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An unexpected tandem enantioselective Michael addition/oxa-nucleophilic rearrangement reaction of β,γ-unsaturated α-keto esters catalyzed by cinchona alkaloids

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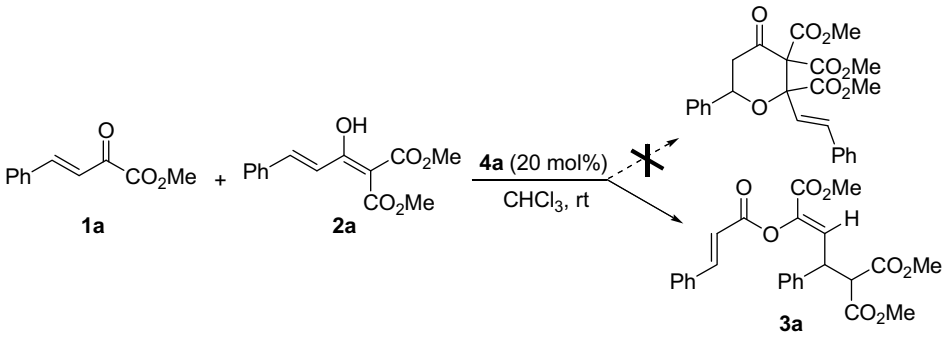
ABSTRACT

Cinchona alkaloids were found to catalyze an enantioselective Michael addition/oxa-nucleophilic rearrangement reaction of β,γ-unsaturated α-keto esters **1** and malonates **2**. Using the optimum catalyst quinine **4a**, a series of the rearranged products **3** were obtained with up to 98% yield and 82% ee under mild reaction conditions.

1. Introduction

Organocatalytic asymmetric carbon–carbon bond-forming reactions have emerged as a powerful tool for the construction of various organic molecules, so they have attracted intensive research interests in recent years.[1] Among the various catalysts used in this field, cinchona alkaloids and their derivatives have demonstrated distintive catalytic proficiency in numerous reactions.[2] On the other hand, as a type of synthetically useful compounds, β,γ-unsaturated α-keto esters **1** have been explored in a variety of enantioselective reactions, such as Diels–Alder and hetero-Diels–Alder reaction,[3] Friedel–Crafts alkylations,[4] nucleophilic substitution, Michael additions and oxa-Michael additions,[5] hydrogenations,[6] and formal [3+3] annulations.[7] However, to the best of our knowledge, the reaction of β,γ-unsaturated α-keto esters catalyzed by cinchona alkaloids has not been reported.

Recently, we have employed compound **1** as a substrate in asymmetric aqueous ketone–ketone aldol reactions to construct compounds with chiral quarternary carbon centers.[8] As a continued interest in the chemistry of compounds **1**, we envisaged a double Michael addition between (*E*)-methyl 2-oxo-4-phenylbut-3-enoate **1a** and (*E*)-dimethyl 2-(1-hydroxy-3-phenylallylidene) malonate **2a** envisaged to synthesize a synthetically useful chiral tetrahydropyran-4-one compound. A new compound **3a** was identified as the sole product under the catalysis of quinine (Scheme 1). Herein, we report the details of this unexpected finding.



Scheme 1. The unexpected formation of **3a** from **1a** and **2a** catalyzed by quinine.

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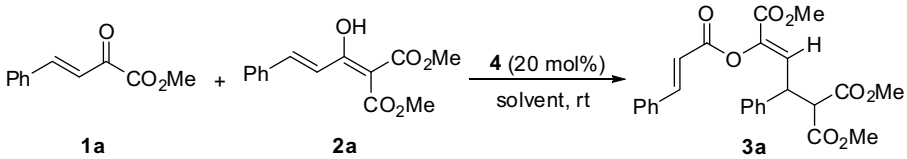
2. Results and discussion

Using the reaction of (*E*)-methyl 2-oxo-4-phenylbut-3-enoate **1a** with (*E*)-dimethyl 2-(1-hydroxy-3-phenylallylidene) malonate **2a** as a model reaction, the results of the optimization of the reaction conditions are summarized in Table 1. Of all the eight cinchona alkaloid catalysts examined, quinine provided the best results in terms of both yield and ee (Table 1, entry 1). Interestingly, quinidine **4b** and cinchonine **4c** provided the desired rearranged product with the opposite absolute configuration with much lower yields (Table 1, entries 5 and 6). Notably, the ineffectiveness of catalysts **4g** and **4h** (Table 1, entries 10 and 11) clearly

Table 1
Screening of the optimal reaction conditions for **1a** and **2a** in the presence of **4**[a]



1a **2a** **3a**

Entry	Catalyst	Solvent	Yield[b] (%)	ee[c] (%)
1	**4a**	$CHCl_3$	68	78
2[d]	**4a**	$CHCl_3$	40	76
3[e]	**4a**	$CHCl_3$	18	76
4[f]	**4a**	$CHCl_3$	53	76
5	**4b**	$CHCl_3$	40	−70
6	**4c**	$CHCl_3$	29	−32
7	**4d**	$CHCl_3$	24	44
8	**4e**	$CHCl_3$	7	n.d.
9	**4f**	$CHCl_3$	20	n.d.
10	**4g**	$CHCl_3$	—[g]	—[g]
11	**4h**	$CHCl_3$	Trace	n.d.
12	**4a**	CH_2Cl_2	33	73
13	**4a**	CCl_4	68	80
14	**4a**	$ClCH_2CH_2Cl$	33	75
15	**4a**	THF	18	63
16	**4a**	Et_2O	68	76
17	**4a**	Toluene	68	79
18	**4a**	CH_3CN	84	71
19	**4a**	EtOAc	79	75
20	**4a**	Acetone	81	68

[a] Unless otherwise noted, the reaction was conducted with 0.1 mmol of **1a** and 0.2 mmol of **2a** in the presence of 20 mol % of **4** in 1.0 mL of solvent at room temperature for 48 h.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis on a chiral AD column.
[d] 0.12 mmol of **2a** was used.
[e] 10 mol % of **4a** was used.
[f] 0.1 mmol of **2a** and 0.2 mmol of **1a** were used.
[g] No reaction occurred and the starting material was recovered.

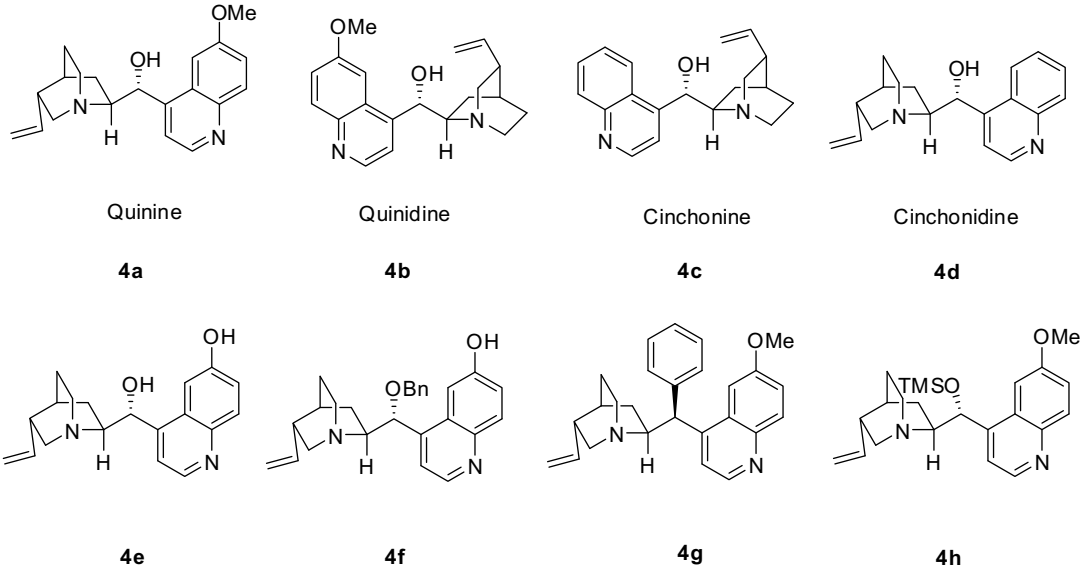
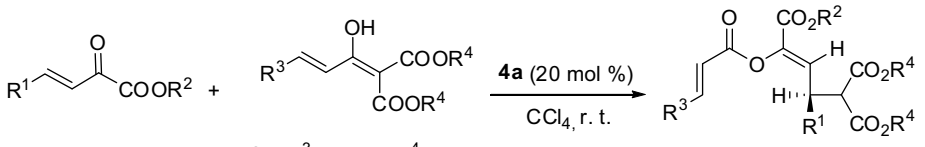


Figure 1. Organocatalysts screened in this study.

Table 2
Asymmetric Michael addition and rearrangement of β,γ-unsaturated α-keto esters catalyzed by **4a**[a]



1a-p

2a: $R^3 = C_6H_5$, R^4 = Me
2b: R^3 = Me, R^4 = Me
2c: $R^3 = C_6H_5$, R^4 = Et
2d: $R^3 = C_6H_5$, R^4 = *i*-Pr
2e: $R^3 = C_6H_5$, R^4 = Bn

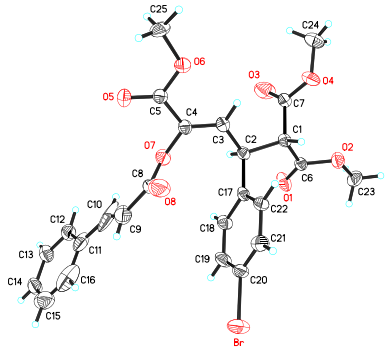
3a-t

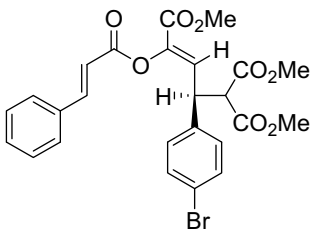
Entry	1	R^1	R^2	2	Time (h)	Product	Yield[b] (%)	ee[c] (%)
1	**1a**	Ph	Me	**2a**	48	**3a**	68	80
2	**1b**	4-FC_6H_4	Me	**2a**	24	**3b**	87	80
3	**1c**	4-ClC_6H_4	Me	**2a**	24	**3c**	88	80
4	**1d**	4-BrC_6H_4	Me	**2a**	24	**3d**	96	80
5	**1e**	3-ClC_6H_4	Me	**2a**	24	**3e**	92	78[d]
6	**1f**	4-$NO_2C_6H_4$	Me	**2a**	15	**3f**	91	72
7	**1g**	4-MeC_6H_4	Me	**2a**	48	**3g**	49	79
8	**1h**	4-$EtOC_6H_4$	Me	**2a**	48	**3h**	51	70
9	**1i**	2,4-diClC_6H_3	Me	**2a**	48	**3i**	31	58
10	**1j**	2-BrC_6H_4	Me	**2a**	48	**3j**	15	54
11	**1k**	Ph	Et	**2a**	15	**3k**	72	79
12	**1l**	Ph	Allyl	**2a**	48	**3l**	50	78
13	**1m**	Ph	*t*-Bu	**2a**	48	**3m**	35	79
14	**1n**	Ph	Bn	**2a**	15	**3n**	70	80[d]
15	**1o**	Ph	*p*-BrBn	**2a**	15	**3o**	74	77[d]
16	**1p**	Ph	*i*-Pr	**2a**	48	**3p**	63	78
17	**1d**	4-BrC_6H_4	Me	**2b**	65	**3q**	70	80
18	**1d**	4-BrC_6H_4	Me	**2c**	48	**3r**	61	82
19	**1d**	4-BrC_6H_4	Me	**2d**	48	**3s**	68	82
20	**1d**	4-BrC_6H_4	Me	**2e**	48	**3t**	98	82

[a] Unless otherwise noted, the reaction was conducted with 0.1 mmol of **1** and 0.2 mmol of **2** in the presence of 20 mol % of **4a** in 1.0 mL of CCl_4 at room temperature.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis on a chiral AD column. The absolute configuration of **3d** was determined to be (*S*) by X-ray crystallographic analysis, and the others **3a**–**3c**, **3e**–**3t** were assigned by assuming that a similar catalytic mechanism was followed.
[d] Determined by chiral HPLC analysis on a chiral AS-H column.

highlighted the importance of the hydroxyl group in quinine for this reaction, and thus suggested a bifunctional role for the catalyst. Lowering the amount of quinine from 20 mol % to 10 mol % diminished both the yield and the ee value (Table 1, entry 3). Decreasing the amount of **2a** also leads to a significant decrease in the yield while with much less appreciable effect on the enantioselectivity (Table 1, entries 2 and 4). No apparent difference was observed when $CHCl_3$, CCl_4, and toluene were used as solvent, except for a slightly higher ee value for CCl_4 (Table 1, entry 13). Higher yields were obtained in the cases of more polar solvents such as CH_3CN, EtOAc, and acetone; however, the enantioselectivity was diminished (Table 1, entries 18–20). Thus, the reaction was best performed with 20 mol % of quinine **4a** in CCl_4 at room temperature (Fig. 1).

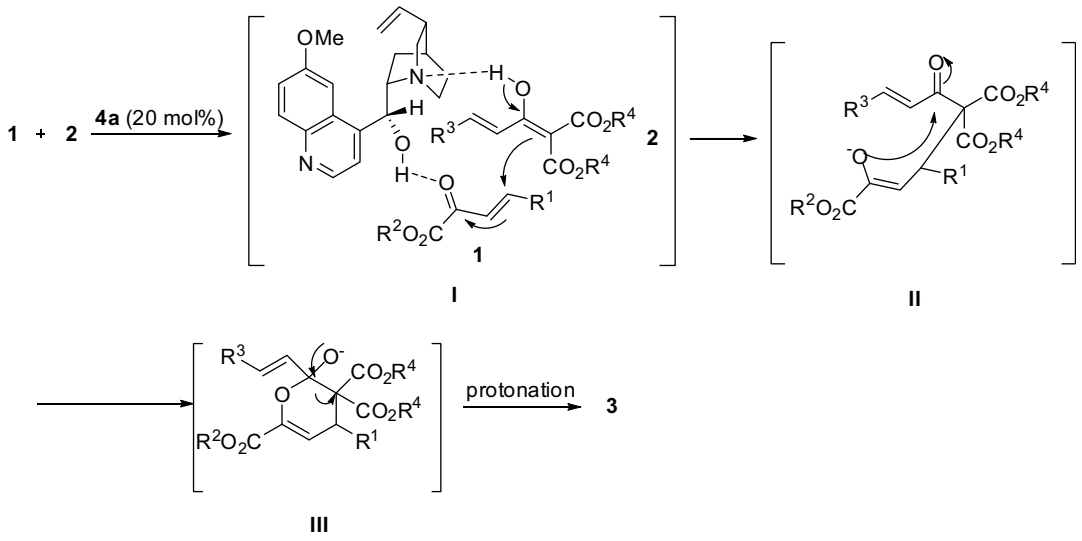
With the optimized reaction conditions, the scope of this reaction was probed with **1** and **2**; the results are summarized in Table 2. In general, the present reaction was rather sensitive to the electronic nature and steric hinderance of both substrates. For substrates **1a–j** with differently substituted phenyl groups (R^1), those with electron-withdrawing substituents required shorter reaction times and provided higher yields than the ones with electron-donating substituents, though no appreciable difference in the enantioselectivity was observed (Table 2, entries 1–8). However, when the substituents were in the *ortho*-position





3d

Figure 2. X-ray structure of compound **3d**.



Scheme 2. Proposed possible catalytic mechanism for the formation of **3**.

of the benzene ring, considerable decreases in both the ee values and the yields were observed (Table 2, entries 9 and 10). In addition, alteration of the ester group (R^2) of **1** did not have any significant influence on the enantioselectivity, but a significantly lower yield was obtained after a relatively long reaction time (48 h) for substrate **1m** bearing a bulky *tert*-butyl group (Table 2, entries 11–16). As for substrates **2c–e** with different ester moieties (R^4), invariably high ees were achieved and up to 98% yield was obtained for the benzyl-substituted substrate **2e** (Table 2, entries 18–20). It is noteworthy that substrate **2b** with a alkyl group (R^3 = Me) also provided the desired product **3q** in 70% yield and 80% ee, although a longer reaction time (65 h) was required (Table 2, entry 17). Furthermore, another feature of this reaction is the complete *Z*-selectivity of the newly formed alkene in products **3**. The absolute configuration of product **3d** was determined to be (*S*) by X-ray crystallographic analysis (Fig. 2).[9]

Based on the numerous previous studies on the bifunctional catalytic activity of cinchona alkaloids,[2] a possible mechanism for the present reaction was proposed (Scheme 2). First, quinine **4a** catalyzed the asymmetric Michael addition of **1** and **2** via dual activation of both the electrophile **1** and the nucleophile **2** (transition state I) to produce intermediate II, which then underwent an oxa-nucleophilic attack at the carbonyl of **2** generating another intermediate III. This intermediate finally rearranged to provide the product **3** after protonation.

3. Conclusion

In conclusion, we have reported the tandem enantioselective Michael addition/oxa-nucleophilic rearrangement reaction of β,γ-unsaturated α-keto esters catalyzed by bifunctional cinchona alkaloids, and a possible catalytic mechanism was also briefly discussed.

4. Experimental

4.1. General

Unless otherwise indicated, chemicals and solvents were purchased from commercial suppliers and purified by standard techniques. Flash column chromatography was performed using silica gel. For thin-layer chromatography (TLC), silica gel plates (HSGF 254) were used and compounds were visualized by irradiation with UV light or by treatment with a solution of phosphomolybdic acid in ethanol followed by heating. The ^{1}H NMR spectra were recorded on a DPX-300 or Varian EM-360 (300 MHz). All chemical shifts (δ) are given in ppm. Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, br = broad, and m = multiplet) and coupling constants (Hz), integration. ^{13}C NMR spectra were recorded on a DPX-400 (100 MHz). Analytical high-performance liquid chromatography (HPLC) was carried out on WATERS equipment using a chiral column. Melting points were determined on a SGW X-4 apparatus, and are uncorrected. Optical rotations were measured on a JASCO P-1030 Polarimeter at λ = 589 nm. IR spectra were recorded on a Perkin-Elmer 983G instrument. Elementary analysis was taken on a Vario EL III elementary analysis instrument. Mass spectra analysis was performed on API 200 LC/MS system (Applied Biosystems Co. Ltd).

4.2. Typical procedure for the preparation of compounds 2

To a solution of dialkyl malonates (40 mmol) in dry tetrahydrofuran (100 mL) was added NaH (40 mmol, 60% wt dispersion in mineral oil) in portions at 0 °C. The mixture was then warmed to room temperature and stirred for 30 min. Cinnamoyl chloride or (*E*)-but-2-enoyl chloride (20 mmol) in dry tetrahydrofuran (20 mL) was then added over 1 h to the above-mentioned system, and the resulting mixture was stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction mixture was then diluted by the addition of saturated NH_4Cl aq (40 mL), evaporated in vacuo to remove most of the solvent (THF), and the residue was extracted with dichloromethane (3 × 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo, and the residue was purified by column chromatography on silica gel, eluted with ethyl acetate and petroleum ether mixture (1:20) to afford pure products **2**.

4.2.1. (*E*)-Dimethyl 2-(1-hydroxy-3-phenylallylidene)-malonate 2a

White solid. Yield 58%. Mp 72–74 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.84 (d, *J* = 5.4 Hz, 6H), 7.02 (d, *J* = 15 Hz, 1H), 7.35–7.37 (m, 3H), 7.51–7.53 (m, 2H), 7.64 (d, *J* = 15 Hz, 1H), 13.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.3, 52.4, 99.3, 119.0, 128.2, 128.9, 130.1, 135.0, 140.8, 166.4, 171.8, 172.3; MS (EI): *m*/*z* 262 (M^+). Anal. Calcd

for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.02; H, 5.36. IR (KBr) ν 2954, 1759, 1733, 1632, 1549, 1442, 1375, 1088 cm^{-1}.

4.2.2. (*E*)-Dimethyl 2-(1-hydroxybut-2-enylidene)malonate 2b

Colorless liquid. Yield 30%. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.92 (d, J = 6.6 Hz, 3H), 3.82 (s, 6H), 6.32 (d, J = 15 Hz, 1H), 6.87–6.99 (m, 1H), 13.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.7, 52.2, 52.3, 98.0, 123.0, 141.0, 166.4, 171.8, 172.0; MS (EI): m/z 200 (M^+); HRMS (EI): calculated for $C_9H_{12}O_5$ (M^+): 200.0685. Found: 200.0687; IR (Film) ν 2955, 1760, 1733, 1647, 1568, 1443, 1087, 963 cm^{-1}.

4.2.3. (*E*)-Diethyl 2-(1-hydroxy-3-phenylallylidene)-malonate 2c[10]

Colorless liquid. Yield 69%. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.27–1.39 (m, 6H), 4.27–4.37 (m, 4H), 7.05 (d, J = 15.6 Hz, 1H), 7.36–7.41 (m, 3H), 7.50–7.53 (m, 2H), 7.64 (d, J = 15.6 Hz, 1H), 13.31 (s, 1H).

4.2.4. (*E*)-Diisopropyl 2-(1-hydroxy-3-phenylallylidene)-malonate 2d

White waxy solid. Yield 75%. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.33 (t, J = 6.6 Hz, 12H), 5.13–5.25 (m, 2H), 7.04 (d, J = 15.6 Hz, 1H), 7.36–7.41 (m, 3H), 7.51–7.53 (m, 2H), 7.62 (d, J = 15.6 Hz, 1H), 13.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 21.8, 64.6, 68.7, 69.2, 70.1, 100.8, 119.0, 128.0, 128.8, 129.8, 135.2, 140.0, 165.6, 170.9, 171.0; MS (EI): m/z 318 (M^+); HRMS (EI): calculated for $C_{18}H_{22}O_5$ (M^+): 318.1467. Found: 318.1471; IR (KBr) ν 2982, 1723, 1634, 1383, 1275, 1020, 971, 693 cm^{-1}.

4.2.5. (*E*)-Dibenzyl 2-(1-hydroxy-3-phenylallylidene)-malonate 2e

Yellow liquid. Yield 72%. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.27 (s, 4H), 7.00 (d, J = 15.6 Hz, 1H), 7.32–7.34 (m, 15H), 7.62 (d, J = 15.6 Hz, 1H), 13.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 67.2, 68.0, 99.4, 119.0, 127.9, 128.1, 128.2, 128.3, 128.6, 128.7, 128.8, 129.0, 130.0, 135.0, 135.2, 135.6, 140.9, 165.7, 171.2, 172.7; MS (EI): m/z 414 (M^+); HRMS (EI): calculated for $C_{26}H_{22}O_5$ (M^+): 414.1467. Found: 414.1472; IR (film) ν 3031, 1725, 1631, 1450, 1396, 1353, 1087, 752 cm^{-1}.

4.3. Typical procedure for the preparation of compounds 3

A mixture of β,γ-unsaturated α-keto ester **1** (0.1 mmol), compound **2** (0.2 mmol) and quinine (0.02 mmol) in 1.0 mL of tetracarbonchloride was stirred at room temperature for the appropriate times until the disappearance of **1** (monitored by TLC). The reaction mixture was then concentrated, and the residue was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether = 1:5) to give the desired products **3**.

4.3.1. (*S,Z*)-Trimethyl 4-(cinnamoyloxy)-2-phenylbut-3-ene-1,1,4-tricarboxylate 3a

White waxy solid. Yield 68%. $[\alpha]_D^{25} = -156.4$ (c 1.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.53 (s, 3H), 3.75 (d, J = 2.4 Hz, 6H), 3.95 (d, J = 10.5 Hz, 1H), 4.53 (t, J = 10.5 Hz, 1H), 6.57 (d, J = 15.6 Hz, 1H), 6.77 (d, J = 10.5 Hz, 1H), 7.23–7.33 (m, 5H), 7.42–7.44 (m, 3H), 7.57–7.60 (m, 2H), 7.80 (d, J = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 42.2, 52.4, 52.5, 52.8, 56.6, 115.9, 127.6, 127.7, 128.3, 128.8, 128.9, 129.0, 130.7, 133.9, 138.2, 138.7, 147.2, 162.1, 164.1, 167.2, 167.5; MS (ESI): m/z 470.2 ($[M+H_2O]^+$); HRMS (ESI): calculated for $C_{25}H_{24}O_8$ (M^+): 452.1471. Found: 452.1469; IR (KBr) ν 2955, 1740, 1634, 1451, 1436, 1311, 1131, 983 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 22.4 min; t_{major} = 28.6 min, λ = 254 nm).

4.3.2. (*S,Z*)-Trimethyl 4-(cinnamoyloxy)-2-(4-fluorophenyl)-but-3-ene-1,1,4-tricarboxylate 3b

White solid. Yield 87%. Mp 96–98 °C. $[\alpha]_D^{26} = -80.5$ (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.55 (s, 3H), 3.76 (d, J = 4.5 Hz, 6H), 3.89 (d, J = 10.2 Hz, 1H), 4.51 (t, J = 10.2 Hz, 1H), 6.56 (d, J = 15.9 Hz, 1H), 6.74 (d, J = 10.2 Hz, 1H), 6.96–7.02 (m, 2H), 7.20–7.26 (m, 2H), 7.40–7.44 (m, 3H), 7.54–7.62 (m, 2H), 7.80 (d, J = 15.9 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: −114.7; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.5, 52.6, 52.7, 53.0, 56.8, 115.7, 115.9 (d, J_{C-F} = 8.9 Hz), 128.4, 128.8, 129.0, 129.5 (d, J_{C-F} = 8.2 Hz), 130.9, 134.0, 134.1 (d, J_{C-F} = 2.0 Hz), 138.9, 147.5, 162.0 (d, J_{C-F} = 244.9 Hz), 162.1, 164.1, 167.3, 167.5; MS (ESI): m/z 488.2 ($[M+H_2O]^+$); HRMS (ESI): calculated for $C_{25}H_{23}FO_8$ (M^+): 470.1377. Found: 470.1386; IR (KBr) ν 2955, 1758, 1634, 1603, 1510, 1436, 983, 766 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 24.2 min; t_{major} = 34.9 min, λ = 254 nm).

4.3.3. (*S,Z*)-Trimethyl 2-(4-chlorophenyl)-4-(cinnamoyloxy)but-3-ene-1,1,4-tricarboxylate 3c

White solid. Yield 88%. Mp 123–125 °C. $[\alpha]_D^{27} = -144.0$ (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.56 (s, 3H), 3.76 (d, J = 4.5 Hz, 6H), 3.90 (d, J = 10.2 Hz, 1H), 4.50 (t, J = 10.2 Hz, 1H), 6.56 (d, J = 15.9 Hz, 1H), 6.73 (d, J = 10.2 Hz, 1H), 7.19 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.40–7.44 (m, 3H), 7.52–7.60 (m, 2H), 7.80 (d, J = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.6, 52.6, 52.7, 53.0, 56.6, 115.8, 128.4, 128.5, 128.9, 129.0, 129.2, 130.9, 133.5, 133.9, 136.9, 139.1, 147.6, 162.0, 164.1, 167.2, 167.4; MS (ESI): m/z 504 ($[M+H_2O]^+$). Anal. Calcd for $C_{25}H_{23}ClO_8$: C, 61.67; H, 4.76. Found: C, 61.40; H, 4.60. IR (KBr) ν 2954, 1740, 1634, 1492, 1436, 1309, 1132, 766 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 25.3 min; t_{major} = 36.2 min, λ = 254 nm).

4.3.4. (*S,Z*)-Trimethyl 2-(4-bromophenyl)-4-(cinnamoyloxy)-but-3-ene-1,1,4-tricarboxylate 3d

White solid. Yield 96%. Mp 126–128 °C. $[\alpha]_D^{27} = -136.0$ (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.56 (s, 3H), 3.76 (d, J = 4.8 Hz, 6H), 3.90 (d, J = 10.2 Hz, 1H), 4.48 (t, J = 10.2 Hz, 1H), 6.56 (d, J = 16.2 Hz, 1H), 6.73 (d, J = 10.2 Hz, 1H), 7.13 (d, J = 8.1 Hz, 2H), 7.38–7.46 (m, 5H), 7.52–7.60 (m, 2H), 7.79 (d, J = 16.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.7, 52.6, 52.7, 53.0, 56.5, 115.8, 121.7, 128.4, 128.5, 129.0, 129.6, 130.9, 132.0, 133.9, 137.4, 139.1, 147.6, 162.0, 164.1, 167.2, 167.4; MS (ESI): m/z 547.8 ($[M+H_2O]^+$). Anal. Calcd for $C_{25}H_{23}BrO_8$: C, 56.51; H, 4.36. Found: C, 56.47; H, 4.23. IR (KBr) ν 2954, 1740, 1634, 1436, 1310, 1132, 766, 682 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 25.8 min; t_{major} = 38.0 min, λ = 254 nm).

4.3.5. (*S,Z*)-Trimethyl 2-(3-chlorophenyl)-4-(cinnamoyloxy)but-3-ene-1,1,4-tricarboxylate 3e

White solid. Yield 92%. Mp 103–105 °C. $[\alpha]_D^{27} = -116.8$ (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.57 (s, 3H), 3.76 (d, J = 5.7 Hz, 6H), 3.91 (d, J = 10.2 Hz, 1H), 4.50 (t, J = 10.2 Hz, 1H), 6.57 (d, J = 15.6 Hz, 1H), 6.73 (d, J = 10.2 Hz, 1H), 7.12–7.17 (m, 1H), 7.20–7.25 (m, 3H), 7.39–7.44 (m, 3H), 7.57–7.60 (m, 2H), 7.80 (d, J = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.8, 52.6, 52.7, 53.0, 56.4, 115.8, 126.0, 127.9, 128.0, 128.2, 128.4, 129.0, 130.1, 130.9, 133.9, 134.6, 139.2, 140.4, 147.6, 162.0, 164.1, 167.1, 167.3; MS (ESI): m/z 504 ($[M+H_2O]^+$). Anal. Calcd for $C_{25}H_{23}ClO_8$: C, 61.67; H, 4.76. Found: C, 61.62; H, 4.68. IR (KBr) ν 2954, 1757, 1634, 1595, 1575, 1435, 1311, 767 cm^{-1}; The enantiomeric excess was determined by HPLC (Chiralpak AS-H column,

hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 13.6 min; t_{major} = 15.0 min, λ = 254 nm).

4.3.6. (*S,Z*)-Trimethyl 4-(cinnamoyloxy)-2-(4-nitrophenyl)but-3-ene-1,1,4-tricarboxylate 3f

White solid. Yield 91%. Mp 131–133 °C. $[\alpha]_D^{27} = -145.2$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.58 (s, 3H), 3.78 (d, *J* = 2.7 Hz, 6H), 3.96 (d, *J* = 9.9 Hz, 1H), 4.63 (t, *J* = 9.9 Hz, 1H), 6.55 (d, *J* = 15.9 Hz, 1H), 6.75 (d, *J* = 9.9 Hz, 1H), 7.38–7.50 (m, 5H), 7.52–7.60 (m, 2H), 7.79 (d, *J* = 15.9 Hz, 1H), 8.17 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 42.1, 53.0, 53.1, 53.4, 56.4, 115.7, 124.3, 127.6, 128.7, 129.2, 129.3, 131.3, 134.0, 140.1, 146.1, 147.5, 148.1, 162.0, 164.3, 167.2, 167.3; MS (ESI): *m*/*z* 515.2 ($[M+H_2O]^+$). Anal. Calcd for $C_{25}H_{23}NO_{10}$: C, 60.36; H, 4.66; N, 2.82. Found: C, 60.27; H, 4.61; N, 2.66. IR (KBr) ν 2955, 1736, 1634, 1523, 1436, 1350, 1130, 858 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 57.1 min; t_{major} = 97.4 min, λ = 254 nm).

4.3.7. (*S,Z*)-Trimethyl 4-(cinnamoyloxy)-2-*p*-tolylbut-3-ene-1,1,4-tricarboxylate 3g

White solid. Yield 49%. Mp 92–94 °C. $[\alpha]_D^{27} = -125.3$ (*c* 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 2.29 (s, 3H), 3.54 (s, 3H), 3.75 (d, *J* = 1.5 Hz, 6H), 3.93 (d, *J* = 10.2 Hz, 1H), 4.49 (t, *J* = 10.2 Hz, 1H), 6.58 (d, *J* = 15.6 Hz, 1H), 6.74 (d, *J* = 10.2 Hz, 1H), 7.04–7.18 (m, 4H), 7.40–7.44 (m, 3H), 7.52–7.60 (m, 2H), 7.80 (d, *J* = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.0, 41.9, 52.5, 52.6, 52.9, 56.7, 116.0, 127.6, 128.4, 128.9, 129.3, 129.6, 130.8, 134.0, 135.2, 137.3, 138.5, 147.3, 162.2, 164.2, 167.4, 167.7; MS (ESI): *m*/*z* 484.2 ($[M+H_2O]^+$). Anal. Calcd for $C_{26}H_{26}O_8$: C, 66.94; H, 5.62. Found: C, 66.85; H, 5.57. IR (KBr) ν 2955, 1738, 1634, 1450, 1436, 1309, 1133, 766 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 21.5 min; t_{major} = 26.5 min, λ = 254 nm).

4.3.8. (*S,Z*)-Trimethyl 4-(cinnamoyloxy)-2-(4-ethoxyphenyl)-but-3-ene-1,1,4-tricarboxylate 3h

White solid. Yield 51%. Mp 85–87 °C. $[\alpha]_D^{27} = -122.2$ (*c* 1.25, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.37 (t, *J* = 6.9 Hz, 3H), 3.54 (s, 3H), 3.75 (d, *J* = 3.9 Hz, 6H), 3.89 (d, *J* = 10.2 Hz, 1H), 3.97 (q, *J* = 6.9 Hz, 2H), 4.46 (t, *J* = 10.2 Hz, 1H), 6.57 (d, *J* = 16.2 Hz, 1H), 6.74 (d, *J* = 10.2 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 2H), 7.14 (d, *J* = 8.7 Hz, 2H), 7.38–7.44 (m, 3H), 7.52–7.59 (m, 2H), 7.79 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.8, 41.6, 52.5, 52.6, 52.9, 56.9, 63.3, 114.8, 116.0, 128.4, 128.8, 128.9, 129.4, 130.0, 130.8, 134.0, 138.4, 147.3, 158.3, 162.2, 164.2, 167.4, 167.7; MS (ESI): *m*/*z* 514.2 ($[M+H_2O]^+$). Anal. Calcd for $C_{27}H_{28}O_9$: C, 65.31; H, 5.68. Found: C, 65.29; H, 5.68. IR (KBr) ν 2954, 1744, 1635, 1511, 1436, 1310, 1129, 767 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 31.8 min; t_{major} = 44.9 min, λ = 254 nm).

4.3.9. (*S,Z*)-Trimethyl 4-(cinnamoyloxy)-2-(2,4-dichlorophenyl)but-3-ene-1,1,4-tricarboxylate 3i

White waxy solid. Yield 31%. $[\alpha]_D^{27} = -50.2$ (*c* 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.60 (s, 3H), 3.76 (d, *J* = 9.6 Hz, 6H), 4.03 (d, *J* = 9.0 Hz, 1H), 4.98 (t, *J* = 9.0 Hz, 1H), 6.49 (d, *J* = 15.6 Hz, 1H), 6.85 (d, *J* = 9.0 Hz, 1H), 7.15–7.26 (m, 2H), 7.35 (s, 1H), 7.40–7.44 (m, 3H), 7.54–7.56 (m, 2H), 7.74 (d, *J* = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 38.4, 52.6, 52.8, 52.9, 55.0, 115.7, 127.4, 127.5, 128.4, 129.0, 129.9, 130.4, 130.8, 133.9, 134.0, 134.4, 134.8, 139.7, 147.4, 161.9, 163.9, 167.1, 167.4; MS (ESI): *m*/*z* 538 ($[M+H_2O]^+$); HRMS (ESI): calculated for $C_{25}H_{22}Cl_2O_8$ (M^+): 520.0692. Found: 520.0684; IR (KBr) ν 2955, 1737, 1634, 1436, 1132, 982, 766, 579 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 21.9 min; t_{major} = 33.6 min, λ = 254 nm).

4.3.10. (*S,Z*)-Trimethyl 2-(2-bromophenyl)-4-(cinnamoyloxy)-but-3-ene-1,1,4-tricarboxylate 3j

White waxy solid. Yield 15%. $[\alpha]_D^{27} = -22.9$ (*c* 0.53, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.59 (s, 3H), 3.76 (d, *J* = 12.3 Hz, 6H), 4.05 (d, *J* = 9.6 Hz, 1H), 5.07 (t, *J* = 9.6 Hz, 1H), 6.50 (d, *J* = 16.2 Hz, 1H), 6.90 (d, *J* = 9.6 Hz, 1H), 7.05–7.11 (m, 1H), 7.26–7.30 (m, 2H), 7.39–7.45 (m, 3H), 7.49–7.60 (m, 3H), 7.76 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.1, 52.5, 52.7, 52.8, 55.4, 116.0, 124.3, 127.8, 128.0, 128.4, 128.9, 129.0, 129.5, 130.7, 133.5, 134.0, 137.8, 139.5, 147.1, 162.1, 163.9, 167.2, 167.5; MS (ESI): *m*/*z* 547.9 ($[M+H_2O]^+$); HRMS (ESI): calculated for $C_{25}H_{23}BrO_8$ (M^+): 530.0576. Found: 530.0577; IR (KBr) ν 2955, 1737, 1634, 1472, 1435, 1311, 1133, 765 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 23.4 min; t_{major} = 29.1 min, λ = 254 nm).

4.3.11. (*S,Z*)-4-Ethyl 1,1-dimethyl 4-(cinnamoyloxy)-2-phenylbut-3-ene-1,1,4-tricarboxylate 3k

White waxy solid. Yield 72%. $[\alpha]_D^{27} = -95.7$ (*c* 1.7, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.25 (t, *J* = 7.2 Hz, 3H), 3.51 (s, 3H), 3.74 (s, 3H), 3.94 (d, *J*= 10.5 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.52 (t, *J* = 10.5 Hz, 1H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.72 (d, *J* = 10.5 Hz, 1H), 7.23–7.31 (m, 5H), 7.32–7.40 (m, 3H), 7.51–7.54 (m, 2H), 7.79 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 42.3, 52.6, 52.9, 56.7, 61.7, 116.1, 127.6, 127.8, 128.4, 128.6, 128.9, 130.8, 134.0, 138.4, 139.0, 147.2, 161.7, 164.2, 167.3, 167.6; MS (ESI): *m*/*z* 484.2 ($[M+NH_4]^+$); HRMS (ESI): calculated for $C_{26}H_{26}O_8$ (M^+): 466.1628. Found: 466.1625; IR (KBr) ν 2955, 1736, 1635, 1435, 1370, 1134, 766, 701 cm^{-1}; The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 20.9 min; t_{major} = 22.5 min, λ = 254 nm).

4.3.12. (*S,Z*)-4-Allyl 1,1-dimethyl 4-(cinnamoyloxy)-2-phenylbut-3-ene-1,1,4-tricarboxylate 3l

White waxy solid. Yield 50%. $[\alpha]_D^{27} = -108.7$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.52 (s, 3H), 3.75 (s, 3H), 3.95 (d, *J* = 10.2 Hz, 1H), 4.54 (t, *J* = 10.2 Hz, 1H), 4.66 (d, *J* = 5.7 Hz, 2H), 5.20–5.33 (m, 2H), 5.83–5.96 (m, 1H), 6.58 (d, *J* = 15.9 Hz, 1H), 6.78 (d, *J* = 10.2 Hz, 1H), 7.23–7.33 (m, 5H), 7.38–7.44 (m, 3H), 7.53–7.62 (m, 2H), 7.80 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 42.3, 52.6, 52.9, 56.7, 66.1, 116.0, 118.5, 127.6, 127.8, 128.4, 128.8, 128.9, 129.2, 130.8, 131.5, 134.0, 138.3, 138.8, 147.3, 161.4, 164.2, 167.3, 167.6; MS (ESI): *m*/*z* 496.2 ($[M+H_2O]^+$); HRMS (ESI): calculated for $C_{27}H_{26}O_8$ (M^+): 478.1628. Found: 478.1636. IR (KBr) ν 2955, 1736, 1634, 1495, 1133, 982, 766, 701 cm^{-1}; The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 21.4 min; t_{major} = 23.0 min, λ = 254 nm).

4.3.13. (*S,Z*)-4-*tert*-Butyl 1,1-dimethyl 4-(cinnamoyloxy)-2-phenylbut-3-ene-1,1,4-tricarboxylate 3m

White waxy solid. Yield 35%. $[\alpha]_D^{27} = -96.7$ (*c* 0.7, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.44 (s, 9H), 3.50 (s, 3H), 3.74 (s, 3H), 3.93 (d, *J* = 10.5 Hz, 1H), 4.50 (t, *J* = 10.5 Hz, 1H), 6.53–6.61 (m, 2H), 7.18–7.36 (m, 5H), 7.38–7.42 (m, 3H), 7.52–7.60 (m, 2H), 7.78 (d, *J* = 16.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.9, 42.3, 52.5, 52.9, 56.8, 82.4, 116.2, 127.4, 127.5, 127.9, 128.3, 128.8, 128.9, 130.7, 134.1, 138.6, 140.0, 146.9, 160.7, 164.2, 167.4, 167.6; MS (ESI): *m*/*z* 512.2 ($[M+H_2O]^+$); HRMS (ESI): calculated

for $C_{28}H_{30}O_8$ (M^+): 494.1941. Found: 494.1944; IR (KBr) ν 2954, 1739, 1635, 1496, 1370, 1311, 1120, 766 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 12.6 min; t_{major} = 13.9 min, λ = 254 nm).

4.3.14. (*S,Z*)-4-Benzyl 1,1-dimethyl 4-(cinnamoyloxy)-2-phenylbut-3-ene-1,1,4-tricarboxylate 3n

White solid. Yield 70%. Mp 107–109 °C. $[\alpha]_D^{27} = -85.9$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.51 (s, 3H), 3.73 (s, 3H), 3.95 (d, *J* = 10.5 Hz, 1H), 4.54 (t, *J* = 10.5 Hz, 1H), 5.20 (dd, *J* = 12.3, 3.0 Hz, 2H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.78 (d, *J* = 10.5 Hz, 1H), 7.20–7.38 (m, 10H), 7.40–7.44 (m, 3H), 7.52–7.60 (m, 2H), 7.80 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 42.3, 52.6, 52.9, 56.7, 67.3, 116.0, 127.7, 127.9, 128.1, 128.3, 128.4, 128.5, 128.9, 129.0, 129.3, 130.8, 134.0, 135.3, 138.3, 138.8, 147.4, 161.6, 164.2, 167.3, 167.6; MS (ESI): *m*/*z* 546.2 ($[M+H_2O]^+$). Anal. Calcd for $C_{31}H_{28}O_8$: C, 70.44; H, 5.34. Found: C, 70.42; H, 5.30. IR (KBr) ν 2955, 1740, 1634, 1496, 1434, 1380, 1131, 766 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AS-H column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 15.2 min; t_{major} = 16.3 min, λ = 254 nm).

4.3.15. (*S,Z*)-4-(4-Bromobenzyl) 1,1-dimethyl 4-(cinnamoyloxy)-2-phenylbut-3-ene-1,1,4-tricarboxylate 3o

White solid. Yield 74%. Mp 113–115 °C. $[\alpha]_D^{27} = -79.7$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.51 (s, 3H), 3.73 (s, 3H), 3.94 (d, *J* = 10.2 Hz, 1H), 4.53 (t, *J* = 10.2 Hz, 1H), 5.13 (s, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.78 (d, *J* = 10.2 Hz, 1H), 7.18–7.32 (m, 7H), 7.40–7.50 (m, 5H), 7.52–7.60 (m, 2H), 7.78 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 42.3, 52.6, 52.9, 56.6, 66.4, 115.9, 122.3, 127.7, 127.9, 128.4, 128.9, 129.0, 129.5, 129.8, 130.9, 131.7, 134.0, 134.3, 138.2, 138.6, 147.5, 161.5, 164.2, 167.3, 167.6; MS (ESI): *m*/*z* 626 ($[M+H_2O]^+$). Anal. Calcd for $C_{31}H_{27}BrO_8$: C, 61.29; H, 4.48. Found: C, 61.40; H, 4.58. IR (KBr) ν 2954, 1737, 1634, 1491, 1451, 1435, 1132, 700 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AS-H column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 18.4 min; t_{major} = 22.0 min, λ = 254 nm).

4.3.16. (*S,Z*)-4-Isopropyl 1,1-dimethyl 4-(cinnamoyloxy)-2-phenylbut-3-ene-1,1,4-tricarboxylate 3p

White waxy solid. Yield 63%. $[\alpha]_D^{27} = -108.7$ (*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.24 (d, *J* = 6.0 Hz, 6H), 3.52 (s, 3H), 3.75 (s, 3H), 3.95 (d, *J* = 10.5 Hz, 1H), 4.53 (t, *J* = 10.5 Hz, 1H), 5.01–5.09 (m, 1H), 6.58 (d, *J* = 15.6 Hz, 1H), 6.68 (d, *J* = 10.5 Hz, 1H), 7.20–7.38 (m, 5H), 7.40–7.44 (m, 3H), 7.52–7.60 (m, 2H), 7.78 (d, *J* = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.6, 21.7, 42.3, 52.5, 52.9, 56.7, 69.5, 116.1, 127.6, 127.9, 128.2, 128.4, 128.8, 128.9, 130.8, 134.1, 138.5, 139.4, 147.1, 161.2, 164.2, 167.3, 167.6; MS (ESI): *m*/*z* 498.2 ($[M+H_2O]^+$); HRMS (ESI): calculated for $C_{27}H_{28}O_8$ (M^+): 480.1784. Found: 480.1789; IR (KBr) ν 2954, 1738, 1634, 1495, 1136, 1101, 980, 765 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 16.3 min; t_{major} = 17.6 min, λ = 254 nm).

4.3.17. (*S,Z*)-Trimethyl 2-(4-bromophenyl)-4-((*E*)-but-2-enoyloxy)but-3-ene-1,1,4-tricarboxylate 3q

White solid. Yield 70%. Mp 111–113 °C. $[\alpha]_D^{26} = -98.4$ (*c* 1.65, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.96 (d, *J* = 6.6 Hz, 3H), 3.55 (s, 3H), 3.72 (d, *J* = 5.4 Hz, 6H), 3.86 (d, *J* = 10.2 Hz, 1H), 4.42 (t, *J* = 10.2 Hz, 1H), 5.97 (d, *J* = 15.6 Hz, 1H), 6.65 (d, *J* = 10.2 Hz, 1H), 7.08–7.18 (m, 3H), 7.41 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.3, 41.6, 52.5, 52.7, 52.9, 56.4, 120.8, 121.6, 128.1, 129.5, 132.0, 137.4, 138.9, 148.2, 162.0, 163.5, 167.2, 167.3; MS (ESI): *m*/*z* 468.9 ($[M+H]^+$). Anal. Calcd for $C_{20}H_{21}BrO_8$: C, 51.59; H, 4.51. Found: C, 51.42; H, 4.57. IR (KBr) ν 2955, 1738, 1653, 1488, 1436, 1312, 1151, 827 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 17.2 min; t_{major} = 22.4 min, λ = 254 nm).

4.3.18. (*S,Z*)-1,1-Diethyl 4-methyl 2-(4-bromophenyl)-4-(cinnamoyloxy)but-3-ene-1,1,4-tricarboxylate 3r

White solid. Yield 61%. Mp 112–114 °C. $[\alpha]_D^{26} = -147.4$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.06 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 3.76 (s, 3H), 3.85 (d, *J* = 10.5 Hz, 1H), 3.96–4.07 (m, 2H), 4.13–4.26 (m, 2H), 4.46 (t, *J* = 10.5 Hz, 1H), 6.55 (d, *J* = 16.2 Hz, 1H), 6.74 (d, *J* = 10.5 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.38–7.46 (m, 5H), 7.52–7.58 (m, 2H), 7.78 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 13.9, 41.6, 52.5, 56.6, 61.7, 62.0, 115.8, 121.5, 128.4, 128.7, 129.0, 129.7, 130.9, 131.9, 133.9, 137.6, 139.0, 147.5, 162.0, 164.1, 166.8, 167.0; MS (ESI): *m*/*z* 575.8 ($[M+H_2O]^+$). Anal. Calcd for $C_{27}H_{27}BrO_8$: C, 57.97; H, 4.86. Found: C, 57.96; H, 4.85. IR (KBr) ν 2955, 1734, 1635, 1308, 1133, 861, 766, 682 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 24.1 min; t_{major} = 36.8 min, λ = 254 nm).

4.3.19. (*S,Z*)-1,1-Diisopropyl 4-methyl 2-(4-bromophenyl)-4-(cinnamoyloxy)but-3-ene-1,1,4-tricarboxylate 3s

White solid. Yield 68%. Mp 127–129 °C. $[\alpha]_D^{28} = -163.1$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.05 (dd, *J* = 13.5, 6.0 Hz, 6H), 1.24 (d, *J* = 6.0 Hz, 6H), 3.70–3.81 (m, 4H), 4.43 (t, *J* = 10.2 Hz, 1H), 4.81–4.89 (m, 1H), 5.02–5.11 (m, 1H), 6.54 (d, *J* = 16.2 Hz, 1H), 6.74 (d, *J* = 10.2 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.32–7.48 (m, 5H), 7.52–7.60 (m, 2H), 7.78 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 21.5, 21.6, 41.6, 52.5, 56.9, 69.4, 69.7, 115.8, 121.4, 128.4, 128.9, 129.0, 129.7, 130.9, 131.8, 134.0, 137.7, 138.9, 147.5, 162.1, 164.1, 166.4, 166.6; MS (MALDI): *m*/*z* 609.1 ($[M+Na]^+$). Anal. Calcd for $C_{29}H_{31}BrO_8$: C, 59.29; H, 5.32. Found: C, 59.42; H, 5.36. IR (KBr) ν 2982, 1732, 1635, 1488, 1100, 983, 911, 766 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 19.2 min; t_{major} = 30.5 min, λ = 254 nm).

4.3.20. (*S,Z*)-1,1-Dibenzyl 4-methyl 2-(4-bromophenyl)-4-(cinnamoyloxy)but-3-ene-1,1,4-tricarboxylate 3t

White waxy solid. Yield 98%. $[\alpha]_D^{27} = -115.1$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 3.75 (s, 3H), 3.98 (d, *J* = 10.2 Hz, 1H), 4.51 (t, *J* = 10.2 Hz, 1H), 4.98 (s, 2H), 5.17 (dd, *J* = 9.9, 12.0 Hz, 2H), 6.49 (d, *J* = 16.2 Hz, 1H), 6.73 (d, *J* = 10.2 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 4H), 7.20–7.38 (m, 10H), 7.40–7.46 (m, 3H), 7.48–7.59 (m, 2H), 7.74 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.8, 52.5, 56.7, 67.5, 67.7, 115.7, 121.7, 128.2, 128.3, 128.4, 128.5, 128.6, 128.9, 129.6, 130.9, 132.0, 133.9, 134.8, 135.0, 137.2, 139.1, 147.6, 161.9, 164.1, 166.5, 166.7; MS (MALDI): *m*/*z* 705.1 ($[M+Na]^+$); HRMS (MALDI): calculated for $C_{37}H_{31}O_8BrNa$ ($[M+Na]^+$): 705.1088. Found: 705.1095; IR (KBr) ν 2954, 1733, 1634, 1488, 1131, 981, 766, 698 cm^{-1}. The enantiomeric excess was determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 80:20, flow rate 0.75 mL/min; t_{minor} = 60.1 min; t_{major} = 71.9 min, λ = 254 nm).

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