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Stereochemical Inversion in the Vinylic Substitution of Boronic Esters To Give Iodonium Salts: Participation of the Internal Oxy Group

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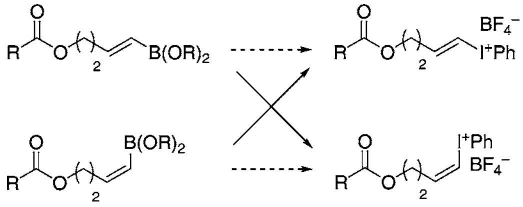
ABSTRACT



Alkenylboronic esters having an acyloxy, alkoxy, or methoxycarbonyl group were employed for the reaction with (diacetoxyiodo)benzene in the presence of $BF_3 \cdot OEt_2$ to provide the alkenyliodonium tetrafluoroborates with inversion of configuration: (*E*)- and (*Z*)-boronates give (*Z*)- and (*E*)-iodonium salts, respectively. This selectivity can be reversed by the addition of ether to the dichloromethane solution. The stereoselectivity can be explained by participation of the neighboring oxy group.

Alk-1-enyl(phenyl)iodonium salts are highly electron-deficient vinyl compounds that undergo a variety of reactions with nucleophiles/bases at the vinylic position.[1] The high reactivity of vinyliodonium salts arises from the powerful electron-withdrawing effects of the positive iodine group and the high nucleofugality of the iodonium group. These properties have provided opportunities for developing synthetically valuable vinylic reactions and for studying reactive intermediates of mechanistic interest. One of the general methods used for the preparation of vinyliodonium salts is electrophilic substitution of the corresponding vinylsilanes and vinylboronic acid esters with iodine(III) species. The reaction of simple (*E*)-alk-1-enylboronates stereoselectively gives (*E*)-alk-1-enyliodonium salts with retention of the olefin geometry (Scheme 1);[2] a result that was also confirmed for the reaction of alkenyltrimethylsilanes.[3,4] In the course of our studies on iodonium chemistry, we tried to prepare some oxy-functionalized alkenyliodonium salts according to the standard method[2] but found that the iodonium salts so obtained were not of the expected configuration. The alkenylboronic esters apparently underwent electrophilic

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[1] For recent reviews, see: (a) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123−1178. (b) Varvoglis, A. *Tetrahedron* **1997**, *53*, 1179−1255. (c) Ochiai, M. In *Chemistry of Hypervalent Compounds*; Akiba, K.-y., Ed.; Wiley-VCH: New York, 1999; p 327. (d) Wirth, T.; Hirt, U. H. *Synthesis* **1999**, 1271−1287. (e) Okuyama, T. *Rev. Heteroatom Chem.* **1999**, *21*, 257−275. (f) Ochiai, M. *J.* Organomet. *Chem.* **2000**, *611*, 494−508. (g) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523−2584. (h) Okuyama, T. *Acc. Chem. Res.* **2002**, *35*, 12−18. (i) Okuyama, T.; Lodder, G. *Adv. Phys. Org. Chem.* **2002**, *37*, 1−56. (j) Okuyama, T.; Fujita, M. *Proc. Japan Acad.* **2002**, *78* (B), 167−172. (k) Ochiai, M. In *Topics of Current Chemistry*; Hypervalent Iodine Chemistry 224; Wirth, T., Ed.; Springer: Berlin, 2003; pp 5−68. (l) Stang, P. J. *J. Org. Chem.* **2003**, *68*, 2997−3008. (m) Okuyama, T.; Fujita, M. *Acc. Chem. Res.* **2005**, *38*, 679−686.

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[3] (a) Ochiai, M.; Sumi, K.; Takaoka, Y.; Kunishima, M.; Nagao, Y.; Shiro, M.; Fujita, E. *Tetrahedron* **1988**, *44*, 4095−4112. (b) Ochiai, M.; Oshima, K.; Masaki, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 869−870. (c) Okuyama, T.; Takino, T.; Sato, K.; Oshima, K.; Imamura, S.; Yamataka, H.; Asano, T.; Ochiai, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 243−257.

[4] (a) Fujita, M.; Sakanishi, Y.; Okuyama, T. *J. Am. Chem. Soc.* **2000**, *122*, 8787−8788. (b) Fujita, M.; Sakanishi, Y.; Nishii, M.; Yamataka, H.; Okuyama, T. *J. Org. Chem.* **2002**, *67*, 8130−8137.

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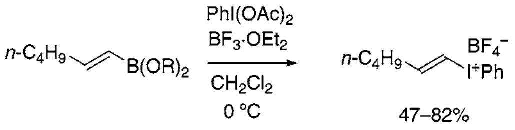
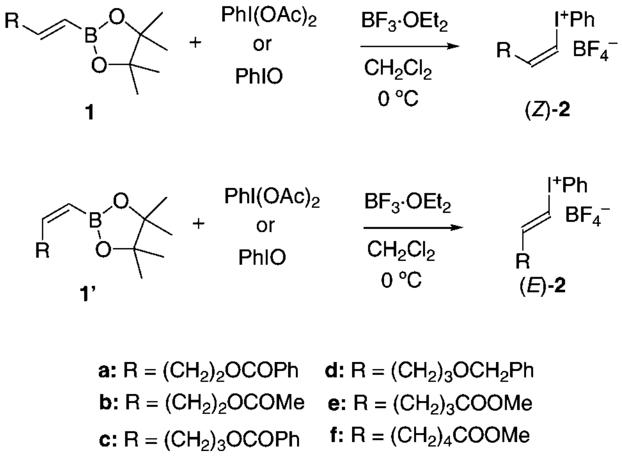
Scheme 1. Preparation of Iodonium Salt with Retention of Configuration



substitution with inversion of configuration. These unexpected observations are detailed in this communication.

(E)-Alkenylboronic esters **1a**−**f** were stereoselectively prepared by conventional hydroboration of alkynes,[5] while the Z isomers **1a′** and **1d′** were obtained by rhodium-catalyzed hydroboration.[6] These boronates contain an oxy function such as acyloxy (**1a**−**c**), alkoxy (**1d**), and methoxycarbonyl (**1e**,**f**) in the alkenyl moiety. They were employed for preparation of alkenyliodonium salts **2** (Scheme 2). The substitution reactions of boronates with (diacetoxyiodo)benzene or iodosylbenzene were carried out in the presence of BF$_3$•OEt$_2$ in dichloromethane at 0 °C. Isolated yields of alkenyliodonium tetrafluoroborates **2** and the E/Z ratios are summarized in Table 1. (Z)-Iodonium salts were obtained from the (E)-boronates **1a**−**f**, and these results stand in contrast to those for the reactions of simple alkenylboronic esters (and acid) which selectively give the iodonium salts with retention of configuration as illustrated in Scheme 1.[2,7]

Scheme 2. Preparation of Iodonium Salt with Inversion of Configuration



The reactions of the (E)- and (Z)-boronates, **1a** and **1a′**, proceeded with complete inversion of olefin geometry, respectively (entries 1 and 2). Similar stereoselectivity was observed for the reaction of the benzyloxy substrates, **1d** and **1d′** (entries 6 and 7). Complete inversion of olefin configuration was observed for the reaction of the methoxycarbonyl substrate (**1e**) as well as the acyloxy (**1a**,**b**) and alkoxy (**1d**) substrates. The reactions with iodosylbenzene proceeded similarly to those with (diacetoxyiodo)benzene except that even higher selectivity was observed for **1c** and **1f**. For the reactions of **1c** and **1f** with (diacetoxyiodo)benzene, a 1:1 mixture of (E)- and (Z)-iodonium salts was obtained (entries 4 and 9). The carbonyl oxygen of these substrates is separated from the double bond by six bonds, while that of **1a** and **1e** is separated by five bonds. These results suggest that the internal oxy group may be playing an important role in the inversion of configuration during vinylic substitution.

Table 1. Stereoselectivity of Displacement of Boronic Ester **1** by the Iodonium Group[a]

entry	substrate	R	yield[b] (%)	(E)-**2**/(Z)-**2**[b]
1	**1a**	(CH$_2$)$_2$OCOPh	45 (47)	<2:98 (<2:98)
2	**1a′**	(CH$_2$)$_2$OCOPh	58 (84)	>98:2 (>98:2)
3	**1b**	(CH$_2$)$_2$OCOMe	32 (51)	<2:98 (<2:98)
4	**1c**	(CH$_2$)$_3$OCOPh	34[c] (57)	44:56 (3:97)
5[d]	**1c**	(CH$_2$)$_3$OCOPh	44	>98:2
6	**1d**	(CH$_2$)$_3$OCH$_2$Ph	50	<2:98
7	**1d′**	(CH$_2$)$_3$OCH$_2$Ph	44	>98:2
8	**1e**	(CH$_2$)$_3$COOMe	30 (59)	<2:98 (4:96)
9	**1f**	(CH$_2$)$_4$COOMe	25[e] (60)	56:44[e] (3:97)

[a] The reaction of **1** (0.4 mmol) with PhI(OAc)$_2$ (0.5 mmol) was typically carried out in the presence of BF$_3$•OEt$_2$ (0.5 mmol) in CH$_2$Cl$_2$ (5 mL) at 0 °C for 0.5 h. Product yields and the E/Z ratios were determined after purification. [b] Values in parentheses are those obtained for the reaction of **1** (0.3 mmol) with iodosylbenzene (0.4 mmol) at 0 °C for 10 min in CH$_2$Cl$_2$ (3 mL) containing BF$_3$•OEt$_2$ (0.4 mmol). [c] Substrate **1c** was recovered in 44% with column chromatography. [d] The reaction was carried out in Et$_2$O/CH$_2$Cl$_2$ = 1:1 (v/v) for 1.5 h. Excess amounts (5 equiv) of PhI(OAc)$_2$ and BF$_3$•OEt$_2$ were used. [e] The reaction time was extended to 4 h to complete the reaction.

To examine the effect of the oxy group, diethyl ether was added to the dichloromethane solution as an external oxy nucleophile, and the reaction of **1c** was carried out in the mixed solvent (entry 5). In this case, excess amounts of reagents BF$_3$•OEt$_2$ and PhI(OAc)$_2$ were needed for the complete conversion of substrate **1c**. The slower reaction in the presence of Et$_2$O may be attributed to deactivation of the Lewis acid. The reaction now proceeds with retention of configuration to selectively give the (E)-iodonium salt. To discuss the stereoselectivity of iodonium formation, careful treatments of product analyses are necessary because (Z)-alkenyliodonium salts are much more reactive than the E isomers, the former decomposing readily to the alkyne via 1,2-elimination.[3] In this regard, prolonged reaction times and workups can result in the decomposition of (Z)-iodonium salts to leave only (E)-iodonium salts. The initial ratio of the products formed is presented in Table 2, where the reaction mixture was analyzed by 600 MHz ^{1}H NMR immediately after the reaction of **1c** for 30 min at 0 °C. The E/Z ratio of **2c** obtained by the usual workup of the mixture is also given in the last column. These results clearly show that added diethyl ether decreases the rate of reaction and switches the product configuration to E.[8]

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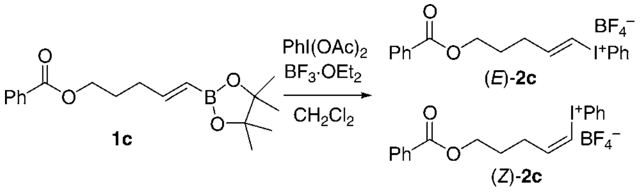
(5) Shirakawa, K.; Arase, A.; Hoshi, M. *Synthesis* **2004**, 1814−1820.

(6) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990−4991.

(7) We confirmed that the reaction of (E)-dec-1-enylborate gave (E)-dec-1-enyl(phenyl)iodonium tetrafluoroborate under the same reaction conditions.

Table 2. Effect of Solvent on the Reaction of **1c**[a]

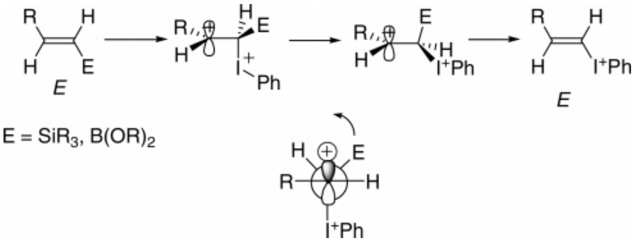


vol % of Et$_2$O	**1c**/(*E*)-**2c**/(*Z*)-**2c**[b]	(*E*)-**2c**/(*Z*)-**2c**[c]
0	54:15:31 (32:68)	29:71
10	87:12:1 (90:10)	91:9
50	86:14:0 (>98:2)	>98:2

[a] The reaction of **1** (0.10 mmol) with PhI(OAc)$_2$ (0.14 mmol) was carried out in the presence of BF$_3$•OEt$_2$ (0.16 mmol) in CH$_2$Cl$_2$/Et$_2$O solvent (2 mL) at 0 °C for 30 min. [b] Product distribution of the reaction mixture determined by ^{1}H NMR before workup. The values in parentheses are the *E*/*Z* ratio of **2c**. [c] Ratio of the isolated products.

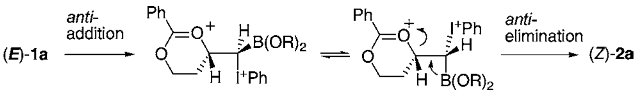
The usual substitution reaction of alkenylborates to form alkenyliodonium salt proceeds with retention of the olefin geometry, and this is rationalized by the addition−elimination mechanism illustrated in Scheme 3.[1k] Electrophilic attack of the iodine(III) reagent to the carbon−carbon double bond of vinylboronic ester must initiate the exchange of boronic ester for the iodonium group. Electrophilic attack is followed by the elimination of the electrofuge, where the cleaving bond is parallel to the vacant orbital on the positive carbon. Favorable rotation around the C1−C2 bond generally occurs as illustrated in Scheme 3 to result in the selective formation of the *E* product with retention of configuration due to the lower rotational barrier.

Scheme 3. Retention of Configuration via Addition−Elimination Mechanism



The opposite selectivity we observed in the reaction of oxy-functionalized alkenylboronic esters may be accounted for as illustrated in Scheme 4. The internal oxy group can interact with the positive charge developed at the β-position of the boronic ester and participates *anti* to the entering electrophile.[9,10] In the ensuing step, the same group departs concertedly with the leaving electrofuge, the boronate group, in an *anti* fashion after bond rotation. That is, the inversion selectivity can be explained by *anti*-addition of the internal oxy group and iodine(III) followed by *anti*-elimination of the oxy group and boronic ester. A similar *anti*-addition-*anti*-elimination mechanism has been proposed for the substitution reaction of alkenylboronic ester with bromine in the presence of base.[11,12]

Scheme 4. A Plausible Mechanism for the Inversion of Configuration



(*E*)-Iodonium salt **2c** was selectively formed with retention of configuration during the reaction of (*E*)-boronate **1c** in the ether−dichloromethane solution, and the stereoselectivity was affected by the content of the ether (Table 2 and entries 4, 5 in Table 1). The ether might be impeding the neighboring group participation process to drive vinylic substitution to the normal retention mode.

In summary, some oxy-functionalized alkenyliodonium salts have been prepared from the corresponding alkenylboronic esters with complete inversion of configuration. The selectivity of substitution is controlled by the reaction conditions used. In particular, both (*E*)- and (*Z*)-**2c** were selectively obtained from *E* substrate **1c** depending on the precise conditions and reagent employed. The unexpected and divergent *E*/*Z* selectivity is rationalized by participation of the internal oxy group.

Supporting Information Available: General procedures and characterization of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) 5-Benzoyloxypent-1-yne was detected in the crude mixture obtained from the reaction of **1c** in the presence of ether, but the content was less than 5%. Thus, (*E*)-**2c** is still a major product under these conditions even if unstable (*Z*)-**2c** is decomposed to the alkyne during the reaction.

(9) (a) Participation of carbonyl oxygen has been discussed for the vinylic substitution of silane for iodine.[9b] The reactions of both (*E*)- and (*Z*)-3-acyloxyprop-1-enyl(trimethyl)silane with *N*-iodosuccinimide gave preferentially (*Z*)-iodide in contrast to retention of configuration for the simple alkenylsilane substrates. The convergent stereoselectivity can also be explained by the thermodynamic stability of the cationic intermediate. (b) Stamos, D. P.; Taylar, A. G.; Kishi, Y. *Tetrahedron Lett.* **1996**, *37*, 8647−8650.

(10) (a) Participation of internal chloride has been reported in the preparation of vinyl-λ^3-bromane (vinylbromonium salt).[10b] The participation does not affect the *E*/*Z* selectivity, but results in internal chloride shift. (b) Ochiai, M.; Nishi, Y.; Mori, T.; Tada, N.; Suefuji, T.; Frohn, H. J. *J. Am. Chem. Soc.* **2005**, *127*, 10460−10461.

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