Pergamon

Tetrahedron Letters 43 (2002) 5813–5815

TETRAHEDRON
LETTERS

New synthesis of α-benzylaldehydes from 2-(dimethylphenylsilylmethylene)alkanals by fluoride promoted phenyl migration

Laura Antonella Aronica, Francesca Morini, Anna Maria Caporusso and Piero Salvadori*

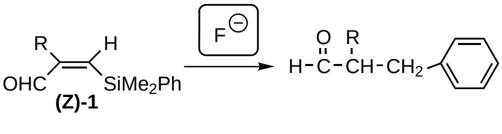
Dipartimento di Chimica e Chimica Industriale, Istituto del CNR di Chimica dei Composti Organo Metallici (ICCOM), sezione di Pisa, Via Risorgimento, 35, 56126 Pisa, Italy

Received 16 May 2002; revised 14 June 2002; accepted 17 June 2002

Abstract—α-Benzyl aldehydes are prepared from easily available β-silylalkenals and fluoride reagents, under mild experimental conditions; the reaction occurs instantaneously with almost quantitative yields. A plausible mechanism is suggested, which involves a 1,2-phenyl migration from the silicon to the adjacent carbon atom. © 2002 Elsevier Science Ltd. All rights reserved.

α-Benzyl aldehydes are extremely useful intermediates in organic synthesis[1] and important industrial substrates.[2] They are usually prepared starting from cinnamaldehydes by hydrogenation or selective addition of alkyl lithium to the carbon–carbon double bond,[3] provided that the carbonyl group is protected. Both these methods suffer from strong experimental conditions, since hydrogenation requires high H_2 pressure and temperature (50 psi, 200–400°C) and carbolithiation must be performed with excess of RLi at −78°C. More complicated methodologies involve multistep sequences starting from Fischer alkenyl carbene complexes,[4] aziridines,[5] pseudoephedrine derivatives[6] and α-benzyloxazolidinones.[7]

In this paper we describe a new convenient synthesis of α-benzyl aldehydes **2** starting from β-silylalkenals (*Z*)-**1**, based on the fluoride affinity for silicon[8] (Scheme 1).



Scheme 1.

Various fluoride sources such as KF, BF_3, TBAF were tested and the obtained results are reported in Table 1. KF/MeOH and TBAF/MeOH were completely ineffective (Table 1, entries 1, 2): (*Z*)-**1** was recovered completely unreacted. This lack of activity could be due to the strong hydrogen bonds between the hydroxy group of methanol and the fluoride ion. As a consequence, F^- resulted shielded and could not coordinate the silicon atom.

The reaction with BF_3–acetic acid complex generated a mixture of (*E*)-2-(dimethylphenylsilylmethylene)hexanal (*E*)-**1a** and 2-benzylhexanal **2a** (Table 1, entry 3). The formation of the *trans* isomer (*E*)-**1a** (thermodynamically more stable) can be easily explained considering the acidic experimental conditions (CH_3COOH) that cause addition of proton to the double bond, formation of a β-stabilised carbocation which, after rotation through the C–C σ bond and consequent deprotonation, affords (*E*)-**1a** (Scheme 2). Indeed, when paratoluensulfinic acid (*p*-TsH) was used, exclusive isomerisation of the β-silylalkenal was observed (Table 1, entry 4).

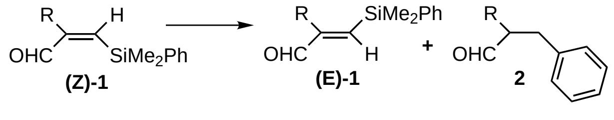
When the reaction was performed at room temperature (25°C) with tetrabutylammonium fluoride in DMSO and hydrolysed immediately after adding TBAF, the complete conversion of the substrate to 2-benzylhexanal **2a** was observed. One mole of fluoride source was sufficient (Table 1, entries 5, 6) and the reaction proceeded in various polar aprotic solvents, such as DMSO, THF, CH_3CN (Table 1, entries 6–8), resulting completely chemoselective: **2a** was exclusively formed.

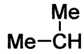
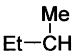
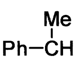
Keywords: α-benzyl aldehydes; alkynes; β-silylalkenal; silicon and compounds.

* Corresponding author. Tel.: +39-050-918273; fax: +39-050-918260; e-mail: psalva@dcci.unipi.it

PII: S0040-4039(02)01178-4

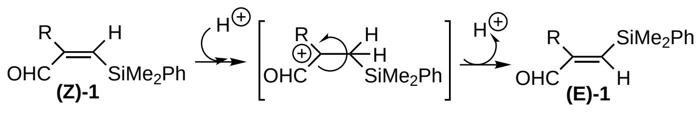
Table 1. Synthesis of 2-benzylaldehydes **2** from β-silylakenals[a] (*Z*)-**1**



Entry	(*Z*)-**1**	R	Reaction conditions	Reagent/substrate (molar ratio)	Yield (%)[b]	
			reagent/solvent/temp./time		(*E*)-**1**	**2**
1	**a**	*n*Bu	KF/MeOH/rt/24 h	10	–	–
2	**a**	*n*Bu	TBAF/MeOH/rt/24 h	1	–	–
3	**a**	*n*Bu	BF_3–$2CH_3COOH$/CH_2Cl_2/rt/24 h	1	80	20
4	**a**	*n*Bu	TsH/CH_3CN/80°C/24 h	0.2	100	–
5	**a**	*n*Bu	TBAF/DMSO/rt/1 min	5	–	100 (68)
6	**a**	*n*Bu	TBAF/DMSO/rt/1 min	1	–	100
7	**a**	*n*Bu	TBAF/THF/rt/1 min	1	–	100
8	**a**	*n*Bu	TBAF/CH_3CN/−60°C/1 min	1	–	100
9	**a**	*n*Bu	TBAF/THF/rt/1 h	0.1	–	100
10	**b**	 $\mathrm{Me{-}\overset{Me}{\overset{\vert}{C}}H}$	TBAF/DMSO/rt/1 min	1	–	100 (46)
11	**c**	 $\mathrm{Et{-}\overset{Me}{\overset{\vert}{C}}H}$	TBAF/DMSO/rt/1 min	1	–	100 (71)
12	**d**	 $\mathrm{Ph{-}\overset{Me}{\overset{\vert}{C}}H}$	TBAF/DMSO/rt/1 min	1	–	100 (60)

[a] Reactions were run with 1 mmol of substrate in 10 ml of solvent. β-Silylalkenals (*Z*)-**1a**–**d** were prepared by rhodium catalysed silylformylation of the corresponding acetylenes, performed in a stainless steel autoclave, under 10 atm of CO, at room temperature for 24 h.[10]

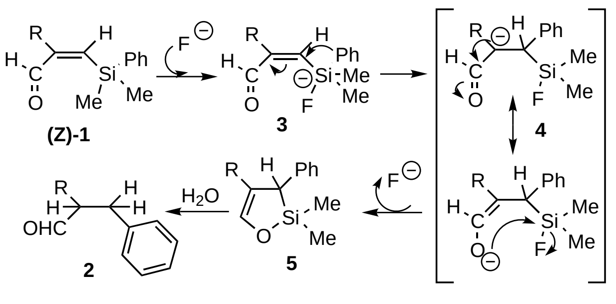
[b] Determined by GLC of the reaction mixture after work up. All new compounds were identified and characterised by FT-IR, NMR (^1H and ^{13}C), GC–MS and elemental analysis. In parentheses the isolated yields of pure compounds are reported.



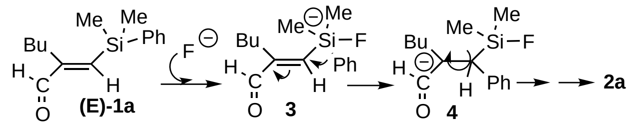
Scheme 2.

For instance, when (*Z*)-**1a** was reacted with an equimolar amount of TBAF in CH_3CN, the yield of 2-benzylhexanal was quantitative within 1 minute at −60°C (Table 1, entry 8). The reaction was successfully extended to branched β-silylalkenals (Table 1, entries 10–12) and afforded the corresponding 2-benzylaldehydes **2b**–**d** with good yields after purification (not optimised), showing the high potentialities of this process.

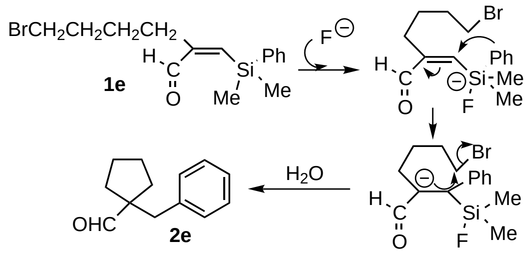
To our knowledge, no data on this fluoride–silicon mediated transformation are reported. The reaction seems to involve a 1,2-migration of phenyl from the silicon atom to the adjacent carbon atom. Indeed, it is known that fluoride ion reacts with phenyltrimethylsilane to generate a phenyl ion[9] which could act as nucleophile on the α,β-unsaturated aldehyde. A possible mechanism is reported in Scheme 3. Fluoride adds to (*Z*)-**1** forming the pentacoordinate silicon derivative **3**, the phenyl group migrates generating the enolate **4** which can intramolecularly cyclise to form silylenolether **5**. After hydrolysis 2-benzylaldehydes **2** are obtained. According to this mechanism, a catalytic amount of TBAF (0.1 mol) in DMSO determines a complete conversion of (*Z*)-**1a** to **2a**, even if a longer reaction time is necessary (Table 1, entry 9). Moreover, when (*E*)-2-(dimethylphenylsilylmethylene)hexanal (*E*)-**1a** was reacted with an equimolar amount of TBAF in DMSO, 2-benzylhexanal **2a** was exclusively obtained, confirming the formation of enolate **4** which can rotate through the *sp*^{3} C–C bond (Scheme 4).



Scheme 3.



Scheme 4.



Scheme 5.

Finally, 1-benzylcyclopentancarbaldehyde **2e** was obtained when (*Z*)-2-(dimethylphenylsilylmethylene)-6-bromohexanal (*Z*)-**1e** was reacted with tetrabutylammonium fluoride (Scheme 5). In this case, after addition of fluoride to silicon and subsequent phenyl transposition to the alpha carbon atom, an intramolecular attachment of the formed carbanion on the carbon bearing bromine could occur. Hydrolysis of the C–Si bond afforded **2e** quantitatively, confirming the mechanism proposed in Scheme 3.

In conclusion, this promoted fluoride regioselective phenyl migration represents a direct methodology for the preparation of 2-benzylaldehydes from β-silylalkenals (*Z*)-**1**. Considering that compounds (*Z*)-**1** can be easily generated by Rh-catalysed silylformylation of 1-alkynes with phenylsilanes,[10] the above results open a new route to the synthesis of 2-benzylaldehydes starting from acetylenic substrates.[11] The extension and optimisation of this method to the preparation of a large variety of aryl and heteroaryl aldehydes is in progress.

Acknowledgements

Financial support for this work was provided by the Ministero dell'Istruzione, dell'Universita' e della Ricerca (MIUR).

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11. 2-Benzylhexanal **2a** (representative procedure): 3 mmol of Me_2PhSiH, 3 mmol of 1-hexyne, 3 mL of toluene and 0.0022 g (3×10^{-3} mmol) of $Rh_4(CO)_{12}$ were put in a Pyrex 'Schlenk' tube, under CO atmosphere. This solution was introduced in a 25 mL stainless steel autoclave fitted with a Teflon inner crucible and a stirring bar, previously placed under vacuum (0.1 mmHg), by a steel siphon. The reactor was pressurised with 10 atm of carbon monoxide and the mixture was stirred at room temperature for 24 h. After removal of excess CO (fume hood), the reaction mixture was diluted with pentane, filtered (Celite) and concentrated by bulb to bulb distillation (1 mmHg). The residue was purified by column chromatography on silica gel using pentane/EtOAc (95/5) as eluent, affording the pure aldehyde[10] (*Z*)-**1a** (85%). To a solution of 0.24 g (1 mmol) of (*Z*)-**1a** in 10 ml of DMSO, was added, at room temperature, 1 ml of TBAF (1 M in THF). The reaction mixture was hydrolysed with water, extracted with Et_2O and the organic layers were dried over Na_2SO_4. After concentration under vacuum, the crude product was purified by column chromatography on silica gel using hexane/EtOAc (90/10) as eluent, affording the title compound **2a** (68%).[3b]