



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

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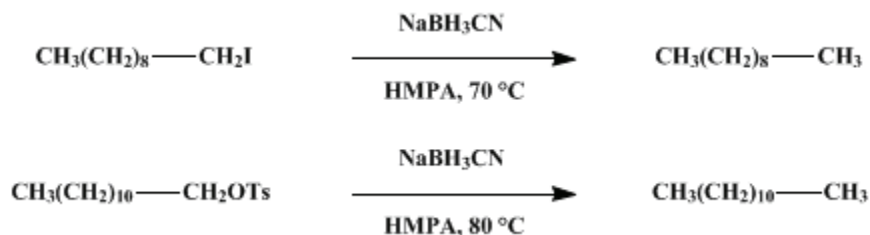
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.376 (1988); Vol. 53, p.107 (1973).

REDUCTION OF ALKYL HALIDES AND TOSYLATES WITH SODIUM CYANOBOROHYDRIDE IN HEXAMETHYLPHOSPHORIC TRIAMIDE (HMPA):

A. 1-IODODECANE TO *n*-DECANE B. 1-DODECYL TOSYLATE TO *n*-DODECANE



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Checked by Ronald I. Trust and Robert E. Ireland.

1. Procedure

Caution! Hexamethylphosphoric triamide (HMPA) vapors have been reported to cause cancer in rats.² All operations with hexamethylphosphoric triamide should be performed in a good hood, and care should be taken to keep the liquid off the skin.

A. *n-Decane*. A dry, 100-ml., three-necked flask equipped with a stirring bar, a thermometer, and a condenser protected with a drying tube is charged with 25 ml. of hexamethylphosphoric triamide (HMPA) (Note 1), 1-iododecane (2.7 g., 0.010 mole) (Note 2) and sodium cyanoborohydride (0.943 g., 0.0157 mole) (Note 3). The solution is stirred at 70° for 2 hours, diluted with 25 ml. of water, and extracted with three 30-ml. portions of diethyl ether. The combined extracts are washed twice with water and dried over anhydrous magnesium sulfate. The solvent is removed by distillation on a steam bath through a 12-in. vacuum-jacketed Vigreux column (Note 4). The residue is distilled at reduced pressure in a short-path apparatus (*Caution! foaming*), yielding 1.25–1.29 g. (88–90%) (Note 5), (Note 6) of *n-decane*, b.p. 68–70° (14 mm.); n_D^{20} 1.4122, n_D^{25} 1.4085 (lit.,³ n_D^{25} 1.4097 (Note 7).

B. *n-Dodecane*. A dry, 200-ml., three-necked flask equipped exactly as described in Section A is charged with 50 ml. of hexamethylphosphoric triamide (HMPA), 1-dodecyl tosylate (6.80 g., 0.0201 mole) (Note 8), and sodium cyanoborohydride (5.02 g., 0.0797 mole) (Note 3). The solution is stirred at 80° for 12 hours (Note 9), diluted with 50 ml. of water, and extracted with three 60-ml. portions of hexane. The hexane solution is washed twice with water, dried over anhydrous magnesium sulfate, and concentrated with a rotary evaporator. Distillation of the residue through a short-path apparatus (Note 5) (*Caution! foaming*) affords 2.49–2.64 g. (73–78%) of *n-dodecane*, b.p. 79–81°; (3.75 mm.) n_D^{24} 1.4217 (lit.,⁴ n_D^{20} 1.4219) (Note 7).

2. Notes

- Commercial hexamethylphosphoric triamide was distilled from calcium hydride and stored over 13X molecular sieves (Linde).
- Commercial 1-iododecane (Eastman Organic Chemicals) was filtered through activated charcoal and distilled before use.
- Sodium cyanoborohydride was used as received from Aldrich Chemical Company, Inc., or Alfa Products, Thiokol/Ventron Division. No purification is necessary. Tan or brown material may be purified by the method of Purcell⁵ or of Borch.⁵
- If a hexane workup is used, and the solvent is removed with a rotary evaporator, considerable loss of

product results from codistillation with the [hexane](#). This should not present a significant problem when higher boiling materials are produced.

5. The condenser was cooled with an [ethylene glycol](#)–water mixture at -5° , and the receiver was cooled to -10° in an ice–salt bath.

6. Considerable mechanical loss was observed because of inability to distill the last portions of the product at 14 mm. To avoid this problem, the pressure was reduced near the end of the distillation to *ca.* 5 mm. This did not affect the purity of the product ([\(Note 7\)](#)).

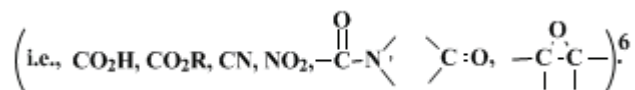
7. Both products showed IR and ^1H NMR spectra identical to those of authentic samples, and no side products were detected by GC or ^1H NMR.

8. [Dodecyl tosylate](#) was prepared from [1-dodecanol](#) by the procedure in *Org. Synth.*, **Coll. Vol. 3**, 366 (1955). Crystallization from a dried ([magnesium sulfate](#)) solution in light petroleum ether afforded white needles, m.p. 27.5–28.5 $^{\circ}$.

9. The large excess of [sodium cyanoborohydride](#) is recommended for the reduction of tosylates. Use of reduced molar excesses led to substantially lower yields. For example, a 3:1 [cyanoborohydride](#) to [tosylate](#) ratio afforded less than 60% yield of product at 80° for 5 hours, while a 1.5:1 excess gave only 52% yield at 70° for 8 hours.

3. Discussion

These preparations illustrate the use of [sodium cyanoborohydride](#) in [hexamethylphosphoric triamide](#) as an effective, selective, and convenient procedure for the reduction of alkyl halides and tosylates, and are essentially the same as previously described.⁶ The very mild reducing ability of [sodium cyanoborohydride](#) makes the method particularly valuable when other functional groups are present in the molecule. In addition, alkene side-products are seldom encountered, contrary to the situation with [lithium aluminum hydride](#)⁷ or [sodium borohydride](#) in aqueous diglyme.⁸ The combination of [sodium borohydride](#) in polar aprotic solvents is also effective for halide and [tosylate](#) removal,⁹ although it is less selective.



References and Notes

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Appendix

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

petroleum ether

diethyl ether (60-29-7)

1-dodecanol (112-53-8)

ethylene glycol (107-21-1)

magnesium sulfate (7487-88-9)

lithium aluminum hydride (16853-85-3)

hexane (110-54-3)

calcium hydride (7789-78-8)

sodium borohydride (16940-66-2)

n-DECANE (124-18-5)

hexamethylphosphoric triamide (680-31-9)

tosylate (104-15-4)

sodium cyanoborohydride (25895-60-7)

cyanoborohydride

1-IODODECANE (2050-77-3)

1-DODECYL TOSYLATE,
Dodecyl tosylate (10157-76-3)

n-DODECANE (112-40-3)