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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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.

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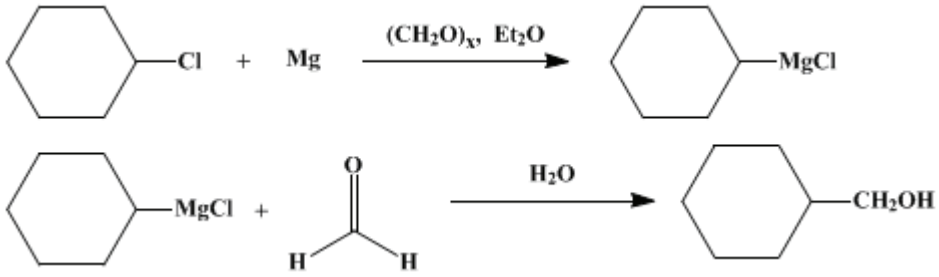
Organic Syntheses, Coll. Vol. 1, p.188 (1941); Vol. 6, p.22 (1926).

CYCLOHEXYLCARBINOL

[Cyclohexanecarbinol]



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1. Procedure

In a dry 1-l. three-necked, round-bottomed flask fitted with a mercury-sealed stirrer, a 500-cc. dropping funnel, and an efficient reflux condenser to the upper end of which a calcium chloride tube is attached, is placed 26.7 g. (1.1 atoms) of magnesium turnings. The reaction requires 450 cc. of ether and 118.5 g. (121 cc., 1 mole) of cyclohexyl chloride (Note 1). About 100 cc. of the ether, 15 cc. of the pure halide, and a crystal of iodine are added to the magnesium. Heat is applied, without stirring, for five to ten minutes after the iodine color has disappeared. When reaction has set in, sufficient ether is added to cover the magnesium while it is stirred, and the remainder of the halide in ether is added in one-half to three-quarters of an hour, the flask being cooled with ice water if necessary. When all the halide has been added, stirring and refluxing are continued fifteen to twenty minutes.

The separatory funnel is now replaced by a wide glass tube (about 12 mm. internal diameter) which reaches almost to, but not below, the surface of the liquid (Note 2). This tube connects directly with a 500-cc. round-bottomed flask containing 50 g. of paraformaldehyde which has been previously dried for two days in a vacuum desiccator over phosphorus pentoxide. This flask contains an inlet tube for admitting dry nitrogen. The stirrer is started (Note 3), and the flask containing the paraformaldehyde is heated in an oil bath to 180–200°. The formaldehyde formed by depolymerization (Note 4) and (Note 5) is carried over into the Grignard reagent by a slow current of dry nitrogen. At the end of about one and three-quarters hours the reaction is complete, as is indicated by a negative color test for Grignard reagent (Note 6).

The reaction mixture is then transferred to a 2-l. wide-necked, round-bottomed flask; 300 g. of cracked ice is added all at once; and the mixture is rapidly agitated until the decomposition is complete (Note 7). Twice the theoretical amount of 30 per cent sulfuric acid is added to dissolve the magnesium hydroxide, and the mixture is then steam-distilled until no more oil is collected (Note 8). The distillate, which amounts to 1500–2500 cc., is saturated with sodium chloride and the ether-alcohol layer separated. The aqueous layer is extracted with two 100-cc. portions of ether and the ether extract added to the ether-alcohol layer. The ether solution is dried over anhydrous potassium carbonate, filtered, and heated carefully on a steam cone until all the ether is distilled. The crude alcohol is warmed one-half hour with 5 g. of freshly dehydrated lime (Note 9). After filtering and washing the lime with a little ether, the ether is distilled, and then the residual alcohol distilled from a Claisen flask (Note 10) under reduced pressure. The carbinol distils at 88–93°/18 mm. (practically all distilling at 91°). The yield is 72.5–78.5 g. (64–69 per cent of the theoretical amount).

2. Notes

1. The cyclohexyl chloride should be pure to insure a prompt reaction with magnesium, using iodine as a catalyst. Reaction between cyclohexyl bromide and magnesium sets in more rapidly than that between

cyclohexyl chloride and magnesium. However, the yield of cyclohexylmagnesium bromide is less than that of cyclohexylmagnesium chloride.[1]
Cyclohexyl chloride can be prepared by heating cyclohexanol, concentrated hydrochloric acid, and anhydrous calcium chloride, with stirring, on a steam bath (W. W. Hartman, private communication).
2. Since a considerable amount of formaldehyde repolymerizes on the walls of the side tube, a wide tube is used to prevent clogging. Clogging by deposition of the reaction product is reduced by having the entry tube about 1 cm. above the surface of the solution.
3. Vigorous stirring is desirable as it materially affects the rate of absorption of the gaseous formaldehyde.
4. The amount of paraformaldehyde used is considerably in excess of 1 mole since it is difficult to tell when the reaction is complete because of repolymerization. For larger runs, the amount of paraformaldehyde need not be increased in direct proportion, as the 20 g. excess used here is sufficient to insure complete reaction in a run of almost any size. An excess of formaldehyde apparently does not decrease the yield provided that the product is steam-distilled from sulfuric acid solution (Note 8) to hydrolyze the acetal.
5. If paraformaldehyde is used directly without depolymerization, the yield is only 40–50 per cent.
6. At the end of about one and one-quarter hours, tests are made at fifteen-minute intervals for the presence of Grignard reagent. The reaction need not be interrupted. About a ½-cc. sample is pipetted out for each test. To this is added an equal volume of a 1 per cent solution of Michler's ketone in dry benzene. The reaction product is then hydrolyzed by the slow addition of 1 cc. of water. The subsequent addition of several drops of a 0.2 per cent solution of iodine in glacial acetic acid develops a characteristic greenish-blue color when Grignard reagent is present. The reaction is complete when no positive test is obtained for the Grignard reagent.[2]
7. The ice must be added all at once so that the mixture stays cold at all times and local overheating does not occur. If this happens, the reaction becomes very vigorous, and the mixture is likely to foam out of the flask.
8. A high-boiling by-product, the cyclohexylcarbinol acetal of formaldehyde, is sometimes obtained, and in particularly large quantities if the steam distillation of the reaction mixture is omitted. The by-product can usually be minimized if twice the amount of 10 per cent sulfuric acid calculated to decompose the Grignard reagent is added to the reaction mixture before steam distillation is carried out. The acetal which may be present is thus hydrolyzed.
If acetal has been isolated, it may best be hydrolyzed by boiling with an equivalent weight of ethyl alcohol and concentrated hydrochloric acid (2 cc. for each 50 cc. of alcohol used) for four or five hours, then distilling off the ethyl alcohol and treating with water.
9. The heating with freshly dehydrated lime not only removes traces of water, but also gives a product which is entirely free from halogen.
10. It is advisable to use a flask with fractionating side arm (p. 130).

3. Discussion

Cyclohexylcarbinol can be prepared by the reduction of ethyl hexahydrobenzoate[3] and of benzyl alcohol,[4] and from cyclohexylmagnesium bromide or chloride with paraformaldehyde.[5]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 186
- Org. Syn. Coll. Vol. 6, 606

References and Notes

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2. Gilman and Schulze, J. Am. Chem. Soc. **47**, 2002 (1925); Gilman and Heck, ibid. **52**, 4949 (1930).
3. Bouveault and Blanc, Compt. rend. **137**, 60 (1903), Ger. pat. 164,294 [Chem. Zentr. II, 1700 (1905)].

4. Adkins and Cramer, J. Am. Chem. Soc. **52**, 4349 (1930).
5. Zelinsky, Bull. soc. chim. (3) **32**, 574 (1904); Sabatier and Mailhe, Compt. rend. **139**, 343 (1904); Freundler, Bull. soc. chim. (3) **35**, 544 (1906); Faworsky and Borgmann, Ber. **40**, 4863 (1907); Hiers and Adams, J. Am. Chem. Soc. **48**, 2385 (1926); Marvel, Blomquist and Vaughn, ibid. **50**, 2810 (1928).

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

halide

Michler's ketone

cyclohexylcarbinol acetal

cyclohexylmagnesium bromide or chloride

ACETAL (105-57-7)

ethyl alcohol,
alcohol (64-17-5)

calcium chloride (10043-52-4)

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

Benzene (71-43-2)

ether (60-29-7)

formaldehyde (50-00-0)

magnesium,
magnesium turnings (7439-95-4)

Cyclohexanol (108-93-0)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

iodine (7553-56-2)

Benzyl alcohol (100-51-6)

cyclohexyl chloride (542-18-7)

cyclohexylmagnesium bromide

Cyclohexyl bromide (108-85-0)

cyclohexylmagnesium chloride

Cyclohexylcarbinol,
Cyclohexanecarbinol (100-49-2)

magnesium hydroxide

ethyl hexahydrobenzoate (3289-28-9)

phosphorus pentoxide (1314-56-3)

paraformaldehyde (30525-89-4)