Halogenation of alkenylaluminums by sulfonyl chloride and bromide

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Abstract

Sulfonyl halides (MsCl, TsCl, PhSO$_2$Cl, MsBr) are convenient and efficient halogenating agents for β,β- and α,β,β-substituted vinylaluminums

Introduction

One of the most widely used methods for the functionalization of organometallic compounds is electrophilic halogenation. Despite the fact that the reaction of diethyl zinc with benzenesulfonyl chloride affording ethyl chloride and zinc sulfinate is known since 19 century [1], we know very few examples of the use of sulfonyl halides as halogenating agents for the functionalization of organometallic species. H. Reinheckel and D. Jahnke have found that triethylaluminum and ethylaluminum sesquichloride react with sulfonyl chlorides to give sulfinic acids and ethyl chloride [2]. J.-F. Normant and co-workers have used benzenesulfonyl chloride for monochlorination of organogem*bis*zinc compounds [3]. Interestingly, the substitution of Zn on Cl may take place at sp^2-, and sp^3-hybridized carbon atom. However, allylzinc reagents have been used for the synthesis of β,γ-unsaturated sulfones through allylation of alkane- or arenesulfonyl chlorides [4]. Grignard reagents react with sulfonyl chlorides to generate the corresponding sulfones [5]. The reaction of alkenyl zirconium derivatives with aryl or alkyl sulfonyl chlorides in the absence of catalyst affords alkenyl sulfones under mild reaction conditions [6]. Aryl sulfonyl chlorides undergo a cross-coupling reaction with trialkylarylstannanes [7a] at 130 ^{o}C and with alkenyl stannanes [7b] in the presence of palladium complexes as catalysts to give arylsulfones. Diarylcadmium reagents react with aromatic sulfonyl chlorides to form mixture of aryl sulfones, aryl halides and sulfinic acids [8]. At the same time, diethylcadmium failed to produce sulfones as products [8b]. Thus, the pathways of the cross-coupling reaction (RM+R'SO$_2$X = RX+R'SO$_2$M *versus* R'SO$_2$R+MX) depend both on the nature of the metal and substituents at the metal.

Earlier we have demonstrated the efficiency of the use of alkyl esters of sulfonic acids for the alkylation of cyclic alkenylaluminums (aluminacyclopen-2-enes) [9]. High yields of the resulting cyclopropanes and selectivity of the transformation called our attention to the prospects of using the derivatives of sulfonic acids for the functionalization of alkenylaluminums. First of all we planned to explore the reaction of substituted alkenylaluminums that were prepared by various methods with sulfonyl halides, which we believed to be effective sources of electrophilic halogen. In this respect, it should be noted that halogens (Br$_2$, I$_2$) [10a], N-halogen succinimides (NCS, NBS, NIS) [10b] and pseudohalogens (BrCN, ICl) [10c] were used earlier for halogenation of alkenylaluminums and sulfonyl halides should be compared to these reagents.
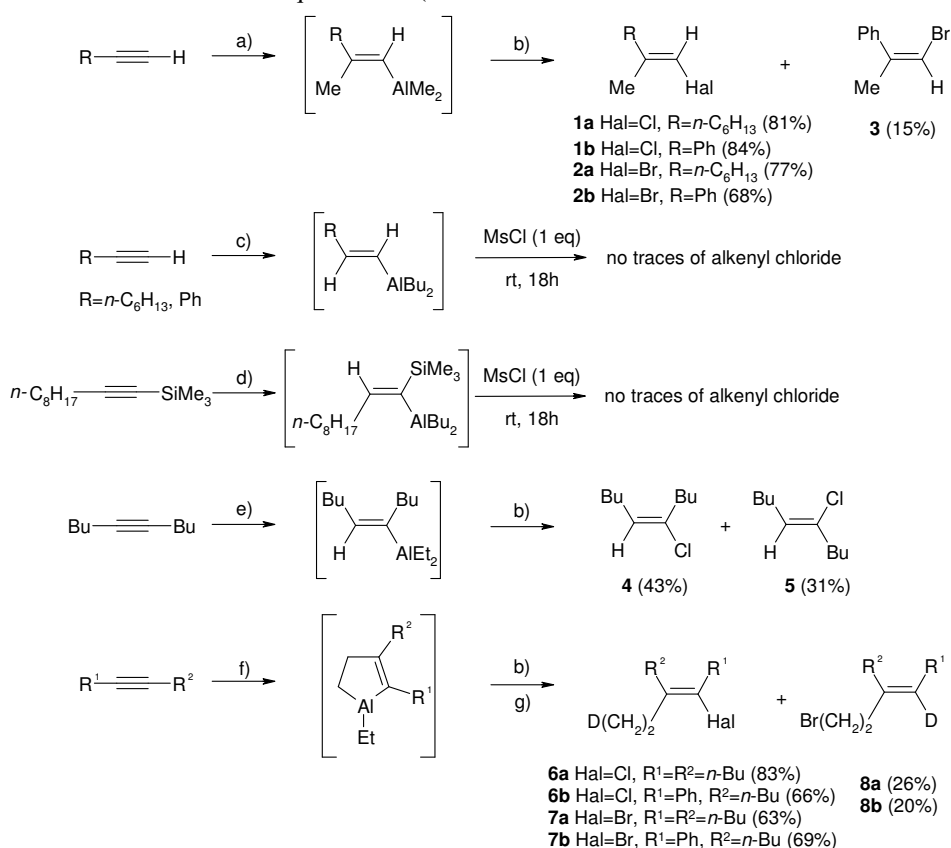
Results and Discussion

The isolation of pure samples of alkenylaluminums to study their reactivity is difficult because of their decomposition during distillation, and is not of interest from a practical point of view. Therefore, we examined the reactivity of alkenylaluminums prepared *in situ* by hydro- and carboalumination of alkynes. Here we should mention Negishi carboalumination [11] as one of the most useful transformation of alkynes. We found that alkenylaluminums obtained in Zr-catalyzed methylalumination of terminal alkynes (1-octyne, phenylacetylene) react with mesyl chloride or mesyl bromide for 15 minutes at room temperature in dichloromethane to give corresponding alkenyl halides **1a,b** or **2a,b** in high yield (Scheme 1). The transformation proceeds with the retention of the configuration of the double bond that was confirmed by NOE experiments [12]. However, the reaction of mesyl bromide with product of phenylacetylene methylalumination gave 15% of *E*-isomer **3** in addition to compound **2b** [13].

On the example of alkenylaluminum that was prepared by 1-octyne methylalumination, a number of sulfonyl halides (TsCl, PhSO$_2$Cl, MsBr, TsF) was examined. The yields of compound **1a** using tosyl chloride and benzenesulfonyl chloride were 88% and 90% respectively, which are virtually identical to that obtained in the case of mesyl chloride. Mesyl fluoride does not react with alkenylaluminums in the above conditions. Reagents for electrophilic fluorination (N-fluoro-*o*-benzenedisulfonimide (NFOBS), N-fluorobenzenesulfonimide (NFSI), and Selectfluor) [14] are characterized by the presence of stronger electron withdrawing groups at fluorine atom compared to sulfonyl group. We did not examine the reaction of alkenylaluminums with sulfonyl iodides due to their

thermal instability and high efficiency of iodine as iodinating agent.

Due to the ease of the procedure and the availability of sulfonyl halides, we studied the possibility of using this methodology for the halogenation of alkenylaluminums of different structure that were prepared by various methods. To our surprise, the reaction of sulfonyl halides (MsCl, TsCl, MsBr) with β-substituted vinylaluminums that were obtained by hydroalumination of terminal alkynes (1-octyne, phenylacetylene) by DIBAL-H does not afford expected alkenyl halides. We assumed that the presence of Cp_2ZrCl_2 in the reaction mixture could promote the reaction, but the addition of 0.1 equivalent (to

alkenylaluminum) did not have any effect. Apparently, this fact can be explained by a lower nucleophilicity of β-substituted vinylaluminums compared to β,β-substituted. Earlier it was found that β-substituted vinylaluminums react with aluminum sulfinates that were produced *in situ* from sulfonyl chlorides and Et_3Al to afford alk-1-enyl sulfoxides in good yields [15a]. The reaction of pyridine-complexed alkenylaluminums with sulfonyl chlorides in the presence of Ph_3PO gives the corresponding sulfones [15b].

1a Hal=Cl, R=n-C_6H_{13} (81%)
1b Hal=Cl, R=Ph (84%)
2a Hal=Br, R=n-C_6H_{13} (77%)
2b Hal=Br, R=Ph (68%)

3 (15%)

4 (43%) **5** (31%)

6a Hal=Cl, R^1=R^2=n-Bu (83%)
6b Hal=Cl, R^1=Ph, R^2=n-Bu (66%)
7a Hal=Br, R^1=R^2=n-Bu (63%)
7b Hal=Br, R^1=Ph, R^2=n-Bu (69%)

8a (26%)
8b (20%)

a) Me_3Al (2 eq), Cp_2ZrCl_2 (1 eq), CH_2Cl_2, rt, 3h; b) MsCl (for **1, 4-6** preparation) or MsBr (for **2, 3, 7, 8** preparation) (1 eq), rt, 15 min; c) DIBAL-H (1.5 eq), hexane, 50 °C, 5 h; d) DIBAL-H (1.1 eq), hexane, rt, 24 h; e) Et_3Al (2 eq), Cp_2TiCl_2 (0.05 eq), hexane, rt, 6 h; f) Et_3Al (2 eq), Cp_2ZrCl_2 (0.1 eq), hexane, 40 °C, 2h; g) D_2O

Scheme 1. Halogenation of alkenylaluminums.

Ti-catalyzed hydroalumination of 5-decyne by Et_3Al affords α,β-substituted vinylaluminum [16] that reacts with mesyl chloride to give a mixture of stereoisomeric alkenyl chlorides **4** и **5** in the ratio of ~4:3 [17]. On the other hand, the attempts to prepare (*E*)- and (*Z*)-1-chloro-1-alkenylsilanes [1b] by the reaction of mesyl chloride with corresponding alkenylaluminums [18] failed (Scheme 1). Apparently, this methodology is not suitable for halogenation of α,β-substituted vinylaluminums.

Thus, the best results were obtained for the halogenation of β,β-substituted vinylaluminums that were prepared by terminal alkynes carboalumination. Zr-Catalyzed cycloalumination of disubstituted alkyne by Et_3Al, also known as cyclic carboalumination, gives aluminacyclopent-2-ene that is a particular case of α,β,β-substituted vinylaluminum [19]. We assumed that nucleophilicity of α,β,β- and β,β-substituted vinyl anions is similar, so we expected that the reaction with sulfonyl halides will successfully proceed. We found that cycloalumination of

1-decyne and phenylacetylene affords aluminacyclopent-2-enes, which react with 1 equivalent of mesyl chloride to give after deuterolysis alkenyl chlorides **6a,b** in high yield. The chlorination proceeds regioselectively only at the sp^2-hybridized carbon atom and with the retention of the configuration of the double bond [20]. The increase in the amount of mesyl chloride up to 5 equivalents does not facilitate the chlorination of the second metal-carbon bond in the ring. Similar regiospecificity we have observed earlier in the alkylation of aluminacyclopent-2-enes by dialkyl sulfates [9]. The monobromination proceeds in the same way when using mesyl bromide instead of mesyl chloride. However, we observed the formation of isomers **8a,b** in an amount of 20-26% in addition to alkenyl bromides **7a,b**. It should be noted that bromination of aluminacyclopent-2-ene that was prepared from 5-decyne with NBS (one volume equivalent of ether, -20 ^{o}C) gives by-product **8** in higher yield (38%). NCS reacted with examined aluminacyclopent-2-enes in the same conditions to afford only compounds **6a,b**. The yields of alkenyl chlorides were close to that were observed when using MsCl, TsCl and $PhSO_2Cl$.

It should be noted that in contrast to our procedure, the halogenation of alkenylaluminums with NCS and NBS requires the use of ether solvents (Et_2O or THF) and low temperature of the reaction (-20 ^{o}C) [10b]. Bromination of alkenylaluminums proceeds with Br_2 at the temperature -70 - (-50) ^{o} C [10a]. However, halogens (Br_2, I_2) and *N*-halogen succinimides (NCS, NBS) have successfully used for the halogenation of β-substituted vinylaluminums that were inactive in our reaction.

Conclusions

Thus, the sulfonyl chloride and bromide are more convenient halogenation agents for β,β- and α,β,β-substituted vinylaluminums that were prepared by Zr-catalyzed methylalumination and cycloalumination compared to NCS and NBS, which is manifested in the facts that: a) the reaction proceeds at room temperature; b) the reaction does not require the use of ether solvent (moreover, the latter inhibits the halogenation), c) higher regioselectivity for the bromination of aluminacyclopent-2-enes is observed.

Experemental

General

The reagents were obtained from Aldrich or Acros. Dichloromethane and hexane were distilled over P_2O_5. Mass spectra were obtained on a Finnigan 4021 instrument. Nuclear Magnetic Resonance spectroscopy was performed on a Brucker Avance-400. The ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra at 100 MHz in $CDCl_3$. The chemical shifts are reported in ppm relative to tetramethylsilane (TMS) as the internal standard. The yields of the products were calculated from GC peak areas by the corrected area normalization method with undecane or hexadecane as the internal standard.

*Synthesis of (1E)-1-chloro-2-methyl-1-octene (**1a**).* To 0.58 g (2 mmol) of Cp_2ZrCl_2 suspended in 5 mL of CH_2Cl_2 was added under an atmosphere of argon 0.29 g (0.38 mL, 4 mmol) of Me_3Al (*caution: organoaluminums are pyrophoric and can ignite on contact with air, water or any oxidizer*) at 23 ^{o}C. All of the Cp_2ZrCl_2 dissolved to give a lemon-yellow solution. To the solution was added 0.22 g (0.30 mL, 2 mmol) of 1-octyne. After 3 h, to the reaction mixture was added 0.23 g (0.15 mL, 2 mmol) of mesyl chloride at 23 ^{o}C and stirred for 15 minutes. The reaction was terminated by dilution with CH_2Cl_2 (10 mL) followed by treatment with a 7 wt% aq. solution of HCl. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were then washed with saturated $NaHCO_3$ solution and dried over anhydrous $CaCl_2$. The solvent was removed under reduced pressure and the residue distilled to give 0.26 g of transparent oily liquid (81 % isolated yield). ^{1}H NMR (δ, ppm, *J*/Hz): 0.91 (t, 3H, *J* = 7), 1.2-1.38 (m, 4H), 1.38-1.5 (m, 4H), 1.78 (s, 3H), 2.07 (t, 2H, *J* = 8), 5.8 (s, 1H). ^{13}C NMR (δ, ppm): 14.06, 16.34, 22.58, 27.46, 28.77, 31.63, 37.09, 111.61, 138.97.

*Synthesis of (5E)-5-chloro-6-(2-deuteroethyl)-5-decene (**6a**).* To 0.058 g (0.2 mmol) of Cp_2ZrCl_2 suspended in 5 mL of hexane was added under an atmosphere of argon 0.36 mL (2 mmol) of 5-decyne and 0.6 mL (4 mmol) of Et_3Al at 40 ^{o}C. After 2 h, to the reaction mixture was added 0.23 g (0.15 mL, 2 mmol) of mesyl chloride at 40 ^{o}C and stirred for 15 minutes. Further treatment was as above. The solvent was removed under reduced pressure and the residue distilled to give 0.34 g of transparent oily liquid (83 % isolated yield). ^{1}H NMR (δ, ppm): 0.88-1.1 (m, 6H), 1.28(m, 2H), 1.5-1.6(m, 2H), 2.05-2.15 (m, 4H), 2.15-2.28 (m, 2H), 2.15-2.45 (m, 6H). ^{13}C NMR (δ, ppm, *J*/Hz): 11.79 (t, 2H, CH_2D, *J* = 19), 13.95, 13.98, 22.01, 22.76, 26.52, 30.26, 30.89, 31.72, 34.83, 129.17, 136.94.

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[12] NOESY spectrum of compound **1a** shows a cross-peak between the singlet of hydrogen atom at the double bond and triplet of α-methylene hydrogen atoms of *n*-hexyl group.

[13] The identification of the *Z*-isomer was carried out by NMR spectroscopy. ^{1}H NMR spectra of *Z*-and *E*-isomers are similar, however, the signals of the methyl group and the hydrogen atom at the double bond in **3** are shifted to strong field by 0.11 and 0.18 ppm, respectively, compared to the signals in the compound **2b** (Davis, D. R.; Roberts, J. R. *J. Am. Chem. Soc.* **1962**, *84*, 2252).

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