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AN EFFICIENT $SbCl_3$-METAL SYSTEM FOR ALLYLATION, REDUCTION AND ACETALIZATION OF ALDEHYDES#

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Dedicated to the 80th birthday of Professor Wang Yu

Abstract: $SbCl_3$-Fe or $SbCl_3$-Al could induce allylation of aldehydes with allylic halides at room temperature to give high yields of the corresponding homoallylic alcohols with high regio- and chemoselectivity. $SbCl_3$-Al or $SbCl_3$-Zn in DMF-H_2O was found to be an efficient reduction system for conversion of aldehydes to alcohols at room temperature in excellent yields. While alcohol was used as solvent instead of DMF-H_2O, the acetalization product was obtained in almost quantitative yield. Catalytic amount of $SbCl_3$ was effective for this purpose. This acetalization method could also be applied to ketones.

Introduction

Only a few reports have appeared in literatures concerning the application of organoantimony compounds in organic synthesis1). In our recent communications we reported the trialkylstibine-mediated olefination reactions of carbonyl compounds with bromoacetates, bromoacetamide, chloroacetonitrile, -bromoketones, bromomalonic ester and dibromomalonic ester2); the reactions of aldehydes with trichloroacetonitrile to form α,α-dichloro- β hydroxynitriles3); and the reaction of dibromomalonic ester and its analogs with electron-deficient olefins to form cyclopropanes4).

In continuation of our studies on application of antimony compounds in organic synthesis, we found $SbCl_3$-metal system is a facile system for allylation, reduction, and acetalization of aldehydes.

Results and Discussion

The allylation of aldehydes to homoallylic alcohols is of synthetic importanceand a number of metals have been used to promote Barbier-type allylation of aldehydes with allyl halides5). Recently, metallic antimony6) and trialkystibine7) mediated Barbier-type reaction at 60-80°C has appeared in literatures. We found that the active zero-valent antimony generated from $SbCl_3$-Fe or -Al could induce allylation of aldehydes with allylic halides at room temperature to give high yields of the corresponding homoallyic alcohols with high regio- and chemoselectivity8).

The results of allylation of aldehydes with allyl iodide mediated by $SbCl_3$-Fe is depicted as shown in Table 1.

Table 1 $SbCl_3$-Fe mediated allylation of aldehydes with allyl iodide (25° C)

RCHO R-	reaction time(hrs)	isolated yields(%)
p-ClC_6H_4	10	95
C_6H_5	20	98
p-$CH_3OC_6H_4$	34	90
p-HOC_6H_4	12	80
o-HOC_6H_4	24	99
$CH_3(CH_2)_5$	24	79

All the products gave satisfactory ^1H NMR and MS specta.

The less reactive allyl bromide reacted with the same aldehydes (see Table 2) to give homoallylic alcohols (80-90%) at 60°C(4.5-7hrs). However, addition of sodium iodide allow the reaction temperature to be reduced to ambient. Metallic aluminium when it replaced metallic iron was also effective in a DMF-H_2O (3:1) medium (Table 2).

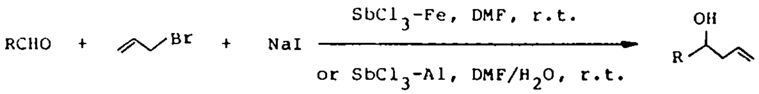


Table 2 $SbCl_3$-Fe or Al mediated allylation of aldehydes with allyl bromide in the presence of NaI (25° C)

Run	RCHO R-	metal	reaction time(hrs)	isolated yields(%)
1	p-ClC_6H_4	Fe[a)]	18	89
2		Al[b)]	24	99
3	C_6H_5	Fe	18	99
4		Al	12	98
5	p-$CH_3OC_6H_4$	Fe	34	98
6		Al	24	86
7	p-HOC_6H_4	Fe	22	61
8		Al	24	97
9	o-HOC_6H_4	Fe	13	98
10		Al	12	67
11	$CH_3(CH_2)_5$	Fe	24	89
12		Al	24	63
13	Ph CH=CH	Fe	20	95
14		Al	24	98

a) RCHO : $CH2$-CH-CH_2Br : $SbCl_3$: Fe : NaI - 1 : 1.2 : 1.5 : 3 : 1 2 (mmol)

b) RCHO : $CH2$-CH-CH_2Br : $SbCl_3$: Al : NaI - 1 : 1.2 : 1.5 : 2 : 1.2 (mmol)

A variety of aldehydes reacted smoothly to give the homoallylic alcohols in good yield α,β-Unsaturated aldehydes afforded only 1,2-addition product (runs 13, 14). Aldehyde containing an hydroxy group gave the corresponding products remaining the OH group unattacked (runs 7-10). Since acetophenone present in benzaldehyde was recovered, the reaction is chemoselective.

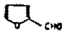
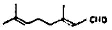
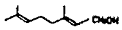
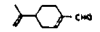
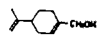
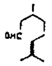
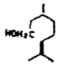
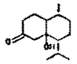
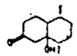
Reaction of crotyl bromide with p-chlorobenzaldehyde under similar reaction conditions provided the homoallylic alcohol with the erythro isomer predominatingly⁹⁾.

The reaction mechanism is suggested as that allylantimony reagent is formed through the oxidative addition of an allyl halide to zero-valent antimony generated in situ by reduction of antimony(III) chloride with metallic iron or aluminium. Because of the erythro selectivity, the reaction with an aldehyde seems to proceed via a non-cyclic transition state¹⁰⁾.

Concerning the reduction of aldehydes to alcohols, we have reported that in the presence of Lewis acids, diphenylstibine reacted with carbonyl compounds to afford, after hydrolysis, alcohols in excellent yields¹¹⁾. Recently, an indirect electroreduction of acetophenone to 1-phenylethanol in the presence of $SbCl_3$ was reported by Ikeda¹²⁾. We found that $SbCl_3$-Al/DMF-H_2O (system A) and $SbCl_3$-Zn/DMF-H_2O (system B) were effective reducing systems for conversion of aldehydes to alcohols in excellent yields. When the reduction was carried out in DMF-D_2O, the aldehydes were converted to deuterium labelled alcohols (RCHDOH) conveniently¹³⁾.

$$\mathrm{RCHO} \xrightarrow[\mathrm{DMF\text{-}H_2O\,(or\ DMF\text{-}D_2O)}]{\mathrm{SbCl_3\text{-}Al\ or\ SbCl_3\text{-}Zn}} \mathrm{RCH_2OH\ (or\ RCHDOH)}$$

Table 3 Reduction of aldehydes with (A) $SbCl_3$-Al/DMF-H_2O or (B) $SbCl_3$-Zn/DMF-H_2O

run	Aldehyde	Reduction system	Reaction time(hrs)	Product*	Isolated yield(%)
1	C_6H_5CHO	A(B)	0.5(3)	$C_6H_5CH_2OH$	98(90)
2	p-ClC_6H_4CHO	A(B)	0.3(3)	p-$ClC_6H_4CH_2OH$	98(90)
3	p-$CH_3C_6H_4CHO$	A(B)	0.8(3)	p-$CH_3C_6H_4CH_2OH$	98(96)
4	p-$CH_3OC_6H_4CHO$	A(B)	2(12)	p-$CH_3OC_6H_4CH_2OH$	98(60)
5		A	1		98
6	$CH_3(CH_2)_8CHO$	A(B)	3(4)	$CH_3(CH_2)_8CH_2OH$	98(94)
7		A(B)	2(4)		95(85)
8		A	1		95
9		A(B)	1(3)		98(95)
10		A(B)	2(5)		50(80)
11		(B)	(4)		(96)
12		A	6		0

* All the products were confirmed by ¹H NMR, MS.

As can be seen in Table 3, a variety of aldehydes were reduced smoothly with either reduction system. In system A, the reaction proceeded faster than in system B. With α,β-unsaturated aldehydes, reduction occurred only at the C—O position (runs 9,10),leaving the carbon-carbon double bonds intact. Neither unconjugated double bond nor cyclic ketone was attacked (runs 9-12). When a mixture of benzaldehyde and acetophenone was allowed to react with system A or B, the former was reduced preferentially.

The reaction mechanism is not clear at present. Some experimental results are noteworthy In the absence of H_2O or antimony trichloride, the reaction did not occur. A dark precipitate, which was probably produced by the reduction of Sb(III) to Sb(0), was found in the course of the reaction. Evolution of hydrogen was also observed.

In the above $SbCl_3$-Al/ or $SbCl_3$-Zn/DMF-H_2O system, when methyl or ethyl alcohol (except isopropyl alcohol) was used as solvent instead of DMF-H_2O, the acetalization product was obtained in almost quantitative yield. Catalytic amount of $SbCl_3$ was effective for this purpose. In the absence of Fe or Al, the reaction did not occur. The results are depicted in Table 4.

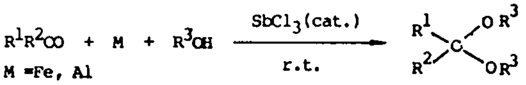
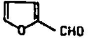
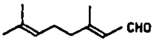


Table 4 Acetalization of carbonyl compounds from R^3OH

Substrate (R^1R^2CO)	R^3	Metal	Reaction time(hrs)	Isolated yield(%)
C_6H_5CHO	CH_3	Fe(Al)	12(4)	98(95)
p-C_6H_4CHO	CH_3	Fe(Al)	12(4)	100(98)
p-$CH_3C_6H_4CHO$	CH_3	(Al)	(15)	(95)
p-$CH_3OC_6H_4CHO$	CH_3	(Al)	(16)	(95)
 CHO	CH_3	(Al)	(10)	(88)
PhCH=CHCHO	CH_3	Fe	24	52
 CHO	CH_3	Fe	24	95
$CH_3(CH_2)_5CHO$	CH_3	Fe(Al)	24(8)	94(92)
 CHO	CH_3	Fe(Al)	20(12)	96(98)
	CH_3	(Al)	(19)	(94)
p-ClC_6H_4CHO	C_2H_5	(Al)	(16)	(96)
$CH_3(CH_2)_5CHO$	C_2H_5	(Al)	(16)	(96)
p-ClC_6H_4CHO	i-C_3H_7	Fe(Al)	24(24)	0(0)

All the products were confirmed by ^1H NMR, MS.

This method could also be applied to diol (ethylene glycol and propylene glycol). The operation is the same as that of monoalcohol. The results are shown in Table 5. This acetalization method could be applied to ketones.

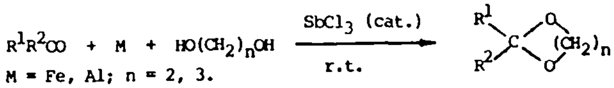
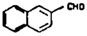
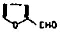
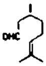
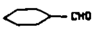


Table 5 Acetalization of carbonyl compounds from $OH(CH_2)_nOH$

Substrate (R^1R^2CO)	Diol (n)	Metal	Reaction time(hrs)	Isolated yield(%)
C_6H_5CHO	2	Al(Fe)	20(22)	98(90)
p-ClC_6H_4CHO	2	Al(Fe)	24(20)	98(98)
	2	Al	24	92
	2	Al	18	95
PhCH=CHCHO	2	Al	20	66
	2	Al	24	96
$CH_3(CH_2)_5CHO$	2	Al	24	90
	2	Al	20	92
	2	Al	22	96
$PhCOCH_3$	2	Al	22	50
C_6H_5CHO	3	Al	24	94
	3	Al	24	99

All the products were confirmed by ^1H NMR, MS.

To our knowledge, the use of $SbCl_3$-metal as a catalyst for acetalization has not been described in the literature, although the acid catalyzed acetalization of aldehydes is a general procedure. Furthermore, our acetalizaton method is suitable for a variety of carbonyl compounds especially for the acid-sensitive heterocyclic compounds such as furfural. The mechanism is not clear at present.

Conclusion

Because of the ready access of reagents, mild reaction conditions, easy work up, and good yields, the $SbCl_3$-metal was a facile system for allylation, reduction and acetalization of aldehydes.

Experimental

^1H NMR spectra were recorded on Varian-360L instrument in CCl_4 solution with Me_4Si as an internal standard and are in δ (ppm). IR spectra were recorded with an Shimadzu IR-440 infrared spectrophotometer and are in cm^{-1} units. Mass spectra were recorded on Finnigan GC-MC 4021 spectrometer.

General Procedure for Barbier-type Allylation

P-Chlorobenzaldehyde (1.0 mmol), sodium iodide (1.2 mmol) antimony(Ⅲ) chloride (1.5 mmol), metallic aluminium (2.0 mmol), allylbromide (1.2 mmol) and DMF 3ml, H_2O 1ml were mixed in a reaction tube under nitrogen and stirred at room temperature. After the reaction was completed (monitored by TLC), ether was added and the reaction mixture was filtered through a small amount of silica gel. The filtrate was washed with water and dried ($MgSO_4$). The solvent was evaporated under reduced pressure. 1-p-Chlorophenyl-3-buten-1-ol was isolated by preparative TLC (silica gel) and was confirmed by ^1H NMR, IR, and MS spectra.

General Procedure for Reduction

A mixture of $SbCl_3$(1.2 mmol), Al or Zn dust(4 mmol), and an aldehyde(1 mmol) in a mixed solvent DMF-H_2O (1:1, 4ml) was stirred at r.t. under nitrogen. After the reaction was completed (monitored by TLC),usual work up yielded the corresponding alcohol. When the reaction was carried out in DMF-D_2O instead of DMF-H_2O, the corresponding deuterium labelled alcohol was obtained.

General Procedure for Acetalization

A mixture of carbonyl compound (1 mmol), Fe powder (4 mmol), $SbCl_3$ (0.4 mmol) and alcohol (2 ml), was allowed to react at room temperature for certain hours with stirring. After the reaction was completed (monitored by TLC), the residue was filtered off and washed with ether. The ethereal solution was concentrated remaining an acetal in almost pure state. Alternatively, a mixture of Al powder (4 mmol), $SbCl_3$ (0.4 mmol) was allowed to stir for 20 min, the carbonyl compound (1 mmol) was added and stirred for further certain hours and work up as before.

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References and Notes:

\# This paper is the 82nd report on the application of elementoorganic compounds of 15th and 16th groups in organic synthesis.

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