

# Highly regio- and stereoselective four-component iodoamination of Se-substituted allenes. an efficient synthesis of *N*-(3-organoseleno-2-iodo-2(*Z*)-propenyl) acetamides†

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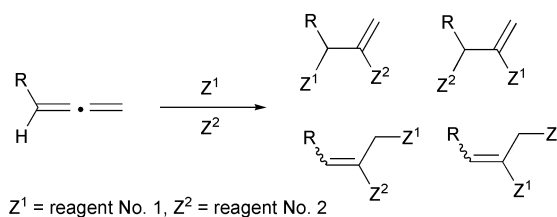
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*Z*-Selectivity was observed for iodohydroxylation of Se-substituted allenes with I<sub>2</sub> and H<sub>2</sub>O, which is opposite to that of 1,2-allenyl sulfoxides. With *n*-hexane as the co-solvent *Z*-iodoamination leading to *N*-(3-organoseleno-2-iodo-2(*Z*)-propenyl)acetamide was observed. A brief rationale for the stereoselectivity of this reaction is provided.

Allenes are useful intermediates for organic synthesis due to the presence of unique cumulated C=C double bonds.<sup>1,2</sup> In our group, we have developed the coupling-cyclization of functionalized allenes<sup>3</sup> and the nucleophilic addition of electron-deficient allenes.<sup>4</sup> For addition reaction of allenes with two different reagents, there would be problems of regio- and stereoselectivity (Scheme 1).<sup>5</sup> In order to make these methodologies synthetically attractive, it is desirable to address the issue of selectivity in these reactions. In our previous studies, we observed that (1) the regioselectivity of hydrohalogenation reaction of electron-deficient allenes leading to β,γ-unsaturated functionalized alkenes can be controlled by the electronic effect of the electron-withdrawing group;<sup>4</sup> (2) the iodohydroxylation reaction of 1,2-allenyl sulfoxides exhibits excellent regio- and *E*-stereoselectivity.<sup>5</sup> Here we wish to report the highly regio- and stereoselective electrophilic addition reaction of Se-substituted allenes with I<sub>2</sub>, H<sub>2</sub>O, and nitriles.

We started this research with the iodohydroxylation of 1,2-propadienyl phenyl selenide (**1a**) with I<sub>2</sub> and H<sub>2</sub>O. Some typical results are summarized in Table 1. From Table 1, it is interesting to note that when the iodohydroxylation of **1a** with I<sub>2</sub> and H<sub>2</sub>O was carried out under the same conditions employed for 1,2-allenyl sulfoxides,<sup>5</sup> the expected product **2a** was isolated in only 28% yield. However, it is interesting to observe that the stereoselectivity is 12.5:1 with the *Z*-isomer being the major product! This is completely opposite to the results for the



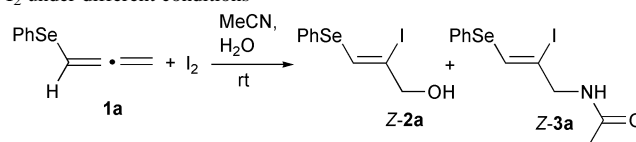
**Scheme 1** Regio- and stereoselectivity of addition reaction involving allenes.

corresponding sulfoxides<sup>5</sup> (entry 1, Table 1). Interestingly, when *n*-hexane was added to a mixture of MeCN and H<sub>2</sub>O as the solvent, besides the formation of **Z-2a**, a new product that is *N*-(2-iodo-3-phenylseleno-2(*Z*)-propenyl)acetamide **Z-3a** was formed (entries 2–4, Table 1). When only 1 equiv of H<sub>2</sub>O was added, the reaction at 25 °C afforded **Z-3a** highly stereoselectively as the only product (entry 7, Table 1). In the presence of 12 or 16 equiv of H<sub>2</sub>O, the stereoselectivity is lower (entries 5 and 6, Table 1). The stereoselectivity, which is opposite to that of 1,2-allenyl sulfoxides, was determined unambiguously by X-ray diffraction study of **Z-3a**.<sup>6</sup>

A typical procedure is as follows: A solution of phenyl 1,2-propadienyl selenide (195 mg, 1 mmol) in 2 mL of MeCN was added slowly (over 30 min) to a solution of iodine (507.6 mg, 2 mmol) in acetonitrile (3 mL) with *n*-hexane (5 mL) under a N<sub>2</sub> atmosphere. After being stirred at 25 °C for 9 hours, the mixture was diluted with ether, then saturated aqueous solutions of NaHCO<sub>3</sub> and Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> were added to the solution. The mixture was extracted with ether (25 mL × 3) and dried over MgSO<sub>4</sub>. Evaporation and column chromatography on silica gel (petroleum ether/ethyl acetate = 1:1) afforded **Z-3a** as a white solid: m.p. 100–102 °C (CH<sub>2</sub>Cl<sub>2</sub>/*n*-hexane). Some typical examples of the four-component reaction between 1-organoselenoallenes, nitriles, I<sub>2</sub> and water are summarized in Table 2. From the results in Table 2, following points are noteworthy: (1)

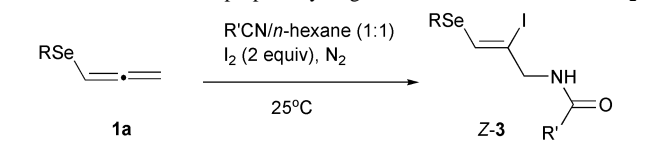
† Electronic supplementary information (ESI) available: experimental section. See <http://www.rsc.org/suppdata/cc/b3/b300879g/>

**Table 1** Addition reaction of **1a** with I<sub>2</sub> under different conditions



Entry	I <sub>2</sub> (equiv)	Solvent	H <sub>2</sub> O (equiv)	T (°C)	Time (h)	<b>2a</b> (%) ( <i>Z/E</i> ) <sup>c</sup>	<b>3a</b> (%) ( <i>Z/E</i> ) <sup>c</sup>
1 <sup>a</sup>	2	MeCN:H <sub>2</sub> O (7:1)	—	21	10	28 (12.5:1)	0
2	2	MeCN:A <sup>b</sup> = (1:1)	8	25	12.5	27 (26:1)	15 (30:1)
3	2	MeCN:A = (1:1)	4	25	12.5	18 (20:1)	36 (22:1)
4	2	MeCN:A = (1:1)	3	25	11.5	22 (15:1)	44 (44:1)
5	2	MeCN:A = (1:1)	16	25	10	63 (6.8:1)	0
6	2	MeCN:A = (1:1)	12	25	11	60 (3.6:1)	0
7	2	MeCN:A = (1:1)	1	25	17	0	64 (28:1)

<sup>a</sup> LiOAc·2H<sub>2</sub>O (2 equiv) was added. <sup>b</sup> A = *n*-Hexane. <sup>c</sup> Determined by 300 MHz <sup>1</sup>H-NMR spectra of the crude product.

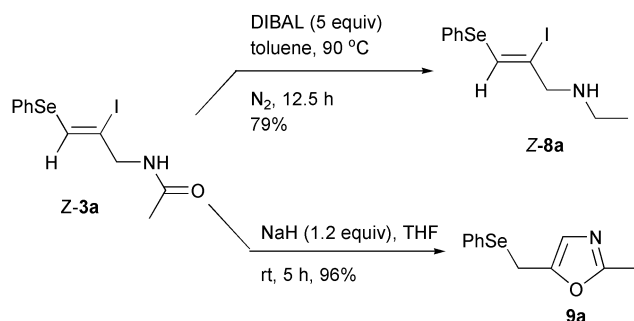
**Table 2** Reaction of 1,2-propadienyl organoselenides with nitriles and I<sub>2</sub>


Entry	R	R'	H <sub>2</sub> O (equiv)	Time (h)	Yield of <b>3</b> (%)	Z/E ratio of <b>3<sup>a</sup></b>
1	C <sub>6</sub> H <sub>5</sub>	Me	1	10.5	59 ( <b>3a</b> )	≥18:1
2	C <sub>6</sub> H <sub>5</sub>	<i>n</i> -Pr	1	10	46 ( <b>3b</b> )	≥21:1
3	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Me	1	14.5	62 ( <b>3c</b> )	≥22:1
4	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Me	0	21	45 ( <b>3c</b> )	≥21:1
5	<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Me	1	11.5	60 ( <b>3d</b> )	≥43:1
6	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub>	Me	1	12	51 ( <b>3e</b> )	≥65:1
7	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	Me	1	10	54 ( <b>3f</b> )	≥26:1
8	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Me	1	9.5	51 ( <b>3g</b> )	≥19:1
9	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Me	0	11.5	23 ( <b>3g</b> )	≥30:1

<sup>a</sup> Determined by 300 MHz <sup>1</sup>H NMR spectra of the crude product.

for the substrates studied, the yields are moderate; (2) The yield in the absence of water is lower.

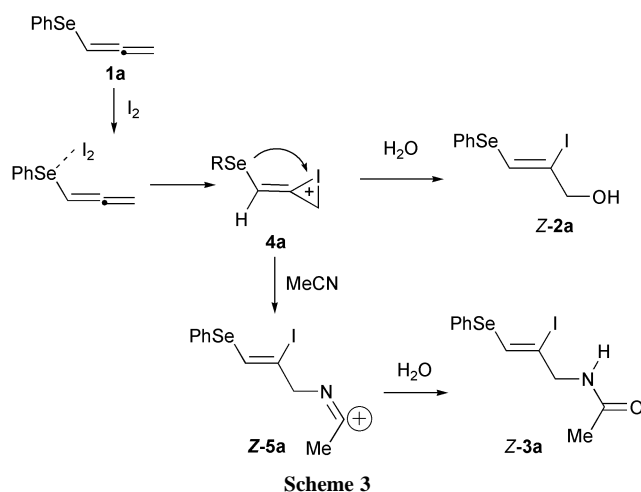
**Z-3a** is a useful synthetic intermediate. Its reduction of the carbonyl group in **3a** with DIBAL in toluene afforded *N*-(3'-phenylseleno-2-iodo-(*Z*)-propenyl) *N*-ethyl amine (**Z-8a**) in 79% yield, while upon its treatment with NaH, the reaction afforded 2-methyl-5-(phenylselenomethyl)oxazole (**9a**) in 96% yield (Scheme 2).<sup>7</sup>

**Scheme 2**

It can be assumed that the lone electron pair of selenium atom would interact with I<sub>2</sub> to form a molecular complex.<sup>8</sup> Intramolecular electrophilic addition of I<sub>2</sub> with the C=C bond remote from the Se group would form intermediate **Z-4a**. The strong soft Lewis acid and base interaction between the positively charged iodine atom and Se<sup>9</sup> may be responsible for the stereoselectivity of this reaction. Upon hydrolysis, the reaction affords **Z-2a**. Its reaction with MeCN leads to intermediate **Z-5a**, which would produce **Z-3a** after hydrolysis (Scheme 3).

In conclusion, we have developed a highly regio- and stereoselective four-component iodoamination reaction of 1,2-allenyl selenides with I<sub>2</sub>, H<sub>2</sub>O, and nitriles. The *Z*-stereoselectivity for this reaction may be controlled by the soft Lewis base and acid interaction between the selenium atom and the positively charged iodine atom.<sup>8</sup> The regioselectivity in this reaction may be controlled by the steric and electronic effects of the Se-containing groups. Although the precise origin of the stereoselectivity observed during this transformation requires more investigation this reaction may open up new area for the control of selectivity in addition reactions of allenes. The scope of this reaction, the real nature of the *Z*-stereoselectivity, and the synthetic application of these reactions are currently being carried out in our laboratory.

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**Scheme 3**

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