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Nucleophilic vinylic substitutions of (*Z*)-(2-aroyloxyvinyl)phenyl-λ^3-iodanes with tetrabutylammonium halides: vinylic S_N2 reactions and ligand coupling on iodine(III)

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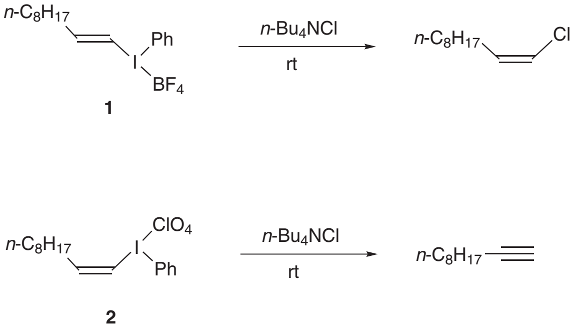
Abstract—Treatment of (*Z*)-(β-benzoyloxyvinyl)phenyl-λ^3-iodanes, readily prepared from ethynyl(phenyl)(tetrafluoroborato)-λ^3-iodane via stereoselective Michael-type addition of benzoic acids in methanol in the presence of sodium benzoates, with tetrabutylammonium halides in THF at 65 °C results in a vinylic S_N2 reaction to give the inverted (*E*)-β-benzoyloxyvinyl halides in high yields.

(*E*)-(β-Alkylvinyl)phenyl-λ^3-iodanes smoothly undergo an unusual vinylic S_N2 reaction under mild conditions to give (*Z*)-vinylic compounds with exclusive inversion of configuration.[1–3] Hyper-nucleofugality of the phenyl-λ^3-iodanyl group is responsible for the unique vinylic S_N2 reaction.[4] Nucleophiles that undergo vinylic S_N2 reactions with (*E*)-(β-alkylvinyl)phenyl-λ^3-iodanes involve halides,[1] dialkyl sulfides and selenides,[2a] phosphoroselenoates,[5a] dithiocarbamates,[5b] carboxylic acids,[6] amides,[7] and thioamides.[8]

In a marked contrast, vinylic S_N2 reactions of (*Z*)-isomers of β-alkylvinyl-λ^3-iodanes have never been reported. In fact, (*Z*)-1-decenyl-λ^3-iodane **2** does not undergo vinylic S_N2 displacement by the reaction with excess amounts of tetrabutylammonium chloride in dichloromethane at room temperature, but instead the reaction affords 1-decyne quantitatively. On the other hand, (*E*)-vinyl-λ^3-iodane **1** affords the inverted (*Z*)-1-chlorodec-1-ene under the conditions in a high yield (Scheme 1).[1a] Stereoelectronically preferred *anti* β-elimination and/or α-elimination-1,2-rearrangement sequence will be responsible for the exclusive formation of 1-decyne. The attempted vinylic S_N2 reactions of **2** by using less basic nucleophiles such as dimethyl sulfide, dibutyl selenide, dibutyl telluride, acetic acid, *N*,*N*-dimethylformamide, and *N*,*N*-dimethylthioformamide were found to be fruitless and all of these reactions produced 1-decyne. We are pleased to report that (*Z*)-(β-aroyloxyvinyl)phenyl-λ^3-iodanes **3** undergo a vinylic S_N2 displacement by the reaction with tetrabutylammonium halides.



Scheme 1.

The required (*Z*)-(β-benzoyloxyvinyl)phenyl-λ^3-iodanes **3** were directly prepared from the commercially available ethynyl(phenyl)(tetrafluoroborato)-λ^3-iodane[9] through a facile Michael-type addition of benzoic acids (Scheme 2).[10] Exposure of the ethynyl-λ^3-iodane to excess amounts of benzoic acid in the presence of sodium benzoate (0.2 equiv) in methanol results in stereoselective Michael-type addition of benzoic acid at room

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Keywords: Vinylic S_N2 reaction; Hypervalent; Iodane; Ligand coupling; Michael-type addition.

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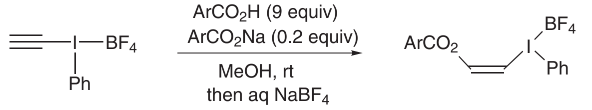


3

3a: Ar = Ph, **3b:** Ar = *p*-MeC_6H_4, **3c:** Ar = *p*-ClC_6H_4

Scheme 2.

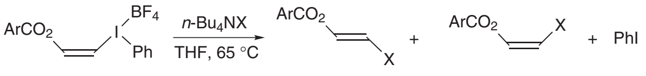
temperature yielding (*Z*)-(β-benzoyloxyvinyl)(phenyl)-(tetrafluoroborato)-λ^3-iodane (**3a**) in a 76% yield as colorless needles, after ligand exchange by the reaction with an aqueous $NaBF_4$ solution. A small vicinal coupling constant ($J = 4.3$ Hz) between the vinylic protons in ^{1}H NMR indicates *trans* conjugate addition of benzoic acid. *p*-Methyl **3b** (66%) and *p*-chloro-λ^3-iodanes **3c** (66%) were also prepared.[11]

When a solution of λ^3-iodane **3a** (4.7×10^{-4} M) and *n*-Bu_4NCl (0.1 M) in THF was heated under reflux for 4.5 h in nitrogen, the inverted (*E*)-β-benzoyloxyvinyl chloride (**4a**) (Ar = Ph, X = Cl) was obtained in 55% yield along with the formation of iodobenzene (84.6%) (Table 1, entry 1). The substitution is exclusively stereoselective and the formation of the retained (*Z*)-isomer **5a** (Ar = Ph, X = Cl) was not detected at all. Interestingly, detailed product analyses showed no evidences for the formation of ethynyl benzoate, which was expected to be produced by *anti* β- and/or α-elimination of **3a**.[12] The observed exclusive inversion of configuration in this nucleophilic vinylic substitution is compatible with the vinylic S_N2 mechanism.

With the decreased concentration of *n*-Bu_4NCl (0.01 M) in refluxing THF, however, (*Z*)-isomer **5a** as well as (*Z*)-vinyl iodide **6a** (Ar = Ph) were produced as minor products (entry 2). Larger amounts of these by-products were obtained in the reaction with 0.001 M of *n*-Bu_4NCl. These results clearly indicate the existence of the competing reaction pathway other than vinylic S_N2 process and the competing pathway becomes significant at lower concentration of nucleophiles. In the nucleophilic substitution of **3a** with *n*-Bu_4NBr and *n*-Bu_4NI, similar concentration-dependent product profiles were observed, as shown in Table 1. Thus, 0.1 M of *n*-Bu_4NBr gave a 99:1 mixture of (*E*)- and (*Z*)-vinyl bromides, **4b** and **5b** (Ar = Ph, X = Br), while an increased amount of (*Z*)-isomer **5b** was produced in the reaction using 0.001 M of *n*-Bu_4NBr (entries 4 and 6). Under the conditions, no isomerization of these vinyl bromides **4b** and **5b** was observed.

A vinylic S_N2 reaction will be a major reaction course in the nucleophilic substitution of (*Z*)-(β-benzoyloxyvinyl)-λ^3-iodanes **3a** with *n*-Bu_4NX, which probably competes with a ligand coupling reaction on iodine(III),[13] as shown in Scheme 3. Very rapid ligand exchange on iodine(III) in **3a** with halides will produce the isomeric vinyl(halo)-λ^3-iodanes **7** and **8** via addition–elimination sequence involving the intermediacy of tetracoordinated species.[14] Both halo-λ^3-iodanes **7** and **8** equilibrate each other through rapid pseudorotation on iodine(III)[15] and undergo a vinylic S_N2 reaction to give the inverted (*E*)-vinyl halides **4**. Solvent-coordinated vinyliodonium ions may participate in part in the vinylic S_N2 reaction.[1] The

Table 1. Nucleophilic substitutions of (*Z*)-(β-benzoyloxyvinyl)phenyl-λ^3-iodanes **3** with tetrabutylammonium halides in THF at 65 °C under nitrogen[a]



3 4 **5:** X = Cl, Br
6: X = I

Entry	3	*n*-Bu_4NX X (M)	Product (yield (%))[b] 4	5	6	PhI	Ratio 5:6	4:(5+6)
1	**3a**	Cl (0.1)	55.0	—	—	84.6		100:0
2	**3a**	Cl (0.01)	61.1	1.9	4.8	86.5	28:72	90:10
3	**3a**	Cl (0.001)	42.0	6.2	24.9	64.0[c]	20:80	57:43
4	**3a**	Br (0.1)	98.4[d]	1.0[d]	0.6[d]	95.5	62:38	98:2
5	**3a**	Br (0.01)	95.9[d]	1.9[d]	2.2[d]	94.9[e]	46:54	96:4
6	**3a**	Br (0.001)	72.4	10.9	16.7	79.0[e]	39:61	72:28
7	**3a**	I (0.1)	77.4	—	6.6	75.4		92:8
8	**3a**	I (0.01)	71.7	—	11.3	77.8		86:14
9	**3b**	Br (0.1)	96.2[d]	1.5[d]	2.3[d]	85	39:61	96:4
10	**3b**	Br (0.01)	90	3.5	6.5	75.8[f]	35:65	90:10
11	**3b**	Br (0.001)	74.6	9.3	16.1	60.6[e]	37:63	75:25
12	**3c**	Br (0.1)	100	—		68.2		100:0
13	**3c**	Br (0.01)	90.5	4.6	4.9	70.5	48:52	91:9
14	**3c**	Br (0.001)	67.6	15.0	17.4	52.4[e]	46:54	68:32

[a] [λ^3-Iodane **3**] = 0.42–0.47 mM, reaction time = 2.5–7 h.

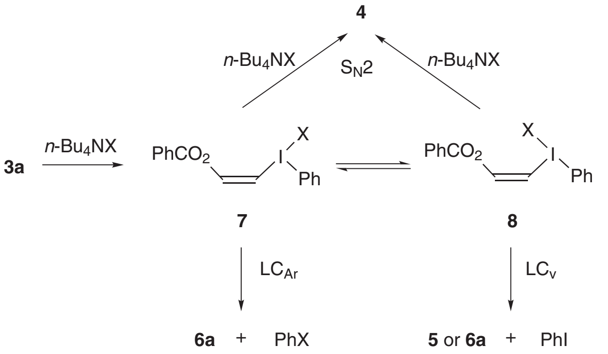
[b] GC yields.

[c] PhCl (2%) was obtained.

[d] ^{1}H NMR yields.

[e] PhBr (1–3%) was obtained.

[f] PhBr (6%) was obtained.

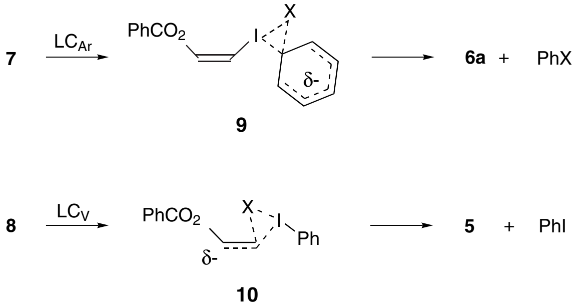


Scheme 3.

competing ligand coupling on aromatic *ipso* carbon atom (LC_{Ar}) of **7** produces (*Z*)-vinyl iodide **6a** and halobenzenes, while that on vinylic carbon atom (LC_V) of **8** affords (*Z*)-vinyl halides **5** or **6a** with retention of configuration and iodobenzene.

The results shown in Table 1 clearly indicate that the ratios of the vinylic S_N2 reaction to the ligand coupling on iodine(III), **4**:(**5** + **6**), decrease with the decreasing concentration of halide nucleophiles. These tendencies probably reflect the differences in the reaction order with respect to halide nucleophiles, that is, second-order in the vinylic S_N2 reaction while first order in the ligand coupling.

Although a detailed mechanism of ligand coupling on iodine(III) has remained obscure,[16] it seems reasonable to assume that the reaction of **3a** with *n*-Bu_4NCl and *n*-Bu_4NBr yielding (*Z*)-vinyl iodide **6a** and (*Z*)-vinyl halides (Cl, Br) **5** probably proceeds via partially polarized transition states, **9** for LC_{Ar} and **10** for LC_V (Scheme 4).[14] A closely related transition state structure for the vinylic ligand coupling LC_V has been proposed by ab initio MO (MP2) calculations of the reaction of chloro(divinyl)-λ^3-iodane.[16a] The presence of an electron-withdrawing *para*-chlorine on the β-benzoyloxy group in **3c** may stabilize a partial negative charge developed on the β-vinylic carbon atom in the LC_V transition state. This type of substituent effect could not be anticipated in the transition state of LC_{Ar}. These arguments are in good agreement with our experimental results, which show larger ratios of **5**:**6** in the reaction of **3c** than that of **3a** (compare entries 5 and 6 with 13 and 14). On the other hand, *para*-methyl substituent in **3b** decreased the ratios of **5**:**6** (compare entries 4–6 with 9–11).



Scheme 4.

In conclusion, we found the first example of vinylic S_N2 reaction of (*Z*)-vinyl-λ^3-iodanes with *n*-Bu_4NX yielding the inverted (*E*)-vinyl halides. The reaction competes with ligand coupling on iodine(III).

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(FAB) *m*/*z* calcd for $C_{15}H_{12}O_2I$ $[(M-BF_4)^+]$ 350.9882. Found: 350.9905. Anal. Calcd for $C_{15}H_{12}O_2BF_4I$: C, 41.14; H, 2.76. Found: C, 40.98; H, 2.81.

12. Treatment of (*Z*)-(β-benzoyloxyvinyl)-λ^3-iodane **3a** with diisopropylethylamine (1.2 equiv) in dichloromethane at room temperature under argon afforded ethynyl benzoate in 89% yield.
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