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# α-Chlorovinylation: Synthesis of 2-Chloropropenyl and Propargyl Alcohols

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**Abstract**: Formal  $\alpha$ -chlorovinylation of aldehydes using CH<sub>3</sub>CCl<sub>3</sub>/CrCl<sub>2</sub> affords 2-chloropropenyl alcohols from which terminal propargyl alcohols are obtained via base induced elimination. © 1999 Elsevier Science Ltd. All rights reserved.

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 $\alpha$ -Chlorovinyl and propargyl moieties are critical structural components in a variety of bioactive natural products of current interest, e.g., halomon,<sup>1</sup> spongistatin,<sup>2</sup> and laurediol.<sup>3</sup> Since introduction of the former subunit via nucleophilic addition of an  $\alpha$ -anionic intermediate is generally precluded by rearrangement and/or decomposition of the metalated carbenoid,<sup>4</sup> indirect and often low yielding procedures must be used.<sup>5</sup> Lithium and magnesium salts of acetylides, on the other hand, are quite stable, but their generation from gaseous acetylene is inconvenient and potentially hazardous. As part of a continuing commitment to the synthesis of structurally challenging, halogenated natural products and their alkynyl analogs,<sup>6</sup> we report herein an efficient and mild  $\alpha$ -chlorovinylation of aldehydes using commercial CH<sub>3</sub>CCl<sub>3</sub> and CrCl<sub>2</sub> (eq 1). Based induced elimination transforms the resultant 2-chloropropen-3-ol adducts into the corresponding terminal propargyl alcohols.



Τ	ab	le	1.

Entry	Aldehyde	Adduct	Yield (%)	Acetylene	Yield (%)
1	∽∽∽∽ <sup>0</sup> H	OH Cl	85	ОН	96
2	С <sup>О</sup> Н	OH Cl	73	OH	89
3	ОН	OH CI	83	OH	95
4	O <sub>V</sub> H	HO	72	HO	92
5	MeO	MeO	70	MeO OH	93
6	F <sub>3</sub> C	F <sub>3</sub> C OH Cl	83	F <sub>3</sub> C OH	95
7	BnO OMe	BnO OMe	75	OH BnO OMe	91
8	С Г Н	OH Cl	81	OT OH	94
9	O Br	OH Br	76	OH Br	94
10	C H	OH Cl	65	OH OH	92
11	L H	OH Cl	71	OH C	90

The scope of the  $\alpha$ -chlorovinylation procedure was explored using a representative panel of aldehydes<sup>7</sup> (Table 1). With a four-fold excess of CH<sub>3</sub>CCl<sub>3</sub>/CrCl<sub>2</sub> in THF, *n*-alkyl

(Entry 1) and cycloalkyl (Entry 2) aldehydes afforded moderate to good yields of adduct as did the aryl examples benzaldehyde (entry 3) and 1-napthaldehyde (Entry 4). Notably, comparable results were achieved at room temperature utilizing a catalytic system<sup>8</sup> based on Mn powder to recycle the  $CrCl_2$ .

The reaction was not significantly influenced by electron donating (Entry 5) or withdrawing (Entry 6) aryl substituents and proved compatible with a variety of functional groups including a benzyl ether (Entry 7), methylenedioxy (Entry 8), and bromide (Entry 9). Preparatively useful yields were also obtained with the  $\alpha$ , $\beta$ -unsaturated systems cinnamaldehyde (Entry 10) and citral (Entry 11) without noticable conjugate addition.

In a mechanistic rationale for the observed addition, outlined in equation 2,  $CrCl_2$  acts as a reducing agent to generate an anionic intermediate that adds to the carbonyl. Proton abstraction and loss of chloride gives rise to  $\alpha$ -chloropropenyl alcohol. In stark contrast to the related Takai reaction,<sup>9</sup> the carbonyl carbon undergoes addition rather than olefination.

$$\begin{array}{c} O \\ R \end{array} \xrightarrow{H} \begin{array}{c} CH_3CCl_3 \\ \hline CrCl_2 \end{array} \end{array} \left[ \begin{array}{c} O \\ R \end{array} \xrightarrow{Cr} H \\ \hline Cl \\ Cl \end{array} \right] \xrightarrow{-HCl} \begin{array}{c} OH \\ R \end{array} \xrightarrow{OH} \begin{array}{c} OH \\ \hline Cl \\ R \end{array} \right] \xrightarrow{-HCl} \begin{array}{c} OH \\ R \end{array} \xrightarrow{OH} \begin{array}{c} OH \\ (eq 2) \end{array}$$

Removal of the elements of HCl from the adducts proceeded smoothly using LDA at low temperature. The uniformly excellent yields of propargyl alcohol (Table 1) make this two-step sequence of  $\alpha$ -chlorovinylation and base-induced elimination an attractive alternative to metal acetylides.

#### **General Procedures**

 $\alpha$ -Chlorovinylation: A solution of aldehyde (1 equiv) and 1,1,1-trichloroethane (3 equiv) in anhydrous THF was added dropwise with stirring to a room temperature suspension of CrCl<sub>2</sub> (4 equiv) in THF under argon. After 12 h, the resultant reddish reaction mixture was quenched with water, extracted trice with Et<sub>2</sub>O, and the combined ethereal extracts were evaporated *in vacuo*. Chromatographic purification on SiO<sub>2</sub> afforded 2-chloropropen-3-ols in the indicated yields (Table 1).

**Mn Supported**  $\alpha$ -Chlorovinylation: To a stirring, room temperature suspension of CrCl<sub>2</sub> (0.7 equiv) and Mn powder (1.7 equiv) in THF was added successively aldehyde (1 equiv), 1,1,1-trichloroethane (2 equiv), and chlorotrimethylsilane (2.4 equiv). After 6 h, the resultant reddish reaction mixture was quenched and the  $\alpha$ -chlorovinyl adduct isolated as described above.

**LDA Elimination**:  $\alpha$ -Chlorovinyl adduct (1 equiv) was stirred with a freshly prepared solution of LDA (3 equiv) in anhydrous THF at -78°C. After 1 h, the reaction was quenched with saturated aqueous NH<sub>4</sub>Cl solution and extracted trice with EtOAc. The combined extracts were evaporated *in vacuo* and the residue purified by SiO<sub>2</sub> chromatography to give the corresponding propargyl alcohols in the yields indicated in Table 1.

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