

Stereochemistry of an Oxidative 1,4-Fragmentation of γ -Stannyl Alcohols with a Hypervalent Organoiodine Compound and the Synthesis of *erythro*-6-Acetoxyhexadecan-5-olide

Masahito Ochiai,^a Tatsuzo Ukita,^b Yoshimitsu Nagao,^a and Eiichi Fujita*^a

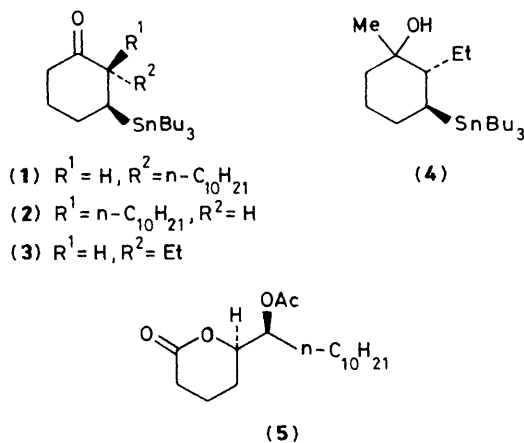
^a Institute for Chemical Research, Kyoto University, Uji, Kyoto-Fu 611, Japan

^b Department of Synthetic Chemistry, Research Laboratory of Applied Biochemistry, Tanabe Seiyaku Co., Ltd., Yodogawa-Ku, Osaka 532, Japan

Iodine(III)-mediated oxidative 1,4-fragmentation of the 2,3-*trans*- and 2,3-*cis*-3-stannyl alcohols, (**6a,b**) and (**6c**), proceeds stereospecifically to give the *E*- and *Z*-enals, (**7**) and (**8**), respectively, and stereoselective synthesis of the mosquito pheromone, *erythro*-6-acetoxyhexadecan-5-olide (**5**), starting from the *E*-enal (**7**), was accomplished.

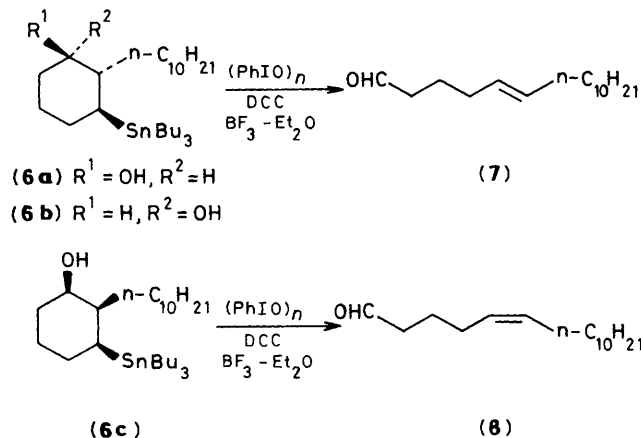
1,4-Fragmentation reactions provide a useful tool for the stereoselective synthesis of acyclic and macrocyclic compounds.^{1,2} The stereochemistry and yields of the products, and the reaction rates depend upon the stereochemical arrangement of nucleofugal and electrofugal groups,¹ especially in one-step synchronous fragmentations.³ Iodine(III)-mediated oxidative 1,4-fragmentation of the cyclic γ -stannyl alcohols has been reported to give unsaturated carbonyl compounds in good yields.⁴ We have now examined the stereochemical course of the fragmentation reaction and the results obtained have been applied to the synthesis of *erythro*-6-acetoxyhexadecan-5-olide (**5**).⁵

Conjugate addition of tributylstannyl-lithium to cyclohex-2-en-1-one in tetrahydrofuran (THF) followed by alkylation of the resulting lithium enolate with *n*-decyl iodide afforded the *trans*-ketone (**1**) stereoselectively in 47% yield. A similar stereochemical outcome was observed in the synthesis of 3-(dimethylphenylsilyl)-2-methylcyclohexan-1-one from cyclohex-2-en-1-one.^{6,7} The LiAlH₄ reduction of (**1**) produced a mixture of stereoisomers, from which 2,3-*trans*-alcohols (**6a**) and (**6b**) were isolated by silica gel column chromatography using hexane-ethyl acetate (10:1) in 51 and 29% yields, respectively. The relative stereochemistry of these alcohols was determined using ¹H and ¹³C n.m.r. spectroscopic data: (**6a**) δ_{H} 3.36 (dt, *J* 4, 10 Hz, C-1-H), δ_{C} 73.9 [³*J*(¹¹⁹Sn-¹³C) 63 Hz, C-1]; (**6b**) δ_{H} 3.93 (dt, *J* 4, 2.5 Hz, C-1-H), δ_{C} 67.5 [³*J*(¹¹⁹Sn-¹³C) 43 Hz, C-1]. Karplus-type dependence of vicinal ¹¹⁹Sn-¹³C coupling has been demonstrated to exist in a series of stereochemically rigid organotin compounds.⁸ 2,3-*cis*-Alcohol (**6c**) was synthesized as follows: isomerization of (**1**) with NaOH in dioxane-MeOH-water afforded an inseparable mixture of *trans*- and *cis*-ketones, (**1**) and (**2**), in a 62:38 ratio (96% yield), which was reduced with LiAlH₄ in THF to give (**6a**), (**6b**), and (**6c**) in a 43:21:36 ratio (96% yield).⁹



Oxidative 1,4-fragmentation of γ -tributylstannyl alcohols (**6**) was found to proceed in a completely stereospecific manner: the 2,3-*trans*-alcohol (**6a**) on treatment with iodosylbenzene, dicyclohexylcarbodiimide (DCC), and boron trifluoride-diethyl ether in dichloromethane at room temperature for 2 h afforded the *E*-enal (**7**)[†] in 77% yield, after purification by preparative t.l.c. using hexane-ethyl acetate (9:1); (**6b**) on the same treatment gave (**7**) in 91% yield. The

[†] Selected spectroscopic data: (**7**), i.r. (neat): 2700, 1730, 965, and 720 cm^{-1} ; ¹H n.m.r. (400 MHz; CDCl₃): δ 0.88 (t, 3H, *J* 6.5 Hz), 1.20–1.38 (m, 16H), 1.70 (quint., 2H, *J* 7.0 Hz), 1.97 (q, 2H, *J* 7.0 Hz), 2.03 (q, 2H, *J* 7.0 Hz), 2.42 (dt, 2H, *J* 2.0 and 7.0 Hz), 5.34, 5.43 [AB type, each 1H, *J* 15.1 Hz; each signal showed a vicinal coupling (t, *J* 7.0 Hz)], and 9.77 (t, 1H, *J* 2.0 Hz); mass spectrum *m/z* 238 (*M*⁺), 220, 194, 166, 98, 82, and 54; *M*⁺: found, 238.2308 (calc. for C₁₆H₃₀O, 238.2296).



400 MHz ^1H n.m.r. spectra of the products from the fragmentation of (6) did not show any signals due to *Z*-enal (8). On the other hand, 2,3-*cis*-alcohol (6c) gave only the *Z*-enal (8)‡ in 45% yield. Thus, the stereochemistry of oxidative fragmentation products depends entirely upon the relative configuration between the substituent at C-2 and tributylstannyl group at C-3; the configuration of the hydroxy group has no effect. Similarly 1,4-fragmentation of an epimeric mixture of alcohol (4), prepared from the ketone (3) by the reaction with methyl-lithium in THF, gave *E*-non-3-en-8-one stereoselectively in 69% yield. The latter has been shown to be an important intermediate for the synthesis of *endo*-brevicomin.¹⁰

Stereoselective synthesis of *erythro*-6-acetoxyhexadecan-5-olide (5), the major component of a mosquito oviposition attractant pheromone, from the fragmentation product (7)

‡ Selected spectroscopic data: (8), i.r. (neat): 2720 and 1720 cm^{-1} ; ^1H n.m.r. (400 MHz; CDCl_3): δ 0.88 (t, 3H, J 6.8 Hz), 1.20–1.38 (m, 16H), 1.70 (quint., 2H, J 7.0 Hz), 2.00 (br. q, 2H, J 7.0 Hz), 2.08 (br. q, 2H, J 7.0 Hz), 2.43 (dt, 2H, J 1.5 and 7.0 Hz), 5.31, 5.42 [AB type, each 1H, J 11.0 Hz; each signal showed vicinal and allylic couplings (tt, J 7.0 and 1.5 Hz)], and 9.77 (t, 1H, J 1.5 Hz); mass spectrum m/z 238 (M^+), 220, 194, 166, 98, 68, and 54; M^+ : found, 238.2312 (calc. for $\text{C}_{16}\text{H}_{30}\text{O}$, 238.2296).

was carried out: oxidation of the *E*-enal (7) with sodium chlorite¹¹ at room temperature for 17 h gave *E*-hexadec-5-enoic acid in 84% yield. Epoxidation of the olefinic acid by treatment with *m*-chloroperbenzoic acid in toluene-cyclohexane at room temperature for 6 h, lactonisation of the resulting oxirane by heating in toluene-cyclohexane at reflux for 24 h, and subsequent acetylation with acetic anhydride in pyridine at room temperature for 48 h afforded the desired compound (5) in 40% yield. The structure of (5) was confirmed by the comparison of the 400 MHz ^1H n.m.r. spectrum with that of the authentic pheromone.

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