylborane are increased. The method is of limited utility for rare olefins. However, the overall simplicity, mild reaction conditions, and absence of any isomeric contaminants recommend the method for reactions involving rarer diazocarbonyl substrates.

Apart from the oxidation of trihexylborane,\(^{15}\) 1-hexanol has been prepared by a previous *Organic Syntheses*\(^{16}\) procedure involving the reaction of ethylene oxide with \(n\)-butylmagnesium bromide; alternate methods of synthesis are reviewed therein.

The present preparation illustrates the hydroboration\(^{17}\) of a terminal olefin and the oxidation of the resultant trialkylborane.

The hydroboration of an olefin involves a cis addition of a boron–hydrogen bond to an alkene linkage, and for unsymmetric olefins occurs in an anti-Markownikoff fashion. 1-Alkenes and simple 1,2-disubstituted olefins undergo rapid conversion to the corresponding trialkylborane, whereas addition of diborane to tri- and tetrasubstituted olefins may be conveniently terminated at the respective di- and monoalkylborane stage. 1-Alkenes yield trialkylboranes in which there is a preponderant (approximately 94%) addition of the boron atom to the terminal carbon.\(^{3,4}\)

The oxidation of a trialkylborane may be effected by perbenzoic acid or by aqueous hydrogen peroxide in the presence of alkali.\(^{19}\) A detailed systematic study of the reaction parameters (oxidation temperature, base concentration, hydrogen peroxide concentration) of the latter method has led to the development\(^{3}\) of a standard and common procedure for oxidising organoboranes, and is illustrated in the present procedure.

The oxidation step occurs with retention of configuration of the carbon atom undergoing migration. The mechanism is believed to proceed as illustrated in the following equation.\(^{3}\) As a result, the sequence involving the hydroboration of an olefin followed by treatment with sodium hydroxide–hydrogen peroxide constitutes a useful device for effecting the overall anti-Markownikoff cis hydration of an olefin.

The principal disadvantage of this procedure resides in its application to terminal olefins. Since the hydroboration step produces ca. 94% primary boron-bound alkyl groups, the maximum purity of primary carbinol is obviously limited to ca. 94%. Isolation of primary alcohol free of the contaminant secondary alcohol requires a tedious, yield-lowering fractionation procedure. This difficulty may be circumvented by employing a more selective hydroboring reagent, disiamylborane, as illustrated in the synthesis of 1-octanol.
1-Octanol has previously been prepared from ethyl caprylate by catalytic hydrogenolysis, and by the Bouveault-Blanc method using sodium and alcohol in toluene. Other preparative methods include the reaction between \( n \)-hexylmagnesium bromide and ethylene oxide, and the oxidation of trioctylborane.

The hydroboration of a trisubstituted olefin, exemplified by the reaction of 2-methyl-2-butene with diborane, is conveniently stopped at the dialkylborane stage, producing disiamylborane. As a result of its rather large steric requirements this reagent selectively hydroborates terminal olefins, placing ca. 99% of the boron atom on the terminal carbon. Consequently, oxidation produces essentially homogeneous 1-alkanol. This procedure is the method of choice for converting terminal olefins to primary alcohols without the accompanying formation of isomers.

The advantages of a hydroboration-oxidation synthesis of alcohols are simplicity of procedure, relatively mild reaction conditions, high overall yields, absence of skeletal rearrangements, and production of a carbinol in which there is an overall cis addition of water to a double bond in an anti-Markownikoff sense.

References and Notes

1. Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G ZGZ.
2. This trivial term, which now finds common usage, was coined as a contraction of the only sec-isoamyl structure possible, \((\text{CH}_3)_2\text{CHCH}(\text{CH}_3)\). 3
17. Although the term hydroboration is most commonly employed\textsuperscript{3,4,14} to denote the addition of a boron–hydrogen linkage to carbon–carbon multiple bonds, it has also been used "for the two-step oxidative process to distinguish it from the process of reduction involving H-B addition and protonolysis."\textsuperscript{18}

Appendix

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

Drierite
brine
diborane
disiamylborane
1-hexane
Bis(3-methyl-2-butyl)borane (disiamylborane)

Benzene (71-43-2)
ether,
diethyl ether (60-29-7)
sodium acetate (127-09-3)
hydrogen (1333-74-0)
sodium hydroxide (1310-73-2)
sodium chloride (7647-14-5)
sodium sulfate (7757-82-6)
nitrogen (7727-37-9)
toluene (108-88-3)
sodium (13966-32-0)

Ethylene oxide (75-21-8)

ethylene glycol (107-21-1)

hydrogen peroxide (7722-84-1)

1-Hexanol (111-27-3)

n-butylmagnesium bromide (693-03-8)

boric acid (10043-35-3)

borane (7440-42-8)

1-Octanol (111-87-5)

3-methyl-2-butanol (598-75-4)

2-methyl-2-butene (513-35-9)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

ethyl caprylate (106-32-1)

1-hexene (592-41-6)

Diazooacetophenone (3282-32-4)

helium (7440-59-7)

Perbenzoic acid (93-59-4)

1-octene (111-66-0)

deuterium oxide (7789-20-0)

Phenyl heptyl ketone, 1-Octanone, 1-phenyl- (1674-37-9)

Trihexylborane

2-hexanol (626-93-7)

octanoyl chloride (111-64-8)

trioctylborane