Pergamon

Tetrahedron Letters 41 (2000) 5009–5012

TETRAHEDRON LETTERS

# Organometallic reactions in aqueous media. Antimony-mediated allylation of carbonyl compounds with fluoride salts

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Received 17 April 2000; accepted 15 May 2000

**Abstract**

Commercial antimony can be used directly for the allylation of carbonyl compounds in aqueous media in the presence of fluoride salts. 

The allylation of carbonyl compounds has proved to be a very important reaction and numerous reagents and methods have been developed to accomplish this transformation.[1] The discovery[2] in the past decade that this transformation could be achieved in aqueous media through a Barbier-type reaction[3] has drawn even more attention to this area of chemistry. Metals such as Zn,[4] In,[5] Bi,[6] Sn,[7] Pb,[8] Mn,[9] Mg,[10] or Sb,[11] have been reported to be effective in mediating the coupling between allyl halides and carbonyl compounds to give the corresponding homoallylic alcohols in aqueous media (Scheme 1). Among these reported metals, all of them except Sb were found to effect the transformation with commercially available metal powder, even though in cases such as Sn or Zn, activation was needed. In the case of antimony, however, commercial antimony metal was apparently not successful in mediating the allylation reaction in aqueous media. Several publications have appeared in the literature to indicate that the antimony metal must be formed in situ through the reduction of antimony trichloride with a reducing reagent such as Al or Fe[11a] or $NaBH_4$.[11b] The 'active' antimony, thus generated, could then mediate the allylation reaction in an aqueous/organic solvent system. As part of our general program[12] to study organometallic reactions in aqueous media, we are interested in finding conditions which can allow the use of commercial antimony directly without the need for the reductive generation step. Recently, we found that some fluoride salts are quite effective in 'activating' aluminum metal in aqueous media to mediate the reduction and/or pinacol coupling of carbonyl compounds.[13] We report here that fluoride salts are equally effective in 'activating' antimony in aqueous media to mediate the coupling of allyl bromide with aldehydes to give the corresponding homoallylic alcohols.

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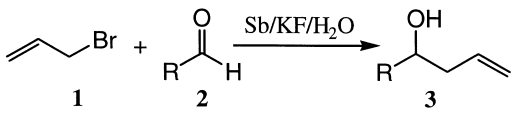
0040-4039/00/$ - see front matter 
PII: S0040-4039(00)00795-4




Scheme 1.

In agreement with previous reports, the reaction performed in distilled water with the molar ratio of Sb:benzaldehyde:allyl bromide at 5:1:2.5 gave no trace of the corresponding homoallylic alcohol even after a week of vigorous stirring of the reaction mixture (Entry 1, Table 1). It was obvious that activation of the metal was needed for this reaction to proceed. Therefore, we tried a number of alkaline metal fluoride salts as additives in the aqueous media. At 1 M concentration, RbF and CsF were found to be quite effective in activating the antimony to give a good yield of the corresponding homoallylic alcohol. At 2 M concentration, NaF and KF were found to be equally effective as RbF and CsF. On the other hand, even at 2 M concentration, KCl or KI were found to be less effective (entries 6 and 8, Table 1) and KBr was completely ineffective (Entry 7, Table 1).

Table 1
The factors that influence the allylation of benzaldehyde

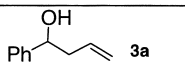
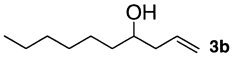
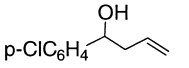
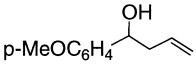
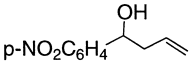
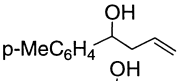
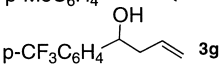
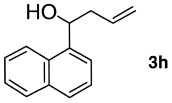
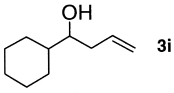
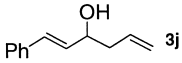
| Entries | Metal Halides | Yield%[a] (hr/d) | |
|---|---|---|---|
| | | 2 M | 1 M |
| 1 | LiF | 34 (16) | 10 (16) |
| 2 | NaF | 100 (16) | 28 (16) |
| 3 | KF | 100 (16) | 53 (16) |
| 4 | RbF | 100 (16) | 89 (16) |
| 5 | CsF | 100 (16) | 92 (16) |
| 6 | KCl | 62 (4d) | |
| 7 | KBr | 0 (4d) | |
| 8 | KI | 90 (4d) | |

[a] Based upon the $^1$H NMR analysis of crude mixture

We thus used 2 M KF as the standard reaction conditions to activate commercial antimony metal and examined its reactions with a number of carbonyl compounds. The results are summarized in Table 2. With these conditions, aldehydes could be allylated to give excellent yields of the products (Entries 1–10, Table 2). The results in Table 2 showed some interesting features of the antimony-mediated allylation reaction. First, the reaction was not sensitive to the nature of the aldehydes used. The reaction proceeded well with either aromatic or aliphatic aldehydes. The allylation of α,β-unsaturated aldehyde as represented by *trans*-cinnamaldehyde (entry 10, Table 2) occurred in a regiospecific manner and gave solely the 1,2-addition product. Furthermore, electron donating or withdrawing groups on the aromatic ring did not seem to affect the reaction significantly either in the yield of the product or the rate of the reaction. Thirdly, the reaction conditions appeared not to be reductive in nature. Thus, we did not detect alcohols or pinacols as side products of the reactions. Similarly, nitro function was not reduced under the reaction conditions. Thus, *p*-nitrobenzaldehyde was successfully allylated. Usually, the nitro group is sensitive to reduction

by metals and could not be allylated under Barbier conditions.[14] In this sense, the use of fluoride salts as activating agent is superior to the use of Al, Fe or $NaBH_4$ reported previously.[11] Finally, the reaction was chemoselective. Efforts to allylate ketones failed (Entries 11–13, Table 2) which is in agreement with literature reports using 'active' antimony.[11] Even the reactive carbonyl in methyl pyruvate (entry 13, Table 2) was left untouched.

Table 2
Allylation of carbonyl compounds mediated by Sb/KF in $H_2O$

| Entries | Carbonyl Compounds R', R" | Products | Yield |
|---|---|---|---|
| 1 | Ph, H |  **3a** | 100 |
| 2 | n-$C_6H_{13}$,H |  **3b** | 92 |
| 3 | p-$ClC_6H_4$,H |  **3c** | 96 |
| 4 | p-$MeOC_6H_4$,H |  **3d** | 87 |
| 5 | p-$NO_2C_6H_4$,H |  **3e** | 88 |
| 6 | p-$MeC_6H_4$,H |  **3f** | 98 |
| 7 | p-$CF_3C_6H_4$,H |  **3g** | 99 |
| 8 | 1-naphthyl,H |  **3h** | 96 |
| 9 | cyclohexyl,H |  **3i** | 94 |
| 10 | cinnamaldehyde |  **3j** | 89 |
| 11 | Ph,Me | | 0 |
| 12 | $(CH_2)_5$ | | 0 |
| 13 |  | | 0 |

*Standard procedures for the allylation of aldehydes are as follows*: To a mixture of aldehyde (1 mmol) in 2 M aqueous potassium fluoride solution (4 mL) and allyl bromide (2.5 mmol), antimony powder (2 mmol) was added in one portion and the mixture was vigorously stirred until the antimony powder was reacted (usually for 16 h). Ethyl ether was added to the reaction mixture and the organic layer was separated. The aqueous phase was extracted with ethyl ether. The organic extracts were combined and dried over $Na_2SO_4$, and was filtered and evaporated. The residue, for

most of the aldehydes, afforded the corresponding homoallylic alcohols of sufficient purity according to $^1$H NMR without the need for further purification. If necessary, purification was performed by flash chromatography over silica gel using EtOAc/hexane (to adjust the $R_f$ value of alcohol at about 0.15–0.2) as eluent. All the homoallylic alcohols reported in Table 2 are known compounds: 1-phenylbut-3-en-1-ol (**3a**),[15] 1-decene-4-ol (**3b**),[16] 1-(4-chlorophenyl)but-3-en-1-ol (**3c**),[17] α-propenyl-cyclohexanemethanol (**3i**),[18] 1-phenyl-1,5-hexadien-3-ol (**3j**),[19] 1-(4-nitrophenyl)-but-3-en-1-ol (**3e**),[20] 1-(4-methoxyphenyl)but-3-en-1-ol (**3d**),[21] 1-naphthylbut-3-en-1-ol (**3h**),[21] 1-(4-trifluoromethylphenyl)but-3-en-1-ol (**3g**),[22] 1-(4-methylphenyl)but-3-en-1-ol (**3f**).[22]

## Acknowledgements

We thank NSERC for financial support of this research.

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