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Anhydrous Deprotection of Dimethyl Acetals with Acetyl Chloride/ZnCl₂

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ANHYDROUS DEPROTECTION OF DIMETHYL ACETALS WITH ACETYL CHLORIDE / ZnCl₂

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Abstract: Dimethyl acetals are converted to the corresponding aldehyde in THF with acetyl chloride/zinc chloride in the presence of dimethyl sulfide

During our course of investigation, we required the chloro ether $\underline{1}$, which we intended to prepare from the dimethyl acetal $\underline{2}$. A brief survey of the literature



shows that there are at least five possible convenient methods 1-5 and among which we chose the acetyl chloride /zinc chloride approach because of the ease of handling

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of the reagents. However, when the dimethyl acetal $\underline{2}$ was treated with acetal chloride (one equivalent) in the presence of about one mole percent of zinc chloride in methylene chloride at 0° C, instead of the expected chloro ether, NMR showed that the curde product was the corresponding aldehyde exclusively. Changing from dimethyl to the diethyl derivative did not alter the course of the reaction nor did the changing of the acid chloride from acetyl chloride to the longer chain myristoyl chloride⁶. A conceivable mechanism is shown in the scheme. The general utility was further investigated and the results are summarized by the table.

As can be seen from the data, the reaction condition can accomodate a reasonable range of acid sensitive groups. The ethylene acetal⁷(example b) stayed very much intact and even the ethylene ketal (example c) was preserved (to our knowledge, no one has done any deprotection on an acetal in the presence of an ethylene ketal) to an acceptable level. In the presence of some other acid sensitive functionalities though, such as an epoxide or an OTHP, mixtures of products were observed. We do feel that this methodology is an effective alternative for the deprotection of a dimethyl acetal.

General procedure: To the dimethyl acetal in THF (about 1 g /10 mL) at 0° C one mole percent of zinc chloride (as a 1 mg /mL THF solution), one equivalent of



All compounds have satisfactory spectral data

* The yield is based on a six-hour reaction in the presence of 3 eq. of dimethyl sulfide and a conversion of 82 %. The major by-product on prolonged period of time is the 1,3-dioxolane $\underline{3}$.



dimethyl sulfide and 1.05 equivalent of acetyl chloride were introduced in the respective order and the resulting mixture was stirred at the cold temperature for 15 hours. At the end of the period, ethyl acetate was added and the reaction was washed with water and brine. Pure product was isolated by column chromatography on silica gel.

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