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ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 10345–10353

Facile stereoselective synthesis of (*E*)- and (*Z*)-α-substituted cinnamates: stereospecific dehydration reaction with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and copper(II) chloride

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Received 11 June 2007; revised 12 July 2007; accepted 17 July 2007
Available online 27 July 2007

Abstract—A highly stereoselective method for the synthesis of (*E*)- and (*Z*)-α-substituted cinnamates in good yield has been achieved by dehydration reaction of *anti*- and *syn*-α-substituted-β-hydroxyphenylpropiolate using EDC. This facile method has been used to synthesize various (*E*)- and (*Z*)-α-substituted cinnamates and (*E*)- and (*Z*)-α-alkylidene-γ-butyrolactones. The reaction mechanism of this highly stereospecific dehydration using EDC can be elucidated by the ω-dimethylamino group of EDC, which is believed to facilitate the deprotonation step.

1. Introduction

Trisubstituted olefins represent an important class of compounds since they are found in a wide variety of natural products and serve as valuable building blocks for the synthesis of various types of natural products and biologically important substances.[1] Highly stereoselective construction of trisubstituted olefins is one of the most challenging problems in synthetic organic chemistry.[2] Since trisubstituted olefins bearing an electron-withdrawing group of *E* geometry are thermodynamically more stable than their *Z* counterparts, they are rather easy to come by. However, the methods available for moderate to highly stereoselective preparation of (*Z*)-trisubstituted olefins are rather limited.

In the course of our synthetic studies and extensive search for biologically active compounds, we needed a facile stereoselective method for the synthesis of (*E*)- and (*Z*)-α-substituted cinnamates. The simplest method we could hit upon was E2 elimination reaction of the corresponding *syn*- and *anti*-β-hydroxyesters. Indeed, stereoselective (*E*)-α-substituted cinnamates were obtained in high yield from the corresponding *syn*-β-hydroxyesters by E2 elimination reaction.

However, preparation of (*Z*)-α-substituted cinnamates from the corresponding *anti*-β-hydroxyesters was not stereoselective (vide infra).[3] This is probably due to the fact that α-proton of the β-hydroxyester is too acidic for E2 elimination reaction to compete with E1cB elimination reaction.[4] Therefore, the thermodynamically stable (*E*)-α-substituted cinnamates were obtained predominantly. Similar results have been reported in the synthesis of α-benzylidene-γ-butyrolactones[5] and α-benzylideneketones.[6] In order to solve this problem, three methods based on Honer–Emmons reaction,[7] Baylis–Hillman reaction,[8] and the reductive elimination reaction of *syn*-β-hydroxy-α-phenylthioester[9] have been reported. However, these methods have disadvantages, such as the use of expensive and not easily accessible reagents, and limitation of substituents at the α-position. Meanwhile, Corey and Letavic have reported that (*E*)- and (*Z*)-α-alkylidene-γ-butyrolactones can stereoselectively be synthesized by dehydration reaction of the corresponding *anti*- and *syn*-α-(1′-hydroxyalkyl)-γ-butyrolactones with *N*,*N*′-dicyclohexylcarbodiimide (DCC) and $CuCl_2$.[10] In this case the isourea-mediated six membered cycloelimination reaction proceeds stereoselectively to provide the (*E*)- and (*Z*)-α-substituted cinnamates from the *anti*- and *syn*-α-substituted-β-hydroxyphenylpropionates, respectively. Recently, we have reported a facile method for the stereoselective synthesis of (*E*)- and (*Z*)-α-substituted cinnamates based on stereoselective dehydration of the easily accessible *anti*- and *syn*-α-substituted-β-hydroxyphenylpropionates by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide

Keywords: α-Substituted cinnamates; α-Alkylidene-γ-butyrolactones; Stereospecific dehydration; *syn*-Elimination; Carbodiimide.
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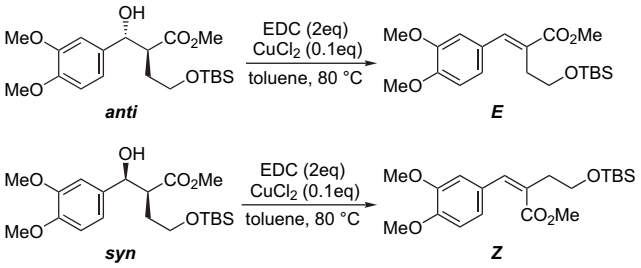
0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.07.069

(EDC) (Scheme 1).[11] Herein we describe in detail our study on the highly stereospecific dehydration of (*E*)- and (*Z*)-α-substituted cinnamates using EDC and the possible reaction mechanism.



Scheme 1. Stereospecific dehydration reaction with EDC and $CuCl_2$.

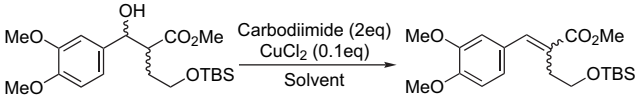
2. Results and discussion

Detail of dehydration reaction of the *anti*- and *syn*-β-hydroxyesters **1** with carbodiimides under different conditions are summarized in Table 1. Dehydration reaction of the *anti*-β-hydroxyester ***anti*-1** with DCC in Et_2O at 35 °C selectively gave the (*E*)-cinnamate ***E*-2** (Entry 1). This reaction proceeded more easily in toluene at 80 °C (Entry 3). However, dehydration reaction of the *syn*-β-hydroxyester ***syn*-1** with DCC in Et_2O at 35 °C did not proceed, instead, isomerization of ***syn*-1** took place (Entry 2). The inversion reaction of secondary alcohol for DCC and CuCl was reported.[12] In toluene at 80 °C, dehydration reaction of ***syn*-1** provided a 2:1 mixture of the *E*- and *Z*-cinnamates in 45% yield although the *Z*-cinnamate had been expected to be the major product if the reaction proceeded in a stereospecific fashion (Entry 4). Because the (*Z*)-isomer obtained did not isomerize to the (*E*)-isomer under our reaction conditions,[13] we considered that isomerization of ***syn*-1** into ***anti*-1** took place before dehydration reaction leading to a mixture of the corresponding cinnamates. In order to avoid isomerization by trapping the liberated water molecule from **1**, we added the molecular sieve 4A into the reaction system. Although the effect of this addition was small, the ratio and yield of ***Z*-2** were improved (Entry 5). Next, we considered that the desired (*Z*)-cinnamate ***Z*-2** can selectively be obtained using an appropriate carbodiimide that promotes the elimination reaction to proceed sufficiently faster than the isomerization reaction. Thus, we examined the sterically less hindering *N*,*N*′-diisopropylcarbodiimide (DIPC) and EDC. Indeed, DIPC improved both the ratio and yield of ***Z*-2**, however, this improvement was unsatisfactory (Entry 6). On the other hand, dehydration reaction of ***anti*-1** and ***syn*-1** with EDC was highly stereospecific giving ***E*-2** and ***Z*-2**, respectively, in high yields (Entries 7 and 8).

With these promising results in hand, we next examined the optimal reaction conditions. The reaction was first examined in toluene at 25, 50, and 100 °C (Table 2). At the low temperatures (25 and 50 °C) the reaction needed rather a long period of time to complete, and both the yield and selectivity were lower than those at 80 °C (Entries 2 and 3). Almost the same yield and selectivity as those obtained at 80 °C were observed when the reaction was carried out at 100 °C (Entry 4).

The reaction was also examined with various solvents at 80 °C or under refluxing conditions (Table 3). In all cases,

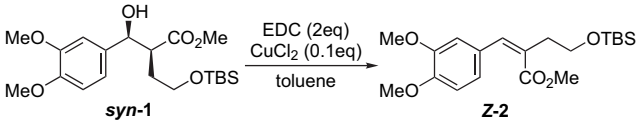
Table 1. Dehydration reaction of **1** with carbodiimide and $CuCl_2$



Entry	Substrate	Carbodiimide	Solvent	Temperature (°C)	Time (h)	Yield[a] (%)	*Z*:*E*[b]
1	***anti*-1**	DCC	Et_2O	35	24	52	1:>99
2	***syn*-1**	DCC	Et_2O	35	24	N.D.[c]	
3	***anti*-1**	DCC	Toluene	80	2	73	1:>99
4	***syn*-1**	DCC	Toluene	80	2	45	33:67
5[d]	***syn*-1**	DCC	Toluene	80	2	63	47:53
6	***syn*-1**	DIPC	Toluene	80	2	41	44:56
7	***anti*-1**	EDC	Toluene	80	2	95	1:>99
8	***syn*-1**	EDC	Toluene	80	2	95	96:4

[a] Combined isolated yield of (*Z*)- and (*E*)-cinnamates.
[b] Determined by ^{1}H NMR measurement of the crude mixture.
[c] ***anti*-1** was isolated in 23% yield and ***syn*-1** was recovered in 30% yield.
[d] Moleculer sieve 4A was used as an additive.

Table 2. Effect of temperature on dehydration reaction of ***syn*-1** with EDC and $CuCl_2$



Entry	Solvent	Temperature (°C)	Time (h)	Yield[a] (%)	*Z*:*E*[b]
1	Toluene	80	2	95	96:4
2	Toluene	25	96	45	88:12
3	Toluene	50	16	69	92:8
4	Toluene	100	2	94	95:5

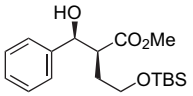
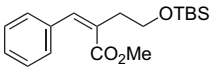
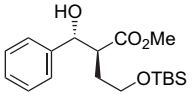
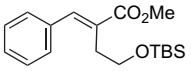
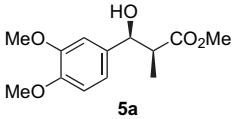
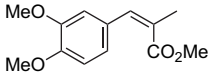
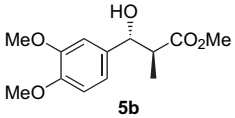
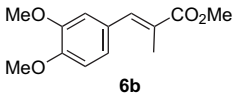
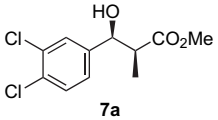
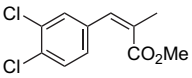
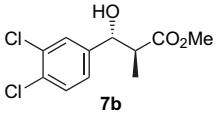
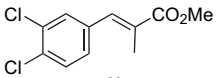
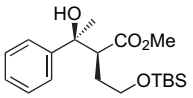
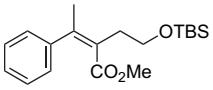
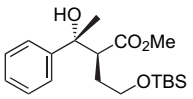
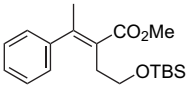
[a] Combined isolated yields of (Z)- and (*E*)-cinnamates.
[b] Determined by ^{1}H NMR measurement of the crude mixture.

Table 3. Effect of solvent on dehydration reaction of ***syn*-1** with EDC and $CuCl_2$

Entry	Solvent	Temperature (°C)	Time (h)	Yield[a] (%)	*Z*:*E*[b]
1	Toluene	80	2	95	96:4
2	$(CH_2Cl)_2$	80	2	67	70:30
3	CH_2Cl_2	40	30	50	78:22
4	AcOEt	80	2	46	85:15
5	^{t}BuOMe	55	24	31	95:5
6	THF	65	2	46	81:19
7	$^i Pr_2O$	70	4	22	66:34
8	Et_2O	35	30	21	86:14
9	Dioxane	80	2	38	85:15
10	DME	80	2	31	75:25
11	DMF	80	2	8	70:30
12	CH_3CN	80	2	57	71:29

[a] Combined isolated yields of (*Z*)- and (*E*)-cinnamates.
[b] Determined by ^{1}H NMR measurement of the crude mixture.

Table 4. Stereoselective synthesis of cinnamate with EDC and $CuCl_2$

Entry	Substrate	Carbodiimide	Product	Yield[a] (%)	*Z*:*E*[b]
1	 **3a**	EDC	 **4a**	60	86:14
2		EDC (100 °C)		99	>99:1
3		DCC		32	25:75
4	 **3b**	EDC	 **4b**	99	1:>99
5	 **5a**	EDC	 **6a**	52	75:25
6		EDC (100 °C)		72	79:21
7		DCC		24	20:80
8	 **5b**	EDC	 **6b**	80	1:>99
9	 **7a**	EDC	 **8a**	50	86:14
10		EDC (100 °C)		96	95:5
11		DCC		20	22:78
12	 **7b**	EDC	 **8b**	96	1:>99
13	 **9a**	EDC	 **10a**	N.D.	
14		EDC (100 °C)		4	>99:1
15		EDC (100 °C, 24 h)		18	>99:1
16	 **9b**	EDC	 **10b**	N.D.	
17		EDC (100 °C)		7	1:>99
18		EDC (100 °C, 24 h)		38	1:>99

Unless otherwise noted, reactions were carried out using carbodiimide (2 equiv) and $CuCl_2$ (0.1 equiv) in toluene at 80 °C for 2 h.
[a] Combined isolated yields of (*Z*)- and (*E*)-cinnamates.
[b] Determined by ^{1}H NMR measurement of the crude mixture.

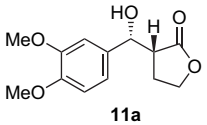
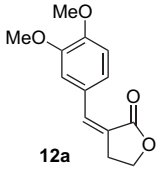
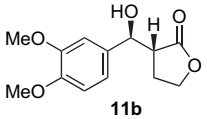
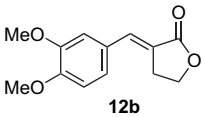
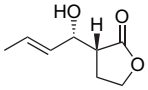
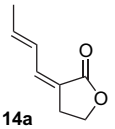
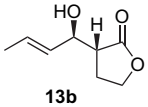
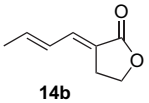
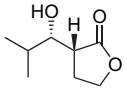
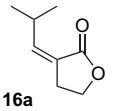
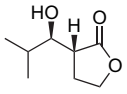
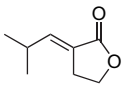
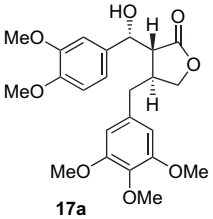
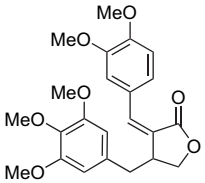
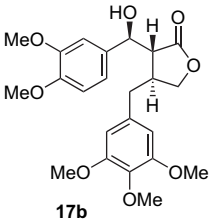
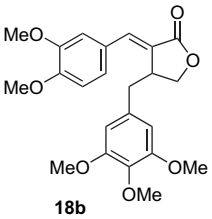
***Z*-2** was obtained predominantly. However, the new solvents only brought about results inferior to those obtained with toluene in terms of yield and stereoselectivity. Reactions at lower temperature were sluggish (Entries 3, 5, and 8). Thus, it was concluded that the reaction proceeds better in toluene at a temperature over 80 °C.

In order to clarify the scope and limitations of the present method, a variety of *anti*- and *syn*-α-substituted-β-hydroxyphenylpropionates were treated with EDC and DCC under various reaction conditions (Table 4). With EDC, the reaction stereoselectively proceeded to give the corresponding (*E*)- and (*Z*)-α-substituted cinnamates in moderate to good yields. In all cases, EDC was superior to DCC. The selectivity and yield decreased in the case of hydroxyester having a methyl group at α-position (Entries 5 and 9), indicating that a more sterically hindered substituent would be favorable for high selectivity. In the case where no good results were obtained at 80 °C, the yield and stereoselectivity were improved at 100 °C (Entries 2, 6, and 10). Tetrasubstituted alkenes were obtained with excellent stereoselectivity in spite of low yield (Entries 13–18).

Dehydration reactions in a variety of α-substituted lactones using EDC and DCC are shown in Table 5. With EDC, (*E*)- and (*Z*)-α-benzylidene-γ-butyrolactones and α-alkylidene-γ-butyrolactones were obtained stereoselectively in moderate to good yields. In all cases, EDC was superior to DCC. When comparing the products, the alkylidenes were obtained in low yield but with high selectivity (Entries 8 and 10). The β-substituted lactones **18a** and **18b** were obtained stereospecifically from the corresponding hydroxylactones **17a** and **17b** (Entries 11 and 12).

Based on these results, we considered the mechanism of the reaction. It has been assumed that dehydration reaction using

Table 5. Stereoselective synthesis of alkylidene-γ-butyrolactone with EDC and $CuCl_2$

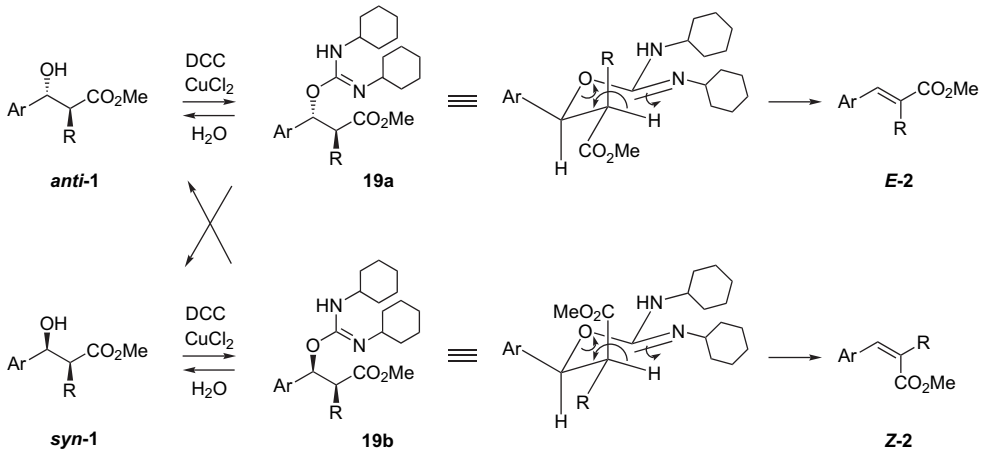
Entry	Substrate	Carbodiimide	Product	Yield[a] (%)	*Z*:*E*[b]
1	 **11a**	EDC	 **12a**	78	80:20
2		DCC		55	32:68
3	 **11b**	EDC	 **12b**	96	1:>99
4	 **13a**	EDC	 **14a**	62	94:6
5		DCC		49	22:78
6	 **13b**	EDC	 **14b**	62	1:>99
7	 **15a**	EDC	 **16a**	31	85:15
8		EDC (100 °C)		42	94:6
9		DCC		53	>99:1
10	 **15b**	EDC	 **16b**	89	1:>99
11	 **17a**	EDC	 **18a**	98	78:22
12	 **17b**	EDC	 **18b**	99	1:>99

Unless otherwise noted, reactions were carried out using carbodiimide (2 equiv) and $CuCl_2$ (0.1 equiv) in toluene at 80 °C for 2 h.

[a] Combined isolated yields of (*Z*)- and (*E*)-γ-butyrolactones.

[b] Determined by ^1H NMR measurement of the crude mixture.

DCC proceeds via a six membered cycloelimination of isourea (Scheme 2).[14] In the case of our reaction, the β-hydroxyesters ***anti*-1** and ***syn*-1** would condense with DCC in the presence of $CuCl_2$ to generate the isourea intermediates **19a** and **19b**, respectively.[15] The six membered cycloelimination reaction of **19a** would easily proceed to afford the ***E*-2**. On the other hand, the six membered cycloelimination reaction of **19b** would hardly proceed at 35 °C, therefore ***syn*-1** would not afford ***Z*-2**. As a result, substitution reaction of the hydroxyl group at the benzylic position[12] occurs and a mixture of ***anti*-1** and ***syn*-1** is obtained. At 80 °C, a mixture of ***E*-2** and ***Z*-2** is obtained because cycloelimination reaction of **19b** proceeds along that of **19a**, which is derived from the isomerized ***anti*-1**. The transition structure (**A**) from the intermediate **19a** and the transition structures (**B**) and (**C**) from the intermediate **19b** are shown in Figure 1. The producing π–π orbital could be conjugated with the aromatic π–π orbital and the carbonyl π–π orbital in the transition structure (**A**) because the aromatic group and the methoxycarbonyl group could be on the same plane



Scheme 2. Proposed reaction mechanism of dehydration reaction using DCC.

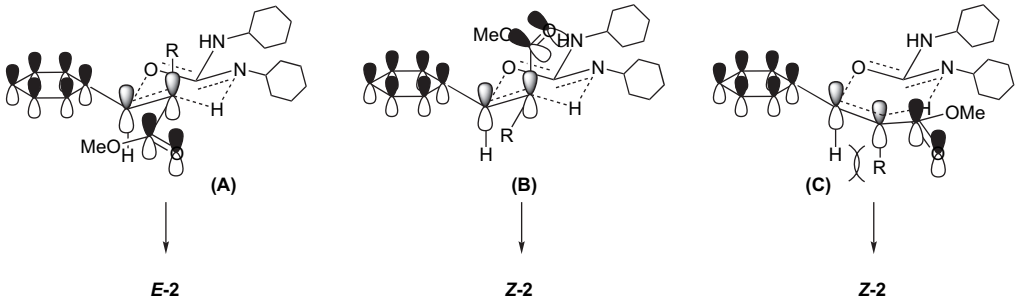
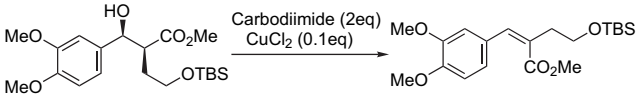


Figure 1. Postulated transition structure from intermediate **19a** and **19b**.

in chair conformation. On the other hand, the transition structures (**B**) and (**C**) could neither be in the same plane nor in chair conformation. Therefore, elimination reaction via (**A**) proceeds more easily than via (**B**) and (**C**) because energy level of (**A**) is sufficiently low, while that of (**B**) and (**C**) is high.

As dehydration reaction of ***anti*-1** and ***syn*-1** with EDC gave ***E*-2** and ***Z*-2** stereospecifically in high yields, we examined the high efficiency of EDC (Table 6). Unlike DCC, EDC possesses an intramolecular basic dimethylamino group. In order to clarify the role of this dimethylamino group in the high efficiency of EDC, we examined the dehydration reaction with DCC in the presence of triethylamine. The product obtained was a mixture of ***E*-2** and ***Z*-2**, but the selectivity was slightly improved (Entries 1 and 2). Deprotonation from the intermediate (**19b**) might have proceeded easily in the presence of triethylamine. Next, we examined dehydration with EDC·HCl, which lacks deprotonation ability. Since EDC·HCl did not dissolve in toluene, the reaction was performed in dichloroethane. EDC·HCl did not give better selectivity than EDC (Entries 3 and 4). This finding was as expected similar to the case of DCC. Although basic reaction conditions can facilitate the deprotonation step, DCC in the presence of triethylamine was not as effective as EDC. Therefore, it was concluded that the dimethylamino group plays an important role in the intramolecular deprotonation step.

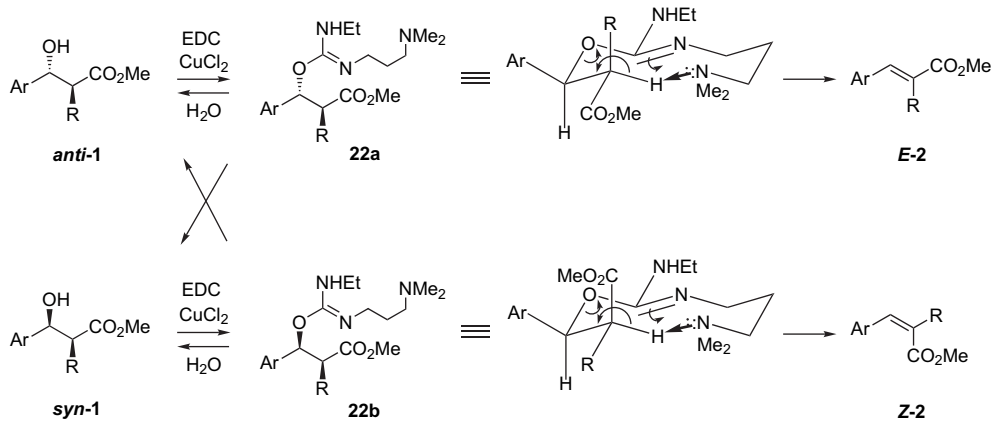
Table 6. Dehydration reaction of ***syn*-1** with carbodiimide and $CuCl_2$



Entry	Carbodiimide	Solvent	Temperature (°C)	Time (h)	Yield[a] (%)	*Z*:*E*[b]
1	DCC	Toluene	80	2	45	33:67
2	DCC (+Et_3N)	Toluene	80	2	37	60:40
3	EDC	$(CH_2Cl)_2$	80	2	67	70:30
4	EDC·HCl	$(CH_2Cl)_2$[c]	80	40	17	15:85
5	EDC	Toluene	80	2	95	96:4
6	(**20**)	Toluene	80	2	42	82:18
7	(**20**)	Toluene	80	8	91	81:19
8	(**21**)	Toluene	80	2	43	88:12
9	(**21**)	Toluene	80	8	87	89:11

[a] Combined isolated yields of (*Z*)- and (*E*)-cinnamates.
[b] Determined by ^1H NMR measurement of the crude mixture.
[c] $(CH_2Cl)_2$ was used since EDC·HCl did not dissolve in toluene.

In order to examine the effect of carbon chain length, we examined the dehydration reaction of ***syn*-1** with 1-ethyl-3-(2-dimethylaminoethyl)carbodiimide (**20**)[16] shortened by one carbon and 1-ethyl-3-(4-dimethylaminobutyl)carbodiimide (**21**) lengthened by one carbon, prepared from *N*,*N*-dimethyl-1,4-butanediamine and ethyl isothiocyanate according to a reported method.[17] The reaction with **20** proceeded more slowly than that with EDC and the selectively slightly was lowered (Entries 6 and 7). Almost the same phenomena were observed in the reaction with **21** (Entries 8 and 9). As shown in Table 6, the dimethylaminopropyl group afforded the best result in yield and selectivity.



Scheme 3. Proposed reaction mechanism of dehydration reaction using EDC.

From these results, the reaction mechanism can be elucidated as illustrated in Scheme 3. The ω-dimethylamino group in EDC does not only play the role of a base that facilitates the deprotonation step, but also participates in the six membered cycloelimination reaction to produce the [6,6]-bicyclic intermediate in **22a** and **22b**. The [6,6]-bicyclic intermediate shows strong deprotonation ability because energy level of the transition state is lowered to allow elimination reaction to proceed easily owing to the effective assistance by the intramolecular ω-dimethylamino group. Therefore, dehydration reaction with EDC can proceed considerably faster than that with DCC and another carbodiimide. As a result, the *anti*- and *syn*-β-hydroxyesters ***anti*-1** and ***syn*-1** could give the (*E*)- and (*Z*)-cinnamates ***E*-2** and ***Z*-2** stereospecifically in high yields.

3. Conclusion

In summary, a highly stereoselective method for the synthesis of (*E*)- and (*Z*)-α-substituted cinnamates and (*E*)- and (*Z*)-α-alkylidene-γ-butyrolactones was developed. It is noteworthy that the (*Z*)-α-substituted cinnamates and the (*Z*)-α-alkylidene-γ-butyrolactones, which had hitherto been difficult to obtain, could be stereoselectively synthesized in good yields. The mechanism of this highly stereospecific dehydration reaction using EDC can be elucidated by the ω-dimethylamino group of EDC, which not only plays a role in facilitating the deprotonation step but also participates in the formation of [6,6]-bicyclic intermediate in the six membered cycloelimination reaction.

4. Experimental

4.1. General

Melting points were measured using a Büchi 535 capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 1640 infrared spectrophotometer. ^{1}H spectra were recorded on a Bruker AC-200 spectrometer and a Bruker AVANCE 400 spectrometer with tetramethylsilane used as an internal standard. Mass spectra were recorded on a Hitachi M-2000A spectrometer. Silica gel column chromatography was performed with Kieselgel 60 (E. Merck). Thin-layer chromatography (TLC) was carried out on E. Merck 0.25-mm precoated glass-backed plates (60 F254). All solvents were dried by standard methods, and all reactions were carried out under an inert atmosphere.

4.1.1. Typical procedure for the dehydration reaction. A solution of β-hydroxyester (0.25 mmol) in toluene (10 mL) was treated with EDC (0.5 mmol) and $CuCl_2$ (0.025 mmol) at 80 °C for 2 h. The reaction mixture was quenched with water and the mixture was extracted with EtOAc. The organic layer was washed with aqueous citric acid, aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel. Elution with hexane–AcOEt gave the product. The *E*/*Z* ratio was determined by ^{1}H NMR. When it was necessary, the isomers were separated by preparative TLC for characterization.

4.1.1.1. (*Z*)-4-(*tert*-Butyldimethylsilanyloxy)-2-(3,4-dimethoxybenzylidene)-butyric acid methyl ester (*Z*-2). Colorless oil. IR (film): 2955, 2850, 1705, 1600, 1515, 1260, 1115, 835, 775 cm^{-1}. ^{1}H NMR ($CDCl_3$) *δ*: 0.05 (6H, s), 0.89 (9H, s), 2.60 (2H, t, *J*=6.6 Hz), 3.67 (3H, s), 3.79 (2H, t, *J*=6.6 Hz), 3.85 (s, 3H), 3.88 (3H, s), 6.67 (1H, s), 6.83 (3H, m). MS (EI): *m*/*z* 380 (M^+), 349, 323 (100%), 291, 89. HRMS calcd for $C_{20}H_{32}O_5Si$ 380.2019, found 380.2026.

4.1.1.2. (*E*)-4-(*tert*-Butyldimethylsilanyloxy)-2-(3,4-dimethoxybenzylidene)-butyric acid methyl ester (*E*-2). Colorless oil. IR (film): 2955, 2850, 1705, 1600, 1515, 1260, 1115, 835, 775 cm^{-1}. ^{1}H NMR ($CDCl_3$) *δ*: 0.03 (6H, s), 0.87 (9H, s), 2.85 (2H, t, *J*=6.6 Hz), 3.81 (3H, s), 3.88 (2H, t, *J*=6.6 Hz), 3.90 (3H, s), 3.92 (3H, s), 6.88 (1H, d, *J*=8.9 Hz), 7.16 (1H, s), 7.18 (1H, d, *J*=8.9 Hz), 7.74 (1H, s). MS (EI): *m*/*z* 380 (M^+), 349, 323 (100%), 291, 89. HRMS calcd for $C_{20}H_{32}O_5Si$ 380.2019, found 380.2024.

4.1.1.3. (*Z*)-2-Benzylidene-4-(*tert*-butyldimethylsilanyloxy)-butyric acid methyl ester (4a). Colorless oil. IR (film): 2955, 1720, 1260, 1095, 835, 775, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$) *δ*: 0.04 (6H, s), 0.88 (9H, s), 2.60 (2H, t, *J*=6.6 Hz), 3.61 (3H, s), 3.78 (2H, t, *J*=6.6 Hz), 6.73 (1H, s), 7.20 (5H, m). MS (SIMS): *m*/*z* 321 (M^++H), 289, 263, 189, 89, 73 (100%). HRMS calcd for $C_{18}H_{29}O_3Si$ (M^++H) 321.1887, found 321.1894.

4.1.1.4. (*E*)-2-Benzylidene-4-(*tert*-butyldimethylsilanyloxy)-butyric acid methyl ester (4b). Colorless oil. IR (film): 2955, 1715, 1260, 1095, 835, 775, 705 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.03 (6H, s), 0.87 (9H, s), 2.80 (2H, t, J=6.8 Hz), 3.81 (3H, s), 3.85 (2H, t, J=6.8 Hz), 7.37 (3H, m), 7.53 (2H, m), 7.79 (1H, s). MS (SIMS): m/z 321 (M^++H), 289, 263, 189, 89, 73 (100%). HRMS calcd for $C_{18}H_{29}O_3Si$ (M^++H) 321.1887, found 321.1891.

4.1.1.5. (*Z*)-3-(3,4-Dimethoxyphenyl)-2-methylacrylic acid methyl ester (6a). Colorless oil. IR (film): 2950, 1720, 1515, 1270, 1145, 1030, 765 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.16 (3H, s), 3.69 (3H, s), 3.86 (3H, s), 3.88 (3H, s), 6.63 (1H, s), 6.80 (1H, d, J=8.2 Hz), 6.84 (1H, dd, J=8.2, 2.0 Hz), 6.86 (1H, d, J=2.0 Hz). MS (EI): m/z 236(M^+, 100%), 221, 205, 176, 161. HRMS calcd for $C_{13}H_{16}O_4$ 236.1049, found 236.1053.

4.1.1.6. (*E*)-3-(3,4-Dimethoxyphenyl)-2-methylacrylic acid methyl ester (6b). Colorless oil. IR (film): 2955, 1705, 1515, 1250, 1115, 1025, 810 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.16 (3H, s), 3.82 (3H, s), 3.90 (3H, s), 3.92 (3H, s), 6.90 (1H, d, J=8.3 Hz), 6.95 (1H, d, J=1.9 Hz), 7.04 (1H, dd, J=8.3, 1.9 Hz), 7.64 (1H, s). MS (EI): m/z 236(M^+, 100%), 221, 205, 176, 161. HRMS calcd for $C_{13}H_{16}O_4$ 236.1049, found 236.1052.

4.1.1.7. (*Z*)-3-(3,4-Dichlorophenyl)-2-methylacrylic acid methyl ester (8a). Colorless oil. IR (film): 2950, 1725, 1470, 1225, 1125, 1030, 910 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.09 (3H, s), 3.83 (3H, s), 7.21 (1H, dd, J=8.1, 1.9 Hz), 7.46 (1H, d, J=1.9 Hz), 7.47 (1H, d, J=8.1 Hz), 7.56 (1H, s). MS (EI): m/z 246(M^+), 244(M^+, 100%), 215, 213, 186, 184, 149, 115. HRMS calcd for $C_{11}H_{10}Cl_2O_2$ 244.0058, found 244.0063.

4.1.1.8. (*E*)-3-(3,4-Dichlorophenyl)-2-methylacrylic acid methyl ester (8b). Colorless oil. IR (film): 2955, 1715, 1475, 1250, 1115, 1030, 820, 750 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.10 (3H, s), 3.67 (3H, s), 6.60 (1H, s), 7.06 (1H, dd, J=8.3, 2.0 Hz), 7.33 (1H, d, J=2.0 Hz), 7.36 (1H, d, J=8.3 Hz). MS (EI): m/z 246 (M^+), 244 (M^+, 100%), 215, 213, 186, 184, 149, 115. HRMS calcd for $C_{11}H_{10}Cl_2O_2$ 244.0058, found 244.0065.

4.1.1.9. (*Z*)-2-[2-(*tert*-Butyldimethylsilanyloxy)ethyl]-3-phenylbut-2-enoic acid methyl ester (10a). Colorless oil. IR (film): 2955, 1715, 1250, 1105, 835, 775, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.07 (6H, s), 0.90 (9H, s), 2.14 (3H, s), 2.69 (2H, t, J=7.0 Hz), 3.36 (3H, s), 3.76 (2H, t, J=7.0 Hz), 7.12 (2H, m), 7.27 (3H, m). MS (EI): m/z 319 (M^+-CH_3), 303, 287, 277 (100%), 245, 89. HRMS calcd for $C_{18}H_{27}O_3Si$ (M^+-CH_3) 319.1617, found 319.1624.

4.1.1.10. (*E*)-2-[2-(*tert*-Butyldimethylsilanyloxy)-ethyl]-3-phenylbut-2-enoic acid methyl ester (10b). Colorless oil. IR (film): 2955, 1720, 1250, 1105, 835, 780, 705 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.05 (6H, s), 0.87 (9H, s), 2.27 (3H, s), 2.45 (2H, t, J=6.8 Hz), 3.60 (2H, t, J=6.8 Hz), 3.85 (3H, s), 7.21 (2H, m), 7.36 (3H, m). MS (EI): m/z 319 (M^+-CH_3), 303, 287, 277 (100%), 245, 89. HRMS calcd for $C_{18}H_{27}O_3Si$ (M^+-CH_3) 319.1617, found 319.1622.

4.1.1.11. (*Z*)-3-(3,4-Dimethoxybenzylidene)-dihydrofuran-2-one (12a). Colorless oil. IR (film): 2955, 2850, 1705, 1600, 1515, 1260, 1115, 835, 775 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.13 (2H, dt, J=2.2, 7.4 Hz), 3.92 (3H, s), 3.94 (3H, s), 4.40 (2H, t, J=7.4 Hz), 6.84 (1H, d, J=8.4 Hz), 6.90 (1H, t, J=2.3 Hz), 7.22 (1H, dd, J=8.4, 2.0 Hz), 8.13 (1H, d, J=2.0 Hz). MS (EI): m/z 234(M^+, 100%), 219. HRMS calcd for $C_{13}H_{14}O_4$ 234.0892, found 234.0900.

4.1.1.12. (*E*)-3-(3,4-Dimethoxybenzylidene)-dihydrofuran-2-one (12b). Colorless prisms (ethyl acetate–hexane, mp 135–136 °C). IR (KBr): 2955, 2850, 1705, 1600, 1515, 1260, 1115, 835, 775 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.24 (2H, dt, J=2.8, 7.5 Hz), 3.92 (3H, s), 3.93 (3H, s), 4.47 (2H, t, J=7.5 Hz), 6.94 (1H, d, J=8.4 Hz), 7.02 (1H, d, J=1.9 Hz), 7.13 (1H, dd, J=8.4, 1.9 Hz), 8.13 (1H, t, J=2.8 Hz). MS (EI): m/z 234 (M^+, 100%), 219. Anal. calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.61; H, 5.94.

4.1.1.13. (*Z*)-3-But-2-enylidenedihydrofuran-2-one (14a). Colorless oil. IR (film): 2915, 1745, 1650, 1195, 1145 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.88 (3H, t, J=6.9 Hz), 2.96 (2H, t, J=7.5 Hz), 4.34 (2H, t, J=7.5 Hz), 6.01 (1H, m), 6.58 (1H, dt, J=11.3, 2.1 Hz), 7.44 (1H, m). MS (EI): m/z 138 (M^+, 100%), 123, 79. HRMS calcd for $C_8H_{10}O_2$ 138.0681, found 138.0687.

4.1.1.14. (*E*)-3-But-2-enylidenedihydrofuran-2-one (14b). Colorless oil. IR (film): 2915, 1750, 1655, 1195, 1140 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.91 (3H, t, J=5.2 Hz), 2.96 (2H, dt, J=1.7, 7.6 Hz), 4.40 (2H, t, J=7.6 Hz), 6.18 (1H, d, J=9.2 Hz), 6.21 (1H, m), 7.08 (1H, dt, J=9.2, 2.5 Hz). MS (EI): m/z 138 (M^+, 100%), 123, 79. HRMS calcd for $C_8H_{10}O_2$ 138.0681, found 138.0685.

4.1.1.15. (*Z*)-3-Isobutylidenedihydrofuran-2-one (16a). Colorless oil. IR (film): 2965, 1755, 1375, 1210, 1135 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.02 (6H, d, J=6.6 Hz), 2.90 (2H, dt, J=2.2, 7.4 Hz), 3.77 (1H, m), 4.31 (2H, t, J=7.4 Hz), 6.02 (1H, dt, J=10.0, 2.2 H). MS (EI): m/z 140 (M^+, 100%), 125. HRMS calcd for $C_8H_{12}O_2$ 140.0837, found 140.0845.

4.1.1.16. (*E*)-3-Isobutylidenedihydrofuran-2-one (16b). Colorless oil. IR (film): 2965, 1755, 1375, 1210, 1135 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.68 (6H, d, J=6.7 Hz), 2.52 (1H, m), 2.89 (2H, dt, J=3.3, 7.6 Hz), 4.38 (2H, t, J=7.6 Hz), 6.59 (1H, dt, J=9.8, 2.9 Hz). MS (EI): m/z 140 (M^+, 100%), 125. HRMS calcd for $C_8H_{12}O_2$ 140.0837, found 140.0844.

4.1.1.17. (*Z*)-3-(3,4-Dimethoxybenzylidene)-4-(3,4,5-trimethoxybenzyl)-dihydrofuran-2-one (18a). Colorless oil. IR (film): 2940, 2840, 1745, 1640, 1590, 1515, 1260, 1125, 775 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.88 (2H, dd, J=7.2, 5.1 Hz), 3.32 (1H, m), 3.81 (6H, s), 3.85 (3H, s), 3.91 (3H, s), 3.94 (3H, s), 4.14 (2H, m), 6.40 (2H, s), 6.53 (1H, d, J=1.4 Hz), 6.83 (1H, d, J=8.4 Hz), 7.15 (1H, dd, J=8.4, 2.0 Hz), 8.10 (1H, d, J=2.0 Hz). MS (EI): m/z 414 (M^+), 266, 233, 181 (100%). HRMS calcd for $C_{23}H_{26}O_7$ 414.1679, found 414.1689.

4.1.1.18. (*E*)-3-(3,4-Dimethoxybenzylidene)-4-(3,4,5-trimethoxybenzyl)-dihydrofuran-2-one (18b). Colorless

prisms (ethyl acetate–hexane, mp 151–152 °C). IR (KBr): 2940, 2840, 1745, 1645, 1590, 1515, 1250, 1125, 805 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.65 (2H, dd, J=14.4, 10.1 Hz), 3.09 (1H, dd, J=14.4, 4.5 Hz), 3.81 (3H, s), 3.84 (6H, s), 3.91 (3H, s), 3.94 (3H, s), 4.30 (2H, m), 6.39 (2H, s), 6.92 (1H, d, J=8.4 Hz), 7.09 (1H, d, J=2.0 Hz), 7.21 (1H, dd, J=8.4, 2.0 Hz), 7.55 (1H, d, J=1.7 Hz). MS (EI): m/z 414 (M^+), 233, 181 (100%). Anal. calcd for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32. found: C, 66.61; H, 6.14.

4.1.2. Typical procedure for substrate preparation. A solution of ester or lactone (11.6 mmol) in dry THF (10 mL) was treated with LDA solution (13.9 mmol) at −78 °C under N_2 for 30 min. The reaction mixture was quenched with aqueous NH_4Cl and the mixture was extracted with EtOAc. The organic layer was washed with aqueous citric acid, aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The mixture of *anti*-isomer and *syn*-isomer was separated by column chromatography on silica gel.

4.1.2.1. Methyl (*syn*)-3-(3,4-Dimethoxyphenyl)-3-hydroxy-2-[2-(*tert*-butyldimethylsilyloxy)-ethyl]-propionate (*syn*-1). Yield 46%. Colorless oil. IR (film): 3515, 2955, 2860, 1735, 1595, 1515, 1260, 835, 775 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.04 (6H, s), 0.88 (9H, s), 1.90 (2H, m), 2.60 (1H, dt, J=2.8, 6.4 Hz), 3.53 (3H, s), 3.63 (2H, m), 3.83 (3H, s), 3.85 (3H, s), 4.90 (1H, d, J=6.4 Hz), 6.78 (1H, d, J=8.2 Hz), 6.83 (1H, d, J=8.2 Hz), 6.86 (1H, s). MS (EI): m/z 398 (M^+), 309, 232, 175 (100%), 166, 139, 89. HRMS calcd for $C_{20}H_{34}O_6Si$ 398.2125, found 398.2136.

4.1.2.2. Methyl (*anti*)-3-(3,4-Dimethoxyphenyl)-3-hydroxy-2-[2-(*tert*-butyldimethylsilyloxy)-ethyl]-propionate (*anti*-1). Yield 46%. Colorless oil. IR (film): 3515, 2955, 2860, 1735, 1595, 1515, 1260, 835, 775 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.02 (6H, s), 0.88 (9H, s), 1.59 (1H, m), 1.82 (1H, m), 2.64 (1H, br s), 2.96 (1H, m), 3.57 (2H, m), 3.71 (3H, s), 3.89 (6H, s), 4.78 (1H, d, J=7.8 Hz), 6.84 (1H, d, J=8.2 Hz), 6.86 (1H, d, J=8.2 Hz), 6.90 (1H, s). MS (EI): m/z 398 (M^+), 309, 232, 175 (100%), 166, 139, 89. HRMS calcd for $C_{20}H_{34}O_6Si$ 398.2125, found 398.2132.

4.1.2.3. Methyl (*syn*)-3-hydroxy-3-phenyl-2-[2-(*tert*-butyldimethylsilyloxy)-ethyl]-propionate (3a). Yield 49%. Colorless oil. IR (film): 3500, 2955, 2850, 1735, 1255, 1100, 835, 775, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.03 (6H, s), 0.85 (9H, s), 1.90 (2H, m), 2.85 (2H, dt, J=5.9, 4.7 Hz), 3.54 (3H, s), 3.59 (2H, m), 4.98 (1H, d, J=5.9 Hz), 7.30 (5H, m). MS (EI): m/z 338 (M^+), 307, 281, 249, 189, 175 (100%), 89. HRMS calcd for $C_{18}H_{30}O_4Si$ 338.1913, found 338.1922.

4.1.2.4. Methyl (*anti*)-3-hydroxy-3-phenyl-2-[2-(*tert*-butyldimethylsilyloxy)-ethyl]-propionate (3b). Yield 45%. Colorless oil. IR (film): 3470, 2955, 2850, 1735, 1255, 1100, 835, 775, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.03 (6H, s), 0.87 (9H, s), 1.63 (1H, m), 1.82 (1H, m), 2.96 (1H, dt, J=7.4, 4.8 Hz), 3.56 (2H, m), 3.66 (3H, s), 4.83 (1H, d, J=7.4 Hz), 7.33 (5H, m). MS (EI): m/z 338 (M^+), 281, 263, 249, 189, 175 (100%), 89. HRMS calcd for $C_{18}H_{30}O_4Si$ 338.1913, found 338.1920.

4.1.2.5. Methyl (*syn*)-3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylpropionate (5a). Yield 46%. Colorless oil. IR (film): 3515, 2950, 2840, 1735, 1595, 1515, 1460, 1265, 1140, 1030, 860, 810, 765 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.15 (3H, d, J=7.2 Hz), 2.78 (1H, dq, J=4.4, 7.2 Hz), 3.68 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 5.04 (1H, d, J=4.4 Hz), 6.84 (1H, d, J=8.0 Hz), 6.86 (1H, d, J=8.0 Hz), 6.90 (1H, s). MS (EI): m/z 254 (M^+), 237, 167 (100%), 139. HRMS calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1159.

4.1.2.6. Methyl (*anti*)-3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylpropionate (5b). Yield 35%. Colorless oil. IR (film): 3505, 2940, 2840, 1735, 1595, 1515, 1460, 1265, 1140, 1025, 855, 820, 765 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.00 (3H, d, J=8.2 Hz), 2.80 (1H, dq, J=8.8, 8.2 Hz), 3.75 (3H, s), 3.88 (3H, s), 3.89 (3H, s), 4.70 (1H, d, J=8.8 Hz), 6.84 (1H, d, J=8.0 Hz), 6.86 (1H, d, J=8.0 Hz), 6.91 (1H, s). MS (EI): m/z 254 (M^+), 237, 167 (100%), 139. HRMS calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1160.

4.1.2.7. Methyl (*syn*)-3-(3,4-dichlorophenyl)-3-hydroxy-2-methylpropionate (7a). Yield 50%. Colorless oil. IR (film): 3485, 2990, 2955, 1730, 1565, 1460, 1350, 1205, 1030, 820, 740 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.09 (3H, d, J=7.2 Hz), 2.75 (1H, dq, J=3.6, 7.2 Hz), 3.15 (1H, br s), 3.72 (3H, s), 5.09 (1H, d, J=3.6 Hz), 7.17 (1H, dd, J=8.2, 2.0 Hz), 7.41 (1H, d, J=8.2 Hz), 7.47 (1H, d, J=2.0 Hz). MS (EI): m/z 264, 262 (M^+), 247, 245, 177, 175, 88 (100%). HRMS calcd for $C_{11}H_{12}Cl_2O_3$ 262.0163, found 262.0159.

4.1.2.8. Methyl (*anti*)-3-(3,4-dichlorophenyl)-3-hydroxy-2-methylpropionate (7b). Yield 35%. Colorless needles (ethyl acetate–hexane, mp 96–97 °C). IR (KBr): 3435, 2955, 1710, 1460, 1435, 1380, 1250, 1205, 1175, 1125, 1050, 875, 830 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.07 (3H, d, J=7.2 Hz), 2.76 (1H, dq, J=8.0, 7.2 Hz), 3.73 (3H, s), 4.72 (1H, d, J=8.0 Hz), 7.17 (1H, dd, J=8.2, 2.5 Hz), 7.43 (1H, d, J=8.2 Hz), 7.45 (1H, d, J=2.5 Hz). MS (EI): m/z 264, 262 (M^+), 247, 245, 177, 175, 88 (100%). Anal. calcd for $C_{11}H_{12}Cl_2O_3$: C, 50.21; H, 4.60; Cl, 26.95. Found: C, 50.18; H, 4.44; Cl, 26.89.

4.1.2.9. Methyl (*syn*)-3-hydroxy-3-phenyl-2-[2-(*tert*-butyldimethylsilyloxy)-ethyl]-butyrate (9a). Yield 28%. Colorless oil. IR (film): 3515, 2955, 2850, 1715, 1500, 1440, 1360, 1250, 1170, 1100, 835, 775, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.07 (6H, s), 0.84 (9H, s), 1.44 (1H, m), 1.52 (3H, s), 1.87 (1H, m), 2.98 (1H, dd, J=3.2, 10.7 Hz), 3.41 (2H, m), 3.76 (3H, s), 7.20–7.47 (5H, m). MS (SIMS): m/z 353 (M^++1), 335, 303, 203 (100%), 175, 121, 73. HRMS calcd for $C_{19}H_{33}O_4Si$ 353.2149, found 353.2152.

4.1.2.10. Methyl (*anti*)-3-hydroxy-3-phenyl-2-[2-(*tert*-butyldimethylsilyloxy)-ethyl]-butyrate (9b). Yield 56%. Colorless oil. IR (film): 3505, 2955, 2855, 1715, 1500, 1435, 1360, 1250, 1170, 1105, 835, 775, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.03 (6H, s), 0.88 (9H, s), 1.47 (3H, s), 1.98 (2H, dt, J=8.2, 5.6 Hz), 3.04 (1H, dt, J=8.2, 6.0 Hz), 3.34 (3H, s), 3.46–3.72 (2H, m), 7.14–7.40 (5H, m). MS (SIMS): m/z 353 (M^++1), 335, 303, 203 (100%), 175, 121, 73. HRMS calcd for $C_{19}H_{33}O_4Si$ 353.2149, found 353.2154.

4.1.2.11. (*syn*)-3-(3,4-Dimethoxy-α-hydroxybenzyl)-dihydrofuran-2-one (11a). Yield 46%. Colorless needles (ethyl acetate–hexane, mp 116–117 °C). IR (KBr): 3490,

2950, 1765, 1595, 1515, 1460, 1235, 1130, 1030, 810, 760 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.02 (1H, m), 2.43 (1H, m), 2.92 (1H, dt, J=2.8, 9.5 Hz), 3.88 (3H, s), 3.89 (3H, s), 4.19 (1H, dt, J=8.8, 7.3 Hz), 4.35 (1H, dt, J=3.6, 8.8 Hz), 5.33 (1H, d, J=2.8 Hz), 6.90 (3H, m). MS (EI): m/z 252 (M^+), 167 (100%), 139. Anal. calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.94; H, 6.51.

4.1.2.12. (*anti*)-3-(3,4-Dimethoxy-α-hydroxybenzyl)-dihydrofuran-2-one (11b). Yield 42%. Colorless oil. IR (film): 3505, 2940, 1765, 1595, 1515, 1460, 1255, 1140, 1025, 820, 765 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.98 (2H, m), 2.91 (1H, dt, J=8.8, 9.8 Hz), 3.88 (3H, s), 3.89 (3H, s), 4.07–4.34 (2H, m), 4.78 (1H, d, J=8.8 Hz), 6.83 (1H, d, J=8.2 Hz), 6.90 (1H, dd, J=8.2, 2.0 Hz), 6.96 (1H, d, J=2.0 Hz). MS (EI): m/z 252 (M^+), 167 (100%), 139. HRMS calcd for $C_{13}H_{16}O_5$ 252.0998, found 252.1002.

4.1.2.13. (*syn*)-3-(1-Hydroxybut-2-enyl)-dihydrofuran-2-one (13a). Yield 25%. Colorless oil. IR (film): 3450, 2950, 1765, 1600, 1380, 1180, 1030 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.75 (3H, d, J=6.4 Hz), 2.15–2.37 (2H, m), 2.76 (1H, dt, J=3.2, 9.6 Hz), 4.26 (1H, m), 4.36 (1H, m), 4.60 (1H, m), 5.48 (1H, m), 5.80 (1H, m). MS: m/z 156 (M^+), 138 (100%), 123, 86, 71. HRMS calcd for $C_8H_{12}O_3$ 156.0786, found 156.0792.

4.1.2.14. (*anti*)-3-(1-Hydroxybut-2-enyl)-dihydrofuran-2-one (13b). Yield 17%. Colorless oil. IR (film): 3445, 2945, 1760, 1605, 1380, 1185, 1025 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.73 (3H, d, J=6.1 Hz), 2.12 (1H, m), 2.28 (1H, m), 2.68 (1H, m), 4.24 (2H, m), 4.39 (1H, m), 5.54 (1H, m), 5.82 (1H, m). MS: m/z 156 (M^+), 138 (100%), 123, 86, 71. HRMS calcd for $C_8H_{12}O_3$ 156.0786, found 156.0791.

4.1.2.15. (*syn*)-3-(1-Hydroxy-2-methylpropyl)-dihydrofuran-2-one (15a). Yield 9%. Colorless oil. IR (film): 3460, 2965, 1760, 1380, 1180, 1025 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.92 (3H, d, J=6.6 Hz), 1.04 (3H, d, J=6.6 Hz), 1.69 (1H, m), 2.18 (1H, m), 2.48 (1H, m), 2.80 (1H, dt, J=2.5, 10.1 Hz), 3.83 (1H, dd, J=2.5, 8.8 Hz), 4.25 (1H, m), 4.39 (1H, m). MS: m/z 159 (M^++1), 140, 130, 115, 86 (100%), 71. HRMS calcd for $C_8H_{15}O_3$ 159.1022, found 159.1025.

4.1.2.16. (*anti*)-3-(1-Hydroxy-2-methylpropyl)-dihydrofuran-2-one (15b). Yield 71%. Colorless oil. IR (film): 3500, 2965, 1755, 1380, 1175, 1000 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.94 (3H, d, J=6.6 Hz), 1.06 (3H, d, J=6.6 Hz), 1.80 (1H, m), 2.05 (1H, m), 2.30 (1H, m), 2.68 (1H, dt, J=11.6, 8.7 Hz), 3.61 (1H, dd, J=3.4, 8.7 Hz), 4.22 (1H, m), 4.42 (1H, dt, J=1.9, 8.9 Hz). MS: m/z 159 (M^++1), 140, 115, 86 (100%), 71. HRMS calcd for $C_8H_{15}O_3$ 159.1022, found 159.1026.

4.1.2.17. (*syn*)-3-[(3,4-Dimethoxyphenyl)hydroxymethyl]-4-(3,4,5-trimethoxybenzyl)dihydrofuran-2-one (17a). Yield 47%. Colorless oil. IR (film): 3485, 2940, 1765, 1590, 1515, 1465, 1230, 1125, 1025, 815, 750 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.26–2.48 (2H, m), 2.68 (1H, m), 2.82 (1H, m), 3.77 (6H, s), 3.80 (6H, s), 3.86 (3H, s), 3.87 (3H, s), 3.96 (1H, m), 4.34 (1H, dd, J=7.7, 8.8 Hz), 5.31 (1H, d, J=2.8 Hz), 6.06 (2H, s), 6.78 (2H, s), 6.88 (1H, s). MS: m/z 432 (M^+), 414, 300, 266, 181, 166 (100%), 151, 95. HRMS calcd for $C_{23}H_{28}O_8$ 432.1784, found 432.1778.

4.1.2.18. (*anti*)-3-[(3,4-Dimethoxyphenyl)hydroxymethyl]-4-(3,4,5-trimethoxybenzyl)dihydrofuran-2-one (17b). Yield 50%. Colorless needles (ethyl acetate–hexane, mp 116–118 °C). IR (KBr): 3490, 2940, 1765, 1590, 1515, 1465, 1240, 1125, 1025, 815, 765 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.18 (2H, m), 2.49–2.71 (2H, m), 3.80 (9H, s), 3.88 (3H, s), 3.90 (3H, s), 4.08–4.21 (2H, m), 4.84 (1H, d, J=7.8 Hz), 6.08 (2H, s), 6.85–6.99 (3H, m). MS: m/z 432 (M^+), 414, 300, 266 (100%), 251, 181, 166, 151, 95. Anal. calcd for $C_{23}H_{28}O_8$: C, 63.88; H, 6.53. Found: C, 63.84; H, 6.51.

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