Tetrahedron Letters, Vol. 34, No. 18, pp. 2927-2930, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

A One Pot Synthesis of α-(Alkoxysilyl)acetic Esters

Olivier Andrey, Yannick Landais* and Denis Planchenault

Institut de Chimie Organique, Université de Lausanne
Rue de la barre, 2, 1005 Lausanne, Switzerland

Abstract: An efficient synthesis of α-(alkoxysilyl)acetic esters by Si-H insertion of carbenes, generated by rhodium catalyzed decomposition of diazoacetic esters, followed by nucleophilic displacement of Cl by ROH has been developed. Alkylation of these α-silyl carbonyls followed by Tamao oxidation of the C-Si bond allow an easy access to terminal diols.

The chemistry of α-silyl carbonyls has mainly concentrated on their use in the preparation of substituted ketones and the elaboration of geometrically defined α,β-unsaturated carbonyl compounds, via Peterson elimination.[1] Since the silicon is lost during these transformations, a majority of the synthesis to date has been restricted to the preparation of trialkyl or alkyl-arylsilyl substituted carbonyls.[2] However, as recently demonstrated by Enders and Nakai,[3] the use of an alkoxysilyl group instead of the trialkyl analog is particularly convenient for the further conversion of the silyl group into hydroxy, using Tamao's oxidation procedures.[4]

Herein, we report a modification of Doyle's $Rh_2(OAc)_4$ catalyzed insertion of diazoacetates into organosilanes,[5] which allow the one pot preparation of α-(alkoxysilyl)acetic esters **1** from readily available dialkyl or diarylchlorosilanes (Scheme 1).[6] We used the dual reactivity of chlorosilanes towards nucleophiles and carbenes to achieve the synthesis of these potentially interesting intermediates (Fig-1). We also describe the elaboration of these compounds by an alkylation-silyl oxidation sequence to give a terminal 1,2-diol.

Reactivity of chlorosilanes

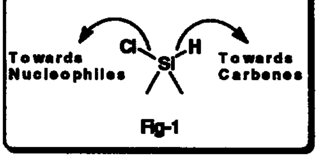
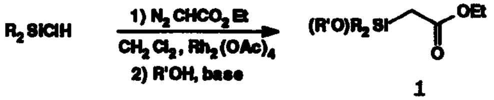


Fig-1

The Si-H insertion readily occured at room temperature with evolution of N_2.[7] It was observed that a rapid addition of diazoacetate resulted in an increasing formation of the carbene dimers, ethyl maleate and fumarate. The substitution of $Rh_2(OAc)_4$ with the less expensive $Cu(acac)_2$ proved to be unsuccessful, the amount of insertion product never exceeding 10% along with carbene dimers.[5] In all cases, the products **1a-i** were easily purified by distillation or rapid filtration through Florisil® and were obtained in good yields, as stable oils (table 1). With the more sterically demanding chlorosilanes **1h** and **1i**, a more polar and basic medium (imidazole, 4-DMAP, DMF) was needed in the last step to form the silicon-oxygen bond.[8]



1

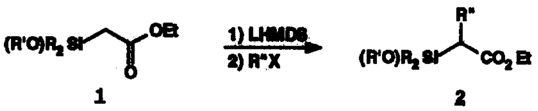
Scheme 1

Table 1. Synthesis of α-silylacetic Esters **1** (Scheme 1).

Product	R	R'	Conditions[a]	Yield %[b]
1a	Me	iPr	A	74
1b	Me	Bn	A	76
1c	Me	Et	A	73
1d	Me	tBu	A	78
1e	Me	Allyl	A	71
1f	Ph	Et	A	74
1g	Ph	iPr	A	65
1h	iPr	Et	B	70
1i	tBu	Et	B	62[c]

[a] Conditions A[7]: R_2SiClH (1.05 eq.), $Rh_2(OAc)_4$ (0.3 mol %), N_2CHCO_2Et (1 eq.), NEt_3 (1.2 eq.) and R'OH (1.2 eq.) in anhydrous CH_2Cl_2.
Conditions B: as described in reference 7, except that the chlorosilane was added to a mixture of EtOH (5 eq.), imidazole (3 eq.) and 4-DMAP (cat.) in DMF.
[b] Isolated yield after filtration over Florisil® or distillation.
[c] accompanied with 20% of the corresponding silanol.

These esters were then treated with 1.1 eq. of LHMDS (Lithium Hexamethyldisilazane) in THF and the resulting enolates quenched with various electrophiles (Scheme 2). The crude esters **2**, obtained in good yields, were usually pure enough to be used in next step without further purifications (table 2). Surprisingly, use of 1.1 equivalent of LHMDS or LDA in ether resulted in complete recovery of starting material.



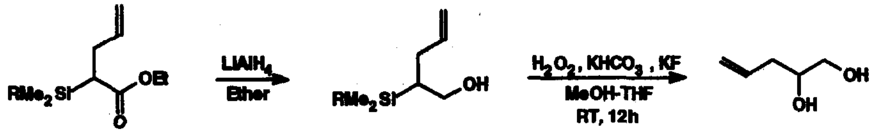
Scheme 2

Table 2. Alkylation of α-silylacetic Esters **1** (Scheme 2).

product	R	R'	R"	Yield (%)[a]
2a	Me	iPr	Allyl	83
2b	Me	iPr	Et	76
2c	Me	iPr	Me	79
2d	Me	Et	Me	78
2e	Me	Et	Et	81
2f	iPr	Et	Me	71[b]
2g	Me	tBu	Me	78
2h	Me	tBu	Et	85
2i	Me	tBu	Allyl	81

Conditions : LHMDS (1.1 eq.), -60°C, 1h, then R"X (5 eq.), -10°C, 2h.
[a] Isolated yield after filtration over Florisil® or distillation.
[b] The enolate was stirred 3h at -50°C prior to the addition of MeI (5 eq.).

To demonstrate the utility of the substrates **2**, we then decided to study the oxidative cleavage of C-Si bond.[4] Direct oxidation of the ester **2a**, using H_2O_2-KF-$KHCO_3$ in MeOH/THF, resulted in extensive decomposition of the starting material without any trace of the desired alcohol.[9] Fortunately, chemoselective reduction of the ester (0.5 eq. of $LiAlH_4$ in ether, 15 min, 0°C),[10] to form the β-hydroxysiloxane **3a** allowed oxidative cleavage of the C-Si bond. The expected homoallylic diol **4** was thus obtained in 59% overall yield (starting from **1a**). All attempts to oxidize the fully reduced hydroxysilane **3c** (obtained by reduction of **2a** with 2 eq. of $LiAlH_4$ in ether, 1h, reflux), or the bulky ester **3b** failed.[11]



2a, R = iPrO
2b, R = tBuO

3a, R = iPrO
3b, R = tBuO
3c, R = H

4

Scheme 3

These preliminary results show that this one pot procedure is particularly efficient and give access to new α-(alkoxysilyl)acetic esters in good yields, starting from cheap, commercially available materials. Moreover, the use of α-(alkoxysilyl) esters not only allows for facile entry to terminal 1,2-diols,[12] but should also prove synthetically useful in the synthesis of α-(alkoxysilyl) ketones[3] or in the C-C bond formation by condensation with carbonyls.[13] Furthermore, parallel studies showed that insertion of carbenes into 4A Metal-H bond seems to follow a general trend as indicated by our result in the tin series.[14] Further elaboration and extension of this method in a homochiral series are now under progress in our laboratory and will be reported in due course.

Acknowledgment. The authors gratefully acknowledge the Swiss National Science Foundation for its financial support.

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6. Me_2SiClH, iPr_2SiClH and tBu_2SiClH are commercially available. Ph_2SiClH has been prepared by a known procedure: Corey, J.Y.; West, R. *J. Am. Chem. Soc.*, **1963**, *85*, 2430.

7. A typical experimental was as follows: A solution of ethyl diazoacetate (0.9 ml, 8.7 mmol) in CH_2Cl_2 (2 ml) was added slowly at RT, using a syringe pump (2 mmol/h), to a solution of dimethylchlorosilane (1 ml, 9.2 mmol) and $Rh_2(OAc)_4$ (14mg, 0.03 mmol) in dry CH_2Cl_2 (3 ml). The mixture was cooled to 0°C and a solution of triethylamine (1.55 ml, 11 mmol) in CH_2Cl_2 (1 ml) was added, followed by isopropanol (0.85 ml, 11 mmol) in CH_2Cl_2 (1 ml). The suspension was stirred for 3 hours then treated at 0°C with a saturated solution of $NaHCO_3$ and the organic layer decanted. The aqueous layer was extracted with CH_2Cl_2 and the combined extracts were washed with brine, dried ($MgSO_4$) and evaporated in vacuo to give a brown oil which was purified by filtration over Florisil® (Petroleum ether/ethyl acetate/NEt_3 98.5/1/0.5) to afford the ester **1a** as a colorless oil (1.32 g, 74%): ^1H NMR ($CDCl_3$) δ 0.22 (s, 6H, $Si(CH_3)_2$), 1.16 (d, 6H, J= 6.0 Hz, $(C\underline{H}_3)_2CH$), 1.24 (t, 3H, J= 7.1 Hz, $OCH_2C\underline{H}_3$), 2.0 (s, 2H, $SiCH_2$), 4.05 (sept, 1H, J= 6.0 Hz, $(CH_3)_2C\underline{H}$), 4.10 (q, 2H, J= 7.1 Hz, $OC\underline{H}_2CH_3$).

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(Received in France 9 February 1993; accepted 12 March 1993)