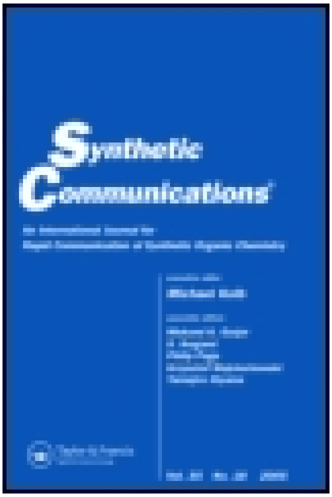

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A Convenient High-Yield Procedure for the β-Hydroxyethylation of Acetylenes with Epoxyethane in Liquid Ammonia

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A CONVENIENT HIGH-YIELD PROCEDURE FOR THE β-HYDROXYETHYLATION OF ACETYLENES WITH EPOXYETHANE IN LIQUID AMMONIA

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Abstract:

3-Butyn-1-ol and homologues, $RC{\equiv}CCH_2CH_2OH$ (R = H or alkyl), have been obtained in excellent yields from alkynyllithium derivatives, $RC{\equiv}CLi$, and epoxyethane in liquid ammonia.

Alkali metal acetylides, $RC{\equiv}C\text{-}M$, are much less reactive towards alkyl halides and epoxides than most other polar organometallic derivatives[1-3]. Their alkylation and β-hydroxyalkylation in organic solvents such as tetrahydrofuran or diethyl ether proceeds sluggishly and successful couplings can be achieved only in the presence of strongly polar co-solvents, *e.g.* dimethylsulfoxide and hexamethylphosphoric triamide.

The most practical solvent for performing these reactions on a sizable scale is anhydrous liquid ammonia. The reaction of alkali alkynylides with epoxyethane at the boiling point of this solvent (–33°C) proceeds slowly, but excellent yields can be obtained when the conditions are properly chosen.

Sodium alkynylides, $NaC{\equiv}CR$, are less suitable, since the primary coupling

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products, $NaOCH_2CH_2C{\equiv}CR$ may react with epoxyethane to give $NaOCH_2CH_2OCH_2CH_2C{\equiv}CR$[2,3]. We have found that this subsequent reaction does not take place with the corresponding *lithium* alkynylides, permitting the use of a large excess of epoxyethane. A further important condition is to minimize losses of the volatile epoxide (b.p. 11°C). This may be realized by performing the reaction under reflux, using a cold finger filled with dry ice and acetone. This method is not practical, however, since dry ice has to be continuously added over a period of 24 to 30 hours. In our procedure, a silvered Dewar flask (a double-walled flask with an evacuated space between the walls, the inner wall being covered with a thin layer of silver) is used. The rate of evaporation of ammonia is very low (of the order of 10 g/ l/ h). Since the reaction mixture is homogeneous, stirring needs not to be carried out, while the dry-ice condenser can be replaced by a beaker hanging over the neck of the flask. If only an unsilvered Dewar-flask is available, the outer wall is covered with aluminum foil and the flask placed in cotton wool: in this case the losses of epoxide due to the somewhat faster evaporation can be compensated for by using a larger excess of the epoxide.

Procedure: (for detailed information about working with liquid ammonia see our laboratory manuals[1,2])

$$HC{\equiv}CH \xrightarrow[\text{liq. } NH_3]{Li} HC{\equiv}CLi \xrightarrow{\text{oxirane}} HC{\equiv}CCH_2CH_2OLi \xrightarrow{NH_4Cl}$$

$$\longrightarrow HC{\equiv}CCH_2CH_2OH$$

$$RC{\equiv}CH \xrightarrow[\text{liq. } NH_3]{LiNH_2} RC{\equiv}CLi \xrightarrow[\text{2. } NH_4Cl]{\text{1. oxirane}} RC{\equiv}CCH_2CH_2OH$$

a. Preparation of the lithium alkynylides.

A solution of 2.0 mol of lithium acetylide $HC{\equiv}CLi$ in 1.5 l of liquid ammonia is prepared starting from 2.0 mol of lithium (cylindrical rods, flattened with a hammer and subsequently cut with a pair of scissors into pieces of 0.5 to 1 g which are immediately introduced into the ammonia) and 2 l of liquid ammonia. For this procedure see[2].

Ammoniacal solutions of the lithium alkynylides $CH_3C{\equiv}CLi$ and $C_2H_5C{\equiv}CLi$ can be made by adding a cold (–50°C) mixture of the alkynes (0.22 mol) and diethyl ether (50 ml) to a suspension of 2.0 mol of lithium amide in 1.5 l of liquid ammonia, cooled to below –50°C (dry ice acetone mixture). For the preparation of $LiNH_2$ and lithium alkynylides see[1,2].

The pre-cooled (~50°C) solutions of $HC{\equiv}CLi$ and $RC{\equiv}CLi$ are cautiously poured into a wide-necked (internal diameter 4 to 5 cm) Dewar-flask (contents 2 to 3 l). Epoxyethane (3.0 mol, pre-cooled at 0°C or lower temperature) is added in portions of 20 to 30 g over a period of 5 h. After addition of each portion the flask is swirled manually for a few seconds. The flask is closed by placing a beaker (upside down) on it, and allowed to stand for at least 24 h. The remaining solution is cautiously poured into a 4 to 5-l wide-necked round-bottomed flask. The Dewar flask is rinsed twice with ~200 ml portions of liquid ammonia and the rinsings combined with the main solution. Finely powdered ammonium chloride (120 g) is added in portions (2 - 5 g) over 15 minutes with occasional swirling by hand. The greater part of the ammonia is removed by placing the flask in a water bath at ~50°C. The remaining mass is dissolved in 500 ml of ice water, after which continuous extraction with ether is carried out (in the cases R = CH_3 and C_2H_5 frequent "manual" extraction presumably can be carried out). The extract is dried over anhydrous potassium carbonate, after which the greater part of the ether is distilled off at atmospheric pressure through a 30-cm Vigreux column. Distillation of the remaining liquid in a water-pump vacuum (in the case of $HC{\equiv}CCH_2CH_2OH$ a *single* receiver, cooled at 0°C is used, in the other cases a fraction collector) gives the alcohols in >80% yields: $HC{\equiv}CCH_2CH_2OH$, b.p. ~30°C/20 mm Hg, n^{20}_D 1.4385; $CH_3C{\equiv}CCH_2CH_2OH$, b.p. 50°C/10 mm Hg, n^{20}_D 1.4555; $C_2H_5C{\equiv}CCH_2CH_2OH$, b.p. 67°C/ 12 mm Hg, n^{20}_D1.4538.

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