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Iodoolefinic polypropionate building blocks from vinyl silanes with control of geometry by solvent and by neighboring group participation

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Dedicate this communication to Professor Harry Wasserman on the occasion of his 90th birthday.

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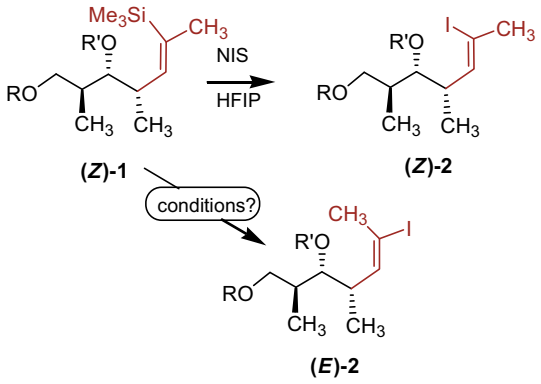
ABSTRACT

Iododesilylation of trisubstituted (*Z*)-silyl olefins proceeds with retention of geometry in hexafluoroisopropanol (HFIP) but, for unhindered cases, with inversion of geometry in DMSO. When an acyloxy substituent is positioned to participate in the reaction, the protocol consistently leads to inversion of geometry.

Vinyl iodides with defined geometry are important chemical intermediates.[1] Their preparation from vinyl silanes with retention of geometry by use of acetonitrile/trichloroacetonitrile[2] or hexafluoroisopropanol (HFIP)[3] as solvent is an attractive synthetic method. We recently took advantage of this transformation in order to convert trisubstituted (*Z*)-vinyl silane **(*Z*)-1** (R = TBS, R′ = MOM) into the corresponding vinyl iodide **(*Z*)-2** (R = TBS, R′ = MOM, Scheme 1); we viewed this iodide as a useful building block for polypropionates in which there is a (*Z*)-trisubstituted olefin.[4]

During the course of our studies, we noted that iododesilylation in some solvent systems gave appreciable amounts of vinyl iodides in which the geometry of the double bond had not been retained.[2,3,5] Therefore, we imagined that we might find conditions that would lead from the now readily accessible, protected homoallylic alcohol substrates **(*Z*)-1**,[4] to trisubstituted vinyl iodides **(*E*)-2** with complete inversion of the geometry of the double bond (Scheme 1).[6,7] A syn, anti (*E*)-isomer of iodide **2** is considered a building block for khafrefungin (**3**)[8] and the anti, anti (*E*)-isomer is a potential building block for tirandamycin A (**4**,[9] see Fig. 1).

We first examined the chemistry of interest in the model homoallylic system **(*Z*)-5**. Iododesilylation of **(*Z*)-5a–d**[10] with **NIS** was studied in three solvent media (Table 1). As expected on the basis of our earlier work,[4] alcohol **(*Z*)-5a**,[11] when treated with NIS in HFIP containing lutidine, gave a mixture of products that contained only a small amount of the expected (*Z*)-vinyl iodide. On the other hand, iododesilylation of substrates **(*Z*)-5b** and **(*Z*)-5c** in HFIP with lutidine gave good yields of vinyl iodides **(*Z*)-6b** and **(*Z*)-6c**,[10] respectively, as the almost exclusive products. These results are consistent with the known propensity of HFIP to favor iododesilylation with high levels of retention of geometry. However, reaction of acetate **(*Z*)-5d** gave a 5:95 mixture of (*Z*)- and (*E*)-vinyl iodides **(*Z*)-6d** and **(*E*)-6d**.[10] This example suggests that the homoallylic ester substituent participates in the reaction, adding to the iodonium ion and then eliminating anti to the TMS group to provide the product with (*E*)-geometry.[12] This pathway is not entirely surprising;[2,3] however, the high level of inverted geometry is impressive and clearly useful.



Scheme 1. Established and postulated iododesilylation of polypropionate building block **(*Z*)-1**.

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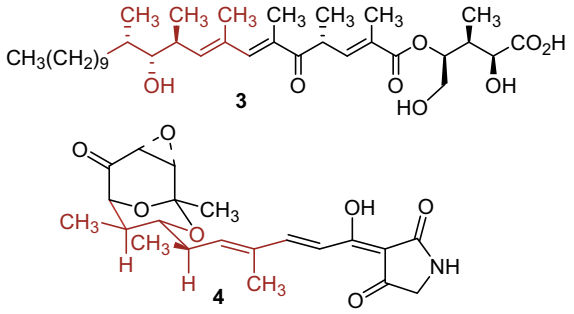
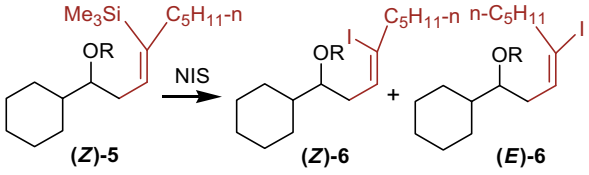


Figure 1. The structures of khafrefungin (**3**) and tirandamycin A (**4**).

Table 1
Yields and stereoselectivity in iododesilylation of vinyl silanes **5** as a function of solvent



Substrate **5**	Yield (ratio of (*Z*)-**6** to (*E*)-**6**)[c] Rxn time (h)		
	HFIP	MeCN/ClCH$_2$CN (4:1)	DMSO
a (R = H)	(–)[a]	82% (86:14)[b]	85% (15:85)[d]
	1.5	18	*67*
b (R = TBS)	72% (97:3)	53% (72:28)	94% (4:96)
	0.5	2	*117*
c (R = MOM)	75% (97:3)	87% (82:18)	86% (3:97)
	0.5	19	6
d (R = Ac)	94% (5:95)	48% (7:93)	43% (*E*)-**6** only
	0.5	17	18

[a] See Ref. 4.
[b] Solvent was neat MeCN.
[c] Determined by integration of the NMR spectrum of the isolated vinyl iodide mixture.
[d] Yield based on 33% recovered starting material.

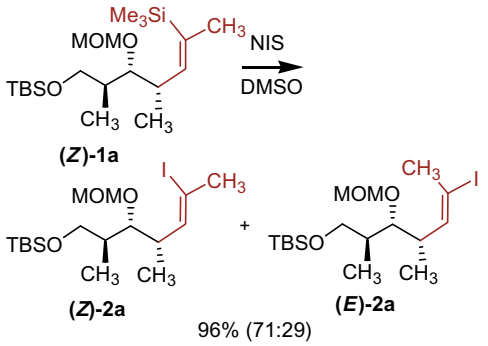
In a 4:1 mixture of MeCN/ClCH$_2$CN, iododesilylation of **(*Z*)-5a–c** gave product mixtures in which the (*Z*)-olefins predominated. Homoallylic acetate **(*Z*)-5d**, under these conditions, again gave almost exclusively the (*E*)-olefin.

Remarkably, reaction of silanes **(*Z*)-5a–c** as well as that of silane **(*Z*)-5d** in DMSO supplied almost entirely the inverted *E*-iodoolefinic products.[10] These results are consistent with the general principles put forth by Tamao[5] for the halodesilylation of disubstituted vinyl silanes. They implicate a high level of participation by solvent or, in the case of **(*Z*)-5d**, by a nearby participating functional group.

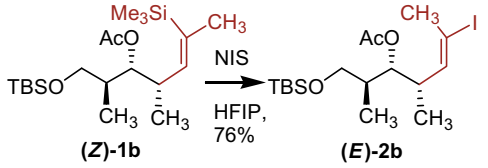
Extension of the solvent-induced inversion of double bond geometry to more complex substrates was partially successful. Application of the DMSO protocol to substrate **(*Z*)-1a** afforded a disappointing 71:29 ratio of the known **(*Z*)-2a** and the desired **(*E*)-2a** (Scheme 2). The appearance of a significant amount of the retention product is consistent with increased steric hindrance at the allylic position[2] in substrate **(*Z*)-1a** relative to that in the model system.

On the other hand, treatment of the acetate **(*Z*)-1b**[10,13] with NIS (in HFIP with 2,6-lutidine) gave only vinyl iodide **(*E*)-2b**[10] (Scheme 3) in 76% yield after 1 h at room temperature.

In summary, both unhindered and chain-substituted (*Z*)-vinyl silanes (**(*Z*)-5** and **(*Z*)-1a**, respectively) give (*Z*)-vinyl iodides under the HFIP conditions; however, only the unhindered compounds were efficiently converted into (*E*)-vinyl iodides in DMSO. On the other hand, a well-positioned participating group led to the inverted (*E*)-geometry in both the simple, unhindered series **5** (i.e., with substrate **(*Z*)-5d**) and in the case of polypropionate substrate **(*Z*)-1b**.



Scheme 2.



Scheme 3.

Acknowledgment

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References and notes

1. Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442.
2. Stamos, D. P.; Taylor, A. G.; Kishi, Y. *Tetrahedron Lett.* **1996**, *37*, 8647.
3. Ilardi, E. A.; Stivala, C. E.; Zakarian, A. *Org. Lett.* **2008**, *10*, 1727–1730.
4. Xie, Q.; Denton, R. W.; Parker, K. A. *Org. Lett.* **2008**, *10*, 5345–5348.
5. As part of an extensive study of solvent effects on the stereoselectivity of the halodesilylation of (*E*)-1-silyloctenes, Tamao had shown that NBS in DMF gave 1-bromooctenes with a high inversion: retention (*Z*:*E*) ratio; see: Tamao, K.; Akita, M.; Maeda, K.; Kumada, M. *J. Org. Chem.* **1987**, *52*, 1100.
6. Complex intermediates that contain trisubstituted (*E*)-olefins adjacent to a series of asymmetric centers are most often prepared from methyl acetylenes by hydrozirconation/iodination or hydrostannylation/iodination; see: (a) Hart, D. W.; Blackburn, T. F.; Schwartz, J. *J. Am. Chem. Soc.* **1975**, *97*, 679; (b) Benechie, M.; Skrydstrup, T.; Khuong-Huu, F. *Tetrahedron Lett.* **1991**, *32*, 7535. They have also been prepared from (*E*)-vinyl silanes by iododesilyation with retention of geometry (our Refs. 2–4).
7. During the course of our work, Oguri and co-workers reported complete inversion of geometry in the iododesilylation of a (*Z*)-trisubstituted olefin, unsubstituted on the carbon chain, in DMF; see: Migita, A.; Shichijo, Y.; Oguri, H. i.; Watanabe, M.; Tokiwano, T.; Oikawa, H. *Tetrahedron Lett.* **2008**, *49*, 1021.
8. For total syntheses and biological activities of khafrefungin and its isomers, see: Shirokawa, S.; Shinoyama, M.; Ooi, I.; Hosokawa, S.; Nakazaki, A.; Kobayashi, S. *Org. Lett.* **2007**, *9*, 849. and references therein.
9. For leading references on tirandamycins A and B, see: Shiratani, T.; Kimura, K.; Yoshihara, K.; Hatakeyama, S.; Irie, H.; Miyashita, M. *Chem. Commun.* **1996**, 21.
10. Each of these compounds was fully characterized.
11. Alcohol **5a** was prepared in three steps from 1-cyclohexyl-3-nonyn-1-ol. Functionalization with tetramethyldisilazane (TMDS) and intramolecular hydrosilylation catalyzed by the cationic ruthenium complex, [Cp Ru(MeCN)$_3$]PF$_6$ gave the dihydrooxasiline. Ring cleavage with methyllithium yielded hydroxy vinyl silane **5a**. See: (a) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2003**, *125*, 30; (b) Mbaye, M. D.; Demerseman, B.; Renaud, J.-L.; Toupet, L.; Bruneau, C. *Adv. Synth. Catal.* **2004**, *346*, 835.
12. For additional evidence for this mechanism, see Refs. 2 and 3.
13. Acetate **(*Z*)-1b** was prepared by 9-BBN hydroboration of our siloxine precursor (Ref. 4), ring opening with methyllithium, selective protection of the primary hydroxyl group with TBSCl, and acetylation of the remaining secondary hydroxyl group.