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Technical Notes

Recyclable Lucas Reagent in Converting Aliphatic Alcohols to Chlorides[1]

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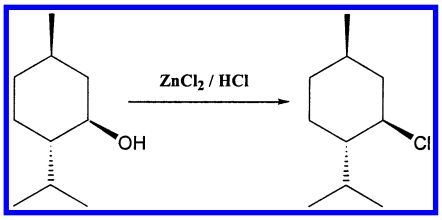
Abstract:

An industrially viable and environmentally friendly process is developed for the synthesis of menthyl chloride from the corresponding alcohol. Menthyl chloride was made in high yield by the reaction of menthol with the Lucas reagent. This chlorinating reagent was then recycled in the subsequent runs by simply replenishing the HCl, making the process simple and commercially viable. This improved procedure minimized the costly disposal of used Zn salts.

Methodology for the generation of alkyl halides from the corresponding alcohols has been extensively examined.[2] Several reagents have been used in this reaction, and the most common are halogen acids and inorganic acid halides. Although halogen acids are more economical to use on an industrial scale, HCl is not the most preferred reagent in converting secondary alcohols to secondary chlorides. During their pioneering work, Norris and Taylor[3] successfully converted alcohols into their corresponding bromides and iodides by treating with the respective halo acids. Since HCl gave poor results in this reaction, its reactivity was improved by adding $ZnCl_2$.[4] Lucas improved this reaction further and extended its scope to an analytical method to distinguish between primary, secondary, and tertiary alcohols.[5] The mild reaction conditions and high yields make the Lucas reaction an attractive methodology to utilize in the industrial-scale preparation of alkyl chlorides from aliphatic alcohols. However, the wide use of the Lucas reagent in industrial settings is limited due to the cost of $ZnCl_2$ and the waste disposal of used Zn salts following the reaction.

As a part of an ongoing research program, we needed large quantities of menthyl chloride. During our initial lab trials, anhydrous $ZnCl_2$ and concentrated HCl at 35 °C conveniently converted L(−)menthol (**1**) to L(−)menthyl chloride (**2**) in excellent yields (Scheme 1).[6] We modified

Scheme 1



this methodology to synthesize multikilogram quantities of menthyl chloride from menthol by minimizing the disposal of used zinc salts. Thus, the Lucas reagent was made by bubbling HCl gas into an aqueous solution of $ZnCl_2$ (70%) to obtain a 1:1 solution of $ZnCl_2$:HCl. Menthol was then introduced into this solution and stirred at ambient temperature to obtain menthyl chloride in 95% yield. The reaction was fast and was complete within 0.5 h, making the process a very cost-effective plant operation.

Smith and Wright have shown from their work that the reaction of $ZnCl_2$/HCl on (−)menthol gives mainly one enantiomer, that is, menthyl chloride. Our results concur with the above observation.[7] The other enantiomer, neomenthyl chloride, undergoes rapid E_2 elimination of HCl to give an isomeric mixture of menthenes. Unlike menthyl chloride, the stable chair conformation of the neomenthyl choride has two axial hydrogen atoms trans to the axial chlorine, thus promoting the E_2 elimination of HCl.[8] The small amount of olefinic byproduct detected by the NMR analysis of the crude product resulted from the decomposition of neomenthyl or menthyl chloride or both.

After completion of the reaction, the organic layer was separated from the aqueous phase, which contained the active reagent. The aqueous phase was then treated with more HCl to maintain the chloride concentration, and the reaction was continued with the next batch of menthol. The reagent was successfully recycled several times without having to dispose of the Zn salts. The activity of the reagent was not diminished for at least four reaction cycles, and the reaction was continued without further addition of $ZnCl_2$. The waste disposal of the process was greatly diminished, making this an envi-

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(7) The resulting chloride is converted to the corresponding diphenyl phosphine by reacting with diphenylphosphide anion. The chiral integrity of the product is confirmed by ^{31}P NMR. A single peak at −14 ppm, which corresponds to neomenthyldiphenyl phosphine was observed (the reaction proceeds via inversion at the chiral center). Thus, menthyl chloride is the major product formed from the halogenation reaction.

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ronmentally friendly process and also a very cost-effective plant operation for the preparation of aliphatic chlorides.

Experimental Section

Materials. Reagents and solvents were obtained from commercial suppliers and were used without further purification. The L-menthol (99%) for the following experiments was obtained from Aldrich Chemicals. GLC analyses were performed on a Hewlett-Packard 5890 series II gas chromatograph (30 m × 0.25 mm HP-5MS column 0.25 μm film thickness) equipped with a flame ionization detector with helium as the carrier gas. The following conditions were used in the GLC analysis: injector temperature 225 °C, 75 °C (hold 3 min) to 250 °C (hold 5 min) at 15 °C/min temperature program.

Preparation of Menthyl Chloride Using Lucas Reagent (Standard Reaction). Anhydrous, solid $ZnCl_2$ (306.3 g, 2.25 mol) was dissolved in cold (0 −5 °C) concentrated HCl acid (209 mL, 2.52 mol). The solution was allowed to warm to room temperature and L-menthol (117 g, 0.750 mol) was added in one portion. The resulting heterogeneous mixture was stirred for 5 h at ambient temperature. The organic phase was removed, and the aqueous phase was extracted with pet ether (35−60 °C). The combined organic phase was washed with water (2 × 35 mL) followed by concentrated H_2SO_4 (8 × 35 mL) and then washed again with water (5 × 35 mL). The organic phase was dried over anhydrous $MgSO_4$. The desiccant was filtered, and the filtrate was concentrated under reduced pressure to obtain menthyl chloride in 91.5% yield (by GLC analysis using an internal standard).

Recycling of Lucas Reagent in Making Menthyl Chloride. HCl gas (550 g, 15 mol) was bubbled into a 70% aqueous solution of $ZnCl_2$ (containing 2500 g of $ZnCl_2$, 13 mol) followed by addition of crystalline L-menthol (600 g, 3.85 mol). The reaction mixture was stirred at ambient temperature for 30 min, and the organic phase was analyzed by GC for menthyl chloride. The conversion of menthol to menthyl chloride was >97%. The organic phase was removed, and anhydrous HCl (280 g, 7.7 mol) gas was bubbled into the aqueous phase. Another 600 g of menthol was added, and the reaction was stirred for 30 min at ambient temperature. When the conversion reached >97% (GC analysis), the organic phase was separated (yield 95%, determined by GLC using an internal standard). The same process was repeated for two more reaction cycles obtaining identical results. The combined organic phases were diluted with toluene and azeotropically distilled to remove water. This process was utilized to make multikilogram quantities of menthyl chloride.

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