

# Highly Selective Hydroiodation of Alkynes Using an Iodine–Hydrophosphine Binary System

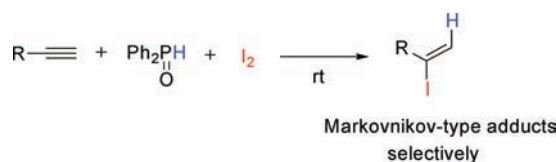
Shin-ichi Kawaguchi and Akiya Ogawa\*

Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, Gakuen-cho 1-1, Nakaku, Sakai, Osaka 599-8531, Japan

ogawa@chem.osakafu-u.ac.jp

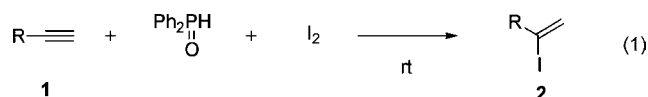
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## ABSTRACT



A novel hydroiodation of alkynes (1) using an iodine/hydrophosphine binary system takes place regioselectively to provide the corresponding Markovnikov-type adducts (2) in good yield. This hydroiodation is advantageous in terms of mild conditions, convenient operation, and tolerance to various functional groups.

Vinyl iodides are important intermediates in organic synthesis and are often employed for transition-metal-catalyzed cross-coupling reactions, halogen–metal exchange reactions, radical reactions, and displacement reactions by nucleophiles. Therefore, the development of highly regio- and stereoselective methods for synthesis of vinyl iodides has been desired strongly. Although one of the most straightforward synthetic methods of vinyl iodides is the addition of HI to alkynes; this reaction commonly does not take place at preparatively useful rates.<sup>1</sup> Therefore, several methods to synthesize vinyl iodides from the corresponding alkynes have been reported.<sup>2–5</sup> However, highly selective synthetic methods to give 2-iodo-1-alkenes are still rare. We report here a novel synthetic method of 2-iodo-1-alkenes from the corresponding alkynes by using a novel I<sub>2</sub>/hydrophosphine binary system (eq 1).



First, we conducted the hydroiodation of 1-octyne under several conditions (Table 1). The hydroiodation of 1-octyne did not take place without hydrophosphine (entry 1). In this case, only diiodation of 1-octyne proceeded slightly. In contrast, the hydroiodation of 1-octyne took place with several hydrophosphines: diphenylphosphine, diphenylphosphine oxide, or diethylphosphite (entries 2–6). When Ph<sub>2</sub>P(O)H/I<sub>2</sub> with the ratio of 1/1 was used, a certain amount of 1,2-diiodido-1-octene was obtained as byproduct (entry 3). The ratio of Ph<sub>2</sub>P(O)H/

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**Table 1.** Optimization of Hydroiodination Using an I<sub>2</sub>/Hydrophosphine Binary System

$${}^n\text{Hex}-\text{C}\equiv\text{C} + \text{Hydrophosphine} + \text{I}_2 \xrightarrow{\text{CDCl}_3} {}^n\text{Hex}-\text{C}(\text{I})=\text{C}$$
  
**1a** (0.3 mmol) +  $(\text{P}^n\text{H})$  → **2a**

entry	hydrophosphine	alkyne/ [P] <sup>n</sup> H/ I <sub>2</sub>	time	temp	yield <sup>a</sup>
1	none	3/ 0/ 1	36 h	rt	0%
2	Ph <sub>2</sub> P <sup>n</sup> H	3/ 1/ 1	16 h	rt	47% <sup>b</sup>
3	Ph <sub>2</sub> P(O) <sup>n</sup> H	3/ 1/ 1	24 h	rt	74% <sup>b</sup>
4	Ph <sub>2</sub> P(O) <sup>n</sup> H	1/ 1.5/ 0.75	16 h	rt	88% <sup>c</sup>
5	(EtO) <sub>2</sub> P(O) <sup>n</sup> H	1/ 1.5/ 0.75	16 h	rt	4% <sup>c</sup>
6	Ph <sub>2</sub> P(O) <sup>n</sup> H	1/ 1.5/ 0.75	16 h	60 °C	50% <sup>c</sup>

<sup>a</sup> Determined by <sup>1</sup>H NMR. <sup>b</sup> Based on phosphine. <sup>c</sup> Based on alkyne.

I<sub>2</sub> (2/1) at room temperature is the most suitable conditions for the desired hydroiodination (entry 4). In this condition, the result indicates that both iodine atoms from one iodine molecule can be used for the hydroiodination.

Next, the hydroiodination of 1-dodecyne using the Ph<sub>2</sub>P(O)H/I<sub>2</sub> binary system was conducted in several solvents (Table 2). In halogenated solvents, the hydroiodination took place

**Table 2.** Hydroiodination in Several Solvents Using the Ph<sub>2</sub>(O)H/I<sub>2</sub> Binary System

$${}^n\text{Dec}-\text{C}\equiv\text{C} + \text{Ph}_2\text{P}(\text{O})\text{H} + \text{I}_2 \xrightarrow[\text{rt, 16 h}]{\text{solvent}} {}^n\text{Dec}-\text{C}(\text{I})=\text{C}$$
  
 0.3 mmol + 1.1 equiv + 0.55 equiv

entry	solvent	yield <sup>a</sup>
1	CHCl <sub>3</sub>	67%
2	CH <sub>2</sub> Cl <sub>2</sub>	62%
3	EtOH	4%
4	THF	0%
5	MeCN	33%
6	toluene	61%
7	benzene	49%

<sup>a</sup> Determined by <sup>1</sup>H NMR.

efficiently (entries 1 and 2). When EtOH or THF<sup>6</sup> was used, iodination of the solvent occurred in preference to the hydroiodination of 1-dodecyne (entries 3 and 4). On the other hand, the hydroiodination in toluene proceeded successfully (entry 6). These results seem to be influenced partly by the solubility of I<sub>2</sub> for each solvent.

Table 3 represents the results of the hydroiodination of several alkynes using a Ph<sub>2</sub>P(O)H/I<sub>2</sub> binary system. The

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**Table 3.** Selective Hydroiodination of Alkynes Using an Iodine–Hydrophosphine Binary System

$$\text{R}-\text{C}\equiv\text{C} + \text{Ph}_2\text{P}(\text{O})\text{H} + \text{I}_2 \xrightarrow[\text{CDCl}_3, 16 \text{ h}]{} \text{R}-\text{C}(\text{I})=\text{C}$$
  
**1** → **2**

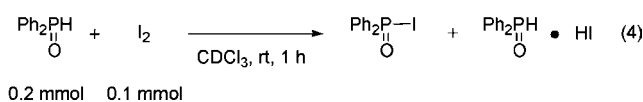
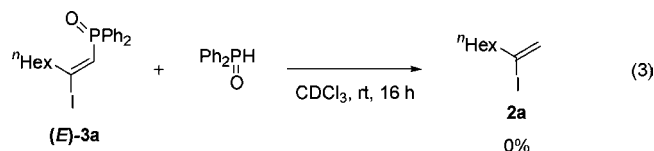
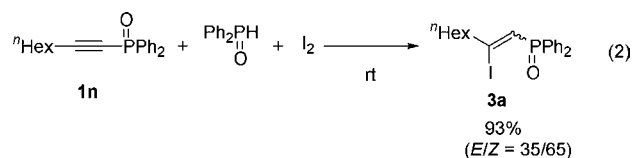
entry	alkyne (alkene)	conditions <sup>a</sup>	product	yield <sup>b</sup>
1	<sup>n</sup> Hex- <b>1a</b>	A	<sup>n</sup> Hex- <b>2a</b>	88% <sup>c</sup>
2	<sup>n</sup> Dec- <b>1b</b>	A	<sup>n</sup> Dec- <b>2b</b>	73% <sup>c</sup>
3 <sup>d</sup>	<sup>n</sup> Hex- <b>1c</b>	A	<sup>n</sup> Hex- <b>2c</b>	91% <sup>c</sup>
4	Cl- <b>1d</b>	A	Cl- <b>2d</b>	59%
5	NC- <b>1e</b>	A	NC- <b>2e</b>	43%
6 <sup>e</sup>	HO- <b>1f</b>	A	I- <b>2f</b>	57%
7 <sup>e, f</sup>	HOC- <b>1g</b>	A	EtOC- <b>2g</b>	96%
8	Ph- <b>1h</b>	B	Ph- <b>2h</b>	95%
9	<sup>n</sup> Pen- <b>1i</b>	B	<sup>n</sup> Pen- <b>2i</b>	77%
10	Br- <b>1j</b>	B	Br- <b>2j</b>	67%
11	MeO- <b>1k</b>	B	MeO- <b>2k</b>	81%
12 <sup>g</sup>	CF <sub>3</sub> - <b>1l</b>	A	CF <sub>3</sub> - <b>2l</b>	81%
13	<b>1m</b>	A	<b>2m</b>	99%

<sup>a</sup> Reaction conditions A: alkyne (alkene) (**1**, 0.20 mmol), Ph<sub>2</sub>P(O)H (0.30 mmol), I<sub>2</sub> (0.15 mmol), CDCl<sub>3</sub> (0.5 mL), room temperature. Reaction conditions B: alkyne (**1**, 0.60 mmol), Ph<sub>2</sub>P(O)H (0.20 mmol), I<sub>2</sub> (0.10 mmol), CDCl<sub>3</sub> (0.5 mL), 0 °C to room temperature. <sup>b</sup> Isolated yield. <sup>c</sup> Determined by <sup>1</sup>H NMR. <sup>d</sup> For 5 h. <sup>e</sup> Ph<sub>2</sub>P(O)H (0.50 mmol) and I<sub>2</sub> (0.25 mmol) were used. <sup>f</sup> After the reaction, EtOH was added. <sup>g</sup> At 0 °C to room temperature for 4 h.

hydroiodination was conducted under two conditions: (A) alkyne (alkene) (**1**, 0.20 mmol), Ph<sub>2</sub>P(O)H (0.30 mmol), I<sub>2</sub> (0.15 mmol), CDCl<sub>3</sub> (0.5 mL), room temperature; (B) alkyne (alkene) (**1**, 0.60 mmol), Ph<sub>2</sub>P(O)H (0.20 mmol), I<sub>2</sub> (0.10 mmol), CDCl<sub>3</sub> (0.5 mL), 0 °C to room temperature. Aliphatic alkynes (**1a**, **1b**, **1d–1g**, **1m**) underwent the hydroiodination under condition A, providing the corresponding 2-substituted vinyl iodides (**2a**, **2b**, **2d–2g**, **2m**), regioselectively. In the case of condition A, the yields were determined based on the employed alkynes. The hydroiodination of alkene such as 1-octene also took place to give the corresponding Markovnikov-type adducts in good yield (entry 3). When the aliphatic alkynes bearing chloro and cyano groups were employed, the hydroiodination proceeded in moderate yields (entries 4 and 5). In the case of the aliphatic alkyne bearing hydroxyl groups, the iodination proceeded simultaneously at

both the alkyne and hydroxyl moieties (entry 6).<sup>7</sup> In the case of the aliphatic alkyne bearing carboxylic acid, the iodation also proceeded simultaneously at both the alkyne and carboxylic acid moieties, providing ethyl 5-iodo-5-hexenoate (**2g**) after quenching iodations with EtOH (entry 7). Entries 6 and 7 clearly indicate that the present system is available to iodations of OH and COOH groups. Aromatic alkynes (**1h–1k**) underwent the hydroiodation at 0 °C to room temperature, providing the corresponding  $\alpha$ -iodostyrene derivatives (**2h–2k**) in good yields (entries 8–11). In the case of condition B, the yields were determined based on the iodine atom employed. When an internal alkyne such as 4-octyne was used in the present system, (*Z*)-4-iodo-4-octene was obtained quantitatively and stereoselectively (entry 13).

To get some information about the mechanism for this hydroiodation, several reactions were examined. The hydroiodation of alkynylphosphine oxide (**1n**)<sup>8</sup> afforded 1-phosphinyl-2-iodo-1-octene (**3a**), regioselectively (eq 2).<sup>9</sup> When the reaction of (*E*)-1-phosphinyl-2-iodo-1-octene with diphenylphosphine oxide was conducted, any product with loss of a phosphinyl group was not obtained at all (eq 3). This result indicates that the present hydroiodation does not proceed via 1-phosphinyl-2-iodoalkene species (**3**) as an intermediate.



When 2 equiv of diphenylphosphine oxide was allowed to react with 1 equiv of iodine, <sup>31</sup>P NMR measurement indicated that diphenylphosphine oxide ( $\delta$  21.6 ppm, in CDCl<sub>3</sub>) completely converted to two different phosphorus compounds ( $\delta$  36.6 and 40.8 ppm, in CDCl<sub>3</sub>). We assume these two peaks are assigned to Ph<sub>2</sub>P(O)I<sup>6,10</sup> and Ph<sub>2</sub>P(O)H·HI,<sup>11</sup> respectively (eq 4).

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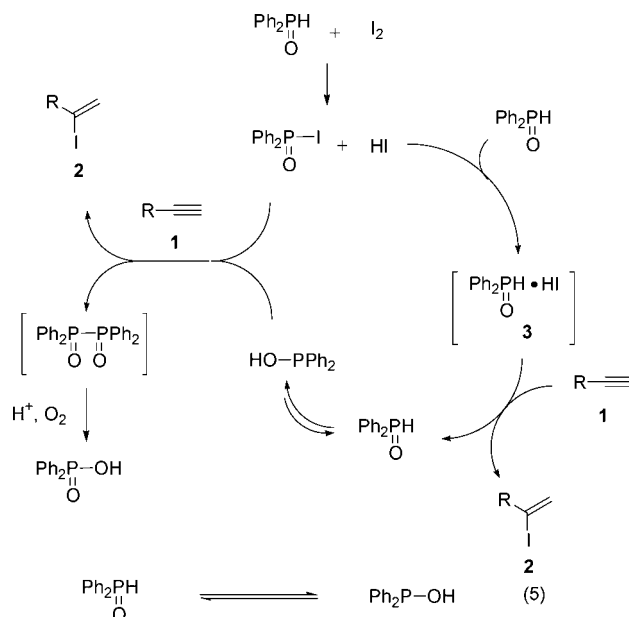
(9) The product **3a** was obtained as an *E/Z* mixture, most probably because acid-induced isomerization might occur during the reaction due to the conjugated system (C=C–P=O). Pure *E* isomer isolated is stable at ambient temperature and does not isomerize to the corresponding *Z* isomer.

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A plausible pathway for the present hydroiodation is shown in Scheme 1. First, Ph<sub>2</sub>P(O)H reacts with I<sub>2</sub>, generat-

**Scheme 1.** Plausible Pathway of Hydroiodation



ing Ph<sub>2</sub>P(O)I and HI. HI is immediately complexed with Ph<sub>2</sub>P(O)H<sup>11</sup> to generate complex **3**, which acts as an active species for the Markovnikov-type hydroiodation of alkynes to give the vinyl iodide **2**. On the other hand, Ph<sub>2</sub>P(O)H has the tautomeric form of three-valent phosphinous acid (Ph<sub>2</sub>POH) (eq 5).<sup>12</sup> Alkynes react with Ph<sub>2</sub>P(O)I and Ph<sub>2</sub>POH, generating vinyl iodides **2**. The resulting phosphine oxide finally changes diphenylphosphinic acid upon treatment with oxygen and proton source.

In summary, we have developed a novel hydroiodation of alkynes using an iodine/hydrophosphine binary system. This hydroiodation proceeds to provide Markovnikov-type adducts in good yield. The advantages of this system are mild conditions, easy handling, and tolerance to functional groups. Furthermore, this system is available to iodations of OH and COOH groups. We hope that this hydroiodation is used in various stages of organic synthesis.

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**Supporting Information Available:** Detailed experimental procedures and compound characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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