



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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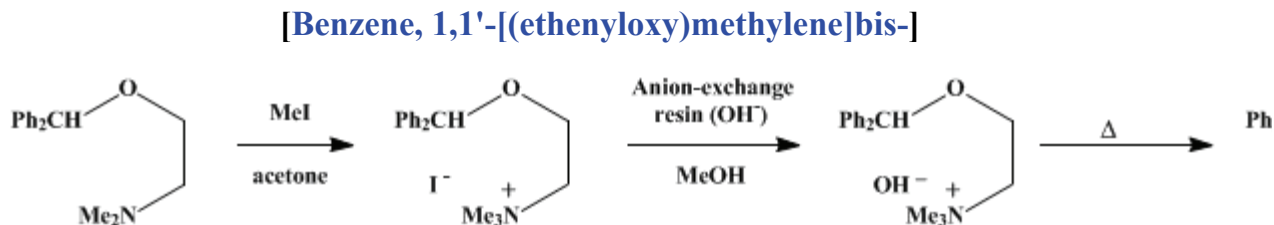
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ALKENES *via* HOFMANN ELIMINATION: USE OF ION-EXCHANGE RESIN FOR PREPARATION OF QUATERNARY AMMONIUM HYDROXIDES: **DIPHENYLMETHYL VINYL ETHER**



1. Procedure

Caution! Methyl iodide, in high concentrations for short periods or in low concentrations for long periods, can cause serious toxic effects in the central nervous system. Accordingly, the American Conference of Governmental Industrial Hygienists² has set 5 p.p.m., a level which cannot be detected by smell, as the highest average concentration in air to which workers should be exposed for long periods. The preparation and use of methyl iodide should always be performed in a well-ventilated fume hood. Since the liquid can be absorbed through the skin, care should be taken to prevent contact.

A 250-ml., three-necked, round-bottomed flask equipped with a sealed mechanical stirrer, a dropping funnel, and a reflux condenser is charged with 13.3 g. (0.0522 mole) of 2-(diphenylmethoxy)-*N,N*-dimethylethylamine (Note 1) and 50 ml. of acetone. The solution is stirred, and 8.1 g. (0.057 mole) of methyl iodide in 15 ml. of acetone is added dropwise over 5 minutes (Note 2). After the addition is complete, the mixture is stirred for 30 minutes, then cooled to 0–10° with an ice bath. The crystalline product is filtered and washed with 15 ml. of acetone and 30 ml. of diethyl ether, yielding 20.0–20.2 g. (97–98%) of colorless, crystalline methiodide, m.p. 194–196°.

An excess (60 g., *ca.* 0.26 equivalent) of anion exchange resin (OH⁻ form, (Note 3)) in a 500-ml. Erlenmeyer flask is stirred with 200 ml. of methanol (Note 4) for 5 minutes. The methanolic slurry of resin is transferred to a 6.5 cm. × 25 cm. chromatography column, using 50–100 ml. of methanol to aid in the transfer. The resin column is washed with 750 ml. of methanol, added gradually so as to maintain about a 1–2.5 cm. solvent head above the upper resin level (Note 5). About two-thirds of the resin slurry is poured from the column (using about 100 ml. of methanol to aid the transfer) into a suspension of 19.9 g. (0.0499 mole) of the methiodide in 50 ml. of methanol (Note 6). The mixture is stirred and heated gently on a water bath, dissolving the crystalline methiodide. The resulting resin suspension is poured onto the column containing the remaining one-third of the resin. Additional methanol (*ca.* 50 ml.) is required to facilitate transferral. The column is eluted with about 500 ml. of methanol until the eluent no longer affords an alkaline reaction to pH paper (Note 7). The methanolic eluent is concentrated under reduced pressure (10–25 mm.), and the residual liquid (Note 8) is gradually heated to 100° under the water-aspirator vacuum. Following completion of thermal decomposition, as evidenced by the end of gas evolution (*ca.* 5–10 minutes), the residue is dissolved in 250 ml. of ether (Note 9). The ether solution is washed with 100 ml. of 0.2 *N* sulfuric acid and 100 ml. of water, dried over anhydrous magnesium sulfate, and filtered. The filtrate is concentrated, and distillation of the residue gives 8.5–9.0 g. (81–86%) of diphenylmethyl vinyl ether as a colorless liquid, b.p. 163–167° (18 mm.), n_D^{25} 1.5716 (Note 10) and (Note 11).

2. Notes

1. The submitters used 2-(diphenylmethoxy)-*N,N*-dimethylethylamine, b.p. 150–165° (2 mm.),³ obtained from Searle Chemicals, Inc., or from the hydrochloride, m.p. 161–162°, which is available commercially from Gane's Chemical Works, Inc., New York, New York, under the generic name, diphenhydramine.
2. The reaction exotherm is just sufficient to cause moderate reflux.
3. A strongly basic, polystyrene, alkyl quaternary amine (hydroxide form) of medium porosity was employed. Research grade Rexyn 201 (OH) (purchased from Fisher Scientific Company) and Amberlite IRA-400 (purchased from Mallinckrodt Chemical Works) were found to be satisfactory. Chloride-form resins must be converted to the hydroxide form before use, as described below (Note 7).
4. It is necessary to wash the resin with methanol prior to packing of the column. If this is not done, swelling of the resin on treatment with the solvent may cause explosion of the column.
5. If the resin was not washed exhaustively with methanol, significant amounts of benzhydrol (α -phenylbenzenemethanol) and diphenylmethyl methyl ether were obtained in the final product.
6. Stirring of the methiodide with the anion exchange resin prior to introduction into the column is necessary, because of the insolubility of this quaternary salt in methanol. For methanol-soluble methiodides, a solution of the salt may be added directly to the methanol-washed resin column.
7. The recovered resin can be reconverted to the hydroxide form by eluting a column of the material with aqueous 10% sodium hydroxide until it is free of halide ion (silver nitrate–nitric acid test), then with water until the eluent is no longer alkaline to pH paper.
8. Heating should be carried out in a 1-l. (oversized) flask because decomposition is accompanied by considerable foaming.
9. A small amount of insoluble material, which is mainly unreacted 2-(diphenylmethoxy)-*N,N*-dimethylethylamine methiodide, can be removed at this point.
10. The product has the following spectral properties; IR (neat) cm^{-1} : 1670, 1200, 770, 710; ^1H NMR (CDCl_3), δ (multiplicity, approx. coupling constant J in Hz., number of protons): 3.97 (d of d, $J_{\text{XY}} = 2$, $J_{\text{AX}} = 7$, 1H), 4.27 (d of d, $J_{\text{XY}} = 2$, $J_{\text{AY}} = 14$, 1H), 5.7 (S, 1H), 6.36 (q, $J_{\text{AX}} = 7$, $J_{\text{AY}} = 14$, 1H), 7.2 (S, 10H). The distilled product was about 98% pure by GC analysis on a 60 cm. \times 0.6 cm. aluminum column packed with 10% SE-30 silicon rubber on Gas Chrom Z, 100–200 mesh, operated at 180°. The retention time was about 2.0 minutes. Minor amounts of benzhydrol and diphenylmethyl methyl ether (retention times 2.5 minutes and 1.8 minutes, respectively) accounted for the remainder of the distillate. The checkers found that GC analysis on a 1.8-m. column packed with 15% SE-30 on GAW, 60–80 mesh at 180°, at an injector temperature of 250° resulted in extensive decomposition. A satisfactory analysis, however, could be performed by lowering the injector temperature to 180°.
11. Reppe⁴ reports b.p. 120° (15 mm.) for diphenylmethyl vinyl ether.

3. Discussion

Diphenylmethyl vinyl ether has also been prepared from benzhydrol and acetylene under high-pressure conditions.⁴ In the described method, an adaptation of the procedure of Weinstock and Boekelheide,⁵ improved yields of the alkene are obtained by using more convenient experimental conditions.

The described method for converting a quaternary halide to the corresponding hydroxide, utilizing an anion-exchange resin, has general application in the Hofmann elimination reaction.⁶ It has been used extensively in the submitters' laboratories for the synthesis of a variety of alkenes⁷ and for the preparation of a number of ethyl 1-benzylcyclopropanecarboxylates *via* abnormal Hofmann elimination of diethyl [2-(*N,N*-dimethylamino)ethyl]benzylmalonates.⁸ It offers several notable advantages over more conventional methods for preparing quaternary hydroxides. Formation of quaternary hydroxides from iodides with bases (e.g., silver oxide) that form insoluble iodides has disadvantages due to the expense of the reagent and, in some instances, the oxidizing power of silver salts in basic solution. Thallous ethoxide has been used to avoid the oxidation effect; however, it is expensive^{9,10,11} and toxic. Quaternary methosulfates may be hydrolyzed to sulfates and converted to the hydroxide with barium hydroxide,¹² but this method has not found general application. The described procedure of exchange of hydroxide ion for halide is suitable for even very sensitive compounds and obviates most of the

objectionable features of the precipitation methods.^{5,6} In the event that [methanol](#) is undesirable, the conversion may be carried out in water.⁵

References and Notes

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Appendix

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

[sulfuric acid](#) (7664-93-9)

[acetylene](#) (74-86-2)

[methanol](#) (67-56-1)

[ether](#),
[diethyl ether](#) (60-29-7)

[sodium hydroxide](#) (1310-73-2)

[silver oxide](#) (20667-12-3)

[ethyl](#) (2025-56-1)

[acetone](#) (67-64-1)

[barium hydroxide](#) (17194-00-2)

[hydroxide](#),
[hydroxide ion](#) (14280-30-9)

[Methyl iodide](#) (74-88-4)

silver (7440-22-4)

magnesium sulfate (7487-88-9)

benzhydrol,
 α -phenylbenzenemethanol (91-01-0)

silicon

Thallos ethoxide (20398-06-5)

Diphenylmethyl vinyl ether,
Benzene, 1,1'-[(ethenoxy)methylene]bis- (23084-88-0)

diphenhydramine,
2-(diphenylmethoxy)-N,N-dimethylethylamine (58-73-1)

diphenylmethyl methyl ether

2-(diphenylmethoxy)-N,N-dimethylethylamine methiodide