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Asymmetric Metal Carbene Insertion into the Si-H Bond.

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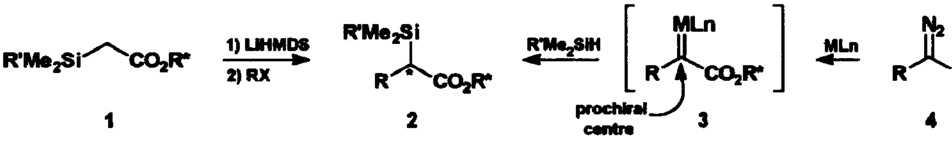
Abstract: α-Silyl-α-substituted acetic esters have been prepared in good yields and reasonable diastereoselectivities using an asymmetric metal carbene insertion into the Si-H bond. Optically active 1,2-diols were then prepared after reduction of the ester and conversion of the C-Si bond into a C-OH bond.

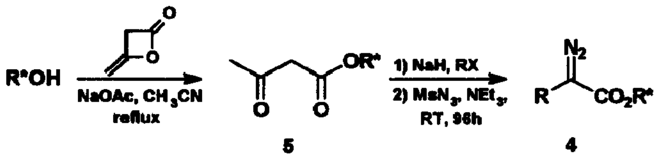
α-Silylcarbonyl compounds are versatile synthons which have recently received an increasing interest.[1] As a part of our program directed towards the development of these compounds in organic synthesis, we have previously shown that α-silylacetic esters (i.e. 1) can be useful synthetic intermediates in the synthesis of 1,2-diols[2a] or in the stereocontrolled synthesis of di- and trisubstituted tetrahydrofurans.[2b] In our strategy, one of the key-substrates is an α-substituted-α-silylacetic ester of type 2, which is readily available by alkylation of the corresponding α-silylacetic esters.[2] However, our attempts to obtain these intermediates in a homochiral series using alkylation of chiral esters 1 have failed, affording 2 with low levels of stereoselectivity.[3] Therefore, we devised an alternative approach where the ester 2 would be formed by a catalyzed insertion of an asymmetric carbenoid species such as 3 into a Si-H bond. It has been shown recently that an achiral version of this insertion gives cleanly α-silylacetic esters with excellent yields.[1c,2a] However, as far as we know the insertion of a homochiral carbenoid intermediate into the Si-H bond has never been reported.[4] The reaction would occur on the prochiral center of the C=M bond of a metallo-carbene intermediate, generated from the corresponding α-diazoester 4 (Scheme 1). We report herein our first results about this new Si-H insertion and show that useful levels of stereoselectivity can be attained using this approach.



Scheme 1

The α-diazoesters 4 were prepared using a three-step sequence starting from the optically active alcohols R*OH. Reaction with diketene afforded the β-ketoesters 5 (90-98% yield) which were alkylated and reacted under diazo-transfer conditions[5] to give the expected diazoesters 4 in excellent overall yields (Scheme 2).

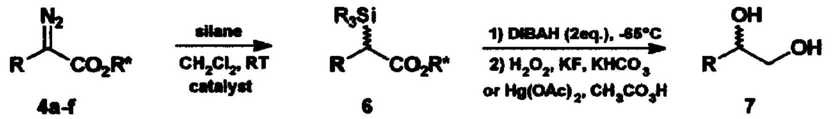
The α-diazoester 4a[4] was chosen as a model to establish the optimum conditions for the insertion reaction (Scheme 3). Different silanes (entries 1 to 5) were studied first, using $Rh_2(OAc)_4$ as catalyst, CH_2Cl_2 as solvent, and the diazoester being added very slowly via a syringe pump (1μmol/min) at room temperature. The diastereoisomeric ratios were determined from ^1H NMR of the crude α-silylesters 6, which were then transformed into the corresponding diols 7, by reduction of the ester function followed by the conversion of the C-Si bond into the C-OH bond.[6] The chiral auxiliary could be recovered in good yield by chromatography after the oxidation sequence. The enantiomeric excesses of the diols 7 were measured from the ^1H NMR of the



Scheme 2

Diazo	R*	R	overall yield (%)
4a	(-)-menthyl	Me	61
4b	(+)-menthyl	Me	60
4c	2-Ph-cyclohexyl	Me	59
4d	(-)-menthyl	iBu	59
4e	(-)-menthyl	$PhCH_2$	54
4f	(-)-menthyl	CH_2CO_2tBu	73

corresponding acetals[7] using $Eu(hfc)_3$, and they were found to match the d.e. of the esters 6, demonstrating that no racemization occured during the DIBAH reduction (table 1). The different silanes we tried gave the desired esters in good yields and we were pleased to find that the reactions occured with reasonable stereoselectivities with $PhMe_2SiH$ (entry 1) and Et_3SiH (entry 5)(44 % d.e.).[8] On the contrary, the bulkier Ph_3SiH (entry 2) gave nearly no diastereoselectivity. $ClSiMe_2H$ (entry 3) was also found slightly less stereoselective than its alkyl and aryl analogs.[9] The low d.e. observed with Whitesell's chiral auxiliary (entry 4) in comparison with the menthyl analog is surprising if we compare this to the generally high stereoselectivities observed with this auxiliary.[10]



Scheme 3

Table 1. Carbene insertion into the Si-H bond (Scheme 3).

Entry	diazoester	silane[a]	catalyst[b]	Yield[c] (%)	ratio[d] (%)	Yield diol[c] (2 steps)	config diol[e]
1	4a	$PhMe_2SiH$	$Rh_2(OAc)_4$	70	72 : 28	48	R
2	4a	Ph_3SiH	"	66	53 : 47	f	-
3	4a	$ClSiMe_2H$	"	74	67 : 33	62	R
4	4c	$ClSiMe_2H$	"	70	58 : 42	54	S
5	4a	Et_3SiH	"	72	72 : 28	f	-
6	4a	$PhMe_2SiH$	$Cu(acac)_2$	50	66 :34	48	R
7	4a	"	$Cu(OTf)_2$	33	56 : 44	"	R
8	4a	"	$Cu(OTf)_2$/sparteine	68	55 :45	"	R
9	4b	"	$Cu(OTf)_2$/sparteine	62	68 :32	"	S
10	4d	"	$Rh_2(OAc)_4$	75	70 : 30	45	R
11	4e	"	"	52	61 : 39	50	R
12	4f	"	"	70	66 : 34	g	-

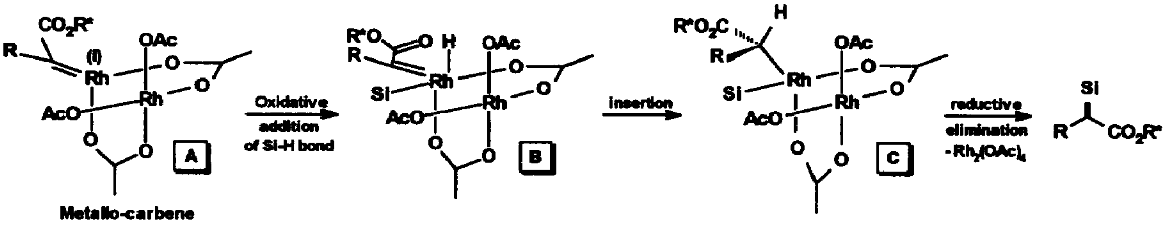
[a] (2 eq.). [b] anhydrous $Rh_2(OAc)_4$ (1 mol %); Cu(II) (10 mol %); sparteine (10 mol %) [c] Isolated yields. [d] determined from ^1H NMR of crude esters. [e] Absolute configuration of the major isomer determined by comparison of optical rotation with that of literature.[11] [f] diol not obtained, see ref 8. [g] Complex mixture obtained on reduction of ester 6f with DIBAH.

We also investigated the influence of the catalyst on the diastereoselectivity using $PhMe_2SiH$ in the same conditions than above (entries 6-9). $Cu(acac)_2$, reported to be very efficient with ethyl diazoacetate[1e] was found to be less stereoselective than $Rh_2(OAc)_4$ and gave the desired ester in only 50% yield (entry 6). $Cu(OTf)_2$ gave even lower yields[1c] (entry 7) but interestingly, the yield could be greatly increased by the use of a catalytic amount of the optically active diamine sparteine, with no change in the diastereoselectivity (entry 8). However, the use of (+)-menthyl diazoester **4b** (entry 9), instead of the (-)-menthyl isomer **4a**, led to a surprising increase of the d.e., demonstrating that a "matched" double stereodifferentiation is probably occuring.[4,12]

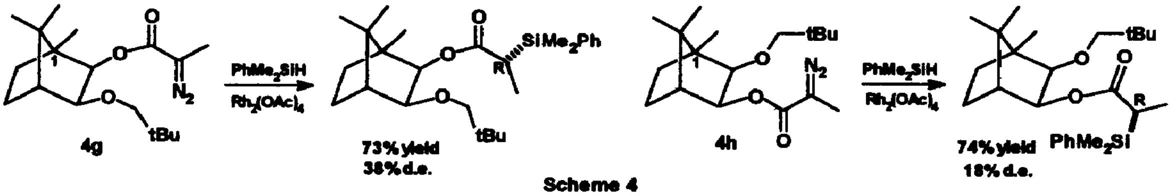
We then extended the methodology to the synthesis of various α-substituted-α-silylacetic esters **6** (entries 10-12). The diastereoisomeric ratios were measured as before. The yields were found to be relatively good and the diastereoselectivities in the range of those obtained with **4a**. In some cases, we observed that the insertion product was accompanied by the corresponding α,β-unsaturated ester (10 to 15% yield). This β-hydride elimination, observed with esters **4d** and **4e** and not with **4a** and **4f**, is in agreement with observations made by Taber[13] on the electronic selectivity of insertion of metallo-carbene into C-H bond. He noticed that methyl C-H was electronically less reactive than methylene and methine C-H bonds towards rhodium-mediated insertion.[14,15] The same trend apply for the electron-poor C-H bond α to the CO_2tBu group (i.e **4f**), less likely to react with the electrophilic metal center than an electron-rich bond.

The mechanism of the rhodium-mediated Si-H insertion has not been proved, however, we can assume that it might be similar to the mechanism of the C-H insertion, which proceeds *via* a Rh(I) carbene complex (i.e. **A**, Fig.-1).[13] Carbene-rhodium(I) complexes have proved to be effective catalysts for the hydrosilylation of ketones and alkenes, which supports this hypothesis.[16] Also, we suppose that our reaction, like hydrosilylation, results from an oxidative addition of the Si-H bond to the rhodium(I) complex **A**, leading to the hydridorhodium complex **B**.[17] Whether the H or Si group is transferred first to the metallo-carbene is unclear.[18] A mechanism involving insertion of Si group first, would probably lead to pronounced steric effects of hydrosilane structure on the diastereoselectivity.[19] However our results (compare entries 1-5) are inconclusive, large silicon groups (Ph_3Si) have the opposite effect of lowering the stereoselectivity. Interestingly, we also observed that the absolute configuration of the diols obtained by Si-H insertion was opposite to that obtained from alkylation of the corresponding menthyl α-silylacetic esters. This supports the formation of an intermediate such as **B** and suggests that similar steric effects operate in these two distinct processes.[20] The α-silylacetic ester and the regenerated catalyst might then be obtained from **C** by reductive elimination with retention of configuration.[21]

Fig.-1. Mechanism of the $Rh_2(OAc)_4$ catalyzed insertion of carbenoids into the Si-H bond.



Finally, in our search for more efficient chiral auxiliaries we observed some contrasting results with camphor-derived chiral auxiliaries (Scheme 4). The two auxiliaries **4g** and **4h** both gave good yields of Si-H insertion products but with a large difference in the magnitude of the stereoselectivity (38 and 18% d.e.). This is presumably an effect of the bridged angular methyl group (C-1) which prevents free rotation of the metallo-carbene intermediate of **4g** by steric interactions, allowing the $tBuCH_2O$ group to efficiently shield one face. Interestingly, Oppolzer reported that in the Diels-Alder reaction of the acrylate derivatives of these chiral auxiliaries, opposite diastereoselectivities were observed.[22]



Scheme 4

Further studies directed towards the search for more efficient chiral auxiliaries and the use of optically active rhodium catalysts[23] are now under way and will be reported in due course.

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14. Reaction of achiral α-diazo-β-alkyl esters with $Rh_2(OAc)_4$ led to high yields of unsaturated esters, reinforcing the idea that electronic factors control the competition between insertion into the Si-H bond and β-hydride elimination.
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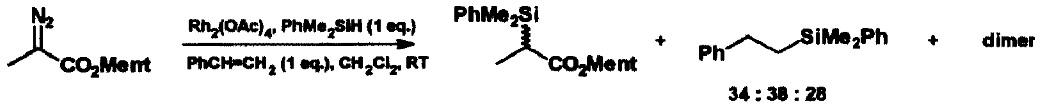
17. Introduction of 1 eq. of styrene to the reaction mixture led to a partial hydrosilylation, supporting the fact that Si-H oxidative addition on Rh(I) intermediate A (Fig.-1) is occuring:



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20. The isopropyl group of the menthyl presumably shields one face of the metallo-carbene, the H or Si group entering on the opposite face. Attempts to increase this effect by using 8-phenylmenthyl esters resulted in insertion of the metallo-carbene into the 8-phenyl ring.
21. Independently, it is also worth mentioning that the small amount of unsaturated esters obtained along with the α-silyl esters is a mixture of *E* and *Z* isomers, contrasting with the complete *Z* selectivity obtained during the $Rh_2(OAc)_4$-diazoesters decomposition, see: Ikota, N.; Takamura, N.; Young, S.D.; Ganem, B. *Tetrahedron Lett.*, **1981**, *22*, 4163-4166. Therefore, it is likely that in our case β-hydride elimination occurs from the catalytic species **B** or **C** and not from the metallo-carbene **A** (Fig.-1).
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