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Stereochemistry in Reactions of Chiral Cyclic Allylsilanes with (Ethoxycarbonyl)nitrene. A New Route to Chiral *N*-substituted Allylamines.

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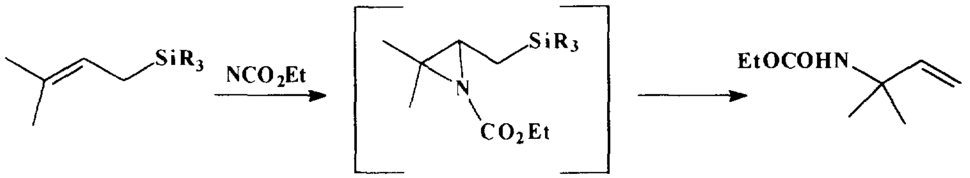
Abstract: The $S_{E'}$ reactions of chiral cyclic allylsilanes with (ethoxycarbonyl)nitrene generated by α-elimination of $NsONHCO_2Et$ with Et_3N permit us to obtain chiral *N*-substituted allylic amines in good diastereomeric excess when stereoelectronic and conformational factors allow the *anti* attack.

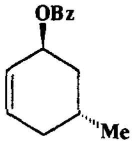
Allylsilanes are important intermediates in organic synthesis.[1] In the last few years the study of their reactivity with electrophiles pointed attention to the regio and stereochemistry of their $S_{E'}$ reactions. It is well known that allylsilanes react with electrophiles through an attack at the γ carbon *anti* to the silyl group with a stereoselective three carbon transfer of chirality.[2]

However, a few examples have been taken on the reaction of allylsilanes with nitrogen electrophiles.[3] In our preceding work we studied the (ethoxycarbonyl)nitrene as a nitrogen donating group in reaction with some electron rich olefins such as silyl enol ethers and silyl ketene acetals.[4] We lately concentrated on the reactivity and regiochemistry of the (ethoxycarbonyl)nitrene reaction with either linear or cyclic allylsilanes. (Ethoxycarbonyl)nitrene reacts with allylsilanes producing (ethoxycarbonyl)aziridines that through an acidic opening of the heterocyclic ring give allylamine derivatives as the main product.[5]



In this paper we extend our analysis to the stereochemistry of reactions of chiral cyclic allylsilanes with (ethoxycarbonyl)nitrene. We chose as substrates the diastereomers of (5-methylcyclohex-2-enyl)silanes in order to determine easily the stereochemical course of the reaction by diastereomeric excesses analysis.

We used diastereomeric mixtures of the (3*S*, 5*S*)-3-dimethyl(phenyl)silyl-5-methylcyclohexene (**1**) and the (3*R*, 5*S*)-3-dimethyl(phenyl)silyl-5-methylcyclohexene (**2**) in the ratio of 80 : 20 and 10 : 90 obtained from the reaction of the corresponding mixture of (1*S*, 5*R*)-5-methylcyclohex-2-enyl benzoate (**3**) and (1*R*, 5*R*)-5-methylcyclohex-2-enyl benzoate (**4**) with dimethyl(phenyl)silyllithium cyanocuprate (**5**) according to Fleming's procedures.[6]



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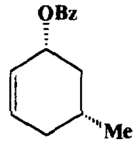
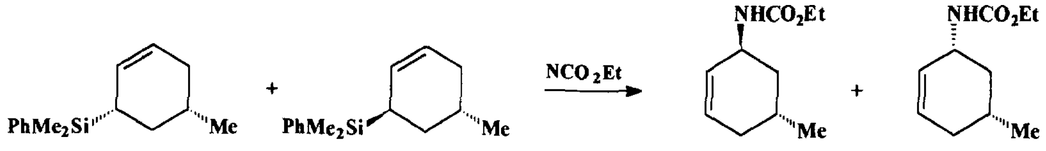


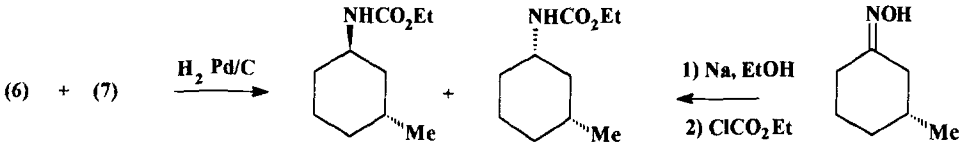
(4)

The reaction of the prevailing *cis* allylsilane (**1**) with (ethoxycarbonyl)nitrene, obtained *in situ* by α-elimination of ethyl *N*-{[(4-nitrophenyl)sulphonyl]oxy}carbamate ($NsONHCO_2Et$) with dry Et_3N as base,[7] gave a mixture of (1*S*, 5*R*)-ethyl 5-methylcyclohex-2-enyl carbamate (**6**)[8] and (1*R*, 5*R*)-ethyl 5-methylcyclohex-2-enyl carbamate (**7**) in the ratio of 88 : 12, probably through an intermediate aziridine which, however, could not be detected by GC-MS. The mixture of the *N*-(ethoxycarbonyl)allylamines (d.e. = 76%) was isolated, after flash chromatography (hexane : ethyl acetate = 95 : 5) in a 30% yield.



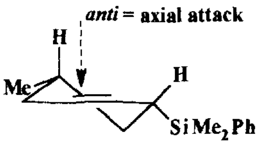
(1) (2) (6) (7)

In order to determine the absolute configuration of the new chiral center the latter unsaturated carbamates were transformed into a mixture of (1*R*, 3*R*)-ethyl 3-methylcyclohexyl carbamate (**8**) and (1*S*, 3*R*)-ethyl 3-methylcyclohexyl carbamate (**9**)[9] by catalytic hydrogenation[10] and compared with the mixture obtained from (*R*)-3-methylcyclohexanone oxime (**10**) after reduction with sodium in EtOH[11] and successive ethoxycarbonylation.[12] This last reaction gives as the minor product the compound (**8**) which corresponds (^{13}C-NMR) to the main diastereomer obtained from the catalytic reduction of (**6**) and (**7**).



(8) (9) (10)

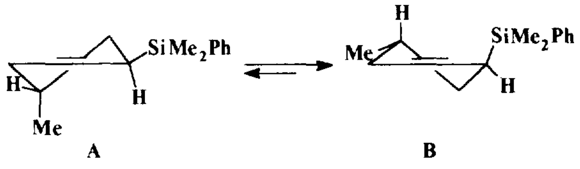
The stereochemistry of the main product (**6**) is in agreement with a preferred *anti* attack of the (ethoxycarbonyl)nitrene to (**1**) in the less energetic conformation which holds the two groups in equatorial position.[13]



Moreover, in this case, the attack is also favoured by the axial approach to the double bond in agreement with the stereochemistry of the attack of electrophiles on the six membered ring olefins.[14]

On the other hand, the diastereomeric mixture containing the major ratio (90 : 10) of the *trans* allylsilane (**2**) gave, in the same reaction conditions, a mixture of (**6**) and (**7**) once again in favour of the *trans* isomer even if with a lower diastereomeric excess (d.e. = 40%) in a 35% yield.

Analysing the two possible conformations of the substrate (**2**) we noted that in conformation A the *anti*-axial approach, which would have been the more favourable, is probably forbidden by the presence of the axial methyl group on the C-5 which occupied the direction of attack of the sterically hindered (ethoxycarbonyl)nitrene.



The prevailing *trans* product (**7**) seemed to derive from a preferred *syn*-axial approach of the electrophile rather than an *anti*-equatorial one in conformation B stabilized by the $\sigma_{C\text{-}Si}$-$\pi_{C\text{-}C}$ interaction. This *syn* attack has already been referred to other cyclic allylsilane systems and is believed to depend on either steric or electronic reasons.[15]

The $S_{E'}$ reactions of chiral cyclic allylsilanes with (ethoxycarbonyl)nitrene appear a facile route to chiral *N*-substituted allylic amines[16] in good diastereomeric excess when stereoelectronic and conformational factors allow the *anti* attack.

The possibility of obtaining chiral linear allylamines with a stereocontrolled reaction prompted us to extend our study to chiral linear allylsilanes. In these cases the *anti* attack of electrophiles is more general and our first results confirm this kind of approach for (ethoxycarbonyl)nitrene.

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7. To a mixture of 3 mmol of allylsilane and 12 mmol of NsNHCO$_2$Et in 80 ml of anhydrous CH$_2$Cl$_2$ a solution of 12 mmol of anhydrous Et$_3$N in 10 ml of anhydrous CH$_2$Cl$_2$ was added during 1 h with

stirring, under argon, at room temperature. After 3 h most of the solvent was removed under reduced pressure and hexane was added. After filtration and removal of the solvent *in vacuo* the crude reaction mixture was chromatographed on silica gel (flash chromatography; hexane : ethyl acetate = 95 : 5) giving the allylamines in the reported yields.

8. Compound (**6**) has: IR (CCl_4) cm^{-1} 3454 (ν_{NH}); 1724 (ν_{CO}). ^1H NMR (200 MHz, $CDCl_3$) δ 0.95 (d, 3 H, $CHC\mathit{H}_3$); 1.22 (t, 3 H, $CH_2C\mathit{H}_3$); 1.5-1.8 (m, 4 H ring); 1.9-2.2 (m, 1 H ring); 4.1 (q, 2 H, $C\mathit{H}_2CH_3$), 4.0-4.2 (m, 1 H, $C\mathit{H}NH$); 4.6 (br s, 1 H, $N\mathit{H}$); 5.6 (dd, 1 H, $C\mathit{H}$=CH); 5.8 (dd, 1 H, CH=$C\mathit{H}$). ^{13}C NMR (200 MHz, $CDCl_3$) δ 14.6 ($CH_2\mathit{C}H_3$); 21.4 ($CH\mathit{C}H_3$), 24.1 ($\mathit{C}HCH_3$), 33.4, 37.3 ($\mathit{C}H_2$ ring); 45.3 ($\mathit{C}HNH$); 60.6 ($\mathit{C}H_2CH_3$); 126.2 (CH=CH), 130.9 (CH=CH); 155.7 (C=O). GC-MS: *m/z (%)* 183 (M^+, 13), 154 (100), 95 (45), 69 (60).
9. The ^{13}C NMR (300 MHz, $CDCl_3$) of the mixtures show for (1*R*,3*R*) (**8**): δ 14.3 ($CH_2\mathit{C}H_3$); 20.3 ($\mathit{C}H_2$ ring); 21.3 ($CH\mathit{C}H_3$); 27.0 ($\mathit{C}HCH_3$); 30.7; 33.5, 38.9 ($\mathit{C}H_2$ ring); 46.1 ($\mathit{C}HNH$); 60.3 ($\mathit{C}H_2CH_3$); for (1*S*,3*R*) (**9**): δ 14.3 ($CH_2\mathit{C}H_3$); 22.1 ($\mathit{C}H_2$ ring); 24.6 ($CH\mathit{C}H_3$); 31.6 ($\mathit{C}HCH_3$); 33.0, 34.0, 42.2 ($\mathit{C}H_2$ ring); 49.9 ($\mathit{C}HNH$); 60.3 ($\mathit{C}H_2CH_3$).
10. The reduction was made with H_2 in MeOH using Pd/C as catalyst.
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