Pergamon

Tetrahedron Letters, Vol. 36, No. 40, pp. 7235-7238, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)01463-2

Reactivity Of Tris(Trimethylsilyl)silyl Radical With β-Alkenyloxyenones

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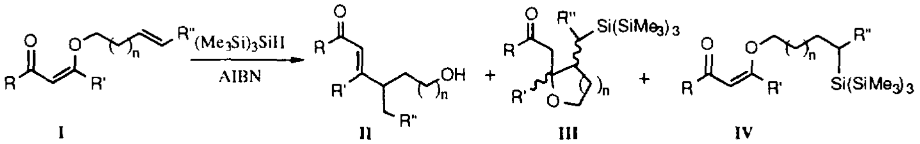
Abstract: *The addition of tris(trimethylsilyl)silyl radical on β-alkenyloxyenones generates an alkyl radical that can add onto the enone moiety. The tetrahydrofuranyl system so-obtained can undergo β-elimination leading to 3-alkylcycloalken-2-ones.*

Free radicals are of considerable importance in the formation of carbon-carbon bonds and have been used in the synthesis of polyfunctional molecules.[1] They can be generated by the reduction of functional groups by tri-*n*-butylstannane hydride and hexaphenyldistannane.[1, 2] However several problems are associated with the use of triorganostannane compounds such as their toxicity,[3] difficulty during the work up and isolation of the products.[4] In the last decade other organometallic hydride such as tri-*n*-butylgermanium hydride,[5] alkylmercuric hydride[6] and organosilanes[7] have been used. Trialkylsilanes are effective reducing agents for organic halides, selenides, xanthates and isocyanides as well as effective hydrosilylating agents for dialkylketones and alkenes.[8] Here, we would like to report that the addition of tris(trimethylsilyl)silyl radical on β-alkenyloxyenones **I** is chemoselective and can lead to compounds of type **II** and/or compounds of type **III** and **IV** depending on the substrate (Scheme 1). The results are reported in the Table.

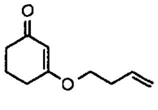
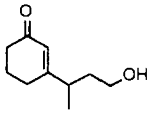
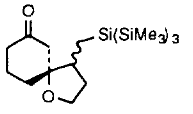
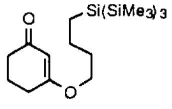
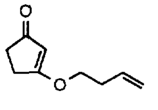
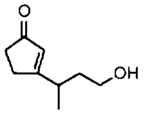
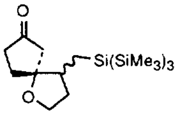
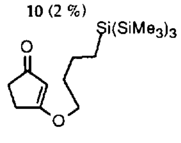
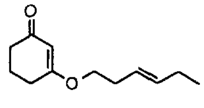
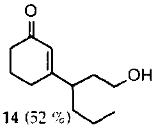
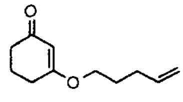
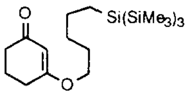
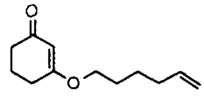
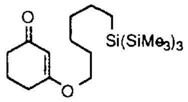
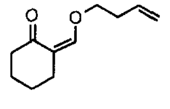
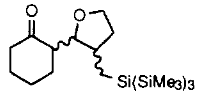
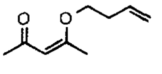
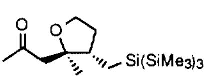
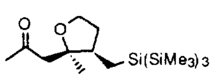
Scheme 1: Reactivity of tris(trimethylsilyl)silyl radical with β-alkenyloxyenones



Alkenyloxyenones **1-7** were prepared by refluxing 1,3-diones in toluene, in the presence of an unsaturated alcohol and a catalytic amount of *p*-toluenesulfonic acid.[9]

Heating 3-butenyloxycyclohex-2-en-1-one **1** with tris(trimethylsilyl)silane [$(Me_3Si)_3SiH$] and azo-bisisobutyronitrile (AIBN) in toluene under reflux allowed us to isolate alcohol **8** (50%), spirofuran **9** (29 %, de = 64%),[10] and β-alkanyloxyenone **10** (2 %). Under the same conditions, β-alkenyloxyenone **2**, gave alcohol **11**, spirofuran **12** (de = 30%) and compound **13** with 53 %, 30 % and 8 % yields respectively. In order to examine whether the substitution of the double bond would influence the chemoselectivity, compound **3** was treated with $(Me_3Si)_3SiH$/AIBN as above. In this case, the formation of the rearranged product **14** (52 %) was observed.

Table: Reactivity of β-alkoxyenones with $(Me_3Si)_3SiH$

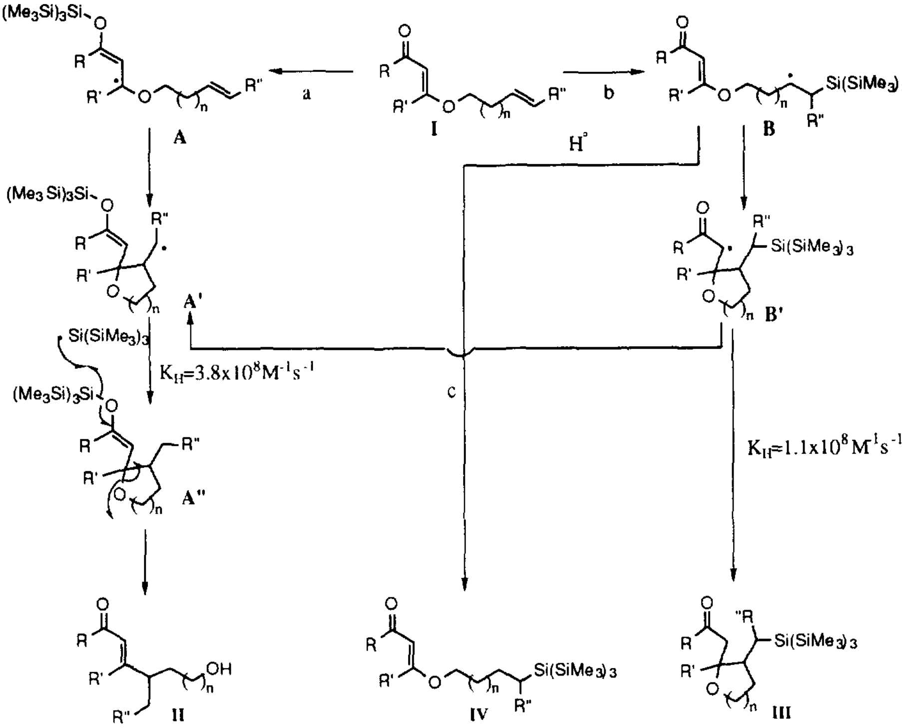
Starting Material	τ_C	Products (yield)		
 **1**	77 %	 **8** (50 %)	 **9** (29 %)	 **10** (2 %)
 **2**	85 %	 **11** (53 %)	 **12** (30 %)	 **13** (8 %)
 **3**	85 %	 **14** (52 %)		
 **4**	43 %	 **15** (31 %)		
 **5**	10 %	 **16** (5 %)		
 **6**	40 %	 **17** (38 %)		
 7	100 %	 **18** (25 %)	 **19** (58 %)	

In the case of enone **4**, substituted by a pent-4-enyloxy chain, and enone **5**, substituted by a hex-5-enyloxy chain, no product of cyclization could be detected.

It is interesting to note that compounds **6** and **7** were transformed into the corresponding tetrahydrofurans **17** and **18**-**19** (de = 41%) with moderate to good yields. The relative configurations of **18** and **19** were established using n.O.e. experiments.

The formation of products **8-19** can be explained by involving initial addition of the tris(trimethylsilyl)silyl radical onto the the carbonyl moiety and/or the exocyclic alkene of the β-alkenyloxyenones giving radicals of type **A** or **B** (Scheme 2)

Scheme 2: Mechanism of addition of the tris(trimethylsilyl)silyl radical onto β-alkenyloxyenones



Products of type **II** are derived from the cyclization (5-exo-trig)[11] of radical **A** into radical **A'** which is reduced with tris(trimethylsilyl)silyl hydride into silylenol ether **A"**. Attack of **A"** by a tris(trimethylsilyl)silyl radical leads to the cleavage of the C-O bond of the tetrahydrofuran and consequently to the formation of product of type **II** (path a).

The formation of compounds of type **III** can be explained by the addition of the tris(trimethylsilyl)silyl radical on the alkene moiety of the enone (path b). The radical **B** thus obtained can attack the β-carbon of the enone, producing the corresponding ketoalkyl radical **B'** (exo-trig process),[11] which can then abstract an hydrogen atom from $(Me_3Si)_3SiH$ very rapidly ($k_H \approx 1.1 \times 10^8\ M^{-1}\ s^{-1}$).[8a] We have to point out that the abstraction of an hydrogen atom by radical **B** from $(Me_3Si)_3SiH$ will lead to compounds of type **IV** (path c).

Compound of type **II** can be obtained only if the rate of the cyclization of radical **A** is faster than the rate of the cyclization of radical **B**, as the rate of the addition of a tris(trimethylsilyl)silyl radical onto an olefin is faster ($k \approx 3.7 \times 10^6\ M^{-1}\ s^{-1}$)[12] than the addition of a tris(trimethylsilyl)silyl radical onto a carbonyl ($k \approx 6.6 \times 10^5\ M^{-1}\ s^{-1}$)[12].

One yet cannot exclude the possibility that radical **B'** can undergo a silyl group transfer to form **A'** concurrently with its reduction.

The formation of **15** and **16** from **4** and **5** respectively as well as their low conversion can be explained by the fact that the rate of the abstraction of an hydrogen atom by **B** from $(Me_3Si)_3SiH$ $(k_H \approx 10^8\ M^{-1}\ s^{-1})$[8a] is faster than the formation of a 6-membered ring according to a 6-exo trig process[10] $(k < 5 \times 10^3\ M^{-1}\ s^{-1})$[13].

In the case of the s-*cis*-enones **6** and **7**, no rearranged products were formed. This can due to the fact that, in s-*cis* enones, π- orbitals are less conjugated than in s-*trans* enones, and consequently radical **A** is more difficult to form.

The addition of organosilyl radicals on alkoxyenones is chemoselective and allows the formation of β-alkylated enones and/or the formation of substituted tetrahydrofurans.

Experimental part

To a solution of enone (1 mmol) in toluene (20 mL), degassed by bubbling Ar, $(Me_3Si)_3SiH$ (1.4 mmol, 1.4 eq) and AIBN (0.1 mmol) were added. The reaction mixture was heated under reflux and every hour more AIBN (0.1 mmol) was added. After 5 h the solvent was evaporated and the residue purified by flash chromatography.

Acknowledgement:

Pr Guetté (CNAM) and Dr Rossey (Synthelabo) are thanked for allowing L. S. to work on this project. L. S. thanks the FONGECIF for financial support.

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10 - The observed diastereoselectivity is probably due to steric effects, see reference 8b.

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(*Received in France* 3 *July* 1995; *accepted* 1 *August* 1995)