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PREPARATION OF IODOALLYLIC ALCOHOLS VIA HYDROSTANNYLATION SPECTROSCOPIC PROOF OF STRUCTURES

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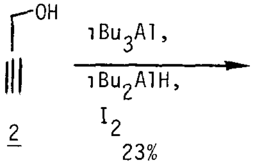
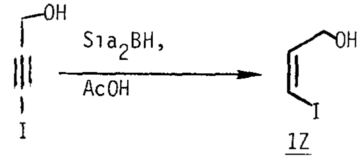
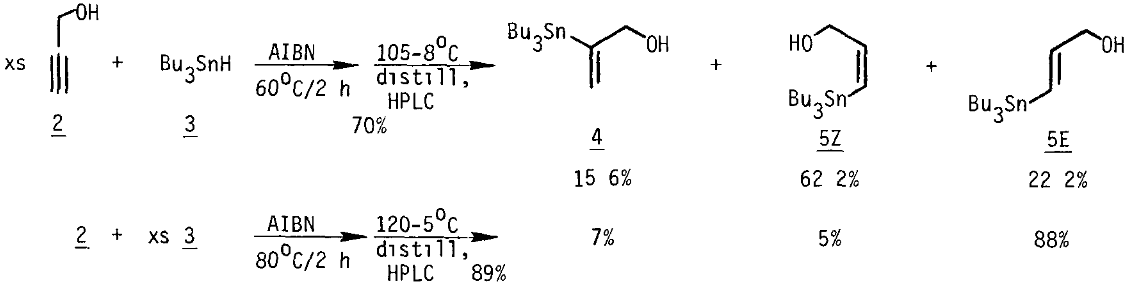
Abstract Hydrostannylation of propargylic alcohols and ethers affords either the E- or Z-β-tributylstannylallylic alcohols and ethers as the major products by the use of excess stannane or acetylenic compound, respectively, europium shift studies in the high field ^{1}H NMR spectra are used to establish the stereochemistry.

For a study of the use of anionic oxy-Cope rearrangements in the synthesis of natural products, we required the E- and Z-1-iodoprop-2-en-3-ols, 1E and 1Z, respectively. Both of the compounds were known, the E-isomer having been prepared by hydroalumination-iodination of propargyl alcohol 2 in 23%[2] yield and 1Z by hydroboration-protonation of 3-iodopropynol in an undetermined yield.[3] Because of the low yields and experimental difficulties of these procedures, we decided to investigate the hydrostannylation[4]-iodination[5] sequence as a general means of preparing E- and Z-1-iodoalk-1-en-3-ols and their ethers. We report here the results of this study and, in particular, the divergence of our results from those reported recently by Seebach.[6]



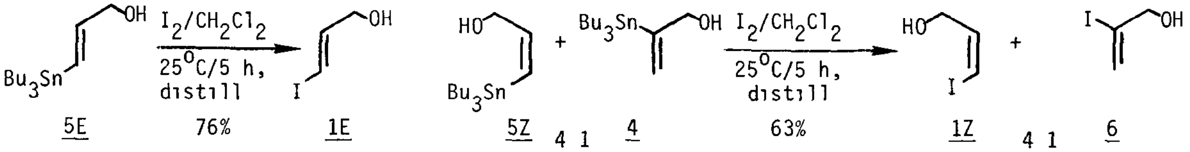


Treatment of 2 equiv of propargyl alcohol 2 with 1 equiv of tributylstannane 3 and a catalytic amount of azobis(isobutyronitrile) (AIBN) at 60°C for 2 h followed by distillation (105-8°C, 0.05 torr) afforded a mixture of the three possible isomers, 4 and 5ZE in 70% overall yield. The ratio of the products was 4 5Z 5E, 15.6 62.2 22.2. The trans-isomer 5Z could be separated in pure form by preparative high pressure liquid chromatography (HPLC), while the 4 1 mixture of 5Z 4 could only be partially separated. This result is in direct contrast to that of Seebach[6] who reported that a 5 1 mixture of 5E 5Z was produced under the identical conditions.[10] When the stannane was used in slight excess, the E-isomer was the major product. Thus treatment of 1 equiv of propynol 2 with 1 3 equiv of tributylstannane 3 and a catalytic amount of AIBN at 80°C for 2 h followed by distillation (120-5°C, 0.25 torr) afforded an 89% yield of a 7 1 mixture of 5E and 4/5Z. Again the pure E-isomer could be readily separated by prep HPLC. Since Seebach[6] reported the ^{13}C NMR data for the two isomers 5EZ, we measured the ^{13}C NMR of all of the isomers in order to assign the structures. However, our ^{13}C NMR data (Table 1) did not correspond to that reported earlier for any of the compounds. Because of the accidental overlap of the two vinyl protons in the ^1H NMR of the E-isomer and the large vinylic coupling constant in the Z-isomer (12.8 Hz), simple proton NMR did not permit a structural assignment. Therefore a europium-induced chemical shift study was undertaken.



The effect of added europium shift reagent on the ^1H NMR of 5E and 5Z is given in Table 2. As indicated, upon addition of the europium shift reagent, H_2 in 5Z is shifted downfield more than twice as much as H_1 while in 5E both protons are shifted nearly the same amount with H_1 being affected slightly more than H_2 (~20%). This data is totally consistent with our structural assignment, namely that in the Z-isomer the H_2 proton would be much closer to the alcohol function and therefore more affected by added Eu, while in the E-isomer the two protons, H_1 and H_2, are more nearly equidistant from the alcohol and thus very similarly affected by added Eu. An additional benefit of adding the shift reagent to 5E was the splitting of the degeneracy of the chemical shifts of the two vinyl protons so that their coupling constant could now be observed (Table 1). This very large value (19.2 Hz) compared to that for 5Z (12.8 Hz) also implies that our structural assignments are correct.

The conversion of the vinylstannanes into vinyl iodides proved very straightforward. Treatment of 5E with 1.1 equiv of iodine in dichloromethane at 25°C for 5 h followed by distillation gave a 76% yield of pure 1E. Similar treatment of the 4.1 mixture of 5Z 4 gave a 63% yield of a 4 1 mixture of 1Z and 2-iodoallyl alcohol 6. In this manner, 1E is prepared from propynol 2 in 60% overall yield while 1Z is available from 2 in 27% overall yield, each in two steps. Again the use of ^1H NMR spectroscopy - both the vinylic coupling constants (Table 1) and the europium-induced chemical shift effects (Table 2) - permit the assignment of structure to 1E and 1Z. As before, H_2 in the Z-isomer is shifted more than twice as much as H_1 upon addition of Eu while in the E-isomer both protons are affected identically. The vinylic coupling constants (14.5 Hz for 1E, 7.6 Hz for 1Z) also are in agreement with the assigned structures.[7,8]



We can put forth no reasons to explain the differences in our results from those of Seebach.[6] In general, our results are in agreement with earlier work on hydrostannylation,[4] namely that excess stannane causes isomerization of the initially formed Z-isomer to the E-isomer.

We have also tested the generality of this hydrostannylation-iodination sequence. Treatment of

Table 1 ^{1}H and ^{13}C NMR data for RC^{1}H=C^{2}H-C^{3}HR''OR'

Cmpd	R	R'	R''	H_1	H_2	H_3	CH_2	Ph	J_{12}	J_{23}	J_{13}	C_1	C_2	C_3	Bu_3Sn			
1Z	I	H	H	6.36	6.49	4.24	----	----	7.6	5.6	1.3							
1E	I	H	H	6.40	6.71	4.10	----	----	14.5	5.4	1.5							
4	-	H	H	5.89	5.25	4.27	----	----	----	---	---	154.8	122.8	69.4	29.2	27.4	13.7	9.6
5Z	Bu_3Sn	H	H	6.07	6.69	4.11	----	----	12.8	5.8	1.1	146.6	131.2	66.0	29.3	27.4	13.7	10.7
5E	Bu_3Sn	H	H	6.19	6.19	4.17	----	----	(19.2)	(4.0)	---	147.3	128.2	66.2	29.2	27.4	13.7	9.5
8E	Bu_3Sn	Bn	H	6.23	6.10	4.05	4.52	7.33	19.1	4.6	0.8							
9	-	Bn	H	5.9	5.3	4.15	4.5	7.33	----	---	---							
10E	I	Bn	H	6.40	6.66	3.95	4.51	7.33	14.5	5.6	1.0							
12E	Bu_3Sn	H	Am	6.14	5.98	4.06	----	----	19.2	5.1	---							
13E	I	H	Am	6.34	6.58	4.09	----	----	14.5	6.2	---							

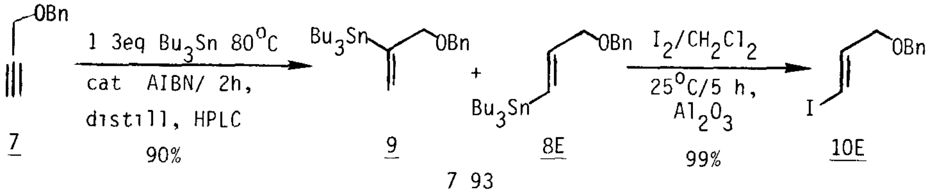
The numbers in parentheses were determined by europium-induced chemical shift experiments.

Table 2. Lanthanide-Induced Chemical Shifts for RC^{1}H=C^{2}H-C^{3}H$_2$OH

	5E		5Z		1E		1Z	
	$\Delta\delta^a$	$\Delta\delta^b$	$\Delta\delta^a$	$\Delta\delta^b$	$\Delta\delta^a$	$\Delta\delta^b$	$\Delta\delta^a$	$\Delta\delta^b$
H_3	1.55	2.50	0.95	2.25	1.12	2.03	0.56	1.43
H_2	0.70	1.25	0.65	1.55	0.64	1.16	0.39	0.98
H_1	0.85	1.45	0.25	0.60	0.65	1.18	0.16	0.39

Positive (downfield) chemical shift difference on addition of ^{a}0.05 and ^{b}0.1 equiv of Eu(fod)$_3$.

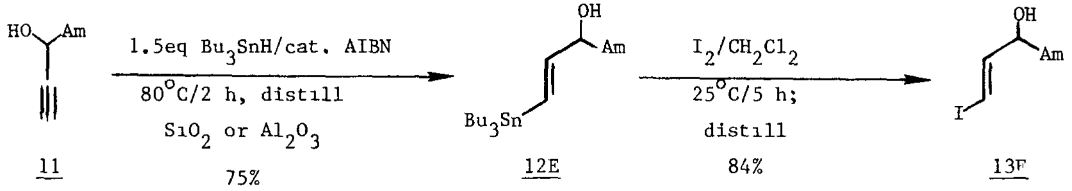
propargyl benzyl ether 7 with 1.3 equiv of tributylstannane 3 and catalytic AIBN at 80°C for 2 h followed by distillation (210-6°C, 0.09 torr) afforded a 90% yield of a 93 7 mixture of 8E 9 which was easily separated by prep HPLC. Iodination of 8E followed by alumina chromatography gave a 99% yield of the iodo benzyl ether 10E, thus making 10E available from 7 in 2 steps in 83% yield.



An important intermediate for prostaglandin synthesis is E-1-iodo-1-octen-3-ol 13E.[9] This is normally prepared in one of two ways 1) addition of iodine to 1-chloro-*trans*-1-octen-3-one followed by LiAlH$_4$ reduction[9a] or 2) hydroalumination-iodination of 1-octyn-3-ol 11,[9b] a sequence which proceeds in 47% yield. This important compound can be prepared by the present method from 11 in 63% overall yield as follows. Treatment of 11 with 1.5 equiv of tributylstannane 3 and catalytic AIBN at 80°C for 2 h followed by distillation (120-5°C, 0.02 torr) and chromatography (silica gel or alumina) furnished 75% of the stannane 12E which was iodinated under the standard conditions to give 13E after distillation (135°C, 1 torr) in 84% purified yield. The structure was assigned by comparison of the ^{1}H NMR and IR data in the literature.[9]

This hydrostannylation-iodination method is applicable for the preparation of either Z- or E-

1-iodo-1-alken-3-ols by varying the initial hydrostannylation procedure. Since vinylstannanes can also by brominated stereospecifically,[5b] this process makes the corresponding bromoalcohols available also.



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10. Stirring the reaction mixture at 20°C for 30 min before heating[6] did not change the outcome and thus this pretreatment was normally omitted.

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