Journal of Fluorine Chemistry 205 (2018) 58–61

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

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

Reductive silylation of *gem*-difluorinated phosphonium salts

Artem V. Tsymbal[a,b], Vitalij V. Levin[a], Marina I. Struchkova[a], Vladimir A. Kokorekin[a,c], Alexander A. Korlyukov[d,e], Alexander D. Dilman[a,*]

[a] *N. D. Zelinsky Institute of Organic Chemistry, 119991, Moscow, Leninsky prosp. 47, Russian Federation*
[b] *M. V. Lomonosov Moscow State University, Department of Chemistry, 119991, Moscow, Leninskie Gory 1-3, Russian Federation*
[c] *I. M. Sechenov First Moscow State Medical University, 119991, Moscow, Trubetskaya st. 8-2, Russian Federation*
[d] *A. N. Nesmeyanov Institute of Organoelement Compounds, 119991, Moscow, Vavilov str. 28, Russian Federation*
[e] *N. I. Pirogov Russian National Research Medical University, Ostrovitianov str., 1, 117997, Moscow, Russian Federation*

ARTICLE INFO

Dedicated to the memory of George Olah

Keywords:
Difluorinated compounds
Phosphonium salts
Silicon reagents
Reductive silylation

ABSTRACT

gem-Difluorinated phosphonium salts, generated from aldehydes and difluorinated phosphobetaine reagent, were converted into corresponding silicon reagents. The reductive silylation of carbon-phosphorus bond is carried out using a combination of magnesium and chlorotrimethylsilane in dimethylformamide. For a model difluoroined phosphonium salt, X-ray structure and reduction potential are provided.

1. Introduction

Fluorinated silicon reagents have found widespread use as reagents for the synthesis of organofluorine compounds [1,2]. The major applications of fluorinated silanes correspond to the use of the Ruppert-Prakash reagent [1], which is associated with significance of the trifluoromethyl group for pharmaceutical research [3] coupled with ready availability of the reagent. At the same time, difluorinated silanes are more difficult to access.

Originally, fluorinated silanes were prepared from fluorinated bromides using highly air sensitive phosphorus (III) compounds [4]. Some silanes can be prepared from bromides and iodies by halogen/metal exchange followed by silylation [5]. However, because of limited stability of fluorinated lithium and magnesium reagents, the scope of this method is narrow. Another approach involves the reductive silylation reaction involving a combined use of a metal and a silylating reagent (for example, Me_3SiCl) [6] (Scheme 1). Besides bromides and iodides, various sulfur compounds such as sulfides, sulfoxides, and sulfones were transformed into the corresponding silanes using magnesium metal [7]. The advantage of this method is that the short-lived intermediate carbanionic species is rapidly trapped by the silylating agent [8]. Herein we report that the reductive silylation reaction can be applied to fluorinated phosphonium salts, which can be obtained from simple staring compounds [9].

2. Results and discussion

Difluorinated phosphonium salts **2** were generated from aldehydes, chlorotrimethylsilane, and difluorinated phosphobetaine reagent **1** [9a,10] (Table 1). The reaction was performed at 45 °C in dimethylformamide. Then, magnesium turnings and excess amount of chlorosilane were added, and the mixture was stirred for two days at room temperature. After work-up, the crude product was desilylated by brief treatment with a solution of hydrogen chloride in methanol. Finally, hydroxy-substituted silanes **3** were purified by flash column chromatography. While aromatic aldehydes gave alcohols **3** in reasonable yields, aliphatic alcohols were problematic. Thus, the reaction of hydrocinnamaldehyde gave a complex mixture containing less than 30% of the expected product according to ^{19}F NMR.

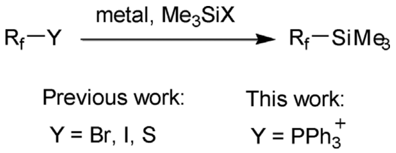
For silane **3a**, the structure was determined by X-ray analysis (Fig. 1) [11]. The structure has staggered conformation along the C—C bond with gauche orientation of hydroxy and trimethylsilyl groups (see projection in Fig. 1). As is typical for other fluorinated trimethylsilyl compounds [12], in the structure of **3a** the bond between the silicon atom and a fluorinated carbon ($Si\text{-}CF_2$, 1.9300(13) Å) is longer than other $Si\text{-}CH_3$ bonds (average 1.85 Å).

The proposed mechanism for the reductive silylation is shown in Scheme 2. It is likely that the reaction starts from the single electron reduction of the phosphonium salt **2** with magnesium to generate free radical **4**, which then leads to organomagnesium species **5**. Subsequent rapid silylation of carbon-magnesium bond of intermediate **5** leads to

---

[*] Corresponding author.
E-mail address: adil25@mail.ru (A.D. Dilman).

https://doi.org/10.1016/j.jfluchem.2017.11.009
Received 5 October 2017; Received in revised form 22 November 2017; Accepted 22 November 2017



Scheme 1. Synthesis of fluorinated silanes.

fluorinated silane **6**. To verify the radical character of the process, the salt **2a** was treated with magnesium in the presence of TEMPO (1 equiv). As a result, a compound originating from the trapping of radical **4** with TEMPO was formed (supported by ^{19}F NMR and GC–MS data). At the same time, attempts to intercept organomagnesium species **5** by other electrophiles such as 4-chlorobenzaldehyde or D_2O were unsuccessful.

Since phosphonium salts **2** can generate free radicals under reductive conditions [13,14], it was important to evaluate their structure and reduction potential. Previously, salts **2** were observed only by NMR spectroscopy [9a,c]. Herein, we were able to isolate a phosphonium salt in crystalline state and preform its complete characterization. Thus, for salt **2a**, derived from 2-chlorbenzaldeyde, the chloride counter ion was exchanged by iodide, and subsequent slow diffusion technique allowed to prepare salt **2a-I** suitable for X-ray analysis (Fig. 2) [11]. Similar to silane **3a**, phosphonium salt **2a-I** has gauche arrangement of silyloxy and phosphonium groups (see projection in Fig. 2).

It is likely that the conformational preference of compounds **2a-I** and **3a** is associated with steric effects. Thus, in observed conformations, bulky trimethylsilyl or tripehnylphosphonium fragments are located in anti-periplanar orientation with respect to the aryl group. Moreover, the structures of **2a-I** and **3a** have a stabilizing anti-periplanar σ(C—H)/σ*(C—F) interaction [15].

The reduction potential of salt **2a-I** in dimethylformamide was measured by cyclic voltammetry, and was determined to be −1.48 V (vs. SCE, see Supplementary data for CV curves). It should be pointed out that the potential of phosphonium salt **2a-I** is notably less negative compared to that of unsubstituted difluorinated iodide ($PhCH_2CF_2I$, −1.11 V [16]) suggesting that for the generation of free radicals, the cleavage of carbon-phosphorus bond requires notably stronger reducing agent compared to that for the reduction of the carbon-iodine bond [17].

3. Conclusions

In summary, a reductive silylation of carbon-phosphorus bond of *gem*-difluorinated phosphonium salts was demonstrated. The reaction is performed using magnesium as a stoichiometric reducing agent, and afforded a series of novel fluorinated silicon reagents.

4. Experimental

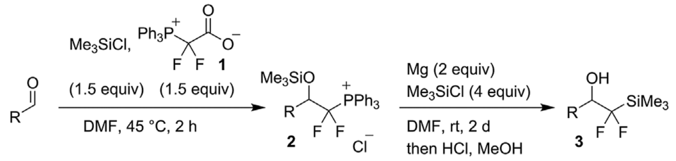
4.1. General experimental procedures

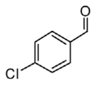
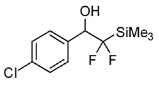
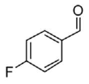
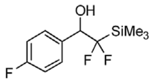
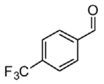
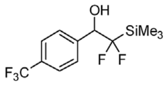
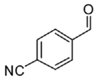
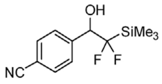
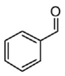
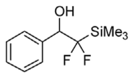
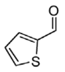
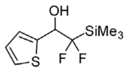
All reactions were performed under an argon atmosphere. DMF was distilled under vacuum from P_2O_5 and stored over MS 4 Å. NMR spectra were recorded on a Bruker AM-300 instrument. Phosphobetaine reagent **1** was obtained according to a literature procedure [10a].

4.2. Preparation of salt 2a-I

A mixture of *p*-chlorobenzaldehyde (176 mg, 1.25 mmol), phosphobetaine (534 mg, 1.50 mmol), and Me_3SiCl (212 µL, 1.66 mmol) in 1,2-dichloroethane (1.2 mL) was heated at 50 °C (water bath) with stirring for 1 h. The resulting colorless solution was cooled to room

Table 1
Synthesis of silanes 3.



Entry	Aldehyde	Silane **3**		Yield of **3**, %[a]
1			**3a**	59
2			**3b**	53
3			**3c**	61
4			**3d**	41
5			**3e**	51
6			**3f**	44

[a]Isolated yield.