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Dehydration-type Ti-Claisen Condensation (Carbonhomologation) of α-Heteroatom-substituted Acetates with Alkyl Formates: Utilization as (*Z*)-Stereodefined Cross-coupling Partners and Application to Concise Synthesis of Strobilurin A

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Abstract.

$TiCl_4$–Et_3N *or* –Bu_3N reagent conducted a highly (*Z*)-stereoselective carbon homologation (dehydration type Ti-Claisen condensation) of alkyl α-heteroatom (halo and sulfonyloxy)-substituted acetates (XCH_2CO_2R) with alkyl formates (HCO_2R) to afford various alkyl β-alkoxy-α-halo *or* sulfonyloxy-substituted acrylates (24 examples; 51%–91% yield). Stereoretentive Suzuki-Miyaura, Negishi, and Sonogashira cross-couplings using the obtained methyl β-methoxy-α-halo or sulfonyloxy-substituted acrylates proceeded smoothly to produce a variety of β-alkoxy-α-substituted acrylates in moderate to high yield (35 examples; 29% – 99% yield). As a successful application, a 3-step straightforward synthesis of strobilurin A was performed utilizing the present reaction sequence (dehydration type Ti-Claisen condensation and Suzuki-Miyaura cross-coupling), wherein the geometry of the three consecutive olefins (2*E*,3*Z*,5*E*) was completely maintained.

Keywords: Synthetic methods; C-C coupling; Cross-coupling; Synthesis design; Ti-Claisen condensation; Suzuki-Miyaura cross-coupling; Negishi cross-coupling; Sonogashira cross-coupling; strobilurin A

Introduction

C-C bond formation at the α-position of carbonyl compounds is a well-recognized pivotal synthetic tool represented by alkylations, aldol additions, Claisen condensations, and Munnich reactions in organic synthesis. Due to the lower enolization ability of simple esters (pKa ~ 25) compared to ketones and aldehydes (pKa ~ 19-21), α-position–functionalized reactions using simple esters generally require harsher conditions.[1] Mild Lewis acid–amine-mediated enolate generation by virtue of the push-pull mechanism is superb, but, successful methods toward this objective for simple ester enolization, are limited to boron-amine-mediated aldol reactions using diazabromoborane (Corey's group),[2] dicyclohexyliodoborane (Brown's group),[3] and boron triflates (Masamune and Abiko's group).[4]

Besides the well-investigated boron ester enolate chemistry, the method using $TiCl_4$–amine reagents contributes to smooth enolate generation from not only ketones or aldehydes, but also simple esters. The inherent potential of the $TiCl_4$–amine system for powerful C-C bond formation undoubtedly originates from the original Mukaiyama aldol reaction.[5] Among $TiCl_4$–amine-mediated reactions, Ti-Claisen condensations using simple ester substrates occupy a central position, categorized as self, crossed, or asymmetric versions to produce a variety of achiral and chiral β-ketoesters.[6-8] A recent Ti-crossed Claisen condensation type between the simple ester and methyl formate provides a reliable carbonhomologation method to α-formyl esters as revealed in *Organic Syntheses*.[7f]

Consistent with our longstanding studies on Ti-Claisen condensations,[6,7b-f,8] relevant Ti-direct aldol-type additions,[9] and Mannich reactions,[10] we next envisage Ti-crossed Claisen condensation using α-heteroatom-substituted acetates with alkyl formates.

Very recently, Massanet's group disclosed a notable dehydration-type condensation of alkyl and aryl acetates with methyl formate using $TiCl_4$–Et_3N reagent,[11] wherein a variety of alkyl (*E*)-2-alkoxyacrylates was produced. This reaction provides an accessible alternative for preparing "(*E*)"-α-alkoxyacrylates (**Scheme 1**).

In the precedent studies, we reported a couple of thioesters undergo specific dehydration-type intramolecular Ti-Claisen (Dieckmann)

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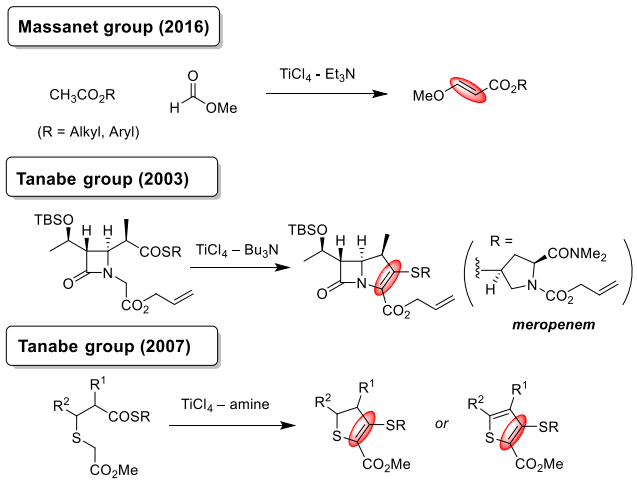
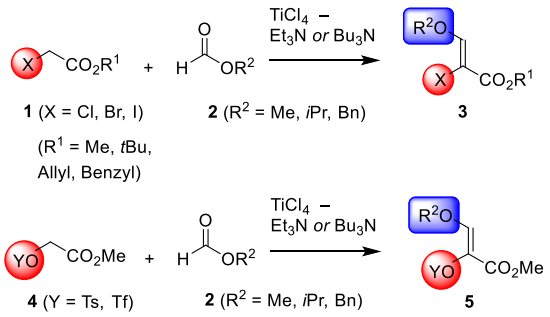
condensations to produce the corresponding vinyl sulfide products (**Scheme 1**): (i) short synthesis of 1β-methylcarbapenem precursors,[12a] including representative meropenem®,[13] and (ii) regioselective synthesis of 3-thiophen-2-carboxylate derivatives.[12b] This background and prospect led us to further investigate the general scope of readily accessible α-heteroatom (halo and sulfonyloxy)-substituted acetate substrates **1** and **4**.

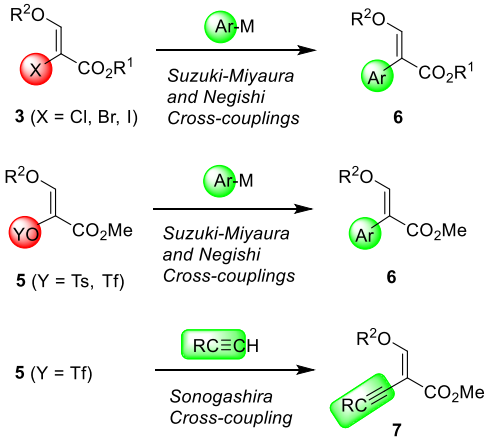


Scheme 1. Reported dehydration-type inter and intramolecular Ti-Claisen condensations.

The present paper disclose a novel (*Z*)-stereoselective dehydration-type Ti-crossed-Claisen condensation (alkoxyvinylidene carbonhomologation) using α- halo *or* sulfonyloxy-substituted acetates **1** ($XCH_2CO_2R^1$: X=Cl, Br, I) and **4** ($YOCH_2CO_2Me$: Y=Ts, Tf) with alkyl formates **2** (HCO_2R^2) to produce alkyl (*Z*)-β-alkoxy-α-halo *or* sulfonyloxy-substituted acrylates **3** and **5**, respectively (**Scheme 2**). The obtained acrylates **3** and **5** were successfully applied as Suzuki-Miyaura (SM), Negishi, and Sonogashira cross-coupling partners with *E*-stereoretention (Note: due to the sequence rule, *E*-geometry is indicated for the setereoretentive reactions). (**Scheme 3**). As a successful application of the present method, concise and convergent synthesis of strobilurin A,[14] natural product possessing the potent fungicidal activity was performed.



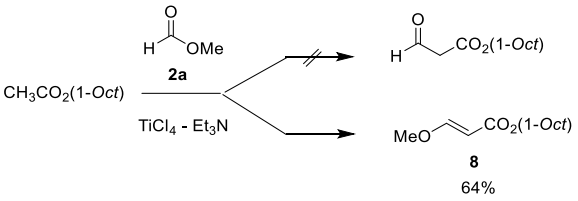
Scheme 2. (*Z*)-Stereoselective dehydration-type Ti-Claisen condensation of esters **1** and **4** with alkyl formates **2**.



Scheme 3. (*Z*)-Stereoretentive Suzuki-Miyaura, Negishi, and Sonogashira cross-couplings using acrylates **3** and **5**.

Results and Discussion

A fundamental Massanet's group reexamination[11] using simple octyl acetate with HCO_2Me (**2a**) was initially tested using $TiCl_4$–Et_3N reagent; octyl (*E*)-2-methoxyacrylate (**8**) was actually obtained as the sole product in 64% yield instead of the expected methyl α-formyl ester[6-8] (**Scheme 4**). The dehydration mode apparently differs from that of the typical Ti-Claisen condensation using α-alkylester substrates (RCH_2CO_2R'; $R \neq H$).[6-8]



Scheme 4. (*E*)-Stereoselective dehydration Ti-Claisen condensation of octyl acetate with methyl formate **2a**.

First, the $TiCl_4$-mediated reaction was applied using α-halogenated propanoates **1a-c** (X = Cl, Br, I) with alkyl formates **2a-c**. Contrary to our expectation, the normal type Ti-Claisen condensation did not occur, but rather a dehydration-type took place to yield alkyl (*Z*)-β-alkoxy-α-halo-substituted acrylates **3**.

Table 1 lists various successful examples, and the salient features are as follows. (i) Good to excellent yield with nearly perfect (*Z*)-selectivity was obtained in almost all cases examined. (ii) Finely tuned conditions (Method *A*-*C*) were adopted for α-haloesters **1a, 1b,** and **1c**, respectively. (iii) Acid-labile *t*Bu esters were also tolerated, although the yield was moderate (Entries 4, 10, 16). (iv) High substrate-generality was demonstrated; The entries

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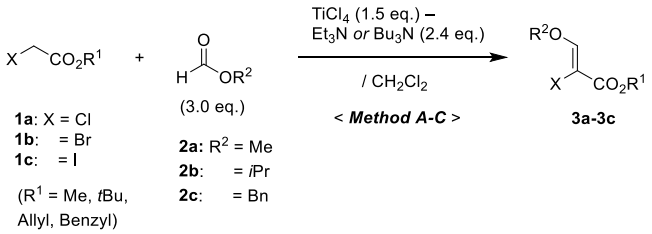
includes three sets of four esters, **1a-1~4**, **1b-1~4, 1c-1~4**, and three formyl esters, **2a-2c**.

Even a trace amount of α-formyl esters was not detected. Concerning this eventful dehydration-mode, we speculate that the produced β-methoxyacrylate is more themodynamically stable than α-formyl esters when using α-heteroatom-substituted ester substrates. Actually, several attempts for the acid hydrolysis of β-methoxyacrylates to convert to α-formyl esters, resulted completely in no reaction.

Notably, compared with the reported methods[15] utilizing α-halogenations both of β-methoxyacrylate and of propiolate, the present one-step preparation provided a wealth of both α-alkoxy and alkyl ester analogues (higher substrate-generality).

Table 1. (*Z*)-Selective dehydration-type Ti-Claisen condensation of α-halogenated esters **1** with alkyl formates **2**



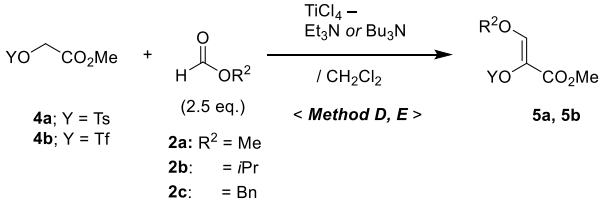
*Method **A***: amine: Bu_3N, –78 °C, 10 min and 0 – 5 °C, 1 h.
*Method **B***: amine: Et_3N, –50 – 45 °C, 10 min and 0 – 5 °C, 1 h.
*Method **C***: amine: Et_3N, –78 °C, 10 min and 0 – 5 °C, 1 h.

Entry	Halo ester X	R^1		Formate R^2		Method	Product	Yield / %[a]
1	Cl	Me	**1a-1**	Me	**2a**	***A***	**3a-1**	97
2				*i*Pr	**2b**		**3a-2**	81
3				Bn	**2c**		**3a-3**	98
4		*t*Bu	**1a-2**	Me	**2a**		**3a-4**	59
5		Bn	**1a-3**				**3a-5**	87
6		Allyl	**1a-4**				**3a-6**	82
7	Br	Me	**1b-1**	Me	**2a**	***B***	**3b-1**	73
8				*i*Pr	**2b**		**3b-2**	81
9				Bn	**2c**		**3b-3**	87
10		*t*Bu	**1b-2**	Me	**2a**		**3b-4**	53
11		Bn	**1b-3**				**3b-5**	77
12		Allyl	**1b-4**				**3b-6**	66
13	I	Me	**1c-1**	Me	**2a**	***C***	**3c-1**	73
14				*i*Pr	**2b**		**3c-2**	50
15				Bn	**2c**		**3c-3**	65
16		*t*Bu	**1c-2**	Me	**2a**		**3c-4**	37
17		Bn	**1c-3**				**3c-5**	77
18		Allyl	**1c-4**				**3c-6**	78

[a] The *Z* purity was >98% based on the ^{1}H NMR spectra.

To extend the scope, a dehydration-type reaction using methyl α-sulfonyloxyester substrates **4a** and **4b** (TsO-, TfO-) was examined. Table 2 lists the successful results, and the salient features are as follows. (i) Moderate to good yield with nearly perfect (*Z*)-selectivity was obtained in all cases examined under the finely tuned optimized conditions (*Methods E* and *F*). (ii) Two sets of (*Z*)-β-alkoxy-α-sulfonyloxyacrylates, **5a-1~5a-3** and **5b-1~5b-3** were successfully obtained. (iii) The reaction using TfO-ester **4b** required smaller amounts of reagents compared with TsO- ester **4a**. (iv) Notably, all six acrylates **5a** (x3) and **5b** (x3) bearing unique triple functional groups, are new compounds, which cannot be accessible by hitherto reported methods.

Table 2. (*Z*)-Selective dehydration-type Ti-Claisen condensation of α-sulfoxy substituted esters **4** with alkyl formates **2**



*Method **D***: $TiCl_4$ (4.6 eq.) - Et_3N (4.8 eq.), – 45 °C, 1 h.
*Method **E***: $TiCl_4$ (2.4 eq.) - Bu_3N (2.6 eq.), –78 °C, 10 min and 0 – 5 °C, 1 h.

Entry	Sulfonyl-oxy ester Y		Formate R^2		Method	Product	Yield / %[a]
1	Ts	**4a**	Me	**2a**	***D***	**5a-1**	70
2			*i*Pr	**2b**		**5a-2**	72
3			Bn	**2c**		**5a-3**	71
4	Tf	**4b**	Me	**2a**	***E***	**5b-1**	70
5			*i*Pr	**2b**		**5b-2**	65
6			Bn	**2c**		**5b-3**	71

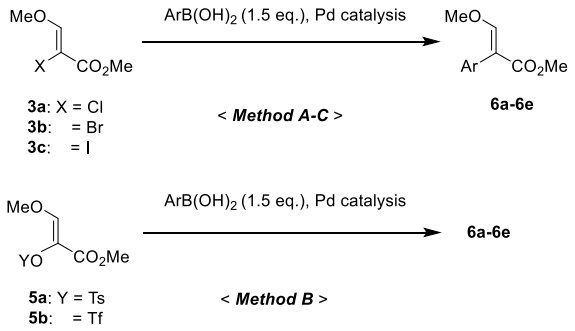
[a] The *Z* purity was >98% based on the ^{1}H NMR spectra.

Following these successful outcomes (Tables 1 and 2), we investigated the utility of obtained (*Z*)-β-alkoxy-α-(halo)- and (sulfonyloxy)-acrylates **3** and **5** bearing α-heteroatom-leaving groups (X, TsO, TfO) as (*E*)-stereoretentive cross-coupling partners (Note: due to the sequence rule, *E*-geometry is indicated for the setereoretentive reactions). While specific Pd-catalyzed Stille,[15b] Suzuki-Miyaura,[15c] and Negishi[15c] cross-couplings using **3b** or **3c** have been reported, they required harsh conditions and/or long reaction periods and produced only low to moderate yields.

To address this problem, we first investigated a (*Z*)-stereoretentive Suzuki-Miyaura cross-coupling

reaction. Table 3 exhibits the successful result of the production of a variety of (*E*)-α-aryl-β-methoxyacrylates **6**. The salient features are as follows. (i) The optimized conditions depended on the leaving groups (Cl, Br, I, OTf) in **3** and **5** (*Methods A-C*) among $Pd(OAc)_2$-PCy_3, $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$, $Pd(dppe)Cl_2$, $Pd(dppp)Cl_2$, $Pd(dppb)Cl_2$, $Pd(dppf)Cl_2$ catalysts (details, ESI). (ii) $PhB(OH)_2$ smoothly coupled with **3a**, **3b**, **3c**, and **5b** in good to excellent yield with nearly perfect (*E*)-stereoretention (Entries 1–3, 5). But, α-(TsO)-acrylate **5a** resulted in no reaction (Entry 4). (iii) Almost all of the reactions using several $ArB(OH)_3$ produced satisfactory results with regard to yield and (*E*)-stereoretention. (i) (Entries 6–13, 15–17, 19). (iv) The use of α-(Cl)-acrylate **3a** with C_6H_4(*p*-Cl) and C_6H_4(*o*-Cl) nucleophiles afforded disappointing results probably due to undesirable further cross-coupling[16] and/or no reactions with *p*-Cl and *o*-Cl groups (Entries 14 and 18).

Table 3. (*E*)-Stereoretentive Suzuki-Miyaura cross-coupling using α-haloacrylates **3** and α-sulfonyloxy acrylates **5**.



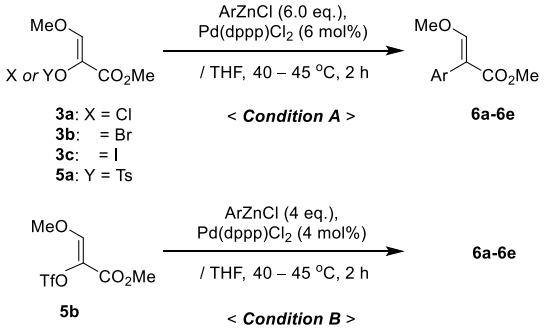
Method ***A***: $Pd(OAc)_2$ (5 mol%), PCy_3 (10 mol%), K_2CO_3 (3.0 equiv) / THF-H_2O (10:1), reflux, 2 h.
Method ***B***: $Pd(PPh_3)_2Cl_2$ (5 mol%), K_2CO_3 (3.0 equiv) / *i*PrOH, reflux, 2 h.
Method ***C***: $Pd(dppe)Cl_2$ (5 mol%), K_2CO_3 (3.0 equiv) / *i*PrOH-H_2O (10:1), reflux, 2 h.

Entry	X or Y	Ar	Method	Product	Yield / %[a]
1	Cl	Ph	***A***	**6a**	93
2	Br		***B***		88
3	I		***C***		89
4	Ts		***B***		NR
5	Tf		***B***		88
6	Cl	C_6H_4(*p*-Me)	***A***	**6b**	91
7	Br		***B***		70
8	I		***C***		99
9	Tf		***B***		94
10	Cl	C_6H_4(*p*-OMe)	***A***	**6c**	94
11	Br		***B***		74
12	I		***C***		93
13	Tf		***B***		92
14	Cl	C_6H_4(*p*-Cl)	***A***	**6d**	Complex mixtures
15	Br		***B***		79
16	I		***C***		80
17	Tf		***B***		93
18	Cl	C_6H_4(*o*-Cl)	***A***	**6e**	NR
19	Br		***B***		77
20	I		***C***		42
21	Tf		***B***		83

[a] The *Z* purity was >98% based on the ^1H NMR spectra.

Next, our attention was focused on an application of the Negishi cross-coupling reaction. Table 4 lists the successful results, and the salient features are as follows. (i) All seven catalysts examined in Suzuki-Miyaura couplings, afforded disappointing results when using α-haloacrylates **3a**-**3c** (Entries 1–3). (ii) On the other hand, sulfonyloxyacrylates **5a** and **5b** underwent the reaction smoothly to furnish the desired products **6a**-**6e** using the $Pd(dppp)Cl_2$ catalyst in good to excellent yield with nearly perfect (*E*)-stereoretention (Entries 4–11). (iii) Only $Pd(dppp)Cl_2$ exhibited remarkable effects, compared with the other six catalysts, which resulted in very low yield. (iv) Even the less reactive C_6H_4(*o*-Cl) nucleophile gave positive results using **5b** (Entry 13).

Table 4. (*E*)-Stereoretentive Negishi cross-coupling using α-haloacrylates **3** and α-sulfonyloxyacrylates **5**.



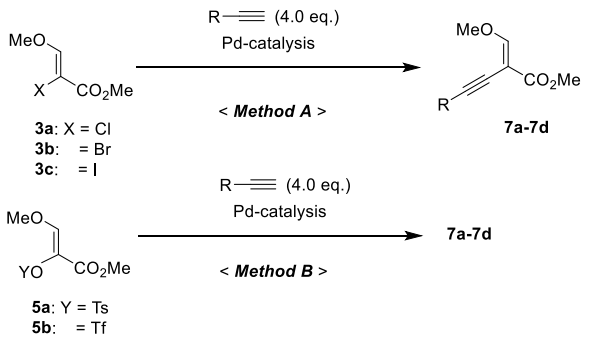
Entry	X *or* Y	Ar	Condition	Product	Yield / %[a]
1	Cl	Ph	***A***	**6a**	NR
2	Br		***A***		NR
3	I		***A***		29
4	Ts		***A***		72
5	Tf		***B***		85
6	Ts	C_6H_4(*p*-Me)	***A***	**6b**	88
7	Tf		***B***		99
8	Ts	C_6H_4(*p*-OMe)	***A***	**6c**	69
9	Tf		***B***		92
10	Ts	C_6H_4(*p*-Cl)	***A***	**6d**	87
11	Tf		***B***		>99
12	Ts	C_6H_4(*o*-Cl)	***A***	**6e**	NR

13	Tf		***B***	56

[a] The *Z* purity was >98% based on the ^{1}H NMR spectra.

The Sonogashira cross-coupling reaction was also investigated, and the results are shown in Table 6. The salient features are as follows. (i) Although α-(Cl)-acrylate **3a** did not undergo the reaction, α-(Br)- and α-(I)-acrylates **3b, 3c** afforded positive results to produce the desired α-alkynyl acrylate **7a** in good yield using the $Pd(PPh_3)_2Cl_2$ catalyst (*Method A*) (Entries 1-3). (ii) α-(TfO)-acrylate **5b** afforded the best results with the $Pd(dppf)Cl_2$ catalyst (*Method B*); The desired α-alkynyl acrylates **7a-7d** were produced in excellent yield with nearly perfect *E*-stereoretention (Entries 4 – 8).

Table 5. (*E*)-Stereoretentive Sonogashira cross-coupling using α-haloacrylates **3** and α-sulfonyloxyacrylates **5**.



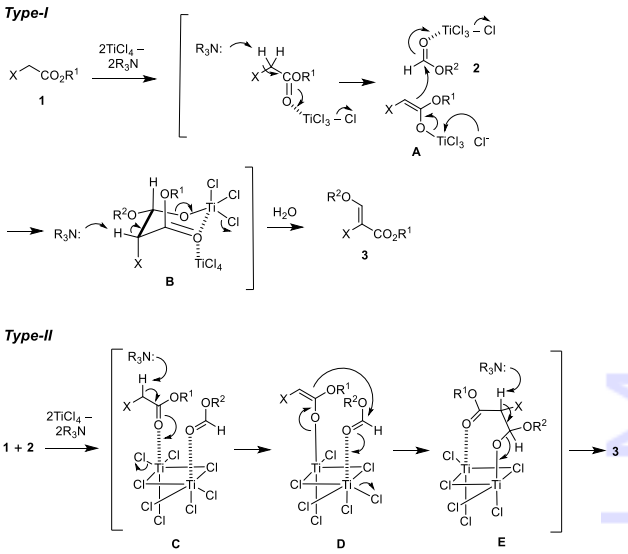
Method ***A***: $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (15 mol%), *i*Pr_2NEt (1.5 equiv) / THF, reflux, 2 h.
Method ***B***: $Pd(dppf)Cl_2$ (5 mol%), CuI (15 mol%), *i*Pr_2NEt (1.5 equiv) / THF, reflux, 2 h.

Entry	X *or* Y	R	Method	Product	Yield / %[a]
1	Cl	Ph	***A***	**7a**	NR
2	Br		***A (B)***		62 (10)
3	I		***A (B)***		81 (20)
4	Ts		***B***		72
5	Tf		***B***		>99
6	Tf		***B***	**7b**	89[b]
7	Tf	*t*Bu	***B***	**7c**	80[b]
8	Tf	TBS	***B***	**7d**	83

[a] The *Z* purity was >98% based on the ^{1}H NMR spectra. [b] CuI (30 mol%) was used.

Scheme 5 shows two plausible mechanisms for the dehydration-type Ti-Claisen condensation, exemplified by α-haloacrylate **1**. [*Type I*]: **1** is converted to ester enolate **A** via a push-pull pathway by the actions of $TiCl_4$ and R_3N. **A**, in turn, attacks formate **2**, which is activated by another $TiCl_4$ (double activation). Through the six-membered cyclic transition state **B**, (*Z*)-α-alkoxy-α-haloacrylates **3** is produced, wherein the R^2O- group locates at an equatorial position and the R^1O- group and X- atom locate at axial positions. [*Type II*]: Massanet's group proposed a related mechanism for the reaction between simple acetates and ethyl formate.[11] Following their speculation, **1** is transformed through bimetallic transition states **C**, **D**, and **E** to produce **3**.

The thermodynamic stabilities of *Z*-**3** and the isomer *E*-**3** were calculated using *Gaussian 16* [B3LYP/6-31+G(d)] (the reference in ESI), exemplified by **3b-1** and **5b-1**, to obtain fundamental insight into the *E* and *Z* selectivity.[17] The total energies of these two sets of compounds were similar [(*Z*)-**3a-1**: 80.68 kcal/mol, (*E*)-**3a-1**: 80.50 kcal/mol, and (*Z*)-**5b-1**: 103.19 kcal/mol, (*E*)-**5b-1**: 102.93 kcal/mol]. This finding implies that *Z*-stereoselectivity does not depend on the stability of the products, but rather on the kinetic pathway.



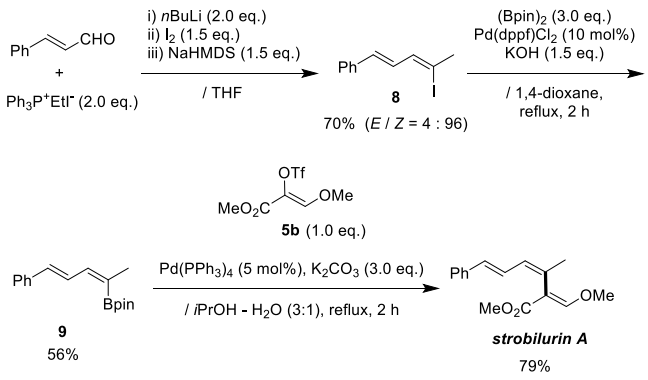
Scheme 5. Proposed mechanism of (*Z*)-dehydration-type Ti-Claisen condensation.

Stereodefined α-dienyl-β-methoxyacrylates comprise a common structural component for agrochemically important natural and unnatural fungicides, as exemplified by strobilurin families.[14] As a final note, application to concise and convergent synthesis of strobilurin A was performed as depicted in Scheme 6, wherein a couple of the present reaction sequences (carbonhomologation and cross-coupling) were involved.

Total syntheses of strobilurins A and B were disclosed utilizing the Peterson reaction (Clough and Beautement)[18] and the Stille cross-coupling (Coleman and Lu)[19] as key steps. Our synthetic strategy entails more accessible and stereoretentive Suzuki-Miyaura cross-coupling between highly reactive (*Z*)-β-methoxy-α-(TfO)-acrylate **5b** and (*Z*,*E*)-dienylboronate **9**.

A one-pot α-methyliodoethylenation of cinnamaldehyde gave dienyl iodide **8** in 70% yield (*E* : *Z* = 4 : 96).[20] Iodide **8** was converted to **9** in 56% yield by $B(pin)_2$/$Pd(dppf)Cl_2$/KOH catalysis (Miyaura-Ishiyama borylation) with stereoretention

of the diene moiety.[21] As a final key step, Suzuki-Miyaura cross-coupling of boronate **9** with α-(TfO)-acrylate **5b** smoothly proceeded to afford strobilurin A in 79% yield with nearly perfect stereocontrol of the three consecutive (2*E*,3*Z*,5*E*) olefins (total 3 steps with overall 31% yield). Compared with the previously reported methods, the present convergent approach is more concise and straightforward.

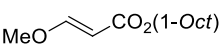


Scheme 6. Synthetic application to strobilurin A utilizing β-methoxy-α-(TfO)-acrylate **5b**.

Experimental Section

Octyl (*E*)-2-methoxyacrylate (8)

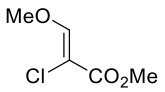
Et_3N (6.66 mL, 48 mmol) and $TiCl_4$ (4.39 mL, 40 mmol) were successively added to a stirred solution of octyl acetate (3.45 g, 20 mmol) and HCO_2Me (3.60 g, 60 mmol) in CH_2Cl_2 (40 mL) at –45 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 2 h. Then, the mixture was poured into ice-water, which was extracted twice with AcOEt. The organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude oil was purified by distillation to give the desired product (**8**; 2.75 g, 64%).



Colorless oil; bp 130 – 135 °C / 11 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.88 (t, *J* = 7.5 Hz, 3H), 1.22–1.41 (m, 10H), 1.64 (quin, *J* = 7.5 Hz, 2H), 3.69 (s, 3H), 4.10 (t, *J* = 7.5 Hz, 2H), 5.19 (d, *J* = 12.6 Hz, 1H), 7.63 (d, *J* = 12.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.8, 22.4, 25.8, 28.6, 28.97, 29.02, 31.6, 56.8, 63.7, 95.7, 162.7, 167.4; IR (neat): ν_{max} = 1711, 1626, 1456, 1327, 1283, 1244, 1219, 1128; HRMS (ESI): *m/z* calcd for $C_{12}H_{22}O_3$ [*M* + Na]$^+$ 237.1467; found: 237.1464.

A typical procedure for the synthesis of methyl (*Z*)-2-chloro-3-methoxyacrylate (3a-1)[15a] **[Method *A*]**

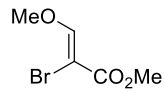
Bu_3N (11.4 mL, 48 mmol) and $TiCl_4$ (3.29 mL, 30 mmol) were successively added to a stirred solution of a methyl chloroacetate (**1a-1**; 2.17 g, 20 mmol) and methyl formate (**2a**; 3.60 g, 60 mmol) in CH_2Cl_2 (40 mL) at –78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 10 min. The mixture was warmed up to 0 – 5 °C, followed by being stirred at the same temperature for 1 h. Then, the mixture was poured into ice-water, which was extracted twice with Et_2O. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 10:1) to give the desired product **3a-1** (2.91 g, 97%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3H), 3.98 (s, 3H), 7.64 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.3, 62.3, 102.6, 157.2, 163.9.

A typical procedure for the synthesis of methyl (*Z*)-2-bromo-3-methoxyacrylate (3b-1)[15a] **[Method *B*]**

Et_3N (3.33 mL, 24 mmol) and $TiCl_4$ (1.64 mL, 15 mmol) were successively added to a stirred solution of a methyl bromoacetate (**1b-1**; 1.53 g, 10 mmol) and methyl formate (**2a**; 1.80 g, 30 mmol) Et_3N (3.33 mL, 24 mmol) and $TiCl_4$ (1.64 mL, 15 mmol) were successively added to a stirred solution of a 2-bromopropanoic ester (**1b**; 10 mmol) and an alkyl formate (**2**; 30 mmol) in CH_2Cl_2 (20 mL) at –40 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 10 min. The mixture was warmed up to 0 – 5 °C, followed by being stirred at the same temperature for 1 h. Then, the mixture was poured into ice-water, which was extracted twice with Et_2O. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 10:1) to give the desired product **3b-1** (1.19 g, 73%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.80 (s, 3H), 3.97 (s, 3H), 7.64 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.4, 62.4, 102.8, 157.3, 164.0.

Conclusion

We developed a highly (*Z*)-stereoselective dehydration-type Ti-crossed-Claisen condensation (carbonhomologation) using α-halo and α-sulfonyloxy (Cl, Br, I, TsO, TfO)-substituted acetates with alkyl formates to produce a variety of alkyl (*Z*)-β-alkoxy-α-halo *or* sulfonyloxy-substituted acrylates.

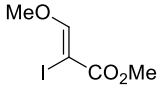
The obtained (*E*)-β-methoxy-α-hetero-substituted acrylates serve as efficient cross-coupling partners for (*E*)-stereoretentive cross-couplings (Suzuki-Miyaura, Negishi, and Sonogashira): (a) Suzuki-Miyaura for Cl, Br, I, and TfO substrates, (b) Negishi for TsO and TfO substrates, and (c) Sonogashira for Br, I, TsO, and TfO substrates. These cross-couplings provided a number of α-aryl and α-ethynyl-(*Z*)-β-methoxyacrylates.

As a synthetic application, we performed a concise and straightforward synthesis of strobilurin A, a representative fungicide.

The present method provides a new avenue for the synthesis of (*Z*)-stereodefined α-substituted β-alkoxyacrylates in the fields of natural product synthesis and process chemistry.

A typical procedure for the synthesis of methyl (*Z*)-2-iodo-3-methoxyacrylate (3c-1)[19] **[Method *C*]**

Et_3N (3.33 mL, 24 mmol) and $TiCl_4$ (1.64 mL, 15 mmol) were successively added to a stirred solution of a methyl iodoacetate (**1c-1**; 2.00 g, 10 mmol) and methyl formate (**2a**; 1.80 g, 30 mmol) in CH_2Cl_2 (20 mL) at –78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 10 min. The mixture was warmed up to 0 – 5 °C, followed by being stirred at the same temperature for 1 h. Then, the mixture was poured into ice-water, which was extracted twice with Et_2O. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 10:1) to give the desired product **3c-1** (1.70 g, 70%).

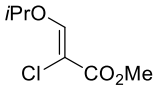


Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (s, 3H), 4.00 (s, 3H), 7.68 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.8, 62.0, 64.8, 164.2, 164.3.

The (Z)-configuration of **3a**, **3b**, **3c** was unambiguously assigned based on ^{1}H and ^{13}C NMRs of the known compounds.

Methyl (*Z*)-2-chloro -3-isopropoxyacrylate (3a-2)

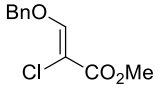
Following the procedure for the preparation of **3a-1**, the reaction of methyl chloroacetate (**1a-1**; 109 mg, 1.0 mmol) with isopropyl formate (**2b**; 264 mg, 3.0 mmol), using Bu_3N (571 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3a-2** (144 mg, 81%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.38 (d, *J* = 6.2 Hz, 6H), 3.80 (s, 3H), 4.32 (sept, *J* = 6.2 Hz, 1H), 7.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 28.0 (2C), 62.1, 82.0, 104.2, 156.3, 162.4; IR (neat): ν_{max} = 2981, 1724, 1630, 1437, 1376, 1282, 1211, 1139 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_{11}O_3Cl$ [*M* + Na]$^+$ 201.0294; found: 201.0294.

Methyl (*Z*)-2-chloro-3-benzyloxyacrylate (3a-3)

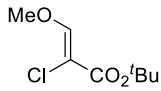
Following the procedure for the preparation of **3a-1**, the reaction of methyl chloroacetate (**1a-1**; 109 mg, 1.0 mmol) with benzyl formate (**2c**; 408 mg, 3.0 mmol), using Bu_3N (571 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3a-3** (192 mg, 98%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.77 (s, 3H), 5.14 (s, 2H), 7.31–7.45 (m, 5H), 7.74 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.4, 76.5, 103.5, 127.6 (2C), 128.8 (3C), 135.1, 155.6, 163.9; IR (neat): ν_{max} = 2952, 1719, 1633, 1497, 1455, 1436, 1377, 1281 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_3Cl$ [*M* + Na]$^+$ 249.0294; found: 249.0297.

***tert*-Butyl (*Z*)-2-chloro-3-methoxyacrylate (3a-4)**

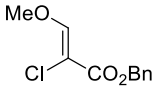
Following the procedure for the preparation of **3a-1**, the reaction of *tert*-butyl chloroacetate (**1a-2**; 151 mg, 1.0 mmol) with methyl formate (**2a**; 180 mg, 3.0 mmol), using Bu_3N (571 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3a-4** (113 mg, 59%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.51 (s, 9H), 3.94 (s, 3H), 7.50 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 28.0 (3C), 62,1, 82.2, 104.3, 156.4, 162.7; IR (neat): ν_{max} = 2983, 2255, 1713, 1637, 1370, 1247, 1140, 1069 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_8H_{13}O_3Cl$ [*M* + Na]$^+$ 215.0451; found: 215.0450.

Benzyl (*Z*)-2-chloro-3-methoxyacrylate (3a-5)

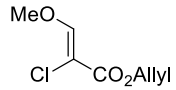
Following the procedure for the preparation of **3a-1**, the reaction of benzyl chloroacetate (**1a-3**; 185 mg, 1.0 mmol) with methyl formate (**2a**; 180 mg, 3.0 mmol), using Bu_3N (571 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3a-5** (198 mg, 87%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.92 (s, 3H), 5.22 (s , 2H), 7.26–7.42 (m , 5H), 7.62 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 62.4, 67.0, 103.0, 128.2 (2C), 128.3, 128.6 (2C), 135.6, 157.5, 163.4; IR (neat): ν_{max} = 2943, 1715, 1633, 1497, 1455, 1379, 1278, 1233 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_3Cl$ [*M* + Na]$^+$ 249.0294; found: 249.0293.

Allyl (*Z*)-2-bromo-3-methyoxyacrylate (3a-6)

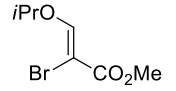
Following the procedure for the preparation of **3a-1**, the reaction of allyl chloroacetate (**1a-4**; 135 mg, 1.0 mmol) with methyl formate (**2a**; 180 mg, 3.0 mmol), using Bu_3N (571 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3a-6** (144 mg, 82%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.98 (s, 3H), 4.64–4.72 (m, 2H), 5.26 (dd, *J* = 1.4, 10.3 Hz, 1H), 5.35 (dd, *J* = 1.4, 17.2 Hz, 1H), 5.94 (ddt, *J* = 5.9, 10.3, 17.2 Hz, 1H), 7.67 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 62.3, 65.7, 102.6, 118.3, 131.7, 157.2, 163.0; IR (neat): ν_{max} = 3649, 2945, 1715, 1627, 1445, 1363, 1270, 1228 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_9O_3Cl$ [*M* + Na]$^+$ 199.0138; found: 199.0137.

Methyl (*Z*)-2-bromo-3-isopropoxyacrylate (3b-2)

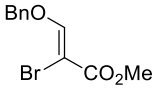
Following the procedure for the preparation of **3b-1**, the reaction of methyl bromoacetate (**1b-1**; 153 mg, 1.0 mmol) with isopropyl formate (**2b**; 264 mg, 3.0 mmol), using Et_3N (333 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3b-2** (180 mg, 81%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.38 (d, *J* = 6.2 Hz, 6H), 3.79 (s, 3H), 4.31 (sept, *J* = 6.2 Hz, 1H), 7.91 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 22.4 (2C), 52.4, 78.9, 90.9, 157.3, 164.1; IR (neat): ν_{max} = 2951, 1731, 1541, 1436, 1414, 1265, 1143, 1094 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_{11}O_3Br$ [*M* + Na]$^+$ 244.9789; found: 244.9785.

Methyl (*Z*)-2-bromo-3-benzyloxyacrylate (3b-3)

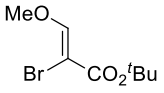
Following the procedure for the preparation of **3b-1**, the reaction of methyl bromoacetate (**1b-1**; 153 mg, 1.0 mmol) with benzyl formate (**2c**; 408 mg, 3.0 mmol), using Et_3N (333 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3b-3** (236 mg, 87%].



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.77 (s, 3H), 5.17 (s, 2H), 7.33–7.44 (m, 5H), 7.90 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.6, 76.4, 92.3, 127.5 (2C), 128.8 (3C), 135.1, 157.9, 163.8; IR (neat): ν_{max} = 2949, 1717, 1627, 1455, 1436, 1379, 1267, 1158 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_3Br$ [*M* + Na]$^+$ 292.9789; found: 292.9796.

***tert*-Butyl (*Z*)-2-bromo-3-methoxyacrylate (3b-4)**

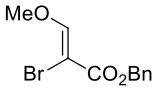
Following the procedure for the preparation of **3b-1**, the reaction of *tert*-butyl bromoacetate (**1b-2**; 195 mg, 1.0 mmol) with methyl formate (**2a**; 180 mg, 3.0 mmol), using Et_3N (333 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3b-4** (126 mg, 53%].



Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.51 (s, 9H), 3.96 (s, 3H), 7.66 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 28.1 (3C), 62,1, 82.2, 93.9, 158.6, 162.3; IR (neat): ν_{max} = 2978, 1692, 1629, 1368, 1295, 1239, 1132, 1052 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_8H_{13}O_3Br$ [*M* + Na]$^+$ 258.9946; found: 258.9949.

Benzyl (*Z*)-2-bromo-3-methoxyacrylate (3b-5)

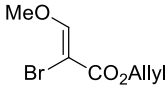
Following the procedure for the preparation of **3b-1**, the reaction of benzyl bromoacetate (**1b-3**; 229 mg, 1.0 mmol) with methyl formate (**2a**; 180 mg, 3.0 mmol), using Et_3N (333 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3b-5** (208 mg, 77%).



Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.97 (s, 3H), 5.24 (s, 2H), 7.30–7.43 (m, 5H), 7.78 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 62.1, 67.0, 91.6, 127.9 (2C), 128.1, 128.4 (2C), 135.5, 159.6, 163.0; IR (neat): ν_{max} = 2977, 1691, 1629, 1368, 1295, 1239, 1132, 1053; cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_3Br$ [*M* + Na]$^+$ 292.9789; found: 292.9785.

Allyl (*Z*)-2-bromo-3-methyoxyacrylate (3b-6)

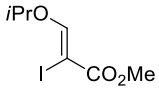
Following the procedure for the preparation of **3b-1**, the reaction of allyl bromoacetate (**1b-4**; 179 mg, 1.0 mmol) with methyl formate (**2a**; 180 mg, 3.0 mmol), using Et_3N (333 μL, 2.4 mmol) and $TiCl_4$ (165 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) gave the desired product **3b-6** (146 mg, 66%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.00 (s, 3H), 4.64–4.81 (m, 2H), 5.26 (dd, *J* = 1.4, 10.3 Hz, 1H), 5.36 (dd, *J* = 1.4, 17.2 Hz, 1H), 5.96 (ddt, *J* = 5.5, 10.3, 17.2 Hz, 1H), 7.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 62.3, 66.0, 91.6, 118.3, 131.7, 159.6, 163.0; IR (neat): ν_{max} = 3649, 2945, 1715, 1627, 1445, 1363, 1270, 1228 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_9O_3Br$ [*M* + Na]$^+$ 242.9633; found: 292.9624.

Methyl (*Z*)-2-iodo-3-isopropoxyacrylate (3c-2)

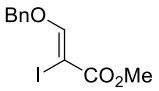
Following the procedure for the preparation of **3c-1**, the reaction of methyl iodoacetate (**1c-1**; 300 mg, 1.5 mmol) with isopropyl formate (**2b**; 396 mg, 4.5 mmol), using Et_3N (499 μL, 3.6 mmol) and $TiCl_4$ (246 μL, 2.3 mmol) in CH_2Cl_2 (3 mL) gave the desired product **3c-2** (202 mg, 50%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.39 (d, *J* = 6.2 Hz, 6H), 3.78 (s, 3H), 4.40 (sept, *J* = 6.2 Hz, 1H), 7.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 22.3 (2C), 52.5, 64.2, 78.5, 161.9, 164.3; IR (neat): ν_{max} = 2978, 2349, 1710, 1610, 1433, 1376, 1265, 1203 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_{11}O_3I$ [*M* + Na]$^+$ 292.9651; found: 292.9651.

Methyl (*Z*)-2-iodo-3-benzyloxyacrylate (3c-3)

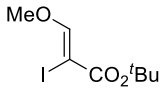
Following the procedure for the preparation of **3c-1**, the reaction of methyl iodoacetate (**1c-1**; 300 mg, 1.5 mmol) with benzyl formate (**2c**; 613 mg, 4.5 mmol), using Et_3N (499 μL, 3.6 mmol) and $TiCl_4$ (246 μL, 2.3 mmol) in CH_2Cl_2 (3 mL) gave the desired product **3c-3** (309 mg, 65%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.61 (s, 3H), 5.04 (s, 2H), 7.17–7.31 (m, 5H), 7.70 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.6, 65.7, 75.9, 127.2 (2C), 128.46, 128.53 (2C), 135.0, 162.6, 164.0; IR (neat): ν_{max} = 2950, 2649, 1708, 1613, 1454, 1433, 1377, 1257 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_3I$ [*M* + Na]$^+$ 340.9651; found: 340.9661.

***tert*-Butyl (*Z*)-2-iodo-3-methoxyacrylate (3c-4)**

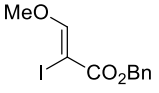
Following the procedure for the preparation of **3c-1**, the reaction of *tert*-butyl iodoacetate (**1c-2**; 484 mg, 2.0 mmol) with methyl formate (**2a**; 360 mg, 6.0 mmol), using Et_3N (666 μL, 4.8 mmol) and $TiCl_4$ (329 μL, 3.0 mmol) in CH_2Cl_2 (4 mL) gave the desired product **3c-4** (212 mg, 37%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.49 (s, 9H), 3.97 (s, 3H), 7.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 28.0 (3C), 61.8, 68.5, 82.0, 162.7, 163.3; IR (neat): ν_{max} = 2977, 2349, 1702, 1616, 1455, 1367, 1235, 1130 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_8H_{13}O_3I$ [*M* + Na]$^+$ 306.9807; found: 306.9815.

Benzyl (*Z*)-2-iodo-3-methoxyacrylate (3c-5)

Following the procedure for the preparation of **3c-1**, the reaction of benzyl iodoacetate (**1c-3**; 414 mg, 1.5 mmol) with methyl formate (**2a**; 270 mg, 4.5 mmol), using Et_3N (499 μL, 3.6 mmol) and $TiCl_4$ (246 μL, 2.3 mmol) in CH_2Cl_2 (3 mL) gave the desired product **3c-5** (366 mg, 77%).

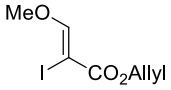


Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.99 (s, 3H), 5.23 (s, 2H), 7.31–7.43 (m, 5H), 7.69 (s, 1H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ = 62.0, 65.4, 67.5, 128.0 (2C), 128.1, 128.5 (2C), 135.7, 163.6, 164.4; IR (neat): ν_{max} = 2942, 2349, 1705, 1615, 1497, 1454, 1376, 1225; cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_3I$ [*M* + Na]$^+$ 340.9651; found: 340.9656.

Allyl (*Z*)-2-iodo-3-methyoxyacrylate (3c-6)

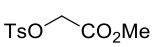
Following the procedure for the preparation of **3c-1**, the reaction of allyl iodoacetate (**1c-4**; 339 mg, 1.5 mmol) with methyl formate (**2a**; 270 mg, 4.5 mmol), using Et_3N (499 μL, 3.6 mmol) and $TiCl_4$ (246 μL, 2.3 mmol) in CH_2Cl_2 (3 mL) gave the desired product **3c-6** (314 mg, 78%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.01 (s, 3H), 4.66–4.73 (m, 2H), 5.26 (dd, *J* = 1.4, 10.3 Hz, 1H), 5.37 (dd, *J* = 1.4, 17.2 Hz, 1H), 5.95 (ddt, *J* = 5.9, 10.3, 17.2 Hz, 1H), 7.70 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 62.0, 65.1, 66.2, 118.1, 131.8, 163.3, 164.3; IR (neat): ν_{max} = 2942, 2349, 1708, 1615, 1442, 1361, 1224, 1132 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_9O_3I$ [*M* + Na]$^+$ 290.9494; found: 290.9500.

Methyl tosyloxyacetate (4a)[22]

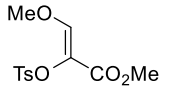
TsCl (8.56 g, 45 mmol) in CH_2Cl_2 (20.0 mL) was added to a stirred solution of methyl glycolate (2.70 g, 30 mmol), NMI (493 mg, 6 mmol), and Et_3N (4.55 g, 45 mmol) in CH_2Cl_2 (40.0 mL) at 20 – 25 °C, followed by being stirred for 1 h at that temperature. Water was added to the stirred mixture, which was extracted twice with EtOAc. The organic phase was washed with water, brine, dried (Na_2SO_4) and consentrated. The obtained crude solid was washed with hexane-Et_2O (20:1, 10 mL) to give the desired product (**4a**; 6.20 g, 85%).



Pale yellow crystals; mp 59 – 61 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.46 (s, 3H), 3.73 (s, 3H), 4.59 (s, 2H), 7.33–7.39 (m, 2H), 7.80–7.86 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 21.6, 52.5, 64.5, 128.1 (2C), 129.9 (2C), 132.5, 145.3, 166.4.

A typical procedure for the synthesis of methyl (*Z*)-3-methoxy-2-(tosyloxy)acrylate (5a-1) [Method *D*]

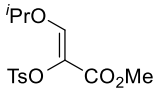
Et_3N (13.3 mL, 96 mmol) and $TiCl_4$ (9.90 mL, 90 mmol) were successively added to a stirred solution of methyl tosyloxyacetate (**4a**; 4.90 g, 20 mmol) and methyl formate (**2a**; 3.00 g, 50 mmol) in CH_2Cl_2 (80 mL) at –45 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Then, the mixture was poured into ice-water, which was extracted twice with Et_2O. The organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 6:1 ~ 3:1) to give the desired product **5a-1** (4.00 g, 70%).



Pale yellow crystals; mp 89 – 93 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.45 (s, 3H), 3.65 (s, 3H), 3.82 (s, 3H), 7.28 (s, 1H), 7.32–7.36 (m, 2H), 7.86–7.91 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.6, 52.0, 62.8, 121.7, 128.4 (2C), 129.5 (2C), 133.6, 144.9, 153.0, 163.2; IR (neat): ν_{max} = 1707, 1653, 1540, 1372, 1256, 1103, 957, 777 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{12}H_{14}O_6S$ [*M* + Na]$^+$ 309.0409; found: 309.0399.

Methyl (*Z*)-3-isopropoxy-2-(tosyloxy)acrylate (5a-2)

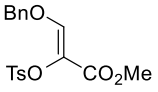
Following the procedure for the preparation of **5a-1**, the reaction of methyl tosyloxyacetate (**4a**; 244 mg, 1.0 mmol) with isopropyl formate (**2b**; 264 mg, 2.5 mmol), using Et_3N (665 μL, 4.8 mmol) and $TiCl_4$ (504 μL, 4.6 mmol) in CH_2Cl_2 (4 mL) gave the desired product **5a-2** (226 mg, 72%).



Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.20 (d, *J* = 6.3 Hz, 6H), 2.45 (s, 3H), 3.69 (s, 3H), 4.16 (sept, *J* = 6.3 Hz, 1H), 7.30–7.34 (2H, m), 7.36 (s, 1H), 7.86–7.90 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 21.3, 21.8 (2C), 51.5, 79.0, 120.8, 128.2 (2C), 129.1 (2C), 133.9, 144.7, 150.2, 163.3; IR (neat): ν_{max} = 1728, 1657, 1595, 1435, 1393, 1369, 1298, 1233, 1180 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{14}H_{18}O_6S$ [*M* + Na]$^+$ 337.0722; found: 337.0713.

Methyl (*Z*)-3-(benzyloxy)-2-(tosyloxy)acrylate (5a-3)

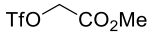
Following the procedure for the preparation of **5a-1**, the reaction of methyl tosyloxyacetate (**4a**; 244 mg, 1.0 mmol) with benzyl formate (**2c**; 340 mg, 2.5 mmol), using Et_3N (665 μL, 4.8 mmol) and $TiCl_4$ (504 μL, 4.6 mmol) in CH_2Cl_2 (4 mL) gave the desired product **5a-3** (257 mg, 71%).



Yellow crystals; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.40 (s, 3H), 3.78 (s, 3H), 4.98 (s, 2H), 7.20–7.31 (m, 3H), 7.34–7.44 (m, 4H), 7.81–7.90 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 21.5, 51.8, 76.6, 121.5, 127.6 (2C), 128.2 (2C), 128.6 (2C), 128.7, 129.2 (2C), 133.8, 134.7, 144.8, 151.1, 163.2; IR (neat): ν_{max} = 2953, 1728, 1658, 1371, 1174, 1090, 723, 664 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{18}H_{18}O_6S$ [*M* + Na]$^+$ 385.0722; found: 385.0720.

Methyl trifluoromethylsulfonyloxy acetate (4b)[23]

Tf_2O (10.0 g, 35 mmol) was added to a stirred solution of methyl glycolate (2.66 g, 30 mmol) and *i*Pr_2NEt (4.58 g, 35 mmol) in CH_2Cl_2 (15 mL) at –20 °C, followed by being stirred for 1 h. Water was added to the stirred mixture, which was extracted twice with EtOAc. The organic phase was washed with 1 M-HCl aq., sat. $NaHCO_3$ aq., brine, dried (Na_2SO_4) and consentrated. The obtained crude product was purified by SiO_2-columun chromatography (hexane-AcOEt = 6:1) to give the desired product (**4b**; 6.1 g, 93%).

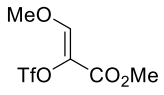


Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.88 (s, 3H), 4.92 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.9, 68.9, 118.4 (q, J_{C-F} = 323 Hz), 165.0.

A typical procedure for the synthesis of methyl (*Z*)-3-methoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (5b-1) [Method *E*]

Bu_3N (6.20 mL, 26 mmol) and $TiCl_4$ (2.60 mL, 24 mmol) were successively added to a stirred solution of a methyl trifluoromethylsulfonyloxyacetate (**4b**; 2.20 g, 10

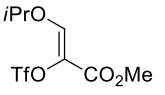
mmol) and methyl formate (**2a**; 1.50 g, 25 mmol in CH_2Cl_2 (20 mL) at –78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 10 min at that temperature. The mixture was warmed up to 0 – 5 °C, followed by being stirred at the same temperature for 1 h. Then, the mixture was poured into ice-water, which was extracted twice with Et_2O. The organic phase was washed with water, 1 M-HCl aq., sat. $NaHCO_3$ aq., brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 6:1) to give the desired product **5b-1** (1.80 g, 70%).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.82 (s, 3H), 3.97 (s, 3H), 7.38 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.0, 63.1, 118.4 (q, $J_{C\text{-}F}$ = 320 Hz), 121.7, 153.0, 161.6 ; IR (neat): ν_{max} = 1666, 1419, 1261, 1202, 1137, 1103, 976, 896, 729 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_6H_7F_3O_6S$ [*M* + Na]$^+$ 286.9813; found: 286.9805.

Methyl (*Z*)-3-isopropoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (5b-2)

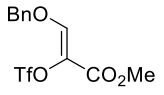
Following the procedure for the preparation of **5b-1**, the reaction of methyl trifluoromethylsulfonyloxy acetate (**4b**; 222 mg, 1.0 mmol) with isopropyl formate (**2b**; 220 mg, 2.5 mmol), using Bu_3N (618 μL, 2.6 mmol) and $TiCl_4$ (263 μL, 2.4 mmol) in CH_2Cl_2 (2 mL) gave the desired product **5b-2** (190 mg, 65%).



Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.38 (d, *J* = 6.3 Hz, 6H), 3.82 (s, 3H), 4.37 (sept, *J* = 6.3 Hz, 1H), 7.49 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 22.1 (2C), 52.1, 80.5, 118.4 (q, $J_{C\text{-}F}$ = 320 Hz), 121.9, 150.4, 162.0; IR (neat): ν_{max} = 1728, 1661, 1420, 1391, 1381, 1331, 1308, 1217 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_8H_{11}F_3O_6S$ [*M* + Na]$^+$ 315.0126; found: 315.0121.

Methyl (*Z*)-3-(benzyloxy)-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (5b-3)

Following the procedure for the preparation of **5b-1**, the reaction of methyl trifluoromethylsulfonyloxy acetate (**4a**; 111 mg, 0.5 mmol) with benzyl formate (**2c**; 177 mg, 1.3 mmol), using Bu_3N (309 μL, 1.3 mmol) and $TiCl_4$ (132 μL, 1.2 mmol) in CH_2Cl_2 (1 mL) gave the desired product **5b-3** (122 mg, 71%).



Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.79 (s, 3H), 5.15 (s, 2H), 7.28–7.47 (m, 5H), 7.49 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.0, 77.4, 118.4 (q, $J_{C\text{-}F}$ = 320 Hz), 122.1, 127.8 (2C), 128.7 (2C), 129.0, 134.2, 151.1, 161.5; IR (neat): ν_{max} = 2957, 1731, 1663, 1419, 1202, 1136, 1103, 974, 723 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{12}H_{11}O_3F_3S$ [*M* + Na]$^+$ 363.0126; found: 363.0130.

General procedure for the (*Z*)-stereoretentive Suzuki-Miyaura cross-coupling using halo esters 3 and sulfonyl oxy esters 5

[Method *A*]

A mixture of an α-chloroacrylate (**3a**; 0.5 mmol) was added to a stirred suspension of an aryl boronic acid (0.75 mmol), $Pd(OAc)_2$ (6 mg, 0.025 mmol), PCy_3 (28 mg 0.1 mmol), and K_2CO_3 (207 mg, 1.5 mmol.) in THF / H_2O (10 : 1) (1.5 mL) at room temperature. The mixture was heated at 110 °C under an Ar atmosphere for 3 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 10:1) to give the desired product **6a** - **6e**.

[Mehod *B*]

A mixture of **3b**, **5a** or **5b** (0.5 mmol) was added to a stirred suspension of an aryl boronic acid (0.75 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 0.025 mmol), and K_2CO_3 (207 mg, 1.5 mmol) in *i*PrOH (1.5 mL) at room temperature. The mixture was heated at 90 °C under an Ar atmosphere for 2 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 10:1) to give the desired product **6a** - **6e**.

[Mehod *C*]

A mixture of α-iodoacrylate (**3c**; 0.5 mmol) was added to a stirred suspension of an aryl boronic acid (0.75 mmol), $Pd(dppe)Cl_2$ (15 mg, 0.025 mmol), and K_2CO_3 (207 mg, 1.5 mmol) in *i*PrOH (1.5 mL) at room temperature. The mixture was heated at 90 °C under an Ar atmosphere for 3 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 10:1) to give the desired product **6a** - **6e**.

General procedure for the (*Z*)-stereoretentive Negishi cross-coupling using halo esters 3 and sulfonyloxy esters 5

[Method *A*]

An ArMgBr (3.0 mmol) in THF was added to a stirred solution of $ZnCl_2$ (408 mg, 3.0 mmol) in THF (2.0 mL) at 0 – 5 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. α-Tosyloxy ester **5a** (0.5 mmol) and $Pd(dppp)Cl_2$ (18 mg, 0.03 mmol) were successively added to the mixture, followed by being stirred at 40 – 45 °C for 2 h. 1M-HCl aq. solution was added to the mixture, which was extracted twice with AcOEt. The obtained organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 15:1) to give the desired product **6a** - **6e**.

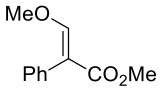
[Method *B*]

An ArMgBr (2.0 mmol) in THF was added to a stirred solution of $ZnCl_2$ (273 mg, 2.0 mmol) in THF (2.0 mL) at 0 – 5 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 0.5 h. α-Trifluoromethanesulfonyloxy ester **5b** (0.5 mmol) and $Pd(dppp)Cl_2$ (18 mg, 0.03 mmol) were successively added

to the mixture, followed by being stirred at 40 – 45 °C for 24 h. 1M-HCl aq. solution was added to the mixture, which was extracted twice with AcOEt. The obtained organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 15:1) to give the desired product **6a** - **6e**.

Methyl (*E*)-2-phenyl-3-methoxy-2-propeonate (6a)[19]

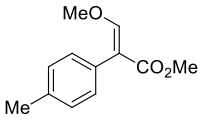
Following the procedure for Suzuki-Miyaura cross-coupling (Method *A*), the reaction of methyl (*Z*)-2-chloro-3-methoxyacrylate (**3a-1**; 75 mg, 0.5 mmol) with phenylboronic acid (91 mg, 0.75 mmol), using $Pd(OAc)_2$ (6 mg, 0.025 mmol), PCy_3 (28 mg, 0.05 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in THF / H_2O (10 : 1) (1.5 mL) gave the desired product **6a** (89 mg, 93%) (Table 3, entry 1).



Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.74 (s, 3H), 3.84 (s, 3H), 7.23–7.39 (m, 5H), 7.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 51.3, 61.7, 111.4, 126.9, 127.6 (2C), 130.0 (2C), 132.4, 159.5, 168.0.

Methyl (*E*)-2-(4-methylphenyl)-3-methoxy-2-propeonate (6b)[15a]

Following the procedure for Suzuki-Miyaura cross-coupling (Method *C*), the reaction of methyl (*Z*)-2-iodo-3-methoxyacrylate (**3c-1**; 61 mg, 0.25 mmol) with 4-methylphenylboronic acid (51 mg, 0.38 mmol), using $Pd(dppe)Cl_2$ (7 mg, 0.013 mmol) and K_2CO_3 (104 mg, 0.75 mmol) in *i*PrOH (0.75 mL) gave the desired product **6b** (89 mg, 93%) (Table 3, entry 8).

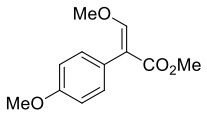


Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.34 (s, 3H), 3.73 (s, 3H), 3.84 (s, 3H), 7.13–7.19 (m, 2H), 7.20–7.24 (m, 2H), 7.53 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.1, 51.4, 61.8, 111.4, 128.5 (2C), 129.4, 129.9 (2C), 136.7, 159.4, 168.2.

Methyl (*E*)-2-(4-methoxylphenyl)-3-methoxy-2-propeonate (6c)[19]

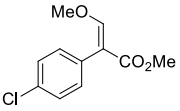
Following the procedure for Suzuki-Miyaura cross-coupling (Method *A*), the reaction of methyl (*Z*)-2-chloro-3-methoxyacrylate (**3a-1**; 75 mg, 0.5 mmol) with 4-methoxyphenylboronic acid (114 mg, 0.75 mmol), using $Pd(OAc)_2$ (6 mg, 0.025 mmol), PCy_3 (28 mg, 0.05 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in THF / H_2O (10 : 1) (1.5 mL) gave the desired product **6c** (104 mg, 94%) (Table 3, entry 10).

Yellow crystals; mp 58 – 62 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.72 (s, 3H), 3.79 (s, 3H), 3.82 (s, 3H), 6.81–6.94 (m, 2H), 7.18–7.31 (m, 2H), 7.51 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 51.5, 55.1, 61.8, 111.0, 113.2 (2C), 124.7, 131.2 (2C), 158.5, 159.1, 168.3.



Methyl (*E*)-2-(4-chlorophenyl)-3-methoxy-2-propeonate (6d)[24]

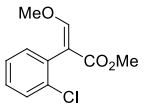
Following the procedure for Suzuki-Miyaura cross-coupling (Method *B*), the reaction of methyl (*Z*)-3-methoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (**5b-1**; 396 mg, 1.5 mmol) with 4-chlorophenylboronic acid (352 mg, 2.25 mmol), using $Pd(PPh_3)_2Cl_2$ (53 mg, 0.075 mmol) and K_2CO_3 (622 mg, 4.5 mmol) in *i*PrOH (4.5 mL) gave the desired product **6d** (316 mg, 93%) (Table 3, entry 17).



Yellow crystals; mp 61 – 62 °C(lit.[24] 61 – 62 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.73 (s, 3H), 3.85 (s, 3H), 7.25–7.31 (m, 4H), 7.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 51.6, 62.0, 110.4, 127.9 (2C), 130.9, 131.4 (2C), 132.8, 159.8, 167.6.

Methyl (*E*)-2-(2-chlorophenyl)-3-methoxy-2-propeonate (6e)[25]

Following the procedure for Suzuki-Miyaura cross-coupling (Method *B*), the reaction of methyl (*Z*)-3-methoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (**5b-1**; 396 mg, 1.5 mmol) with 2-chlorophenylboronic acid (59 mg, 0.375 mmol), using $Pd(PPh_3)_2Cl_2$ (9 mg, 0.013 mmol) and K_2CO_3 (104 mg, 0.75 mmol) in *i*PrOH (0.75 mL) gave the desired product **6e** (47 mg, 83%) (Table 3, entry 21).



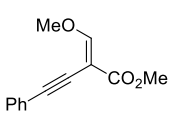
Yellow crystals; mp 55 – 56 °C (lit.[25] 61 – 62 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.71 (s, 3H), 3.85 (s, 3H), 7.20–7.51 (m, 4H), 7.57 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 51.6, 62.0, 109.7, 126.3, 128.9, 129.2, 131.9, 132.2, 134.4, 160.3, 167.5.

General procedure for the (*Z*)-stereoretentive Sonogashira cross-coupling using 3 or 5

An alkyne (1.0 mmol) and *i*Pr_2NEt (0.25 mL, 1.47 mmol) were added to a stirred solution of α-trifluoromethanesulfonyloxy ester **5b** (0.25 mmol), CuI (7 mg, 0.38 mmol), and $Pd(dppf)Cl_2$ (9 mg, 0.13 mmol) in THF (0.25 mL) at c.a. 80 °C under an Ar atmosphere, and the mixture was stirred at same temperature for 14 h. Water was added to the mixture, which was extracted with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 30:1 ~ 25:1) to give the desired product **7a - 7d**.

Methyl (*E*)-3-methoxy-2-phenylethynyl-2-propeonate (7a)

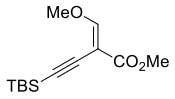
Following the procedure for Sonogashira cross-coupling (Method *B*), the reaction of methyl (*Z*)-3-methoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (**5b-1**; 198 mg, 0.75 mmol) with ethynylbenzene (306 mg, 3.0 mmol), using $Pd(PPh_3)_2Cl_2$ (27 mg, 0.04 mmol) and CuI (21 mg, 0.11 mmol) in THF (0.75 mL) / *i*Pr_2NEt (0.75 mL) gave the desired product **7a** (162 mg, 99%) (Table 5, entry 5).



Brown crystals; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.72 (s, 3H), 3.91 (s, 3H), 7.16–7.28 (m, 3H), 7.35–7.50 (m, 2H), 7.72 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 52.0, 62.6, 80.2, 95.3, 96.0, 123.2, 128.1 (3C), 131.4 (2C), 166.3, 166.5; IR (neat): ν_{max} = 2949, 1713, 1614, 1267, 1220, 1144, 1101, 756; HRMS (ESI): *m/z* calcd for $C_{13}H_{12}O_3$ $[M + Na]^+$ 239.0684; found: 239.0695.

Methyl (*E*)-2-*tert*-butyldimethylsilylethynyl-3-methoxy-2-propeonate (7b)

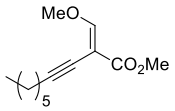
Following the procedure for Sonogashira cross-coupling (Method *B*), the reaction of methyl (*Z*)-3-methoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (**5b-1**; 66 mg, 0.25 mmol) with (*tert*-butyl)ethynyldimethylsilane (306 mg, 3.0 mmol), using $Pd(PPh_3)_2Cl_2$ (9 mg, 0.013 mmol) and CuI (21 mg, 0.11 mmol) in THF (0.25 mL) / *i*Pr_2NEt (0.25 mL) gave the desired product **7b** (104 mg, 89%) (Table 5, entry 6).



Yellow crystals; mp 77 – 79 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.15 (s, 6H), 0.97 (s, 9H), 3.75 (s, 3H), 3.97 (s, 3H), 7.67 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = -4.7 (2C), 16.7, 26.0 (3C), 51.9, 62.5, 95.6, 96.0, 100.1, 166.3, 167.5; IR (neat): ν_{max} = 2952, 2153, 1710, 1615, 1254, 1116, 909, 731; HRMS (ESI): *m/z* calcd for $C_{13}H_{22}O_3Si$ [*M* + Na]$^+$ 277.1236; found: 227.1228.

Methyl (*E*)-3-methoxy-2-(1-octinyl)-2-propeonate (7c)

Following the procedure for Sonogashira cross-coupling (Method *B*), the reaction of methyl (*Z*)-3-methoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (**5b-1**; 132 mg, 0.5 mmol) with 1-octyne (164 mg, 2 mmol), using $Pd(PPh_3)_2Cl_2$ (18 mg, 0.025 mmol) and CuI (29 mg, 0.15 mmol) in THF (0.5 mL) / *i*Pr_2NEt (0.5 mL) gave the desired product **7c** (78 mg, 80%) (Table 5, entry 7).

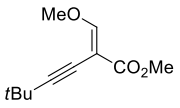


Brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.81 (t, *J* = 6.5 Hz, 3H), 1.13–1.30 (m, 4H), 1.30–1.42 (m, 2H), 1.43–1.59 (m, 2H), 2.33 (t, *J* = 6.8 Hz, 2H), 3.67 (s, 3H), 3.87 (s, 3H), 7.54 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.8, 19.6, 22.3, 28.3, 28.5, 31.1, 51.7, 62.1, 70.9, 95.6, 97.3, 165.6, 166.5; IR (neat): ν_{max} = 2932, 2856, 1714, 1616, 1254, 1192, 1122, 765; HRMS (ESI): *m/z* calcd for $C_{13}H_{20}O_3$ [*M* + Na]$^+$ 247.1310; found: 247.1322.

Methyl (*E*)-2-*tert*-butylethynyl-3-methoxy-2-propeonate (7d)

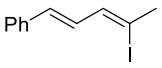
Following the procedure for Sonogashira cross-coupling (Method *B*), the reaction of methyl (*Z*)-3-methoxy-2-(((trifluoromethyl)sulfonyl)oxy)acrylate (**5b-1**; 132 mg, 0.5 mmol) with 1-octyne (280 mg, 2 mmol), using $Pd(PPh_3)_2Cl_2$ (18 mg, 0.025 mmol) and CuI (14 mg, 0.075 mmol) in THF (0.5 mL) / *i*Pr_2NEt (0.5 mL) gave the desired product **7d** (106 mg, 83%) (Table 5, entry 8).

Colorless crystals; mp 50 – 52 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.30 (s, 9H), 3.75 (s, 3H), 3.94 (s, 3H), 7.59 (s, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 28.2, 30.9 (3C), 51.8, 62.2, 69.5, 95.6, 105.4, 165.4, 166.8; IR (neat): ν_{max} = 2968, 1707, 1612, 1436, 1371, 1241, 1116, 999, 766; HRMS (ESI): *m/z* calcd for $C_{11}H_{16}O_3$ [*M* + Na]$^+$ 219.0997; found: 219.1006.



((1*E*,3*Z*)-4-Iodopenta-1,3-dien-1-yl)benzene (8)[26]

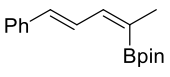
*n*BuLi (1.6 M in hexane, 2.09 mL, 3.34 mmol) was added to a stirred suspension of (ethyl)triphenylphosphonium iodide (1.40 g, 3.34 mmol) in THF (17 mL) at 20 – 25°C, followed by being stirred at the same temperature for 10 min. The mixture was added to a stirred solution of iodine (589 mg, 2.50 mmol) in THF (20 mL) at –78 °C. After stirring at –78 ˚C for an additional 5 min, the suspension was warmed to 0 °C, then NaHMDS (1 M in THF, 2.50 mL, 2.50 mmol) was added. After stirring at 0–5 ˚C for an additional 5 min, *trans*-cinnamaldehyde (210 μL, 1.67 mmol) was added, followed by being stirred at the same temperature for 1 h. The mixture was quenched with sat. NH_4Cl aq., which was filtered through Celite®. The obtained filtrate was extracted twice with Et_2O. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane) to give the desired product (**8**; 337 mg, 70%, *E* / *Z* = 4 / 96).



Pale yellow crystals; mp 51 – 52 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.64 (s, 3H), 6.23 (d, *J* = 9.7 Hz, 1H), 6.68 (d, *J* = 15.5 Hz, 1H), 6.82 (dd, *J* = 9.7, 15.5 Hz, 1H), 7.22–7.27 (m, 1H), 7.30–7.36 (m, 2H), 7.42–7.48 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 34.1, 102.5, 126.6 (2C), 127.9, 128.6 (2C), 131.0, 134.3, 134.4, 137.0; IR (neat): ν_{max} = 2901, 1572, 1485, 1447, 1437, 1427, 1288, 1236; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}I$ [*M* + Na]$^+$ 292.9803; found: 292.9805.

4,4,5,5-Tetramethyl-2-((2*E*,4*E*)-5-phenylpenta-2,4-dien-2-yl)-1,3,2-dioxaborolane (9)

A mixture of dienyl iodide (**8**; 135 mg, 0.5 mmol) was added to a stirred suspension of bis(pinacolato)diboron (381 mg, 1.5 mmol), $Pd(dppf)Cl_2$ (37 mg 0.05 mmol), and KOH (42 mg, 0.75 mmol.) in 1,4-dioxane (3.0 mL) at room temperature. The mixture was hearted at reflux under an Ar atmosphere for 2 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 50:1) to give the desired product (**9**; 76 mg, 56%).

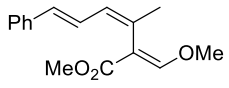


Pale yellow crystals; mp 74 – 76 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.33 (s, 12H), 1.95 (s, 3H), 6.52 (d, *J* = 15.5 Hz, 1H), 6.76 (d, *J* = 10.9 Hz, 1H), 7.19–7.24 (m, 1H), 7.29–7.34 (m, 2H), 7.39–7.44 (m, 1H), 7.65 (dd, *J* = 10.9, 15.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 22.7 (2C), 24.9 (4C), 83.1, 126.5 (2C), 127.3, 128.5 (2C), 129.1, 133.3 (2C), 137.8, 145.4; IR (neat): ν_{max} = 1715, 1680, 1626, 1599, 1485, 1447, 1371, 1325; HRMS (ESI): *m/z* calcd for $C_{17}H_{23}O_2B$ [*M* + Na]$^+$ 293.1692; found: 293.1689.

Methyl (2*E*,3*Z*,5*E*)-2-(methyoxymethylene)-3-methyl-6-phenylhexa-3,5-dienoate: strobilurin A[14c]

A mixture of α-trifluoromethanesulfonyloxy ester **5b** (53 mg, 0.2 mmol) was added to a stirred suspension of dienylborate **9** (54 mg, 0.2 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), and K_2CO_3 (83 mg, 0.6 mmol.) in *i*PrOH (1.2 mL) and H_2O (0.4 mL) at room temperature. The mixture was hearted at reflux under an Ar atmosphere for 2 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with

water, brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by SiO_2-column chromatography (hexane-AcOEt = 10:1) to give the desired product (**10**; 41 mg, 79%).



Pale yellow oil; ^{1}H NMR (500 MHz, acetone-6d) δ = 1.93 (d, *J* = 1.2 Hz, 3H), 3.67 (s, 3H), 3.90 (s, 3H), 6.20 (dq, *J* = 1.2, 10.3 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.72 (dd, *J* = 10.3, 16.0 Hz, 1H), 7.17–7.22 (m, 1H), 7.27–7.34 (m, 2H), 7.38–7.42 (m, 2H), 7.49 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 22.9, 51.3, 62.1, 111.0, 126.9 (2C), 127.9, 128.0, 129.4 (2C), 130.3, 131.2, 132.5, 138.8, 160.0, 167.6; IR (neat): ν_{max} = 1703, 1624, 1489, 1433, 1395, 1373, 1234, 1188; HRMS (ESI): *m/z* calcd for $C_{16}H_{18}O_3$ [*M* + Na]$^+$ 281.1154; found: 281.1154. Physical properties of the present synthetic strobilurin A exhibited in good agreement with those derived from natural and synthetic specimens (^{1}H and ^{13}C NMRs).[14c]

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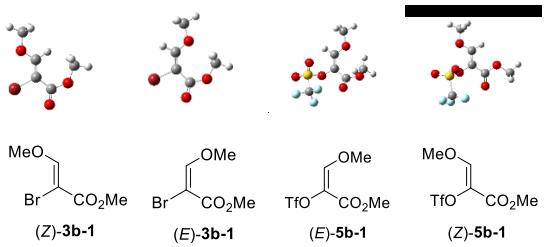

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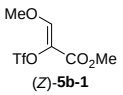

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Update

Dehydration-type Ti-Claisen Condensation (Carbonhomologation) of α-Heteroatom-substituted Acetates with Alkyl Formates: Utilization as Novel (*Z*)-Stereodefined Cross-coupling Partners and Application to Concise Synthesis of Strobilurin A

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