3-Iodo-3-trimethylsilylpropenal as a Useful Unit for Pinacol Coupling and Subsequent Functional Group Transformations

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Titanium tetraiodidesilyl-mediated pinacol coupling reaction of (*Z*)-3-iodo-3-trimethylsilylpropenal is used for the preparation of *trans*-4,5-bis[(*Z*)-2-iodo-2-(trimethylsilyl)vinyl]-2,2-dimethyl-1,3-dioxolane, which is utilized for the subsequent C–C bond-forming reactions.

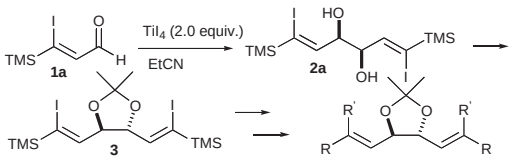
We have been interested in the reaction using TiI_4 and have already reported the pinacol coupling reaction of aromatic aldehydes.[1] However, TiI_4 could not sufficiently promote the pinacol coupling reaction of aliphatic aldehydes due to its mild reducing ability. During these investigations α,β-unsaturated aldehydes possessing a halogen have been found to serve as excellent substrates for pinacol coupling, and the subsequent hydrogenation furnished saturated 1,2-diols in good overall yields.[1b] For further functional group manipulations, introduction of a silicon moiety attracted us, since silyl groups could be transformed into a variety of functionalities.[2] This paper describes TiI_4-mediated stereoselective pinacol coupling of (*Z*)-3-iodo-3-trimethylsilylpropenal (**1a**)[3] and the subsequent reactions of the coupling product **2a** (Scheme 2).

The pinacol coupling reaction was conducted under the reported conditions using TiI_4[1] (Table 1).

As shown in Table 1, (*Z*)-3-bromo-3-TMS-substituted propenal gave a moderate dl-selectivity, whereas its E derivative also recorded a slightly decreased dl-selectivity (Entries 1 and 2). No diastereoselectivity was observed using the TBDPS derivative (Entry 5). In terms of the product yield, (*Z*)-3-iodo-3-TMS-substituted derivative gave the best result, although a perfect dl-selectivity was obtained using the TBS analogue (Entries 3 and 4). For further functional group manipulations and due to the ease to separate each diastereomer, (*Z*)-3-iodo-3-TMS derivative was chosen as the substrate for the present study. For purification and functional group manipulations, the diol dl-**2a** was transformed into the acetonide **3** in good yield ($Me_2C(OMe)_2$, cat. PPTS, PhMe, 80 °C, 4 h, 95%), and the dl isomer **3** was readily separated from its meso-counterpart by simple silica gel column chromatography. The alkyne and aryl coupling reactions were carried out to check the reactivity of the iodovinyl moiety. Both the Sonogashira[5] and the Suzuki[6] coupling reactions gave the products **4** and **5** (Chart 1) in good yields without affecting the geometry of the starting olefins.

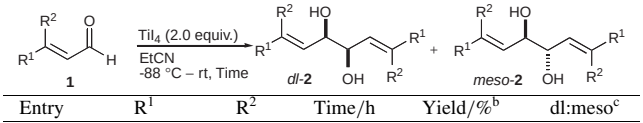
For the C–C bond formation using the trimethylsilylvinyl moiety, we have tried several reaction conditions, and found that the fluoride-catalyzed reaction[7] gave the addition products most efficiently. Table 2 summarizes the results.

Although TBAF effected the addition reaction to give the adduct in low yield, use of TASF increased the product yield (Entries 1 and 2). The reaction carried out at low temperature considerably improved the product yields, where the presence of MS 4A and quenching the reaction at −70 °C made possible the isolation of the product as its bis(silyl ether) (Entries 4 and 5). This addition reaction was also carried out in the presence of a catalytic amount of TASF. The reaction could proceed even in



Scheme 1. The present strategy.

Table 1. Pinacol coupling reaction of the enal **1** promoted by TiI_4[a]



Entry	R^1	R^2	Time/h	Yield/%[b]	dl:meso[c]
1	TMS	Br	15	84	82:18
2	Br	TMS	16	84	79:21
3	TMS[d]	I	16.5	88	92:8
4	TBS	I	18	78	>99:1
5	TBDPS[e]	I	11	33	50:50

[a]The reaction was carried out according to the typical procedure (Ref 4). [b]Isolated yield. [c]Determined by ^{1}H NMR and/or HPLC, and for the explanation of the high dl-selectivity, see Ref. 1. [d]Carried out at −88 to −20 °C. [e]Carried out at −78 to −10 °C.

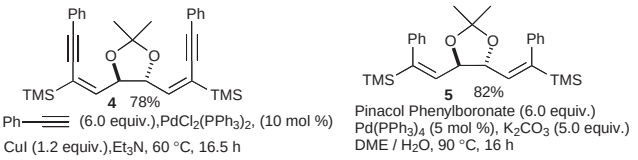
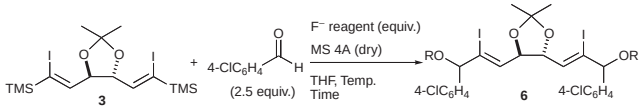


Chart 1.

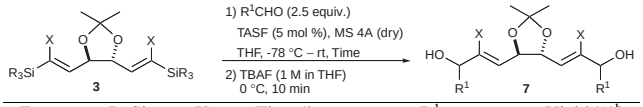
Table 2. Fluoride-mediated C–C bond-forming reaction of **3**[a]



Entry	F^- Source/equiv.	Temp/°C	Time/h	R = H/%[c]	R = TMS/%[c]
1[b]	TBAF (2.5)[d]	rt	18	15	0
2[b]	TASF (2.2)[e]	rt	18	31	0
3[b]	TASF (2.2)	−78 to rt	15	77	0
4	TASF (2.2)	−78 to rt	15	84	0
5	TASF (2.2)	−78 to −70	1	0	84
6	TASF (1.0)	−78 to rt	16	75	0
7	TASF (0.5)	−78 to rt	16	27	60
8	TASF (0.1)	−78 to rt	16	6	84
9	TASF (0.05)	−78 to rt	16	6	85
10	TASF (0.02)	−78 to rt	16	9	0

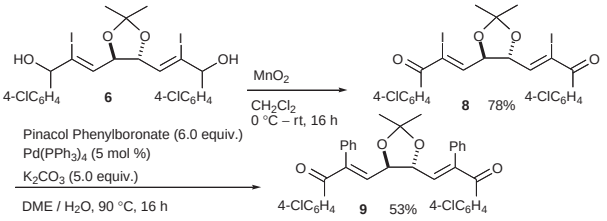
[a]Carried out according to the typical procedure (Ref. 8). [b]In the absence of MS 4A. [c]Isolated yield. [d]*n*-Bu_4NF. [e][$(Me_2N)_3S$](Me_3SiF_2).

Table 3. Addition reaction using various aldehydes[a]



Entry	R_3Si	X	Time/h	R^1	Yield/%[b]
1	TMS	I	16	Ph	65
2	TMS	I	16	4-$MeOC_6H_4$	50
3	TMS	I	16	(*Z*)-*t*-Bu(Cl)C=C	78
4	TMS	I	16	(*E*)-PhC=C	37
5	TMS	I	16	(*E*)-*n*-PrC=C	54
6	TMS	I	16	PhC≡C	77
7	TMS	I	16	*cyclo*-C_6H_{11}	57
8	TMS	Br	14	4-ClC_6H_4	75
9	TMS	Br	14	Ph	64
10	TBS	I	16	4-ClC_6H_4	21
11	TBS	I	11	Ph	16

[a]Reaction was carried out according to the typical procedure (Ref. 8). [b]Isolated yield as a mixture of diastereomers.



Scheme 2. Functional group transformations.

the presence of 5 mol % of the fluoride source (Entries 7–9). Under the optimized conditions a variety of aldehydes were subjected to the addition reaction (Table 3).

The reaction proceeded well with aromatic aldehydes (Entries 1 and 2). Although use of cinnamaldehyde gave the adduct in moderate yield, those of chlorovinyl, phenylethynyl, and aliphatic aldehydes recorded better yields (Entries 3–7). The use of dibromo derivative as substrate gave essentially the same results as in the case with the diiodinated starting material (Entries 8 and 9). The bis-TBS derivative was not as reactive as its TMS counterpart (Entries 10 and 11). The products were obtained after desilylation with TBAF in the work-up process. For further C–C bond-forming reaction with the adduct, we carried out the following Suzuki coupling reaction.

The adduct was first oxidized with MnO_2 to give the diketone **8**, which was treated with pinacol phenylboronate in the presence of Pd^0 to give the diphenylated product **9** in moderate yield, making a useful addition to the synthesis of this class of compounds (Scheme 2).[9]

In conclusion, we have shown that (*Z*)-3-iodo-3-trimethylsilylpropenal (**1a**) is an excellent substrate for the dl-selective pinacol coupling under the influence of TiI_4. The trimethyliodovinyl moiety of the coupling product was in turn efficiently utilized for the C–C bond-forming reactions.

References and Notes

1 a) R. Hayakawa, M. Shimizu, *Chem. Lett.* **2000**, 724. b) M. Shimizu, H. Goto, R. Hayakawa, *Org. Lett.* **2002**, *4*, 4097.

2 a) J. Yoshida, K. Tamao, T. Kakui, M. Kumada, *Tetrahedron Lett.* **1979**, *20*, 1141. b) T. Hiyama, Y. Hatanaka, *Pure Appl. Chem.* **1994**, *66*, 1471. c) K. A. Horn, *Chem. Rev.* **1995**, *95*, 1317. d) K. Itami, T. Nokami, Y. Ishimura, K. Mitsudo, T. Kamei, J. Yoshida, *J. Am. Chem. Soc.* **2001**, *123*, 11577. e) H. Taguchi, K. Ghoroku, M. Tadaki, A. Tsubouchi, T. Takeda, *J. Org. Chem.* **2002**, *67*, 8450. f) M. Yamane, K. Uera, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2005**, *78*, 477.

3 **1a** was prepared by the oxidation of the known (*Z*)-3-iodo-3-trimethylsilylpropenol **10** with PCC/Celite® in 86–90% yield. For the synthesis of **10**, see: a) K. D. Kim, P. A. Magriotis, *Tetrahedron Lett.* **1990**, *31*, 6137. b) S. Ma, F. Liu, E. Negishi, *Tetrahedron Lett.* **1997**, *38*, 3829. c) D. Beruben, I. Marek, J. F. Normant, N. Platzert, *J. Org. Chem.* **1995**, *60*, 2488.

4 Propionitrile (10 mL) was added to TiI_4 (2222 mg, 4.0 mmol) at ambient temperature under an argon atmosphere. The solution was stirred for 10 min, and a propionitrile (10 mL) solution of **1a** (508.2 mg, 2.0 mmol) was added at −88 °C during 2 h. After being stirred at −88 to −20 °C for 16.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$, 10% aqueous $NaHSO_3$, and triethylamine. The whole mixture was filtered through a Celite pad and extracted with ethyl acetate. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification on preparative silica gel TLC (2:1 *n*-hexane/ethyl acetate as an eluent) gave **2a** (383.7 mg, 75%) as a colorless oil. dl:meso = 92:8. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.19 (s, 18H), 2.45 (brs, 0.16H), 2.58 (brs, 1.84H), 4.50–4.54 (m, 1.84H), 4.68–4.70 (m, 0.16H), 6.23–6.27 (m, 0.16H), 6.32–6.35 (m, 1.84H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −1.7, 79.6, 116.9, 143.9.

5 K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467.

6 N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457.

7 a) E. Nakamura, T. Murofushi, M. Shimizu, I. Kuwajima, *J. Am. Chem. Soc.* **1976**, *98*, 2346. b) R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura, M. Shimizu, *J. Am. Chem. Soc.* **1977**, *99*, 1265. c) A. Hosomi, A. Shirahata, H. Sakurai, *Tetrahedron Lett.* **1978**, *19*, 3043. d) H. Oda, M. Sato, Y. Morizawa, K. Oshima, H. Nozaki, *Tetrahedron Lett.* **1983**, *24*, 2877. e) K. Matsumoto, K. Oshima, K. Utimoto, *Chem. Lett.* **1994**, 1211.

8 Under an argon atmosphere to a suspension of TASF (0.5 mg, 0.004 mmol) in THF (1.0 mL) in the presence of molecular sieves 4A (300 mg) was added a mixture of benzaldehyde (8.9 mg, 0.084 mmol) and **3** (18.4 mg, 0.033 mmol) in THF (2.0 mL) at −78 °C, and with stirring the mixture was allowed to stand at rt for 16 h. The mixture was cooled to 0 °C, and a THF solution of TBAF (0.07 mL, 0.07 mmol, 1 M solution) was added to it. After being stirred for 10 min at 0 °C, the whole mixture was quenched by adding water and sat. aqueous NH_4Cl. After a usual work-up, the crude product was purified on preparative silica gel TLC (3:1 *n*-hexane/ethyl acetate as an eluent) to give **7** (R^1 = Ph) as a mixture of diastereomers (13.4 mg, 65%). R_f = 0.33 (*n*-hexane/ethyl acetate = 3:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.50 (s, 3H), 1.50 (s, 3H), 2.32–2.37 (m, 2H), 4.64–4.70 (m, 2H), 5.08–5.11 (m, 1H), 5.16–5.19 (m, 1H), 6.32–6.37 (m, 1H), 6.40–6.44 (m, 1H), 7.25–7.38 (m, 10H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 26.9, 80.0, 80.0, 80.3, 80.4, 83.5, 83.6, 83.6, 110.5, 117.2, 117.4, 117.9, 126.8, 126.8, 127.0, 127.0, 128.2, 128.2, 128.3, 128.5, 131.7, 131.9, 132,0, 139.7, 139.8, 139.8.

9 a) A. G. M. Barrett, W. W. Doubleday, K. Kasdorf, G. J. Tustin, *J. Org. Chem.* **1996**, *61*, 3280. b) E. P. Schreiner, A. Pruckner, *J. Org. Chem.* **1997**, *62*, 5380. c) N. K. Dunlap, W. Mergo, J. M. Jones, J. D. Carrick, *Tetrahedron Lett.* **2002**, *43*, 3923.

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