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Preparation of *E*-α-stannyl-β-trimethylsilylethynylacrylate, building block for polyconjugated ylidenebutenolide and its derivatives, by novel *E*-selective ethynylstannylation of propiolate

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ABSTRACT

E-α-Stannyl-β-trimethylsilylethynylacrylates, which are effective building blocks for the polyconjugated ylidenebutenolides and its modified derivatives, were directly synthesized via novel *E*-selective ethynylstannylation of propiolic acid esters. These building blocks were applied to the syntheses of the ylidenebutenolide segment in the previous peridinin synthesis and a short chain *Z*-eneyne ester derivative, by the sequential Stille and Sonogashira couplings with the corresponding epoxide and vinyl iodide segments.

Among a significant number of carotenoids (over 750 different types),[1] peridinin (**1**, Fig. 1) isolated from the planktonic algae dinoflagellates[2] is a representative light-harvesting pigment in photosynthesis in the sea, and exhibits exceptionally high (>95%) energy transfer efficiencies to chlorophyll (Chl) *a* in the peridinin–Chl *a*–protein (PCP) complex.[3] Many efforts have been devoted to the synthesis of this unique carotenoid,[4] and we achieved the first stereocontrolled synthesis.[4b,c] This molecule is a novel C37 nor-carotenoid that possesses an allene and an ylidenebutenolide in the main conjugated polyene chain. In these functional groups, the ylidenebutenolide function has been generally accepted to play the key role for the highly efficient energy transfer ability of this carotenoid.[5] In the course of our study to understand the mechanism of this quite attractive phenomenon,[5,6] we reported the synthesis of the ylidenebutenolide-modified derivatives, such as eneyne ester derivative **2** (Fig. 1), which has been regarded as the biosynthetic and also artificial synthetic precursor of peridinin, to investigate the relative thermodynamic stability of *E*- and *Z*-isomers at the C13–14 double bond along with its spectral characteristics of the exited state,[5a,b] and also reported the synthesis of the different π-electron-chain length derivatives along with their spectral features.[6] In order to provide more valuable ylidenebutenolide-modified derivatives to elucidate this particular mechanism, we intended to develop a further simple and versatile method for the construction of both polyconjugated ylidenebutenolide function and ester-substituted eneyne system. We have then designed *E*-α-stannyl-β-trimethylsilylacrylates **3a** and **4** as new bidirectionally extensible building blocks for the construction of the polyconjugated eneyne esters, such as **6** and **7** (Fig. 2).

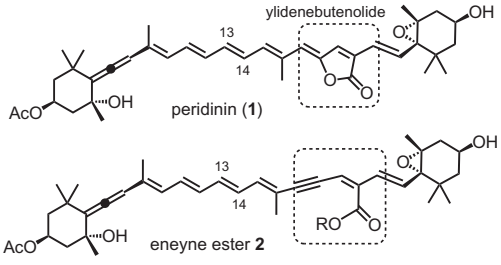

Figure 1. Peridinin and its ylidenebutenolide-modified derivative.

Compound **6** is the synthetic precursor of the ylidenebutenolide segment **5** in our previous peridinin synthesis,[4c] and compound **7** is the short-chain derivative of **2** (C5-unit missing), whose relative stability of the geometrical isomers and its spectral characteristics were of interest in connection with our previous

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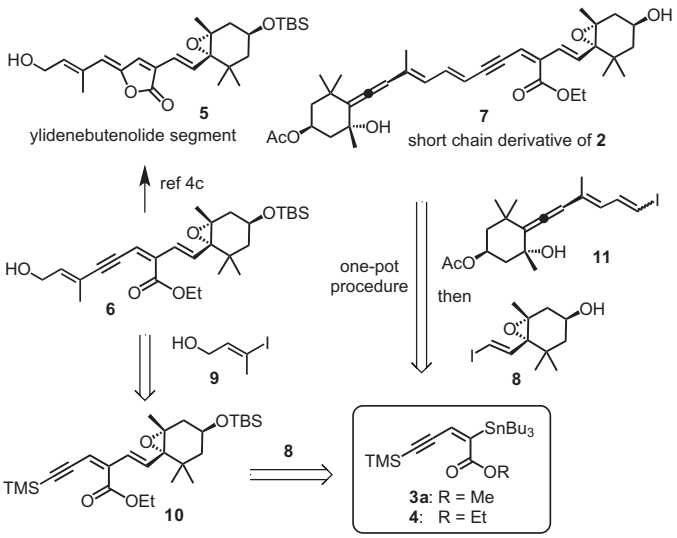


Figure 2. Synthetic plan for ylidenebutenolide segment and short chain derivative of **2**.

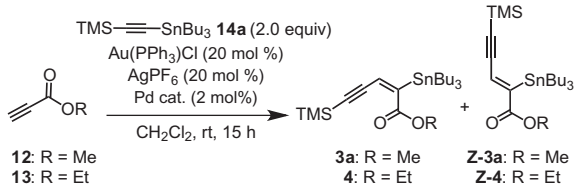
studies.[5a,b,7] Compound **6** could be easily synthesized from the building block **3a** or **4** through **10** by repeating the Stille and Sonogashira couplings with the suitable vinyl iodides **8** and then **9**, respectively, and the one-pot synthesis of **7** from **3a** or **4** by the sequential Stille and Sonogashira couplings with two kinds of vinyl iodides, **8** and **11**, might be possible (Fig. 2). These syntheses would exemplify the availability of these building blocks for the construction of the polyconjugated ester-substituted eneyne system.

In this Letter, we describe the straightforward preparation of the bidirectionally extensible building blocks **3a** and **4** by the novel *E*-selective ethynylstannylation of the propiolic acid esters (Table 1), and also describe the availability of these building blocks by applying them to the synthesis of the ester **6** (Scheme 1) and the one-pot synthesis of the short-chain *Z*-derivative, *Z*-**7** (Scheme 2).

As the synthetic method for α-stannyl-β-ethynylacrylate, the alkynylstannylation of propiolate was found in the literature. Shirakawa et al. reported the carbostannylation of alkynes catalyzed by their originally prepared palladium–iminophosphine catalyst, and described in the Letter that the alkynylstannylation of propiolate produced *Z*-α-stannyl-β-alkynylacrylates in a highly stereo- and regioselective manner.[9] Blum's group also reported the regio- and stereoselective alkynylstannylation of propiolate to produce *Z*-α-stannyl-β-alkynylacrylates in the Letter of the Au- and Pd-cocatalyzed synthesis of tri- and tetra-substituted olefins.[10] It was noteworthy that both methods selectively provided *Z*-isomers resulting from *syn* addition of alkynylstannanes to propiolates.

The newly designed vinylstannanes **3a** and **4** consist of a conjugated *E*-olefin and an ethynyl group with a trimethylsilyl group, which is an easily removable protecting group of the alkyne terminus. We then tried to investigate the Au- and Pd-cocatalyzed ethynylstannylation of propiolates **12** and **13** using trimethylsilylethynylstannane **14a** as a substrate (Table 1). The reaction was performed in the following sequence: (1) a mixture of $Au(PPh_3)Cl$ and $AgPF_6$ in CH_2Cl_2 was stirred for 10 min at room temperature, (2) $Pd_2(dba)_3$ and **14a** were added into the reaction mixture, and then (3) **12** was added dropwise to the resulting mixture.[11] Gratifyingly, the reaction successfully proceeded in a stereo- and regioselective manner to produce the desired *E*-α-stannyl-β-trimethylsilylethynylacrylate **3a** as the major isomer along with the *Z*-stereoisomer *Z*-**3a** (43%, **3a**:*Z*-**3a** = 8.9:1, entry 1).[12,13] The screening of the Pd catalyst revealed that $PdCl_2(PPh_3)_2$ and Pd

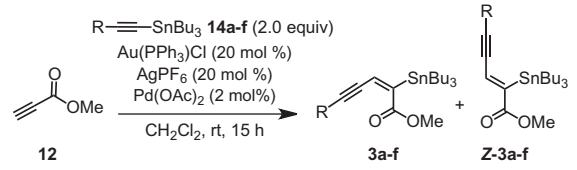
Table 1
Ethynylstannylation of propiolates[a]



Entry	Propiolates	Pd cat.	Products	Yield[b]	Ratio[c] (**3a**:*Z*-**3a**)
1	**12**	$Pd_2(dba)_3$	**3a** and *Z*-**3a**	43%	**8.9**:**1**
2	**12**	$PdCl_2(PPh_3)_2$	**3a** and *Z*-**3a**	10%	1:1
3	**12**	$Pd(PPh_3)_4$	**3a** and *Z*-**3a**	Decomposition	
4	**12**	$Pd(OAc)_2$	**3a** and *Z*-**3a**	35%	**10.5**:**1**
5[d]	**12**	$Pd(OAc)_2$	**3a** and *Z*-**3a**	44%	8.0:1
6[e]	**12**	$Pd(OAc)_2$	**3a** and *Z*-**3a**	67%	1:>20
7	**13**	$Pd(OAc)_2$	**4** and *Z*-**4**	49%	6.3:1[f]

[a] Reaction conditions: **12** or **13** (0.1 mmol), **14a** (0.2 mmol), $Au(PPh_3)Cl$ (20 mol %), $AgPF_6$ (20 mol %), Pd cat. (2 mol %), CH_2Cl_2 (1 mL), rt, 15 h.
[b] Mixture of stereoisomers.
[c] Determined by ^1H NMR analysis.
[d] Reaction was performed in a 3.0 mmol (for **12**) scale.
[e] Reaction was performed in the absence of $Au(PPh_3)Cl$ and $AgPF_6$.
[f] Ratio of **4**:*Z*-**4**.

Table 2
Scope of alkynylstannylation with various alkynylstannanes[a]



Entry	Alkynyl stannanes	R	Products	Yield[b] (%)	Ratio (**3a–f**:*Z*-**3a–f**)[c]
1	**14a**	TMS	**3a** and *Z*-**3a**	35	10.5:1
2	**14b**	TES	**3b** and *Z*-**3b**	76	3.2:1
3	**14c**	TBS	**3c** and *Z*-**3c**	37	3.1:1
4	**14d**	TIPS	**3d** and *Z*-**3d**	53	1:6.4
5[d]	**14e**	Propyl	**3e** and *Z*-**3e**	25	2:1
6[d]	**14f**	*t*-Bu	**3f** and *Z*-**3f**	24	3.6:1

[a] Reaction conditions: **12** (0.1 mmol), **14a–f** (0.2 mmol), $Au(PPh_3)Cl$ (20 mol %), $AgPF_6$ (20 mol %), $Pd(OAc)_2$ (2 mol %), CH_2Cl_2 (1 mL), rt, 15 h.
[b] Mixture of stereoisomers.
[c] Determined by ^1H NMR analysis.
[d] Reaction was performed at 45 °C.

$(PPh_3)_4$ were undesirable (entries 2 and 3), however fortunately, $Pd(OAc)_2$ effectively increased the *E*-selectivity (35%, **3a**:*Z*-**3a** = 10.5:1, entry 4). A good *E*-selectivity was also observed during the experiment on a 3 mmol scale for **12** under the same reaction conditions (44%, **3a**:*Z*-**3a** = 8: 1, entry 5). When the $Pd(OAc)_2$ catalyzed reaction was performed in the absence of both $Au(PPh_3)Cl$ and $AgPF_6$, the *Z*-isomer *Z*-**3a** was selectively obtained (67%, **3a**:*Z*-**3a** = 1:>20, entry 6).[14] Employing ethyl propiolate (**13**) slightly decreased the *E*-selectivity (49%, **4**:*Z*-**4** = 6.3:1, entry 7).[12,13] The reaction did not take place in polar solvents such as THF, DMF and MeOH.

We next examined the scope of this novel *E*-selective alkynylstannylation with respect to various alkynylstannanes **14b–f** under the optimized reaction conditions using $Pd(OAc)_2$ (Table 2). The TES substituted ethynylstannane **14b** instead of TMS resulted in a better yield of the adducts **3b** and *Z*-**3b** (76%), however decreased