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Synthesis of (Z)-1,2-Dihalo-1-alkenes by the Reaction of (Z)-(β-Halovinyl)phenyliodonium Salts with n-Bu$_4$NX or KX/CuX. Competitions between Nucleophilic Vinylic Substitutions and Aromatic Substitutions1)

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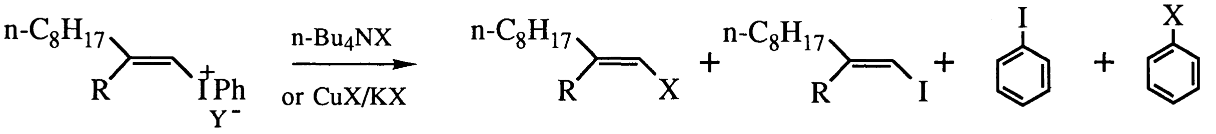
Nucleophilic vinylic substitutions of (Z)-(β-halovinyl)phenyliodonium salts with tetrabutylammonium halides proceed in a stereoselective manner with retention of configuration yielding vicinal (Z)-vinyl dihalides. This reaction competes with nucleophilic aromatic substitutions. Similar competition was observed in the reactions with potassium halides/cuprous halides.

Vicinal dihaloalkenes are usually prepared by the addition reaction of halogens and interhalogens to alkynes.2) This reaction gives (*E*)-1,2-dihalo-1-alkenes predominantly. The method for stereo- and regioselective synthesis of (Z)-1,2-dihalo-1-alkenes, however, are very limited.3) We report herein nucleophilic vinylic substitutions of (Z)-(β-halovinyl)phenyliodonium salts **1** with halides, which provide an efficient route for the stereo- and regioselective synthesis of vicinal (Z)-vinyl dihalides. This reaction competes with nucleophilic aromatic substitutions.

Because of a superleaving ability of a phenyliodonio group, vinyl(phenyl)iodonium salts serve as the highly activated species of alkenyl halides toward the substitution reactions with a variety of nucleophiles.4) Nucleophilic vinylic substitutions of (*E*)-(β-alkylvinyl)phenyliodonium tetrafluoroborates with n-Bu$_4$NX (Cl, Br, and I) at room temperature proceed with exclusive inversion of configuration yielding alkenyl halides of (Z) stereochemistry.5) Substitutions of (Z)-(β-(phenylsulfonyl)vinyl)phenyliodonium tetrafluoroborates, however, lead to exclusive retention of configuration.6) Vinylic S$_N$2 type mechanism for the inversion of configuration and addition-elimination mechanism for the retention of configuration were proposed.5,6) Both the reactions are highly chemoselective in the sense that halide anions attack the α-vinylic carbons and not the *ipso*-aromatic carbons, while the *ipso* aromatic substitutions of diaryliodonium salts with halides have been well established.7)



1a: R = Br, Y = BF$_4$
1b: R = Cl, Y = BF$_4$
1c: R = F, Y = I

2a: R = Br
2b: R = Cl

3a: R = Br
3b: R = Cl
3c: R = F

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5a: X = Br
5b: X = Cl

Reaction of (*E*)-(β-alkylvinyl)- and (Z)-(β-(phenylsulfonyl)vinyl)phenyliodonium salts with n-Bu$_4$NX proceeds smoothly at room temperature.5,6) Introduction of halogens at β-olefinic carbons of vinyliodonium

Table 1. Reaction of (Z)-(β-Halovinyl)iodonium Salts **1** with n-Bu_4NX[a]

Entry	**1**	X	Solvent	Reaction time	Product (yield)[b] **2**	**3**	**4**	**5**
1	**1a**	Cl	CH_3CN	4 h	**2a**(X=Cl, 91%)	**3a**(9%)[c]	**4**(82%)	**5b**(10%)
						(91:9)[d]		(89:11)[e]
2	**1a**	Br	CH_3CN	3 h	**2a**(X=Br, 94%)[c]	**3a**(6%)	**4**(88%)	**5a**(9%)
						(94:6)[d]		(91:9)[e]
3	**1a**	I	CH_3CN	10 min		**3a**(88%)	**4**(94%)	
4	**1b**	Cl	CH_3CN	8 h	**2b**(X=Cl, 81%)	**3b**(19%)	**4**(80%)	**5b**(15%)
						(81:19)[d]		(84:16)[e]
5	**1b**	Cl	hexane	2 d	**2b**(X=Cl, 80%)	**3b**(12%)	**4**(82%)	**5b**(11%)
						(87:13)[d]		(89:11)[e]
6	**1b**	Br	CH_3CN	4 h	**2b**(X=Br, 85%)	**3b**(13%)	**4**(85%)	**5a**(13%)
						(87:13)[d]		(87:13)[e]
7	**1b**	I	CH_3CN	0.5 h		**3b**(100%)	**4**(100%)	
8	**1c**	I	CH_3CN	8 h		**3c**(80%)	**4**(83%)	

a) Reactions were carried out using 1.2 equiv. of n-Bu_4NX under refluxing under nitrogen. b) Yields were determined by GC. c) S. Hara, T. Kato, H. Shimizu, and A. Suzuki, *Tetrahedron Lett.*, **26**, 1065 (1985). d) Ratio of **2**:**3**. e) Ratio of **4**:**5**.

Table 2. Reaction of (Z)-(β-Halovinyl)iodonium Salts **1** with CuX/KX[a]

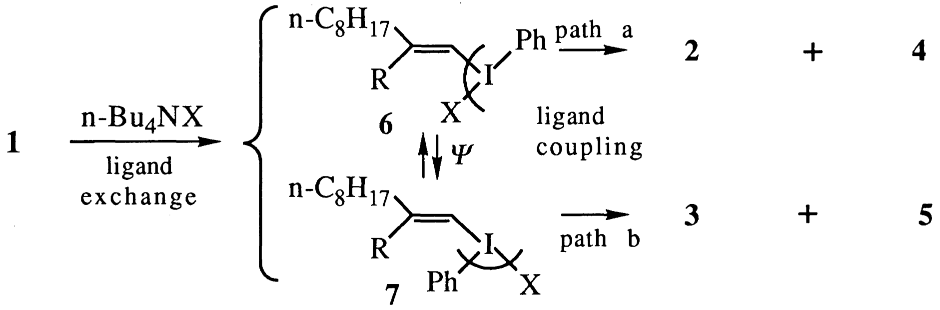
Entry	**1**	X	Solvent	Reaction time	Product (yield)[b] **2**	**3**	**4**	**5**
9	**1a**	Cl	CH_2Cl_2	2 d	**2a**(X=Cl, 80%)	**3a**(16%)	**4**(73%)	**5b**(18%)
						(84:16)[c]		(80:20)[d]
10	**1a**	Br	CH_2Cl_2	2 d	**2a**(X=Br, 73%)	**3a**(13%)	**4**(64%)	**5a**(14%)
						(85:15)[c]		(81:19)[d]
11	**1a**	I	CH_2Cl_2	3 d		**3a**(85%)	**4**(83%)	
12	**1b**	Cl	CH_2Cl_2	1 d	**2b**(X=Cl, 72%)	**3b**(24%)	**4**(74%)	**5b**(23%)
						(75:25)[c]		(76:24)[d]
13	**1b**	Br	CH_2Cl_2	1 d	**2b**(X=Br, 73%)	**3b**(23%)	**4**(74%)	**5a**(21%)
						(76:24)[c]		(78:22)[d]
14	**1b**	I	CH_2Cl_2	1 d		**3b**(98%)	**4**(99%)	

a) Reactions were carried out using CuX(10 equiv.)/KX(10 equiv.) at room temperature under nitrogen in the dark. b) Yields were determined by GC. c) Ratio of **2**:**3**. d) Ratio of **4**:**5**.

salts, however, makes the reaction very sluggish. Thus, prolonged treatment of (Z)-β-bromo- **1a** and (Z)-β-chlorovinyliodonium tetrafluoroborates **1b**[8] with n-Bu_4NCl or n-Bu_4NBr in dichloromethane at room temperature recovered more than 90% of the vinyliodonium salts. The major reaction observed was a ligand exchange on iodine(III) atom. However, refluxing the reaction mixture in CH_3CN led to the formation of nucleophilic substitution products; treatment of **1b** with n-Bu_4NCl (1.2 equiv.) in refluxing CH_3CN under nitrogen for 8 h gave a mixture of the vinylic substitution products, the vicinal (*Z*)-vinyl dichloride **2b**9) (X = Cl; 81%) and iodobenzene (80%), and the aromatic substitution products, the β-chlorovinyl iodide (*Z*)-**3b** (19%) and chlorobenzene (15%) (Table 1, entry 4). Slightly higher ratios of vinylic to aromatic substitutions were obtained by using hexane as a solvent (entry 5), or by replacing the nucleophile from n-Bu_4NCl to n-Bu_4NBr (entry 6).10) These nucleophilic vinylic substitutions were completely stereoselective to the limits of NMR detection at 270 MHz with retention of configuration, and the Z stereochemistry of **2b** and **3b** was established by the observation of a nuclear Overhauser effect (NOE) enhancement between the vinylic and allylic protons. Similar competitions between nucleophilic vinylic substitutions and aromatic substitutions were observed in the reaction of **1a** with n-Bu_4NX, which gives a mixture of (*Z*)-β-bromovinyl halides and halobenzenes. Reaction of (*Z*)-β-fluorovinyliodonium salt **1c** with n-Bu_4NI also gave (*Z*)-β-fluorovinyl iodide **3c** in high yield.

Table 1 shows that the rate of nucleophilic substitutions depends on the halide ions, and decreases in the order of n-Bu_4NI > n-Bu_4NBr > n-Bu_4NCl, reflecting the decreasing softness of halide ions. On the other hand, n-Bu_4NF does not undergo nucleophilic substitutions, and acts as a base for α-proton abstraction from **1**. For instance, the reaction of **1b** with n-Bu_4NF generates an (α-chloroalkylidene)carbene *via* α- and/or β-elimination, which undergoes intramolecular 1,5-carbon-hydrogen insertions and 1,2-migration of an α-chlorine atom.11)

Nucleophilic substitutions of (*E*)-(β-alkylvinyl)phenyliodonium tetrafluoroborates with a combination of cuprous halides and potassium halides have been shown to proceed chemoselectively at an α-vinylic carbon, yielding (*E*)-vinyl halides with retention of configuration;5) however, nucleophilic vinylic substitutions of **1** with cuprous halides and potassium halides yielding **2** also compete with the nucleophilic aromatic substitutions yielding **3**, as was observed in the reaction with n-Bu_4NX. These results are summarized in Table 2.



Scheme 1.

Both an addition-elimination route12) and a ligand coupling mechanism13) (Scheme 1; path a) on the iodine(III) of the intermediate iodonium halide **6** produced by rapid ligand exchange14) are compatible with the stereochemical outcome observed in this nucleophilic vinylic substitution using n-Bu_4NX. An alternative ligand coupling (path b) of the halide **7** generated by pseudorotation (Ψ) on iodine(III) of **6** leads to the formation of the nucleophilic aromatic substitution products. Whatever mechanism operates in the reactions of **1** with halides, the methods developed provide an efficient route for the stereo- and regioselective synthesis of vicinal (Z)-vinyl dihalides.

References

1) This paper is dedicated to Professor Yoshifumi Maki on the occasion of his retirement from Gifu Pharmaceutical University in March 1994.

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8) (*Z*)-β-Bromo- **1a** and (*Z*)-β-chlorovinyliodonium salts **1b** were prepared by stereoselective Michael-type addition of one equiv. of LiX (X = Cl and Br) to 1-decynyl(phenyl)iodonium tetrafluoroborate in acetic acid in 82% and 80% yields, respectively. Similarly, (*Z*)-β-fluorovinyliodonium iodide **1c** was prepared by the reaction of the alkynyliodonium salt with CsF (2 equiv.) and H_2O (20 equiv.) in acetone, followed by the ligand exchange using KI, in 12% yield.

9) All new compounds were fully characterized by spectroscopic means and/or elemental analyses. ^1H NMR (270 MHz, $CDCl_3$) data are the following; **2a** (X = Cl): δ 0.88 (t, 3 H, J = 6.5 Hz), 1.2-1.7 (12 H), 2.47 (dt, 2 H, J = 1, 7.5 Hz), 6.35 (t, 1 H, J = 1 Hz). **2b** (X = Cl): δ 0.88 (t, 3 H, J = 6.5 Hz), 1.2-1.7 (12 H), 2.37 (dt, 2 H, J = 1, 7.5 Hz), 6.13 (t, 1 H, J = 1 Hz). **2b** (X = Br): δ 0.89 (t, 3 H, J = 6.5 Hz), 1.2-1.7 (12 H), 2.40 (dt, 2 H, J = 1, 7.5 Hz), 6.27 (t, 1 H, J = 1 Hz). **3b**: δ 0.88 (t, 3 H, J = 6.5 Hz), 1.2-1.7 (12 H), 2.49 (t, 2 H, J = 7.5 Hz), 6.41 (s, 1 H). **3c**: δ 0.88 (t, 3 H, J = 6.5 Hz), 1.2-1.7 (12 H), 2.33 (dt, 2 H, J = 7.5 Hz, $^3J(^{19}F-^1H)$ = 16.1 Hz), 5.17 (d, 1 H, $^3J(^{19}F-^1H)$ = 35.2 Hz).

10) Interestingly, pyrolysis of (*Z*)-(2-chloro-1-decenyl)phenyliodonium bromide at 140 °C for 2 min without using solvent gave a similar ratio of substitution products: **2b** (X = Br; 65%), iodobenzene (59%), **3b** (14%), and bromobenzene (12%).

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14) When a dichloromethane solution of **1b** was shaken with an aqueous NaCl or NaBr solution using separatory funnel, the corresponding vinyliodonium halides were produced *via* rapid ligand exchange in high yields.

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