Journal of Fluorine Chemistry 173 (2015) 69–76

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Highly regio- and stereoselective hydrosilylation of β-fluoroalkylated α,β-unsaturated ketones

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A R T I C L E I N F O

Article history:
Received 19 January 2015
Received in revised form 6 February 2015
Accepted 7 February 2015
Available online 28 February 2015

Keywords:
Hydrosilylation
β-Fluoroalkylated α,β-unsaturated ketones
Dicobalt octacarbonyl
Regioselective
Stereoselective
Aldol reaction

A B S T R A C T

Treatment of β-fluoroalkylated α,β-unsaturated ketones with 10.2 equiv of triethylsilane in the presence of 3 mol% of $Co_2(CO)_8$ in dichloroethane at the reflux temperature for 4 h gave 1,4-hydrosilylated adducts in a highly regio- and stereoselective manner. Thus-obtained silyl enol ethers underwent a smooth Mukaiyama aldol reaction with benzaldehyde in the presence of 1.2 equiv of $TiCl_4$ in CH_2Cl_2 at −78 °C for 1 h, affording the corresponding α-(2,2,2-trifluoroethyl)-β-hydroxy ketones with high *syn* stereoselectivity in good yields.

1. Introduction

Transition metal-catalyzed hydrosilylation of α,β-unsaturated carbonyl compounds has been recognized as one of the most important and valuable synthetic methods for the preparation of silyl enol ethers [1]. This is because the reaction generally proceeds in a 1,4-addition manner to produce the corresponding silyl enol ethers, which can participate well in the subsequent various reactions, such as Mukaiyama aldol reaction [2], Michael addition [3], alkylation [4], halogenation [5], oxidation [6], and so on [7] (Scheme 1). Therefore, it is not surprising that there have been voluminous researches on hydrosilylation reactions of *nonfluorinated* α,β-unsaturated carbonyl compounds. However, most of the researches are concerned with the hydrosilylation catalyzed by very expensive rhodium, palladium, platinum, or gold catalysts, and little attention has been paid to inexpensive transition metal-catalyzed hydrosilylation thus far [8]. In addition, to the best of our knowledge, hydrosilylations of *fluorinated* α,β-unsaturated carbonyl compounds have hardly been reported [9].

As a part of our research project on hydrometallation reactions of various fluorinated substances [10], herein is described the highly regio- and stereoselective hydrosilylation reaction of various β-fluoroalkylated α,β-unsaturated ketones **1** in the presence of relatively inexpensive cobalt catalyst in detail (Scheme 2). Moreover, we wish to disclose the highly *syn*-selective aldol reactions using thus-obtained hydrosilylated adducts **2**.

2. Results and discussion

2.1. Preparation of β-fluoroalkylated α,β-unsaturated ketones

Initially, we began with the preparation of various β-fluoroalkylated α,β-unsaturated ketones **1A**–**H**. As shown in Scheme 3, **1A**–**C** were easily prepared from commercially available fluorinated hemiacetals **3**, **4** or hydrate **5** and the enamine **6** according to the literature (Scheme 3, eq. 1) [11]. On the other hand, **1D**–**H** were prepared with slight modifications of the reported procedure (Scheme 3, eq. 2) [12]. Thus, treatment of 2-bromo-3,3,3-trifluoropropene **7** (1.0 equiv) with LDA (2.2 equiv) in THF at −78 °C for 5 min, followed by the addition of various aldehydes (1.0 equiv) into the resultant reaction mixture, gave the corresponding γ-fluoroalkylated propargyl alcohols **8** [12,13]. Without purification, thus-obtained propargyl alcohols **8** were subjected to an excess amount of $NaBH_4$ in ethanol at room temperature for 14 h, affording the corresponding γ-fluoroalkylated allylic alcohols **9** in good yields. Finally, the allylic alcohols were easily oxidized by MnO_2 at the reflux temperature to provide the desired β-fluoroalkylated α,β-unsaturated ketones **1**.

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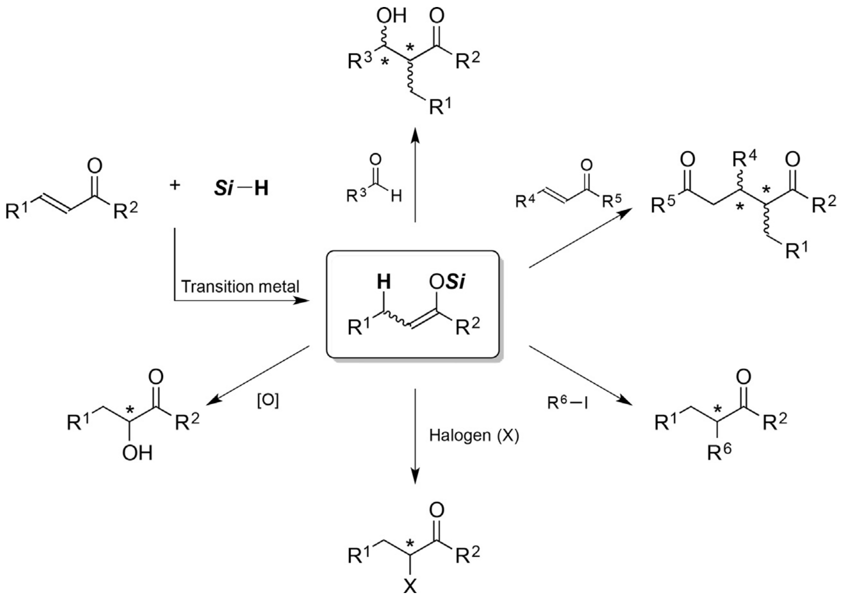
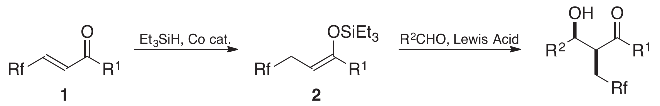
http://dx.doi.org/10.1016/j.jfluchem.2015.02.010



Scheme 1. Hydrosilylation of α,β-unsaturated carbonyl compounds and the synthetic applications.



Scheme 2. Present work.

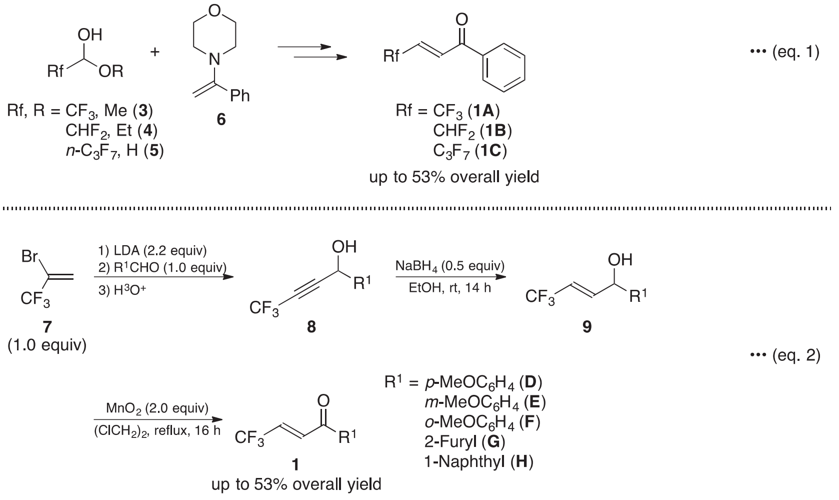
2.2. Hydrosilylation of β-fluoroalkylated α,β-unsaturated ketones

With various types of substrates in hand, our attention was directed toward the examination of the hydrosilylation reaction of **1A**–**H**. First of all, we started the exploitation of the optimum reaction conditions by using **1A**, as shown in Table 1. Thus, treatment of **1A** with 1.2 equiv of Et_3SiH in the presence of 5 mol% of $Co_2(CO)_8$ in dichloroethane at the reflux temperature for 12 h resulted in a complete consumption of the starting ketone, affording the 1,4-hydrosilylated adduct **2Aa** with high *Z* selectivity in 78% yield, together with 7% of the 1,2-hydrosilyated adduct **10Aa** [14]. It was also revealed that the reaction completed within 2 h without any decrease of the yield and the stereoselectivity (Entry 2). Although a lower loading of the catalyst afforded the desired product in only 61% yield (Entry 3), prolonged reaction under 3 mol% loading of the catalyst afforded the desired product quantitatively (Entry 4). At lower temperature, the reaction hardly proceeded (Entry 5). Very interestingly, rhodium or platinum catalysts, very frequently employed for hydrosilylation of the nonfluorinated substances, were found not to be suitable for this reaction (Entries 6–9).

We next examined a series of silanes as summarized in Table 2. In the case of $PhMe_2SiH$, the desired **2Ab** was obtained in only 54% yield though the starting material was completely consumed (Entry 2). Additionally, the stereoselectivity of **2Ab** still remained very high, but the regioselectivity significantly decreased. It was also revealed that use of $(EtO)_2MeSiH$ and $(EtO)_3SiH$ caused a significant decrease of the regioselectivity (Entries 3 and 4) [15].

With the best reaction conditions in hand, we next tested a variety of β-fluoroalkylated α,β-unsaturated ketones for the hydrosilylation reaction. The results are summarized in Table 3.

As shown in Entries 2–4, the position of a substituent on the benzene ring in the substrate did not influence on the reaction at all, providing the corresponding silyl enol ethers **2Da**, **2Ea**, **2Fa** in a highly regio- and stereoselective manner. Additionally, the ketones



Scheme 3. Preparation of various β-fluoroalkylated α,β-unsaturated ketones.