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ACYCLIC DIASTEREOFACIAL SELECTION IN RADICAL ADDITION.

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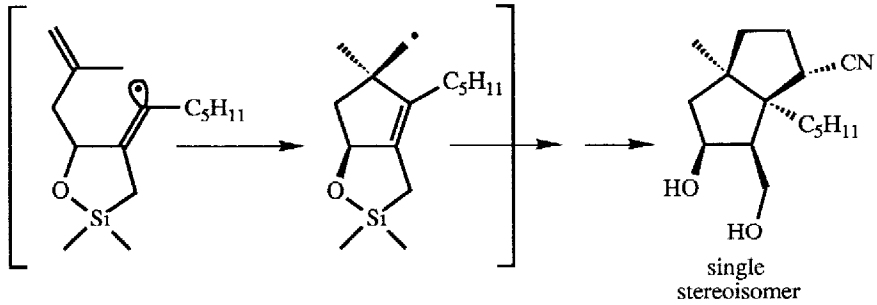
Abstract *: 1,2-asymmetric induction with up to 83 % of diastereoisomeric excess has been observed during intermolecular addition of silicon centered radical to carbon-carbon double bond of chiral non-racemic α,β-unsaturated esters derived from glyceraldehyde acetonide. The stereoselectivity observed should be mainly due to some electronic effects.*
Key Words *: Acyclic diastereofacial selection / Intermolecular radical addition / 1,2-Asymmetric induction / Stereoelectronic control.*

The control of stereochemistry in free radical reaction has received increased attention in recent years.[1,2]

For the **intra**-molecular addition of carbon centered radical to chiral olefins, the 1,3-asymmetric induction is well documented[3] and the stereochemistry has been rationalized in term of steric effects in a chair-like transition state.[4] However, in our recent access to a diquinane[1], the high stereoselectivity observed could also be due to electronic effect of homoallylic ether linkage[5] (Scheme 1).



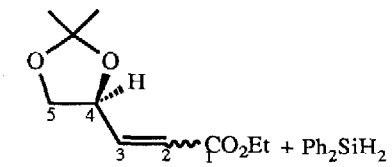
Scheme 1

For the **inter**-molecular addition of carbon-centered radicals[2] (cyclohexyl and tBu) to olefins substituted with chiral amides, an extremely high level of stereoselectivity (24 : 1 to 40 : 1 respectively) has very recently been achieved and this stereoselectivity was shown to be steric in origin.[6]

In this paper, we describe our results for the stereoselective **inter**-molecular addition of silicon centered radical to chiral alkenes and the probable intervention of some electronic effect. Thus, the chiral non-racemic α,β-unsaturated ester **1**[7] derived from acetonide of glyceraldehyde was chosen as a substrate since both

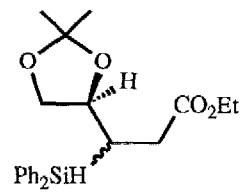
geometrical isomers are commercially available. Among the three silanes we tested [Et_3SiH, Ph_2SiH_2[8] and $(TMS)_3SiH$[9]] only diphenylsilane was shown to afford addition products when azobisisobutyronitrile (AIBN) was used as radical initiator. This silane was already known to be a good reducing agent in the presence of Et_3B-air as an initiator.[8] The diphenylsilyl radical formation was initiated by the Polarity Reversal Catalysis (PRC) described by Roberts and coworkers[10] and using the bulky tertiododecanethiol (tDSH) as catalyst.

Thus, the radical-induced hydrosilylation of acyclic *Z* and *E*-α,β-unsaturated chiral non racemic esters **1** was shown to be stereoselective.[11] The major stereoisomer **2**, the same from both *Z* and *E* esters **1**, can reach as high as 91 % (Scheme 2). The stereoselectivity observed was kinetically controlled since no *Z* to *E*-isomerization of the double bond could be detected in the recovered starting material during the partial transformation of the *Z*-ester **1**. Interestingly and surprisingly, only one hydrogen atom of the diphenylsilane was involved in the radical addition reaction studied.



AIBN, tDSH
hexane reflux

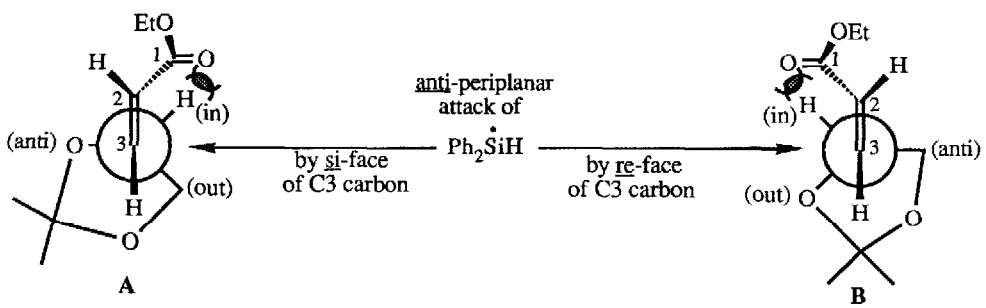
3 to 6 hours



Z (S) - **1**	69 % yield 83 % de	(*Major : Minor*) **2** (91 : 9)
E (S) - **1**	63 % yield 40 % de	(*Major : Minor*) **2** (70 : 30)

Scheme 2

Competition experiment with an equimolar mixture of *Z* and *E*-esters **1** indicated that the latter is twice more reactive than the former. This result is in agreement with the nucleophilicity of the diphenylsilyl radical and a decreasing electrophilicity of the carbon-carbon double bond of the *Z*-ester **1**. This reduced resonance delocalisation is probably due to a twisting of the ester group because of its 1,5-steric interaction with allylic hydrogens in *inside* positions for the most reactive conformers **A** and/or **B** (Scheme 3). Furthermore, increasing stereoselectivity is in agreement with the decreasing reactivity of starting material going from *E* to *Z* substrates **1**.[2]



Scheme 3 : The most reactive conformers of the Z-(S)-**1** enantiomer

Whatever the configuration of the major silylation product **2** (Scheme 2) the stereoselectivity observed should be due to some electronic effects, since, if we assume an *anti*-periplanar attack[12] of the π-diastereofaces of the chiral carbon-carbon double bond by silyl radical, the allylic substituents of the chiral center in *outside* and position, namely O and CH_2, are of about the same bulkiness (Scheme 3).

Deacetalisation[13] of the adduct **2** followed by Peterson olefination is in progress to define, from the direction of the diastereofacial selection observed, which type of stereoelectronic factors is operative[14] for the transition state stabilisation by either electron donating[15] or electron withdrawing[16] groups both located in *anti* position (Scheme 3). Finally and importantly these adducts can be used as cheap reactive intermediate for enantioselective hydrosilylation of *pro*chiral olefins and ketones derivatives.

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11. **Typical Procedure :**
A solution of 200 mg (1 mmol) of ester **1** 369 mg (2 mmol. eq) of diphenylsilane, 4 mg (2 % mol. eq.) of tertiododecanethiol and 7 mg (5 % mol. eq.) of AIBN in 5 ml of hexane was heated for 3 to 6 hours at 70°C under argon. After each hour, 7 mg (5 % mol. eq.) of AIBN was added. The reaction mixture was concentrated in vacuo and flash chromatographed on silicagel. The *major* and *minor* adducts **2** have retention times of $R_f = 0.30$ and $R_f = 0.32$ respectively when the eluant is the petroleum ether with 20 % of diethyl ether and are isolated in 69 % of overall yield.
Spectroscopic data for *major* adduct-**2** :
$[\alpha]_D^{22°C} = +3$ (c = 2.5 $CHCl_3$), $[\alpha]_{365} = +15$ (c = 2.5 $CHCl_3$)
^{1}H-NMR ($CDCl_3$, 200 MHz) : 7.60-7.69 (m, 4H, phenyl) ; 7.30-7.43 (m, 6H, phenyl) ; 4.86 ppm (m, SiH) ; 4.23 (m, 4H) ; 4.00 (q, J=7.2 Hz, 1.5 H, H5) ; 3.90 (d, J=6.0 Hz, 0.5 H, H5) ; 3.87 (d, J=6.2 Hz, 0.5 H, ?) ; 3.55 (d, J=8.1 Hz, 0.5 H, H2) ; 3.48 (m, 2.3 H, H3) ; 1.28 (s, 3H, H7 or H8) ; 1.25 (s, 3H, H8 or H7) ; 1.16 (q, J=7.2 Hz, 3H, H10).
^{13}C-NMR ($CDCl_3$, 50 MHz) : 173.21 (C1) ; 108.53 (C6) ; 76.98 (C4) ; 66.10 (C5) ; 60.53 (C9) ; 31.68 (C2) ; 26.18 (C7 or C8) ; 25.38 (C8 or C7) ; 23.84 (C3) ; 14.08 (C10) ; two diastereotopic phenyl groups : 135.69 and 135.64, 134.31, 129.93 and 129.78, 128.10 and 127.96.
Spectroscopic data for *minor* adduct-**2** :
$[\alpha]_D^{22°C} = +2$ (c = 0.8 $CHCl_3$), $[\alpha]_{365} = +7.9$ (c = 0.8 $CHCl_3$)
^{1}H-NMR ($CDCl_3$, 200 MHz) : 7.44-7.67 (m, 4H, phenyl) ; 7.32-7.39 (m, 6H, phenyl) ; 4.83 ppm (d, J=3.3 Hz, SiH) ; 4.20 (dt, J=5.9 and 7.9 Hz, 1.0 H, H4) ; 3.95 (dd, J=5.9 and 7.2 Hz, 1.0H, H5) ; 3.81 (dd, J=5.9 and 8.3 Hz, 1H, H5') ; 3.44 (t, J=8.0 Hz, 1H, ?) ; 2.61 (dd, J=7.4 and 16.7 Hz, 1H, H2) ; 2.44 (dd, J=5.7 and 16.7 Hz, 1H, H2') ; 2.20 (m, 1H, H3) ; 1.37 (s, 3H, H7 or H8) ; 1.27 (s, 3H, H8 or H7) ; 1.14 (q, J=7.1 Hz, 3H, H10).
^{13}C-NMR ($CDCl_3$, 50 MHz) : 173.59 (C1) ; 108.45 (C6) ; 77.00 (C4) ; 68.65 (C5) ; 60.41 (C9) ; 32.33 (C2) ; 26.62 (C7 or C8) ; 26.65 (C8 or C7) ; 24.64 (C3) ; 14.05 (C10) ; two diastereotopic groups : 135.66 and 135.58, 132.23 and 131.99, 129.96 and 129.11.

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