A Convenient Method for Conversion of Allylic Chlorides to α,β-Unsaturated Aldehydes

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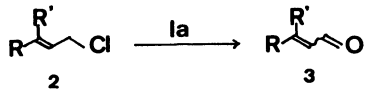
(Received May 15, 1986)

Synopsis. Tertiary amine *N*-oxides were found to be effective for converting allylic chlorides to α,β-unsaturated aldehydes.

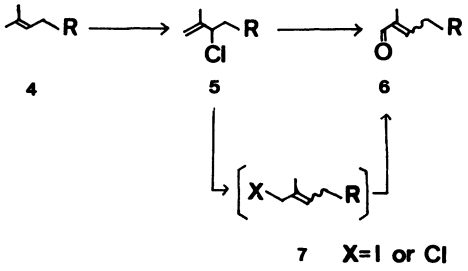
Oxidation of allylic chlorides provides a convenient method for synthesizing α,β-unsaturated aldehydes. Unfortunately, however, only a few successful results have been reported which had recourse to dimethyl sulfoxide oxidation[1,2] or a potassium salt of 2-*aci*-nitropropane-tetrakis(triphenylphosphine)palladium system[3] whereas allylic bromides proved to be oxidized by a potassium salt of 2-*aci*-nitropropane[4] or potassium chromate.[5,6] In our continuing efforts to develop an efficient method to synthesize α,β-unsaturated compounds as a raw material for the vitamin A synthesis,[7] we have now disclosed that tertiary amine *N*-oxides (**1**) effect a smooth conversion of allylic chlorides into α,β-unsaturated aldehydes.

Various tertiary amine *N*-oxides were reported to oxidize benzylic halides successfully.[8-10] We have found that treatment of primary allylic chlorides **2** with 3 equiv of *N*-ethylmorpholine *N*-oxide (**1a**) in DMF at 50°C for 4 h affords the desired α,β-unsaturated aldehydes **3** in excellent yields according to Eq. 1 (Table 1, Entries 1—5) (Method A). Other tertiary amine *N*-oxides derived from *N*-methylmorpholine, *N*-methylpyrrolidine, *N*-methylpiperidine, trimethylamine, *N*,*N*-dimethylcyclohexylamine, *N*,*N*-dicyclohexylmethylamine, and *N*,*N*-diethylcyclohexylamine gave rise to lower yields of **3**.



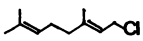
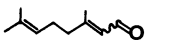
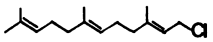
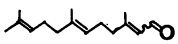
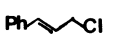
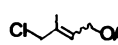
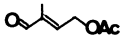
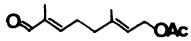
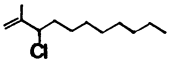
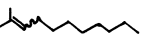
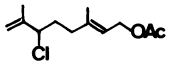
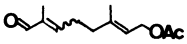
2 3 (1)

When this reaction was applied to secondary allylic chlorides **5**, no satisfactory results were obtained. The difficulty was overcome, however, by conducting the reaction in the presence of an alkali metal iodide such as lithium iodide (Table 1, Entries 6 and 7) (Method B) or in the presence of a catalytic amount of copper (I) chloride (Table 1, Entry 8) (Method C). Since **5** can be readily prepared by the ene-type chlorination of the corresponding alkenes **4**,[11] the effective method for converting **4** into **6** has been established (Eq 2). The



(2)

Table 1. Oxidation of Allylic Chlorides by Tertiary Amine *N*-Oxides (**1**)

Entry	Allyl chloride	Method	α,β-Unsaturated aldehyde[a]	Yield/%	*E*/*Z*[b]
1		A		88[c]	70/30
2		A		82[d]	53/47
3		A		97[c]	100/0
4		A		88[d]	100/0
5		A		90[d]	100/0
6		B		47(89)[d,e]	77/23
7		B		71[d]	68/32
8		C		61[d]	100/0

a) All products were confirmed by comparison with authentic samples. b) Determined by means of GLC or ^{1}H NMR spectra. c) Isolated yield after distillation. d) Isolated yield after column chromatography. e) The starting material was recovered (47%). The value in the parenthesis indicates the yield based on the consumed starting material.

reaction can be viewed as proceeding via initial formation of the primary allylic halides **7**.[12]

Experimental

Reaction of Primary Allylic Chlorides with *N*-Ethylmorpholine *N*-Oxide (1a): Method A (Typical Procedure). A DMF solution (3 cm^3) of geranyl chloride (346 mg, 2 mmol) and **1a** (787 mg, 6 mmol) was stirred at room temperature for 1 h and at 50 °C for additional 4 h under an argon atmosphere. The reaction mixture was combined with 2.5% H_2SO_4 (10 cm^3) and ethyl acetate (10 cm^3). The organic layer was washed successively with 2.5% H_2SO_4, saturated $NaHCO_3$, and 10% Na_2SO_3 solutions. Drying ($MgSO_4$) followed by evaporation afforded a crude oil which was distilled to give 3,7-dimethyl-2,6-octadienal (268 mg, 88%, *E*/*Z*=70:30, bp 93 °C/400 Pa, .Kugelrohr bath temperature).

Reaction of Secondary Allylic Chlorides with Tertiary Amine *N*-Oxide: Method B (Typical Procedure). A DMF solution (3 cm^3) containing (*E*)-6-chloro-3,7-dimethyl-2,7-octadienyl acetate[11] (461 mg, 2 mmol), **1a** (787 mg, 6 mmol), and $LiI \cdot 2H_2O$ (680 mg, 4 mmol) was stirred at room temperature for 1 h and at 50 °C for additional 4 h. Workup as described above and column chromatogrpahy of the crude oil on silica gel (10:1 hexane-ethyl acetate) gave 8-acetoxy-2,6-dimethyl-2,6-octadienal (298 mg, 71%, 2*E*/2*Z* 68:32).

Method C: A dioxane solution (5 cm^3) containing (*E*)-6-chloro-3,7-dimethyl-2,7-octadienyl acetate (2.17 g, 9.41 mmol), triethylamine *N*-oxide (**1b**) (3.47 g, 29.6 mmol), and copper(I) chloride (92 mg, 0.93 mmol) was stirred at 50 °C for 10 h. Workup and chromatographic purification as described above gave (2*E*,6*E*)-8-acetoxy-2,6-dimethyl-2,6-octadienal (1.21 g, 61%). In this reaction, **1a** gave rise to a lower yield.

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