Stereoselective Dioxygenation of Allylstannanes: Synthesis of Enantiomerically Enriched Allyl Hydroperoxides

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Received November 29, 1993

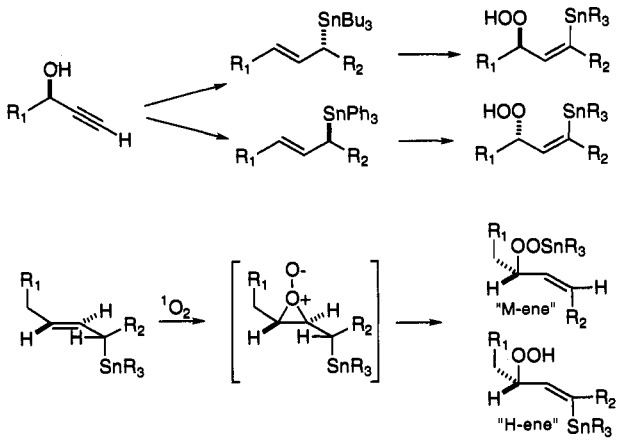
As part of a program targeting stereoselective synthesis of unsaturated hydroperoxides, we have become interested in improved strategies for alkene dioxygenation.[1] The reaction between singlet oxygen ($^1O_2$) and prochiral alkenes, perhaps the most direct method for the synthesis of allyl hydroperoxides, nevertheless produces racemic products, often as a mix of regioisomers.[2]

No general strategy exists for enantioselective oxygenations with $^1O_2$. The simultaneous inclusion of alkenes and $^1O_2$ within a chiral cyclodextrin cavity furnishes hydroperoxides with only modest enantioselectivity.[3] Neighboring stereocenters and a chiral auxiliary have both shown the ability to induce highly stereoselective dioxygenation, but neither approach is broadly applicable.[1,4-6] We report herein a general method for the stereoselective conversion of a chiral propargyl alcohol to either enantiomer of an allyl hydroperoxide through dioxygenation of chiral allylstannanes. (Scheme 1).

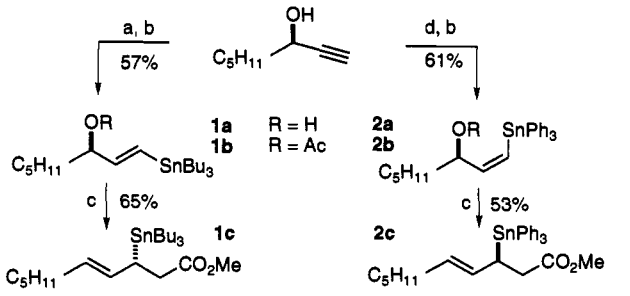
Our interest was prompted by recent reports describing stannyl-directed regioselective dioxygenation of acyclic and cyclic allyl stannanes; in one example, a stannylated cholestene underwent oxygenation to produce a single hydroperoxide stereoisomer.[7] The established preference for *anti*/ S_E2' electrophilic addition to chiral allylsilanes and -stannanes led us to explore the dioxygenation of chiral allylstannanes as a general strategy for the asymmetric synthesis of acyclic allyl hydroperoxides.[8] (Scheme 1) The selective formation of a single perepoxide upon addition of $^1O_2$ to a chiral allylstannane would result in a stereoselective synthesis of an allyl hydroperoxide, regardless of whether subsequent isomerization occurred through migration of hydrogen (H-ene) or tin (M-ene).[7a-c]

Synthesis of racemic models was accomplished as shown in Scheme 2. Radical addition of tributyltin hydride to 1-octyn-3-ol afforded a 4:1 mixture of the (*E*)- and (*Z*)-alkenyltributylstannanes **1a** from which the desired *E* isomer was separated by chromatography. In contrast, Et_3B-catalyzed addition of triphenyltin hydride afforded only the (*Z*)-alkenyltriphenylstannane **2a**.[9] Ester–enolate Claisen rearrangement of the corresponding acetates **1b** and **2b** afforded the 3-tributylstannyl- and 3-triarylstannyl-4(*E*)-alkenoate methyl esters **1c** and **2c** in good yield.[10]

Scheme 1



Scheme 2[a]



[a] Key: (a) *n*-Bu_3SnH, AIBN; (b) Ac_2O, pyr; (c) (i) $KN(TMS)_2$, TMSCl, (ii) H_2O, (iii) CH_2N_2; (d) Ph_3SnH, Et_3B.

Dye-sensitized photooxygenations were conducted with visible light in a jacketed cell.[11] The tributylstannyl enoate **1c** underwent oxidation to produce the β-stannylallyl hydroperoxide **1d** as the major (H-ene) product accompanied by 10–15% of a 1,2-dioxolane (**1f**) derived upon migration of the tributylstannyl group; no destannylated allyl hydroperoxide (M-ene) was observed. (Chart 1) Dioxygenation of the triphenylstannyl enoate **2c**, in contrast, afforded only H-ene product **2d**; the absence of dioxolane may be due to the lower migratory aptitude of the triarylstannyl moiety.[7c] Configurational assignments for **1d** and **2d** are based upon both the olefinic $^3J_{Sn-H}$ coupling and the observation of a strong NOE between the olefinic hydrogen and the C_2 methylene group.[12] Although the configuration of dioxolane **1f** has not been elucidated, stereoselective formation of the perepoxide as described in Scheme 1, followed by migration of the trialkylstannyl moiety, would be anticipated to produce a *cis*-3,5-disubstituted 1,2-dioxolane;[7bc,13] *cis*-3,5-disubstituted tetrahydrofurans have been

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(12) Cawley, S.; Danyluk, S. S. *J. Phys. Chem.* **1964**, *68*, 1240–1242. Selective production of (*Z*)-alkenes has been previously observed (refs 7b and 7d).
(13) **1f**: $^3J_{Sn-H3}$ = 32 Hz, $^3J_{Sn-H5}$ = 39 Hz, $^3J_{H3-4}$ = 7.6 Hz, $^3J_{H4-5}$ = 9.5 Hz.
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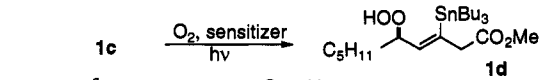
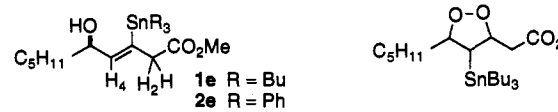
Chart 1



e.e of 1c[a]	Solvent	Sensitizer	Yield	e.e.
-	CCl_4	TPP	45%	-
-	CH_2Cl_2	TPP	56%	-
80%	CH_2Cl_2	TPP	52%	80%
-	CH_3CN	RB	58%	-
80%	CH_2Cl_2/CH_3CN	RB	52%	80%

e.e of 2c[a]	Solvent	Sensitizer	Yield	e.e.
-	CCl_4	TPP	60%	-
-	CH_2Cl_2	TPP	60%	-
-	CH_3CN	RB	74%	-
85%	CH_2Cl_2/CH_3CN	RB	60%	86%



[a] Based upon ^1H NMR analysis of corresponding Mosher ester.

isolated from silyl migrations during additions of allylsilanes to carbonyl electrophiles.[14]

Enantiomerically enriched allylstannanes were prepared through the same route employed for the racemates (Scheme 2). Reduction of 1-octyn-3-one with Alpine-Borane produced the desired (*R*)-propargyl alcohol in 80–85% ee.[15] Elaboration as before produced (*R*)-allyltributylstannane **1c** and (*S*)-allyltriphenylstannane **2c**. The photooxygenation-derived hydroperoxides **1d** and **2d** were reduced to the corresponding alcohols **1e** and **2e** with Ph_3P. Comparison of the ^1H NMR spectra of the (*R*)-(–) Mosher esters derived from racemic and enantiomerically enriched **1e** and **2e** allowed determination of both enantiomeric excess and absolute stereochemistry.[16] (Chart 1) The absolute stereochemical outcome is in agreement with the mechanism illustrated in Scheme 1, implying complete stereospecificity during the Claisen rearrangement and complete stereoselectivity during the subsequent photooxygenation.

In summary, the stereoselective reaction of $^1O_2$ with chiral allylstannanes allows the conversion of an enantiomerically enriched propargyl alcohol into either enantiomer of an allyl hydroperoxide. Further investigations into the applications of this new transformation are in progress and will be reported in due course.

Acknowledgment. We thank Professor Richard Shoemaker for valuable assistance with NMR experiments. The generous financial support of the American Cancer Society is gratefully acknowledged.

Supplementary Material Available: ^1H NMR spectra of **1a-f**, **2a-e**, Mosher esters of **1e** and **2e** (21 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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