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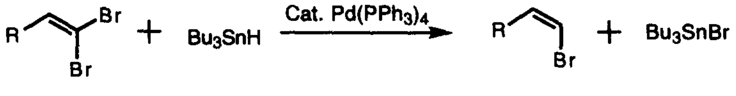
A General and Convenient Synthetic Method of Geometrically Pure (Z)-1-Bromo-1-alkenes

Jun'ichi Uenishi,* Reiko Kawahama, Yasuhiko Shiga, and Osamu Yonemitsu
Department of Chemistry, Faculty of Science, Okayama University of Science
Ridaicho, Okayama 700, Japan

Jiro Tsuji
Department of Chemical Technology, Kurashiki University of Science and the Arts
Tsurajima-cho, Kurashiki, Okayama 712, Japan

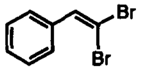
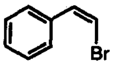
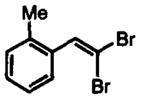
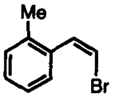
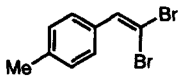
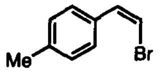
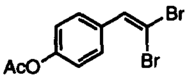
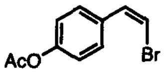
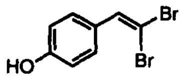
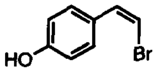
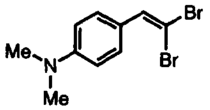
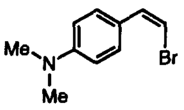
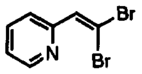
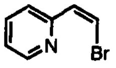
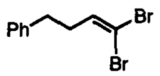
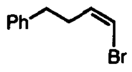
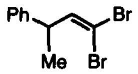
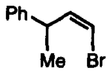
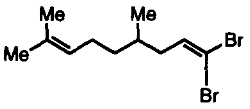
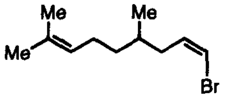
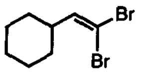
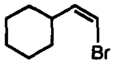
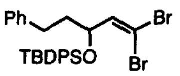
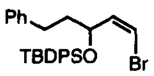
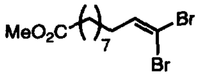
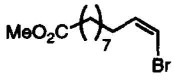
Abstracts: Palladium catalyzed hydrogenolysis of 1,1-dibromo-1-alkenes by tributyltin hydride proceeds smoothly to give (Z)-1-bromo-1-alkenes with excellent stereoselectivity in good yields. Dibromomethylenation of aldehydes by a combination of CBr_4 and Ph_3P in methylene chloride and the successive hydrogenolysis affords (Z)-1-bromo-1-alkenes in one-pot.

(Z)-1-Halo-1-alkene is an important building block for stereospecific synthesis of organic compounds possessing a Z-olefin unit in the molecules.[1] To date, (Z)-1-halo-1-alkenes have been prepared using several methods, including *cis* hydrogenation of 1-halo-1-alkynes with diimine,[2] haloalkenylation of aldehydes with Wittig type reagents,[3] stereospecific substitution of *Z*- or *E*-metalloalkenes with halogen-groups,[4] and others.[5] Sometimes, however, they are unsatisfactory, having low reactivity, poor stereoselectivity, or undesired side reactions including over-reduction. Herein, we report a very simple and reliable method for preparing geometrically pure (Z)-1-bromo-1-alkenes from 1,1-dibromo-1-alkenes. The method can be expressed in the following general scheme.



When β,β-dibromostyrene (**1a**) was treated with tributyltin hydride (1.05~1.15 eq) in the presence of tetrakis(triphenylphosphine)palladium (4 mol%) in benzene[6] at room temperature, (Z)-β-bromostyrene (**2a**) was obtained in 76% yield. The reaction was completed in 15 min and none of the *E*-isomer was detected in the crude product.[7] The starting 1,1-dibromoalkenes, **1a**-**1m**, were prepared from the corresponding aldehydes in 70 to 98% yields by a standard method.[8] Results of the hydrogenolysis for **1a**-**1m**, are summarized in Table 1.[9, 10] *Ortho* and *para* methyl substituted styrenes, **1b** and **1c**, gave the corresponding (Z)-bromostyrenes, **2b** and **2c**, in both 79% yields. An acetoxy group substituting on the aromatic ring did not influence the reaction, thus, 4-acetoxy-(Z)-β-bromostyrene (**2d**) was obtained in 83% yield. Even in the presence of a phenol group,

Table 1. Palladium Catalyzed Hydrogenolysis of 1,1-Dibromoalkenes with Bu$_3$SnH

Entry	1,1-Dibromoalkene		*Z*-Bromoalkene[a]		Yield[b] (%)
1		1a		2a	76
2		1b		2b	79
3		1c		2c	79
4		1d		2d[c]	83
5		1e		2e	82
6		1f		2f[d]	90
7		1g		2g	61
8		1h		2h	79
9		1i		2i	84
10		1j		2j	70
11		1k		2k	77
12		1l		2l	56
13		1m		2m	80

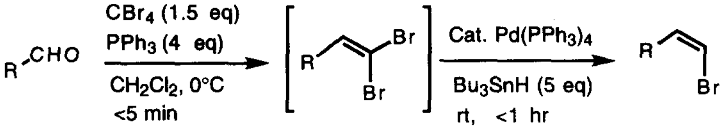
[a] Geometric purities were determined to be greater than 98% by ^{1}H NMR. [b] Isolated yields. [c] mp 44-46°C. [d] mp 49-50°C.

this reaction proceeded smoothly to give 4-hydroxy-(*Z*)-β-bromostyrene (**2e**) in 82% yield. Compounds **2f** and **2g**, having a tertiary amine and pyridine ring, were yielded in 90 and 61% from 4-(2,2-dibromovinyl)-*N*,*N*-dimethylaniline and 2-(2,2-dibromovinyl)pyridine, respectively. These results (entries 1-7) indicate that this method is widely applicable for the preparation of (*Z*)-β-bromostyrenes.

The reaction was also effective for aliphatic substrates shown in entries 8-13. The reaction of 4-phenyl- and 3-phenyl-1,1-dibromo-1-butenes, (**1h**) and (**1i**), afforded (*Z*)-1-bromobutenes, **2h** and **2i**, in 79 and 84% yields, respectively. The dibromoalkenes, **1j** and **1k**, derived from citronellal and cyclohexanecarboxaldehyde, lead to the corresponding (*Z*)-bromoalkenes, **2j** and **2k**, in 70 and 77% yields. Reactions of the (*tert*-butyldiphenylsilyl)oxy substituted substrate **1l** and the substrate bearing a long carbon chain ester **1m** provided **2l** and **2m** in 56 and 80% yields.

The high selectivities of the reaction is certainly due to facile oxidative addition of Pd(0) to the carbon-bromine bond located at the less hindered *trans* position. Then, transmetallation with tributyltin hydride followed by reductive elimination takes place to give the (*Z*)-bromoalkene selectively. In only a few cases, nearly perfect discrimination of the two halogen groups in 1,1-dihalo-1-alkenes has been reported. They were found in the palladium catalyzed Suzuki coupling and Tamao coupling reactions,[11, 12] in which a halide located at the *trans* position reacted faster than that at the *cis*. In fact, when no palladium catalyst was used with tributyltin hydride, a radical reaction of 1,1-dibromoalkenes proceeded non-stereoselectively to give a mixture of stereoisomers.[13] Although Oshima and Utimoto reported hydrogenolysis of 1-bromo-1-alkene with tributyltin hydride under the palladium catalyzed conditions, the bromide was replaced by hydride very poorly even under refluxing conditions.[14] Our results indicate that 1,1-dibromoalkenes are remarkably more reactive than 1-bromoalkenes in the palladium catalyzed hydrogenolysis by tributyltin hydride.

The dibromomethylenation of aldehydes took place cleanly to give 1,1-dibromoalkenes in excellent yields. Since both the dibromoalkene formation and hydrogenolysis were performed in methylene chloride,[8, 6] these reactions could be carried out from the aldehydes in one-pot. Thus, *para*-tolualdehyde was treated with carbon tetrabromide (1.5 eq) and triphenylphosphine (4 eq) in methylene chloride at 0°C. Then after the formation of 1,1-dibromoalkene, **1c**, addition of tributyltin hydride (5 eq) and a catalytic amount of $Pd(PPh_3)_4$ (6 mol%) to the reaction flask afforded **2c** in 84% yield. An aliphatic aldehyde, 2-phenylpropanal, was also converted to **2i** in 81% yield under the above one-pot conditions. Although the reaction required a considerable amount of tributyltin hydride,[15] the one-pot procedure was very effective, particularly when 1,1-dibromoalkenes were unstable.



R = *p*-tolyl
α-phenethyl

2c 84%
2i 81%

In conclusion, we have succeeded in the stereoselective hydrogenolysis of 1,1-dibromoalkenes leading to *Z*-bromo-1-alkenes exclusively. The resulting (*Z*)-bromoalkenes would be valuable compounds for stereospecific synthesis of polyenes or other systems possessing a *Z*-olefin unit in the molecules.

Acknowledgment

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6, Other solvents, such as THF, ether, toluene and CH_2Cl_2 are also suitable for the hydrogenolysis.

7, For (*E*)- and (*Z*)-β-bromostyrenes; see Miller, R. B.; McGarvey, G. *J. Org. Chem.* **1978**, *43*, 4424-4431.

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9, A typical experimental procedure is as follows: To a stirred solution of dibromoalkene, **1** (1 mmol) and $Pd(PPh_3)_4$ (0.04 mmol) in anhydrous benzene (7 mL) was added Bu_3SnH (1.1 mmol) in anhydrous benzene (3 mL) under Ar atomosphere. After the mixture was stirred for 15 to 60 min at room temperature, an extractive work up with hexane or benzene and a purification by alumina column chromatography gave **2**.

10, The stereochemistries of all the products were confirmed by comparison with previous data reported in the literature, or determined by a coupling constants of the olefinic protons in proton nmr spectra.

11, Roush, W. R.; Moriarty, K. J.; Brown, B. B. *Tetrahderon Lett.* **1990**, *31*, 6509-6512.

12, Minato, A.; Suzuki, K.; Tamao, K. *J. Am. Chem. Soc.* **1987**, *109*, 1257-1258.

13, For example, the reaction of **1a** and **1i** gave a 1 : 1 mixture of (*E*)- and (*Z*)-bromoalkenes along with a mixture of other complex products.

14, The desired alkenes were obtained in 35~37% yields, although these authors succeeded in stereospecific hydrogenolysis of 1-iodo-1-alkenes with tributyltin hydride using a slow addition technique. See, Taniguchi, M.; Takeyama, Y.; Fugami, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2593-2595.

15, Theoretically, five equivalents of tributyltin hydride are totally required in this case; three for the reaction with Ph_3PBr_2 (1.5 eq), one for the reaction with the remaining $Ph_3P{=}CBr_2$ (0.5 eq), and an additonal equivalent for the hydrogenolysis.

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