Halogenative Allylation and Reduction of Aromatic Acetals by Double Substitution of Alkoxyl Groups in Acetal

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Synopsis. In the presence of excessive amount of acetyl halide along with a catalytic amount of tin(II) halide, aromatic acetals react with allyltrimethylsilane or triethylsilane to give α-allylbenzyl halides or benzyl halides, respectively, in good to excellent yields.

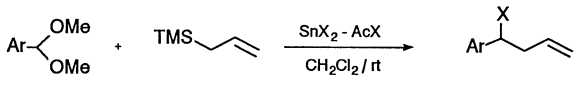
In continuation of our studies of the new carbon-carbon bond formation between acetals and silyl nucleophiles effected by the combined use of a catalytic amount of tin(II) halide (SnX_2) and an excessive amount of reactive organic halide such as acetyl chloride (AcCl) and methoxymethyl chloride (MOMCl), we have already demonstrated a convenient synthesis of conjugated enones from acetals and silyl enol ethers.[1]

Now we wish to report novel reaction of aromatic acetals with allyltrimethylsilane[2] or triethylsilane[3] as a silyl nucleophile to give α-allylbenzyl halides or benzyl halides respectively.

In the first place, we have examined the allylation according to the procedure similar to that for the aldol-type reaction reported in the previous paper.[1] Reaction of benzaldehyde dimethyl acetal (**1**) with allylsilane using a combined activator, $SnCl_2$ and AcCl both in a catalytic amount, afforded the known product, 4-methoxy-4-phenyl-1-butene (**3**), in 72% yield (Run 1 in Table 1). In a striking contrast, when 2.5 molar amount of AcCl to the acetal was employed, an allylation with concomitant substitution of methoxyl for chloride[4] occurred to give 4-chloro-4-phenyl-1-butene (**2**, X=Cl) in 83% yield (Run 2 in Table 1). AcCl did not function as an electrophile to acylate allylsilane. Screening of various combined activator system using benzaldehyde dimethyl acetal as a reference substrate revealed that SnX_2/AcX (molar ratio of acetal : SnX_2 : AcX=1.0 : 0.05 : 2.0—2.5) gave the best result as shown in Table 1. When a combination of $SnBr_2$/AcBr was used as an activator, corresponding 4-bromo-1-butene was obtained as a sole product (Run 8 in Table 1). The results of the reaction with various acetals are summarized in Table 2.

The reaction is similarly effective to ketone acetal,

Table 2. Synthesis of 4-Aryl-4-halo-1-butene (**5**) from Acetals (**4**)[a,b]



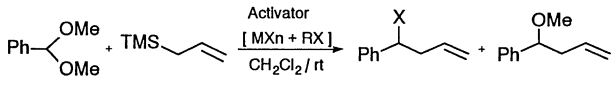
(2)

4 **5**

Run	Ar	X	Time/h	Yield of **5**[c]/%
1	Ph	Cl	2	83
2	Ph	Br	2	87
3	Ph[d]	Cl	2	79
4	*p*-BrC_6H_4	Cl	12	85
5	*p*-BrC_6H_4	Br	24	84
6	*p*-ClC_6H_4	Br	6	65
7	*m*-$MeOC_6H_4$	Br	3	63

a) Molar ratio of acetal : SnX_2 : AcX=1.0 : 0.05 : 2.0—2.5. b) All the products gave satisfactory ^1H NMR and IR spectra. c) Isolated yield. d) Diethyl acetal was used in place of dimethyl acetal.

Table 1. The Effect of Activator System of the Reaction between Benzaldehyde Dimethyl Acetal (**1**) and Allyltrimethylsilane[a]



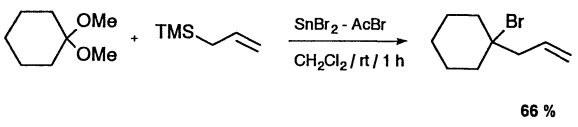
(1)

1 **2** **3**

Run	Activator [MX_n+RX] (molar ratio to the acetal)			Time/h	Yield[b]/%	
					2	**3**
1	$SnCl_2$	(0.05) + AcCl	(0.05)	2.5	0	72
2	$SnCl_2$	(0.05) + AcCl	(2.5)	2	83	0
3	$ZnCl_2$	(0.05) + AcCl	(2.5)	2	87	Trace
4	$Sn(OTf)_2$	(0.05) + AcCl	(2.5)	2	59	16
5	$SnCl_2$	(0.05) + MOMCl	(2.5)	2	66	0
6	$SnCl_2$	(0.05) + TMSCl	(2.0)	6	Trace	69
7	$SnBr_2$	(0.05) + MOMBr	(2.5)	2	77	0
8	$SnBr_2$	(0.05) + AcBr	(2.0)	2	87	0

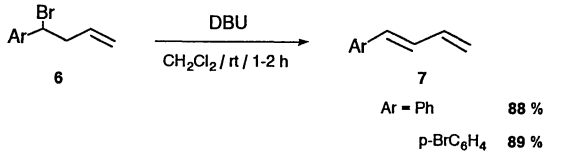
a) Molar ratio of acetal : allylsilane=1 : 1.2. b) Isolated yield.

e.g. cyclohexanone dimethyl acetal, to result in 1-allyl-1-bromocyclohexane (Eq. 3).



(3)

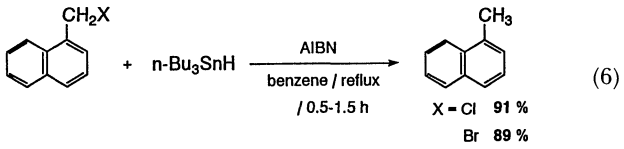
4-Aryl-4-bromo-1-butenes (**6**), above obtained, were easily converted to 1-aryl-1,3-butadienes (**7**) by a convenient procedure as illustrated in Eq. 4.



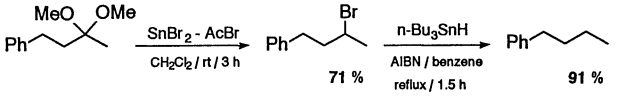
(4)

The above shown double substitution of alkoxyl groups in acetal by a nucleophile from reactive silanes and a halogen from reactive organic halides has led us to examine the hydride reduction of acetals with simultaneous halogen substitution to obtain benzyl halides. Thus, the reduction of aromatic dimethyl acetals by triethylsilane in the presence of a combined AcX/SnX_2 reagent was tried and was proven to be successful as well. The results are summarized in Table 3.

Reaction of alkyl halides with *n*-Bu_3SnH under radical conditions[5] gave the corresponding alkane in good yield as shown in Eqs. 6 and 7. This overall three step reduction from carbonyl to methylene provides a mild and effective alternative to conventional Wolff-Kishner[6] and Clemmensen reductions,[7] both of which necessitate drastic reaction conditions.

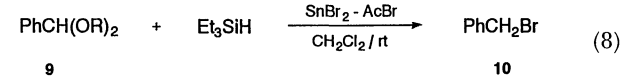


(6)



(7)

Table 4. Halogenative Reduction of Various Acetals of Benzaldehyde (**9**)[a,b]



(8)

Run	R, R	Time/h	Yield of **10**[c]/%
1	Me, Me	3	89
2	Et, Et	3	91
3	$-(CH_2)_2-$	3	96
4	$-(CH_2)_3-$	3	82
5	Ac, Ac	3[d]	77

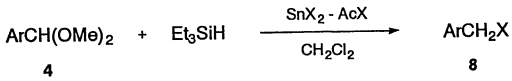
a) Molar ratio of acetal : SnBr : AcBr=1.0 : 0.05 : 2.5. b) All the products gave satisfactory ^1H NMR and IR spectra. c) Isolated yield. d) The reaction was carried out in refluxing 1,2-dichloroethane.

Benzaldehyde diethyl acetal, ethylene acetal, and acylal were also transformed to benzyl bromide in good yield as shown in Table 4.

Experimental

General Procedure. To a suspension of tin(II) bromide

Table 3. Synthesis of Benzyl Halides (**8**) from Acetals (**4**)[a,b]



(5)

Run	Ar	X	Temp/°C	Time/h	Yield of **8**[c]/%
1	Ph	Cl	R.T.	3	76
2		Br	R.T.	3	89
3	*m*-$MeOC_6H_4$	Cl	R.T.	3	97
4		Br	R.T.	2	99
5	*p*-MeC_6H_4	Cl	R.T.	3	89
6		Br	R.T.	3	86
7	*p*-ClC_6H_4	Cl	R.T.	12	79
8		Br	R.T.	2	87
9	*p*-BrC_6H_4	Cl	R.T.	5	92
10		Br	R.T.	7	97
11	α-Naph	Cl	0	2	92
12		Br	0	1	96
13	β-Naph	Cl	0	5	91
14		Br	0	3	94

a) Molar ratio of acetal : SnX_2 : AcX=1.0 : 0.05 : 2.5. b) All the products gave satisfactory ^1H NMR and IR spectra. c) Isolated yield.

(5.1 mg, 0.02 mmol) and benzaldehyde dimethyl acetal (54.8 mg, 0.36 mmol) in dichloromethane (2.5 ml) were added triethylsilane (65.0 mg, 0.56 mmol) in dichloromethane (1.5 ml) and acetyl bromide (96.8 mg, 0.79 mmol) in dichloromethane (1 ml), successively at room temperature under argon atmosphere. The mixture was stirred for 3 h at this temperature, and quenched with a phosphate buffer (pH 7). The organic materials were extracted with dichloromethane and dried over Na_2SO_4. Benzyl bromide (54.7 mg, 89%) was isolated by thin layer chromatography on silica gel.

It should be noted that the present halogenative allylation and reduction of aromatic acetals are extremely mild and exceptionally simple in operation.

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References

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