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Photooxygenation of γ-Hydroxy Vinylstannanes and their Acyl Derivatives: Mechanistic Insight into the Hydroxy-Directing Effect

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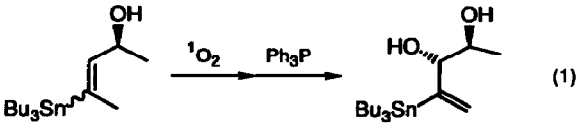
Abstract : The photooxygenation of *E*- as well as *Z*-configurated γ-hydroxy vinylstannanes proceeded in high regio- and diastereoselectivity to yield, after subsequent triphenylphosphine reduction, the corresponding *threo*-stannyl diols **2** in high excess. Their acylated derivatives showed only low and solvent-dependent stereoselectivity, which was not significantly influenced by the steric and electronic demand of the ester group.

The singlet oxygen ene reaction (Schenck reaction[1]) of chiral allylic alcohols[2] and amines[3] proceeds in a highly regio- and *threo*-selective manner in unpolar solvents; vinylstannanes[4] exhibit a pronounced *gem* selectivity. Accordingly, γ-hydroxy vinylstannanes, in which expectedly both the hydroxy directing effect and the *gem* selectivity of the stannyl moiety act synergistically, should display high regio- and stereocontrol in the ene reaction with singlet oxygen (eq. 1). After subsequent reduction of the resulting hydroperoxides, stannylated



(1)

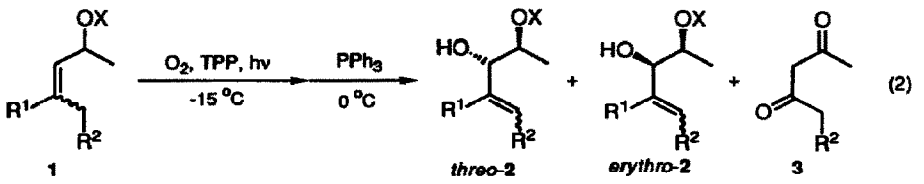
diols would result, which constitute useful building blocks for synthetic purposes.[5] On the other hand, such γ-hydroxy vinylstannanes are valuable for mechanistic studies, since the stereochemistry of the singlet oxygen ene reaction with allylic alcohols can be assessed without complications by regioisomeric ene products. Thus, through the facile stereoselective synthesis of (*E*)- and (*Z*)-γ-hydroxy vinylstannes from the corresponding propargylic alcohols,[6,7] the opportunity is offered to examine the stereochemical consequence of 1,3-allylic strain between the hydroxy-bearing chirality center and the towards ene reaction inert (no allylic H abstraction) *gem*-selective stannyl group by placing the latter *cis* or *trans* to the hydroxy-steering functionality. The corresponding carbon analogues, e.g. *tert*-butyl groups, are cumbersome to prepare in a stereochemically defined manner and have, consequently, not been subjected to the Schenck reaction.

Moreover, it has been demonstrated that the photooxygenation of an allylic acetate proceeded in low *erythro* selectivity in carbon tetrachloride;[2] in fact, for allylic amines protection of the amino functionality by the large phthalimido group[3] led to complete inversion of the *threo* selectivity displayed by the free amine. Thus, it was of interest to determine the stereoselectivity in the photooxygenation of chiral allylic esters by varying the steric

and electronic demand of the ester group. Herein we demonstrate that the photooxygenation of chiral γ-hydroxy vinylstannanes and their acyl derivatives occurs in high regio- and stereoselectivity, which provides valuable mechanistic insight into the oxyfunctionalization of allylic alcohols by $^1O_2$.

The required (*E*)-γ-hydroxy vinylstannanes (*E*)-**1a,b** were prepared from the corresponding propargylic alcohols according to the literature[6] (44-56 % yield). The substrates (*Z*)-**1a,b** were obtained by the addition of $Bu_3SnCu/Me_2S/LiBr$[7] to the respective propargylic ketones and subsequent reduction of the resulting stannyl enones with diisobutylaluminium hydride. The allylic esters (*E*)-**1c-g** were prepared from (*E*)-**1a** by acylation with the appropriate acid chloride for derivatives **1c-f** or anhydride for **1g** (2.5 equiv. pyridine, DMAP, CH_2Cl_2, 0 °C), while substrate **1h** was obtained as previously reported.[2]

The photooxygenation of these substrates **1** was conducted at low temperature (-15 °C) in CH_2Cl_2 (eq 2, Table I) with tetraphenylporphine as sensitizer. Subsequent triphenylphosphine reduction (CH_2Cl_2, 0 °C) yielded the corresponding vinylstannanes **2** in 70-93 % yield after flash chromatography on silica gel.



1 *threo*-2 *erythro*-2 3

Table I: Photooxygenation of γ-Hydroxy Vinylstannanes **1** and Related Esters

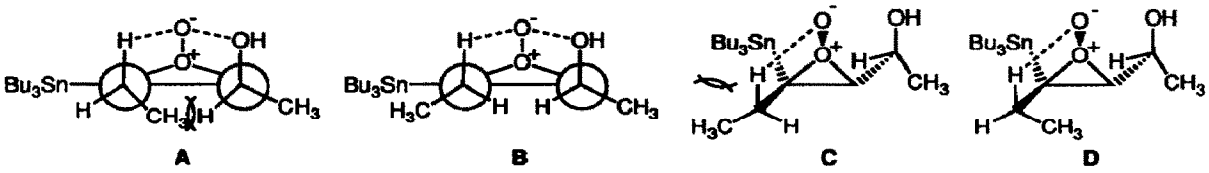
entry	substrate 1	R^1	R^2	X	t (h)[a]	conversion[b] (%)	regioselectivity 2 : 3	yield 2 (%)	diastereoselectivity *threo*-2 : *erythro*-2
(1)	(*E*)-**1a**	$SnBu_3$	H	H	2.5	100	100 : 0	93	95 : 5
(2)	(*Z*)-**1a**	$SnBu_3$	H	H	15	100	89 : 11	76	76 : 24
(3)	(*E*)-**1b**	$SnBu_3$	CH_3	H	4	100	100 : 0	78	95 : 5[c]
(4)	(*Z*)-**1b**	$SnBu_3$	CH_3	H	24	35	85 : 15	71[e]	94 : 6[d]
(5)	**1c**	$SnBu_3$	H	$COCH_3$	53	>95	100 : 0	84	68 : 32
(6)	**1d**	$SnBu_3$	H	COtBu	42	> 95	100 : 0	82	62 : 38
(7)	**1e**	$SnBu_3$	H	$COOCH_3$	44	> 95	100 : 0	70	76 : 24
(8)	**1f**	$SnBu_3$	H	$COC_6H_4NO_2$	42	73	100 : 0	84[e]	67 : 33
(9)	**1g**	$SnBu_3$	H	$COCF_3$	18.5[f]	14	100 : 0	-[g]	66 : 34
(10)	**1h**	CH_3	H	$COCH_3$	20	93	92 : 8[i]	-[g]	57 : 43
(11)	**1h**	CH_3	H	$COCH_3$	3.5[h]	68	87 : 13[i]	-[g]	42 : 58

a) Photooxygenation in CH_2Cl_2 at -15 °C with tetraphenylporphine as sensitizer; two 250-W sodium lamps; b) mass balance >90 %; c) *Z* : *E* = 92 : 8; d) *Z* : *E* = 14 : 86; e) corrected for conversion; f) in $CDCl_3$; in CH_2Cl_2 no reaction; g) NMR scale; h) in CCl_4; i) the other regioisomer was observed as 1,2-dioxolane, cf. ref.[2]

As shown in Table I, the introduction of the tributylstannyl group in the substrates (*E*)-**1a** to **1g** completely suppressed the formation of regioisomeric ene products, which result from the abstraction of a hydrogen α to

an oxygen atom. High regioselectivities were also obtained for the respective *Z* isomers. This was expected in view of the established *gem*-directing propensity of the stannyl moiety.

The photooxygenation of the vinylstannanes (*E*)-**1a,b** (entries 1,3) proceeded in high *threo* diastereoselectivity.[9] Additionally, the new double bond was formed *Z*-selectively in a ratio of 92 : 8 (entry 3). This was expected in view of the synergism between the regio- and *Z*-selective photooxygenation of (*E*)-vinylstannanes and that of allylic alcohols with *cis* alkyl groups to the chiral hydroxyethyl functionality. The remarkable *threo*-selectivity was previously explained[2] by an attractive interaction of the electrophilic singlet oxygen with the nucleophilic hydroxy group. The pronounced *Z* selectivity is rationalized in terms of appreciable 1,3-allylic strain due to methyl-hydrogen interaction in the intermediate **A**, which dominates the 1,2-allylic strain between the geminal stannyl and methyl groups in intermediate **B**. In view of the long tin-carbon bond, the lower steric demand of the stannyl group[10] is expected.



The corresponding (*Z*)-γ-hydroxy vinylstannanes (*Z*)-**1a,b** (entries 2,4), nonetheless, also reacted in good regiocontrol (> 85 : 15), but considerably slower, as expected for substrates in which the *cis* effect[8] is absent. Also the diones **3** were formed, which result from decomposition of the intermediary, regioisomeric α-hydroperoxy allylstannanes. Furthermore, these photooxygenations also occurred in moderate *threo* selectivity for **1a** and in an excellent one for **1b** , which for the latter is as high as for the *E* isomer (entry 4). This was surprising, since during the H abstraction step the singlet oxygen cannot coordinate to the hydroxy group in view of the *trans* stereochemistry. The high preference of singlet oxygen to attack the double bond of the stannylated substrates from the hydroxy side is in contrast to those substrates which bear a hydrogen atom instead; the latter do not exhibit any significant stereoselectivity.[2] 1,3-Allylic strain is presumably again responsible in fixing the conformation at the chirality center to result in such a high stereoselectivity. This 1,3-allylic strain is more prominent in substrate **1b**, since the preference for the *E*-configurated double bond (*Z* : *E* = 14 : 86) in **2b** suggests that significant 1,2-allylic strain is built up between the stannyl and the allylic methyl group (perepoxide **C**), which is not the case for **D**. Thus, (*Z*)-**1b** is sterically more compressed and should also exhibit larger 1,3-allylic strain, which is corroborated by the higher diastereoselectivity. Since for olefins with low electron density exciplex formation can be reversible,[11] we propose coordination of singlet oxygen to the hydroxy functionality in form of an exciplex and subsequent suprafacial migration followed by H transfer to singlet oxygen for rationalizing the high selectivities.

The photooxygenation of the allylic acetate **1h** revealed a small, but within the experimental error definite solvent effect (entries 10,11). Whereas the Schenck reaction proceeded in slight preference *erythro*-selectively (*threo* : *erythro* = 42 : 58) in carbon tetrachloride,[2] in the more polar dichloromethane an inverted selectivity (*threo* : *erythro* = 57 : 43) was observed. Only small energy differences govern these low diastereoselectivities, presumably through minor conformational changes in the transition state. Analogously, the photooxygenation of the stannylated allylic acetates in dichloromethane (*E*)-**1c** to **1g** (entries 5-9) displayed also a small *threo* preference and yielded the corresponding hydroxy esters **2c-g**. This low selectivity was not influenced

significantly by the electronic demand of the ester (cf. entries 5,7,8,9), except that the reaction rate was significantly slowed down, as becomes evident for the trifluoroacetate **1g** (entry 9) *versus* the acetate **1c** (entry 5). Furthermore, also the steric demand of the ester group changed only slightly the diastereoselectivity (entries 5,6); e.g. the pivalate **1d** (entry 6) showed a slightly higher *erythro* selectivity than the acetate **1c** (entry 5). Contrary to the allylic amines,[3] the diastereoselectivity in the singlet oxygen ene reaction of chiral allylic alcohols cannot be inverted by acylation. Thus, substitution by electron-withdrawing ester functionalities (entry 8,9) only causes a decrease in reactivity, while steric factors affect the stereoselectivity only nominally through a slight increase of the *erythro* product even for bulky ester groups. The higher conformational flexibility of esters obviates effective shielding of the double bond for appreciable diastereomeric control.

In conclusion, γ-hydroxy vinylstannanes are photoooxygenated regioselectively to the corresponding stannylated diols. In these allylic alcohols, the chirality center is fixed by 1,3-allylic strain and a strong preference for the *threo* product, irrespective of the double bond configuration in the starting material is observed. Photooxygenation of the corresponding acylated vinylstannanes does promote *erythro* selectivity through steric effects, but not to a sufficient degree to be useful for preparative applications.

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   (*E*)-**1a**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.70-1.10 (m, 15 H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.20-1.70 (m, 13H), 1.89 (d, *J* = 1.8 Hz, 3H), 4.74 (m, 1H), 5.56 (dq, *J* = 7.8, 1.8 Hz, J_{HSn}= 68.4 Hz, 1H).
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   The cuprate additions and the subsequent reduction were performed as described for the synthesis of (*E*)-3-(tri-*n*-butylstannyl)-2-penten-1-ol; however, cuprate addition to the propargylic ketones, contrary to the coreresponding esters, led predominantly (90 : 10) to the corresponding (*Z*)-enones (93 %), which on reduction gave 47-83 % (*Z*)-**1a,b** , as evident from the large J_{HSn} coupling constants.
   (*Z*)-**1a**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.76-1.11 (m, 15 H), 1.25 (d, *J* = 6.2 Hz, 3H), 1.20-1.70 (m, 13H), 1.91 (d, *J* = 1.6 Hz, 3H), 4.07 (m, 1H), 6.06 (dq, *J* = 8.5, 1.6 Hz, J_{HSn}= 122/127 Hz, 1H).
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9. The stereochemical asignment of **2** rests on the fact that all *threo*-diols **2a,b** and their acylated derivatives **2c-g** show significantly larger vicinal coupling constants $J_{2,3}$ (6.6-8.5 Hz) than the *erythro* isomers (3.8-4.5 Hz).[2] Further support was obtained by NOE experiments on the cyclic acetonides of the diols [*S**, *R**-(*Z*)]-**2b** and [*S**, *R**-(*E*)]-**2b**. For rigorous structure assignment, the isomeric hydroxy esters **2e** were converted to the diol **2a** through reductive deprotection by diisobutylaluminium hydride.
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