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LETTERS

Rhodium Catalysed Reactions of Silylated Diazoacetates: Stereoselective Synthesis of α-Silylated γ-Lactones *via* C-H Insertion

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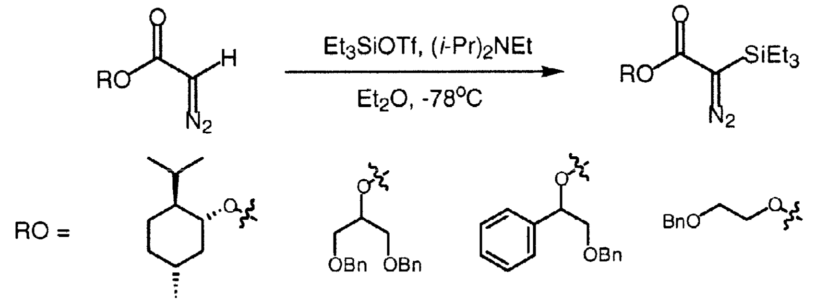
Abstract: The rhodium catalysed C-H insertion reactions of α-(triethylsilyl)diazoacetates have been studied, facilitating the stereoselective synthesis of α-(triethylsilyl)-γ-lactones. An intriguing and unprecedented inversion of stereoselectivity is observed upon changing from rhodium (II) carboxylates to rhodium (II) acetamide as catalyst for insertion to acyclic esters.

Keywords: Carbenes and carbenoids; Diazo compounds; Lactones; Silicon and compounds

Organosilicon compounds have assumed an important role in modern synthetic chemistry. Although α-silyl diazocarbonyl compounds have been known for many years, they have been little used in synthesis. We have been studying the chemistry of these compounds with the aim of developing new, efficient, functional group tolerant approaches to a variety of organosilicon reagents. α-Silyl ketones and esters are useful reagents in synthesis: they undergo mild and efficient fluoride or base promoted alkylation,[1] aldol[1] and Michael reactions,[2] while the lithiated derivatives effect the construction of α,β-unsaturated esters with aldehydes, ketones and lactones.[3] In this Letter, we describe a novel approach to α-silylated γ-lactones, based upon the intramolecular C-H insertion reactions of α-silyldiazoacetates.[4]

Examining the literature of silyl diazocarbonyl compounds, we noted isolated reports of inter-[5] and intramolecular[6] C-H insertion reactions of photolytically generated carbenes, albeit in modest yields. Concerning reactions promoted by transition metal complexes, products arising through C-H insertion into the silyl function of (triisopropylsilyl)diazoketones have been observed with copper (I) triflate.[6] Rhodium based catalysts appeared less promising. The highly electrophilic rhodium (II) tetra(perfluorobutyrate) caused skeletal rearrangements of methyl silyldiazoacetates, while less electrophilic rhodium (II) carboxylate caused only simple carbene dimerisation.[7] The latter catalysts were reported to be inert towards silylated diazoketones.[6] We reasoned that silyldiazoacetates bearing ester groups more susceptible to insertion than methyl[8] would offer a more rapid and productive reaction pathway for any rhodium carbenoids formed, and thereby allow the catalyst to turn over more readily. We therefore set out to prepare some suitable substrates to test this hypothesis.

The α-silyldiazoacetates used in this study were prepared by the method of Regitz,[9] by reaction of the parent diazoacetates[10] with a silyl triflate in the presence of Hünigs base (Scheme 1).



Scheme 1 Compound (% Yield) 1 (85) 2 (87) 3 (82) 4 (70)

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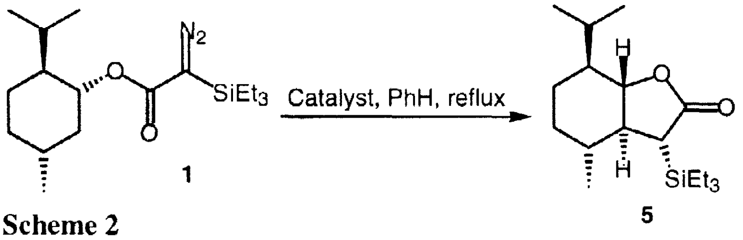
Initial efforts employing trimethylsilyl triflate met with limited success, since the products invariably partially desilylated upon chromatography. Use of the more robust triethylsilyl group results in good to excellent yields of the desired silyldiazoacetates.

We commenced our studies with an examination of the decomposition of menthol derived diazoacetate **1**, since the C-H insertion reaction of the related menthyl diazoacetoacetate has been studied by Doyle.[11] Initial experiments under Doyle's conditions (slow addition of the diazoester to a refluxing solution of the catalyst) gave 38% of the desired silyl lactone **5**, together with 11% of the product of carbene insertion into adventitious water. Further experimentation showed that faster and cleaner reactions could be achieved simply by heating a pre-mixed solution of the silyldiazoacetate and catalyst, giving the silyl lactone in an isolated 80% yield as a single diastereoisomer. The stereochemistry was assigned on the basis of *J* values in the ^{1}H nmr spectrum of **5**.[12]

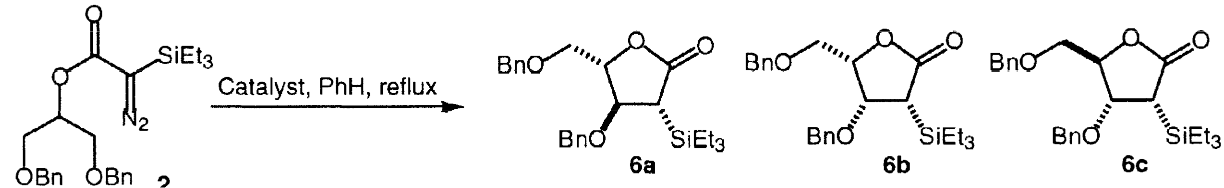


Conditions:	Yield (%):
1% $Rh_2(OAc)_4$	80
2% $Rh_2(octanoate)_4$	72
1% $Rh_2(acam)_4$	64

Scheme 2

Using this operationally simpler procedure, no other products could be detected in the ^{1}H and ^{13}C nmr spectra or the mass spectrum of the crude reaction mixture. In particular, we were gratified to find no traces of the silylated maleates and fumarates which would have been the products of the carbene dimerisation observed by Maas.[7] Similar experiments using $Rh_2(octanoate)_4$ and $Rh_2(acam)_4$ also furnished **5**, albeit in slightly lower yield.

We next turned our attention to the cyclisation of the glycerol derived silyldiazoacetate **2** (Scheme 3). Under the optimum conditions developed for **1**, we isolated a 71% yield of three diastereomeric silyl lactones **6a-c** in a ratio of 64:26:10. Repeating this reaction with $Rh_2(octanoate)_4$ lead to a slight increase in yield (74%) and essentially the same ratio of diastereomers (62:31:7). The relative stereochemistry of isomers **6a** and **6b** was determined by X-ray crystallographic analysis of crystalline derivatives.[13] Isomer **6c** was demonstrated to be epimeric to **6a** at the silicon bearing carbon, since the two isomers converged to 3,5-dibenzyl-2-deoxyribonolactone upon desilylation in acidic methanol.

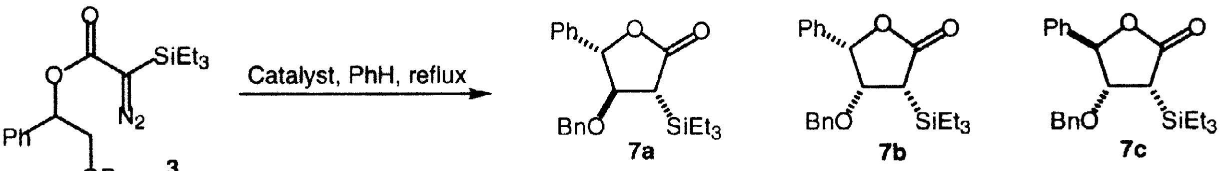


Conditions:	Yield (%):	Ratio **6a** : **6b** : **6c**
1% $Rh_2(OAc)_4$	71	64 : 26 : 10
1% $Rh_2(octanoate)_4$	74	62 : 31 : 7
5% $Rh_2(acam)_4$	60	19 : 5 : 76

Scheme 3

When the catalyst was changed to $Rh_2(acam)_4$, the yield dropped slightly to 60%, but most remarkably the diastereomeric ratio changed to 19:5:76. Whilst it has commonly been observed that the outcome of intramolecular C-H insertion reactions can be influenced by the nature of the catalyst, this is to our knowledge the first example of an *achiral* catalyst prompting a complete reversal in the observed sense of diastereoselection.[14]

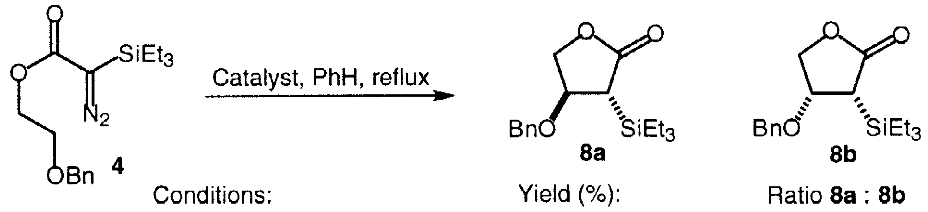
Similar results were observed in the C-H insertions of the styrene diol derived silyldiazoacetate **3** (Scheme 4). Using $Rh_2(OAc)_4$ as the catalyst, an 80% yield of three diastereomeric silyl lactones **7a-c** was obtained, in a ratio (61:25:14) very close to that for the formation of **6a-c** from **2**. The stereochemistry of the isomers of **7** was therefore assigned as shown by analogy with compounds **6a-c**, and further corroboration of these assignments was gained by examination of the H-3/H-4 and H-4/H-5 coupling constants, which were found to be in close agreement for the respective pairs of diastereomers.[15] Once again, the use of $Rh_2(octanoate)_4$ as catalyst had only a minor effect on both the yield (78%) and diastereomeric ratio (62:26:12) observed. However, the use of $Rh_2(acam)_4$ gave an 89% yield of the three isomers in a ratio of 18:5:77, *i.e.* this catalyst again favours the formation of isomer **7c**, and the diastereomeric ratio is very close to that observed for decomposition of **2**.



Conditions:	Yield (%):	Ratio **7a** : **7b** : **7c**
5% $Rh_2(OAc)_4$	80	61 : 25 : 14
1% $Rh_2(octanoate)_4$	78	62 : 26 : 12
5% $Rh_2(acam)_4$	89	18 : 5 : 77

Scheme 4

We next investigated whether such a dependence of the product stereochemistry upon catalyst type would exert itself in the formation of lactones with a different substitution pattern. We therefore examined the cyclisation of silyldiazoacetate **4** (Scheme 5).



Conditions:	Yield (%):	Ratio **8a** : **8b**
5% $Rh_2(OAc)_4$	54	50 : 50
1% $Rh_2(octanoate)_4$	55	50 : 50
5% $Rh_2(acam)_4$	84	32 : 68

Scheme 5

Somewhat disappointingly, cyclisation of **4** under both $Rh_2(OAc)_4$ and $Rh_2(octanoate)_4$ catalysis gave an equimolar mixture of the two possible diastereomers **8a,b** in moderate (54-44%) yield. The use of $Rh_2(acam)_4$ as catalyst gave an improved 84% yield of the two diastereomers in a 32:68 ratio. While we have not yet obtained rigorous proof of the identities of diastereomers **8a/b**, we tentatively assign the stereochemistry as shown, since in the cyclisations of **2** and **3** the 3,4-*cis* relationship has been favoured in reactions catalysed by $Rh_2(acam)_4$. This assignment should clearly be regarded as speculative until concrete evidence has been obtained.

The inversion of stereoselectivity observed on changing from $Rh_2(O_2CR)_4$ to $Rh_2(acam)_4$ as catalyst is striking. A possible explanation for this phenomenon, based upon Doyle's transition state model for C-H insertion reactions[14] (Figure 1), is given below.

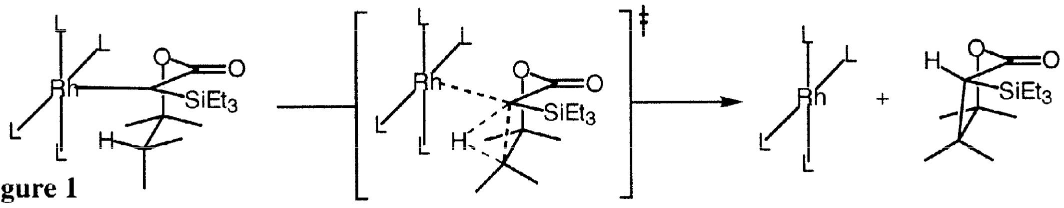


Figure 1

In Figure 2 are shown the four possible diastereomeric transition states **9a-d**, which give rise to lactones **6/7a-d**. There are three destabilising interactions which can occur in these transition states: (i) between the OBn group and the ligands on rhodium (**9a**, **9d**); (ii) eclipsing interactions between the OBn and R groups (**9b**, **9d**); and (iii) interactions between the OBn and $SiEt_3$ groups (**9b**, **9c**). Isomer **d**, which suffers from interactions (i) and (ii), is not observed with any of the catalysts used. When rhodium carboxylates are employed, transition state **9a** dominates, indicating that interaction (i) is smaller than (iii) for these catalysts. Since $Rh_2(acam)_4$ is generally viewed as being isosteric to $Rh_2(OAc)_4$, the likely explanation for the inversion of stereoselection rests upon the electronic differences between the carboxylate and carboxamide catalysts. In accordance with the studies of Pirrung,[16] the more polarisable carboxamide ligands should facilitate enhanced rhodium to carbene back-bonding, leading to much shorter rhodium-carbon bond lengths. This would sharply increase the destabilising effects of interaction (i), and thus transition state **9c** dominates. A more comprehensive model is still required to account for the relative proportions of isomers **6/7b** observed, and further experimentation upon substituent effects is under way in an attempt to refine this model.

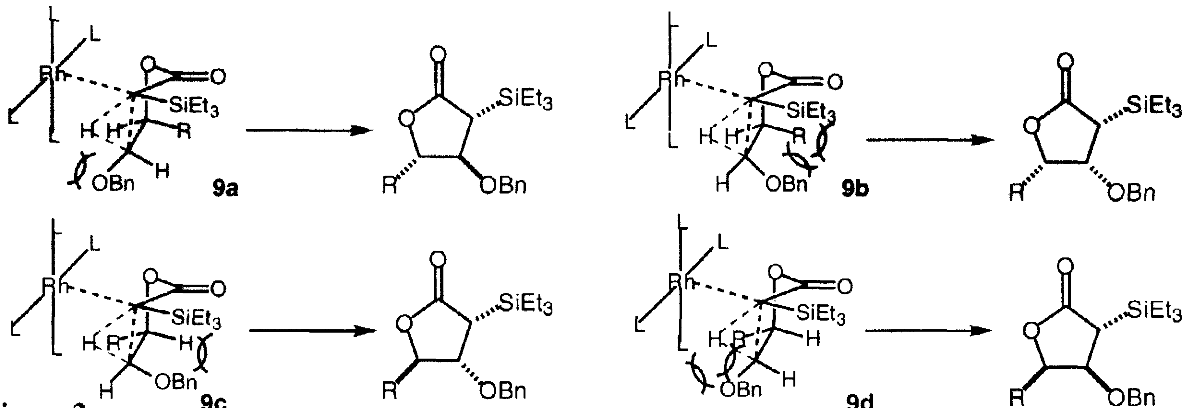


Figure 2

In conclusion, we have demonstrated that rhodium catalysed intramolecular C-H insertion reactions of silylated diazoacetates is possible, leading to a new method for the stereoselective construction of α-silylated lactones. Further details of our studies in this area will be reported in due course.

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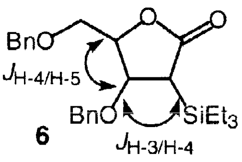
12. In the case of the lactone formed in the intramolecular C-H insertion of menthyl diazoacetoacetate, the *trans*-ring fusion and *trans*-disposition of the pendant acetyl group were assigned on the basis of *J* values of 10.7 and 12.4Hz respectively.[11] In compound **5**, the corresponding *J* values are 10.4 and 11.0Hz.
13. The lactones were reduced to 1,4-diols using DIBAL-H, then converted to their crystalline *bis*-(3,5-dinitrobenzoate) esters. We thank Professor D. J. Williams and Dr A. J. P. White of this department for determining these structures, details of which will be published elsewhere.
14. The effects of chiral rhodium catalysts upon diastereoselection in C-H insertion reactions have been discussed: Doyle, M. P.; Kalinin, A. V.; Ene, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 8837
15. The relevant coupling constants are shown below. The signals for H-4 and H-5 are obscured in the spectrum of **6b**, hence no *J* value is shown for this compound.



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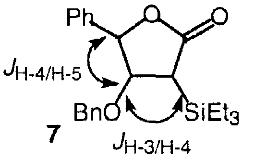
	6a	7a	6b	7b	6c	7c
$J_{H-3/H-4}$(Hz)	3.4	3.5	6.5	6.2	7.8	7.2
$J_{H-4/H-5}$(Hz)	2.7	2.7	-	3.7	2.0	2.4



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