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Catalytic asymmetric homo-1,3-dipolar cycloadditions of azomethine ylides: diastereo- and enantioselective synthesis of imidazolidines

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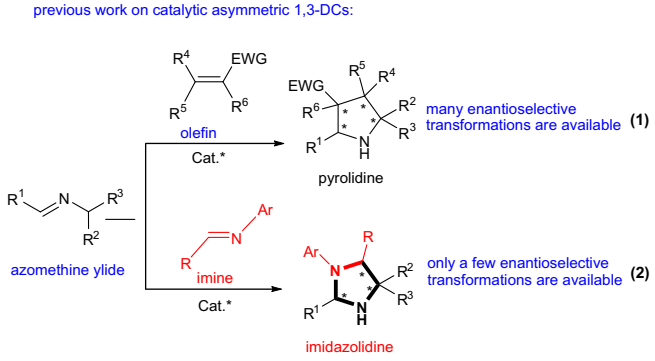
ABSTRACT

The first catalytic asymmetric homo-1,3-dipolar cycloadditions of azomethine ylides have been established via SPINOL-derived chiral phosphoric acid-catalyzed pseudo four-component reactions of aldehydes and 2-aminomalonates, resulting in the stereoselective construction of chiral imidazolidine scaffolds with two stereogenic centers in generally high yields and with good stereoselectivities (up to 81% yield, all >20:1 dr, up to 93% ee). This protocol provides easy access to synthetically and pharmaceutically important chiral imidazolidines via the formation of one ring system, two stereogenic centers, and four new bonds in a single step.

1. Introduction

Catalytic asymmetric 1,3-dipolar cycloadditions (1,3-DCs) of azomethine ylides to unsaturated bonds have proven to be a powerful tool to access chiral nitrogenous heterocyclic motifs, which existed in numerous natural products and artificial molecules with pharmaceutical relevance.[1] As a result, many enantioselective transformations have been developed in the catalytic asymmetric 1,3-DCs of azomethine ylides to electron-deficient olefins, leading to the formation of chiral pyrolidine scaffolds (Eq. 1).[2] However, in sharp contrast, only a few enantioselective variants have been found for the catalytic asymmetric 1,3-DCs of azomethine ylides to electronically poor carbon—nitrogen double bonds, which involves the use of imines derived from anilines and aldehydes as dipolarophiles as reported by Gong et al. and Wang et al. (Eq. 2).[3]



On the other hand, the catalytic asymmetric 1,3-DCs of azomethine ylides to imines would allow for the creation of a chiral imidazolidine skeleton, which constitutes the core structure of many natural products, bioactive compounds, and important catalysts or ligands in organic synthesis. For example, as illustrated in Figure 1, fumiquinazolines A and B **I** are natural alkaloids.[4] Compounds **II**–**IV** possess antipyretic, anticonvulsant, and aldose reductase inhibitory activities, respectively.[5] Compounds **V**–**VII** are well known organocatalysts or ligands, which have enabled a variety of enantioselective transformations.[6] Therefore, this transformation is highly desirable for the stereoselective construction of the imidazolidine moiety and remains a challenge with regard to the limited examples employing carbon—nitrogen double bonds as dipolarophiles.

We have already established a series of 1,3-DCs of azomethine ylides to electron-deficient olefins[7] or alkynes[8] with excellent enantioselectivity using chiral phosphoric acids (CPAs)[9] as catalysts. Inspired by this success and with the aim of synthesizing stereoselective imidazolidines, we envisioned that the precursors of azomethine ylides, that is, the aldimines generated from aldehydes and amino-esters would serve as carbon—nitrogen double bonds to react with the same azomethine ylides via homo-1,3-DCs under the catalysis of CPA, thus affording chiral imidazolidines with multiple stereogenic centers (Scheme 1). In this approach, azomethine ylides would act as both 1,3-dipoles and dipolarophiles to perform diastereo- and enantioselective homo-1,3-DCs, which have not been reported so far during the development of catalytic asymmetric 1,3-DCs of azomethine ylides.

Herein we report the first catalytic asymmetric homo-1,3-DCs of azomethine ylides, which assemble aldehydes and 2-aminomalonates in a highly ordered reaction sequence to efficiently

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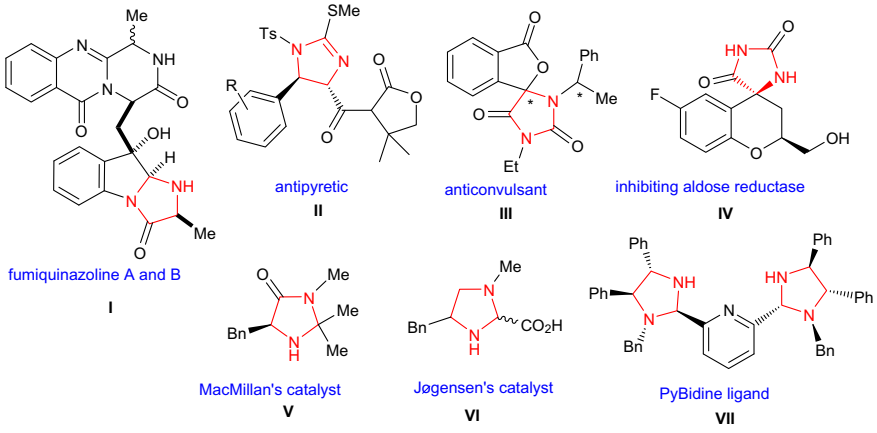
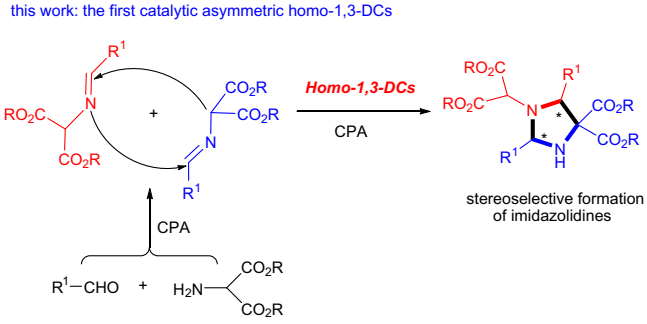


Figure 1. Selected natural alkaloids, bioactive compounds, and important catalysts or ligands containing a chiral imidazolidine skeleton.



Scheme 1. The design of catalytic asymmetric homo-1,3-DCs of azomethine ylides.

construct chiral imidazolidines with two stereogenic centers in high yields (up to 81%) and with good stereoselectivities (all >20:1 dr, up to 93% ee). This approach also takes advantage of a *pseudo* four-component reaction, which forms one ring system, two stereogenic centers, and four new bonds in a single step.

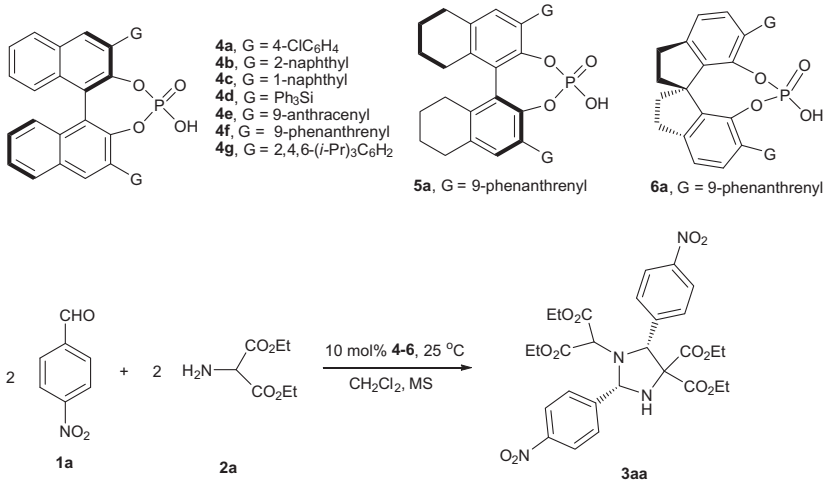
2. Results and discussion

The initial experiments to test our hypothesis started with a *pseudo* four-component reaction of 4-nitrobenzaldehyde **1a** and diethyl 2-aminomalonate **2a** in the presence of various BINOL-derived CPAs **4** at 25 °C in chloromethane (Table 1, entries 1–7). Although these reactions afforded the desired imidazolidine product **3aa**, the yield was rather low, which indicated that the homo-1,3-DCs of azomethine ylides were challenging because of the relatively low activity of azomethine ylides acting as dipolarophiles. The preliminary screening of catalysts also revealed that CPAs **4f** and **4g** could give product **3aa** with higher enantioselectivity than others (entries 6 and 7 vs 1–5). Changing CPA **4f** to H_8-BINOL-derived CPA **5a** with the same 3,3′-substituents of the BINOL backbone improved the enantioselectivity to 69% ee, but without any improvement in the yield (entry 8). Recently, SPINOL-derived CPAs have been recognized as a type of chiral Brønsted acids that possess higher capability in enantioselective control than their BINOL-based analogues.[10] Hence, we changed the H_8-BINOL backbone of catalyst **5a** to a SPINOL scaffold and employed this type of spiro-CPA **6a** to the same reaction. As expected, this structurally more rigid catalyst **6a** enabled the model reaction to proceed in a much more efficient and enantioselective manner, affording imidazolidine **3aa** in 68% yield and 87% ee (entry 9). In the presence of CPA **6a**, the screening of molecular sieves (MS) were subsequently performed, which showed that 4 Å MS was much superior to 3 Å and 5 Å MS, both in terms of reactivity and enantioselective control (entry 9 vs 10 and 11).

Next, other reaction parameters including solvents, temperature, and catalyst loading were optimized to further improve the enantioselectivity (Table 2). The screening of solvents (entries 1–5) found that chloroform was the most suitable one, enabling the model reaction to proceed in a high yield of 74% and with an excellent enantioselectivity of 90% ee (entry 3). With regard to the temperature (entries 6 and 7), we found that 40 °C gave the best performance in providing product **3aa** in 76% yield and 91% ee (entry 6). However, increasing the catalyst loading was detrimental to the enantioselectivity of the reaction without any obvious improvements in the yields (entries 8 and 9). The most suitable reaction conditions are found in entry 6.

With the optimal reaction conditions in hand, we next investigated the substrate scope of the catalytic asymmetric homo-1,3-DCs of azomethine ylides. As shown in Table 3, this protocol was amenable to a wide range of aromatic, heteroaromatic aldehydes **1a**–**1m** and different amino-esters **2a**,**2b**, providing chiral imidazolidines **3** with structural diversity in generally acceptable yields and with good stereoselectivities. Most of the electronically poor aldehydes proved to be suitable substrates in giving the homo-1,3-DCs with high enantioselectivities (80–93% ee, entries 1–5, 8, 10, and 14–17). Nevertheless, for some of the benzaldehydes substituted with electron-withdrawing groups, the enantioselectivities were moderate (entries 6, 7, and 9), which indicated that the electronic nature of the substituents might have an effect on the enantioselectivity. The position of the substituents also affected the reactivity and enantioselectivity. For instance, *p*-nitrobenzaldehyde **1a** exhibited a higher reactivity and enantioselectivity than its *meta*- or *ortho*-substituted counterparts **1b**,**1c** (entry 1 vs 2 and 3). Electronically neutral or electron rich aldehydes **1k**,**1l** could participate in the homo-1,3-DCs with good yields, but the enantioselectivities were unsatisfactory (entries 10 and 11), which was largely ascribed to the low reactivity of such aldehydes in 1,3-DCs.[8a,c] Similarly, heteroaromatic aldehydes as exemplified by **1m** could also take part in the reaction although the yield and enantioselectivity were not satisfactory (entry 13). Aliphatic aldehydes such as 3-phenylpropanal could not be utilized as suitable substrates to afford the homo-1,3-DC products, and just generated the corresponding azomethine ylide using the current conditions. Moreover, when dimethyl 2-aminomalonate **2b** was used in the reaction, *o*-nitrobenzaldehyde **1c** showed the highest capability in terms of enantioselective control (93% ee), albeit with moderate yield (entry 14). It should be noted that all of the

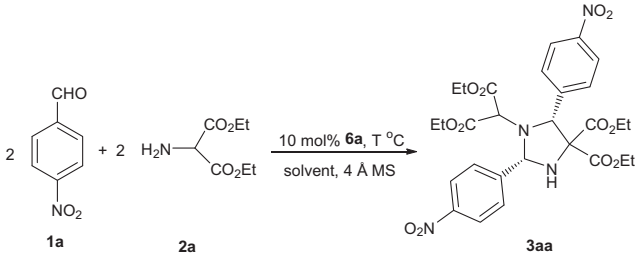
Table 1
Screening of catalysts and MS[a]



Entry	4	MS (Å)	Yield[b] (%)	dr[c]	ee[d] (%)
1	**4a**	4	31	>20:1	43
2	**4b**	4	38	>20:1	3
3	**4c**	4	15	>20:1	20
4	**4d**	4	—	>20:1	—
5	**4e**	4	20	>20:1	48
6	**4f**	4	33	>20:1	52
7	**4g**	4	33	>20:1	65
8	**5a**	4	34	>20:1	69
9	**6a**	4	**68**	**>20:1**	**87**
10	**6a**	3	34	>20:1	53
11	**6a**	5	10	>20:1	56

[a] Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale in CH_2Cl_2 (1 mL) with MS (100 mg) for 24 h, and the ratio of **1a**/**2a** was 1.2:1.
[b] Isolated yields.
[c] The diastereomeric ratio (dr) was determined by ^{1}H NMR spectroscopy.
[d] The enantiomeric excess (ee) was determined by HPLC.

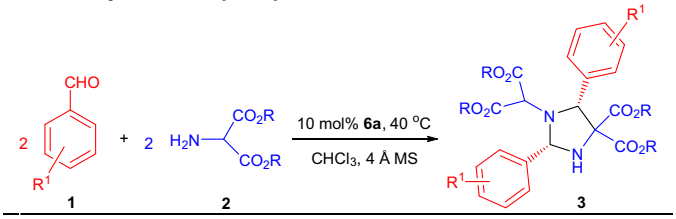
Table 2
Further optimization of reaction conditions[a]



Entry	Solvent	*T* (°C)	Yield[b] (%)	dr[c]	ee[d] (%)
1	CH_2Cl_2	25	68	>20:1	87
2	DCE	25	69	>20:1	81
3	$CHCl_3$	25	74	>20:1	90
4	CCl_4	25	66	>20:1	66
5	$PhCH_3$	25	35	>20:1	72
6	**$CHCl_3$**	**40**	**76**	**>20:1**	**91**
7	$CHCl_3$	55	76	>20:1	86
8[e]	$CHCl_3$	40	76	>20:1	86
9[f]	$CHCl_3$	40	79	>20:1	86

[a] Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale in a solvent (1 mL) with 4 Å MS (100 mg) for 24 h, and the ratio of **1a**/**2a** was 1.2:1.
[b] Isolated yields.
[c] The diastereomeric ratio (dr) was determined by ^{1}H NMR.
[d] The enantiomeric excess (ee) was determined by HPLC.
[e] Catalyzed by 15 mol % **6a**.
[f] Catalyzed by 20 mol % **6a**.

Table 3
Substrate scope of the catalytic asymmetric homo-1,3-DCs[a]



Entry	3	R^1 **1**	R **2**	Yield[b] (%)	dr[c]	ee[d] (%)
1	**3aa**	4-NO_2 **1a**	Et **2a**	76	>20:1	91
2	**3ba**	3-NO_2 **1b**	Et **2a**	66	>20:1	87
3	**3ca**	2-NO_2 **1c**	Et **2a**	47	>20:1	89
4	**3da**	4-CN **1d**	Et **2a**	81	>20:1	85
5	**3ea**	3-CN **1e**	Et **2a**	68	>20:1	82
6	**3fa**	4-CO_2Me **1f**	Et **2a**	61	>20:1	47
7	**3ga**	4-CF_3 **1g**	Et **2a**	36	>20:1	44
8	**3ha**	4-F **1h**	Et **2a**	49	>20:1	87
9	**3ia**	2-F **1i**	Et **2a**	45	>20:1	41
10	**3ja**	4-F–3-CN **1j**	Et **2a**	51	>20:1	87
11	**3ka**	H **1k**	Et **2a**	51	>20:1	27
12	**3la**	4-MeO **1l**	Et **2a**	62	>20:1	23
13	**3ma**	2-Thiophenyl **1m**	Et **2a**	38	>20:1	37
14	**3ab**	4-NO_2 **1a**	Me **2b**	72	>20:1	84
15	**3bb**	3-NO_2 **1b**	Me **2b**	75	>20:1	83
16	**3cb**	2-NO_2 **1c**	Me **2b**	45	>20:1	93
17	**3db**	4-CN **1d**	Me **2b**	77	>20:1	80

[a] Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale in chloroform (1 mL) at 40 °C with 4 Å MS (100 mg) for 24 h, and the ratio of **1**/**2** was 1.2:1.
[b] Isolated yields.
[c] The diastereomeric ratio (dr) was determined by ^{1}H NMR.
[d] The enantiomeric excess (ee) was determined by HPLC.

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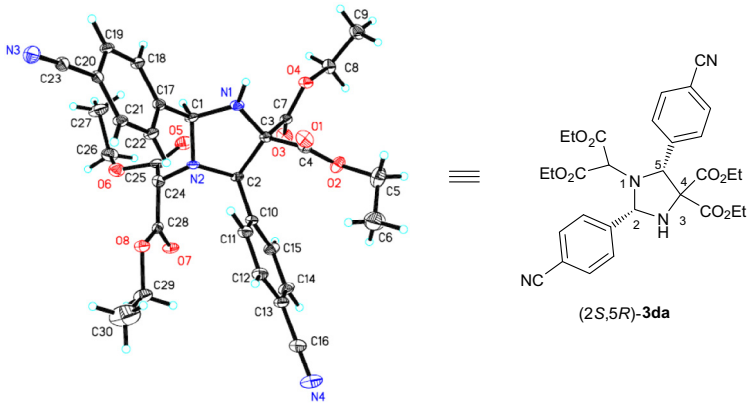
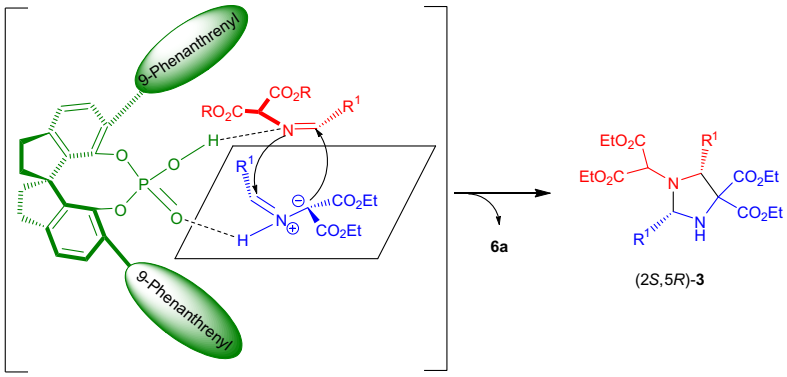


Figure 2. The absolute configuration of imidazolidine **3da**.



Scheme 2. Possible reaction pathway and transition state.

reactions proceeded in a highly diastereoselective manner with more than 20:1 dr due to the fact that only one diastereomer could be observed in the reaction.

The absolute configuration of compound **3da** was unambiguously determined to be (2*S*,5*R*) by single-crystal X-ray diffraction analysis (Fig. 2).[11] Moreover, the relative configuration of compound **3da** was also confirmed to be *cis* by its X-ray structure. The relative and absolute configurations of other imidazolidines **3** were assigned by analogy.

Based on our experimental results and previous studies on the reaction mechanism,[3a,7,12] we propose a possible reaction pathway and transition state to explain the stereochemistry of this catalytic asymmetric homo-1,3-DCs of azomethine ylides. As illustrated in Scheme 2, CPA **6a** acted as a Brønsted acid/Lewis base bifunctional catalyst to simultaneously activate both the azomethine ylide and the aldimine via hydrogen bonding interactions, which facilitated subsequent [3+2] cycloadditions. Due to the chiral environment created by the (*R*)-SPINOL backbone and the bulky 6,6′-(9-phenanthrenyl)-substitutents of catalyst **6a**, the homo-1,3-DCs of the azomethine ylides occurred in a diastereo- and enantioselective mode, leading to the generation of the experimentally observed (2*S*,5*R*)-configured imidazolidines **3**.

3. Conclusion

In conclusion, we have established the first catalytic asymmetric homo-1,3-DCs of azomethine ylides generated in situ from aldehydes and 2-aminomalonates. This approach utilized a structurally rigid SPINOL-derived CPA as the organocatalyst, resulting in the stereoselective construction of a chiral imidazolidine scaffold with two stereogenic centers in generally high yields and with good stereoselectivities (up to 81% yield, all >20:1 dr, up to 93% ee). This protocol takes advantage of a *pseudo* four-component reaction, leading to the formation of one ring system, two stereogenic centers, and four new bonds in a single step. Therefore, this study will not only enrich the chemistry of catalytic asymmetric 1,3-DCs of azomethine ylides, but also provide an easy access to synthetically and pharmaceutically important chiral imidazolidines.

4. Experimental

4.1. General

NMR spectra were measured respectively at 400 and 100 MHz. The solvent used for NMR spectroscopy was $CDCl_3$, using tetramethylsilane as the internal reference. HRMS spectra were recorded on a LTQ-Orbitrap mass spectrometer. Enantiomeric excess (ee) was determined by chiral high-performance liquid chromatography (chiral HPLC). The chiral columns used for determination of the enantiomeric excess by chiral HPLC were Chiralpak OD-H, IA, and IC columns. Optical rotation values were measured with instruments operating at $\lambda = 589$ nm, corresponding to the sodium D line at the temperatures indicated. Analytical grade solvents for column chromatography and commercially available reagents were used as received.

4.2. General procedure for the catalytic asymmetric synthesis of imidazolidines 3

To a solution of aldehyde **1** (0.24 mmol), catalyst **6a** (0.01 mmol), and 4 Å molecular sieves (100 mg) in chloroform (1 mL), amino-ester **2** (0.2 mmol) was added and then stirred at 40 °C for 24 h. The reaction mixture was then filtered to remove molecular sieves and the solid powder was washed with ethyl acetate. The resultant solution was concentrated under the reduced pressure to give the residue, which was purified by flash column chromatography on silica gel to afford pure product **3**.

4.3. Characterization of compounds 3

4.3.1. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-bis(4-nitrophenyl)imidazolidine-4,4-dicarboxylate 3aa

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 76%; >20:1 dr; colorless solid; $[\alpha]_D^{20} = -7$ (*c* 0.33, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 5.59 (s, 1H), 5.29 (d, *J* = 7.6 Hz, 1H), 4.46–4.28 (m, 1H), 4.26–4.08 (m, 1H), 4.02 (s, 1H), 3.96–3.88 (m, 1H), 3.88–3.83 (m, 1H), 3.83–3.79 (m, 1H), 3.79–3.73 (m, 2H), 3.53 (d, *J* = 8.1 Hz, 1H), 3.44–3.28 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 167.5, 166.0, 165.8, 148.6, 147.7, 146.4, 144.9, 129.3, 123.9, 123.0, 67.3, 62.8, 62.6, 62.0, 61.72, 61.6, 13.9, 13.8, 13.7, 13.4; IR (KBr): 3273, 2985, 1734, 1629, 1523, 1385, 855, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{32}N_4O_{12}-H)^-$ requires *m*/*z* 615.1939, found *m*/*z* 615.1917; enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 80:20, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 9.410 min (major), t_R = 7.793 - min (minor).

4.3.2. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-bis(3-nitrophenyl)imidazolidine-4,4-dicarboxylate 3ba

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 66%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = +27$ (*c* 0.36, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.44 (s, 1H), 8.30 (t, *J* = 8.9 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 7.62–7.52 (m, 1H), 5.75 (s, 1H), 5.45 (d, *J* = 9.7 Hz, 1H), 4.49–4.44 (m, 1H), 4.41–4.27 (m, 1H), 4.06 (s, 1H), 4.01–3.98 (m, 1H), 3.95–3.87 (m, 1H), 3.86–3.77 (m, 2H), 3.77–3.68 (m, 1H), 3.58 (d, *J* = 9.8 Hz, 1H), 3.46–3.38 (m, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 0.85 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 167.3, 166.1, 165.9, 148.4, 147.9, 141.3, 140.2, 134.6, 134.4, 129.9, 129.0, 124.4, 123.6, 123.5, 123.1, 67.1, 62.8, 62.6, 61.9, 61.7, 61.7, 14.0, 13.8, 13.6, 13.3; IR (KBr): 3255, 2963, 1737, 1629, 1532, 1388, 1008, 869, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{32}N_4O_{12}-H)^-$ requires *m*/*z* 615.1939, found *m*/*z* 615.1873; enantiomeric excess: 87%, determined by HPLC (Daicel Chirapak IA, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 8.200 min (major), t_R = 5.800 min (minor).

4.3.3. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-bis(2-nitrophenyl)imidazolidine-4,4-dicarboxylate 3ca

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 47%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = -109$ (*c* 0.24, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.7 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 6.36 (s, 1H), 5.72 (d, *J* = 5.8 Hz, 1H), 4.47–4.38 (m, 2H), 4.37–4.22 (m, 2H), 4.20 (s, 1H), 4.08–4.03 (m, 1H), 3.86–3.74 (m, 3H), 3.57–3.48 (m, 1H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H), 0.85 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 167.7, 166.1, 165.9, 140.4, 139.4, 133.1, 132.8, 132.2, 131.8, 129.7, 129.0, 112.8, 112.1, 67.1, 62.7, 62.6, 61.8, 61.7, 61.6, 13.9, 13.8, 13.7, 13.4; IR (KBr): 3235, 2990, 1738, 1629, 1540, 1379, 1200, 1006, 866, 745 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{32}N_4O_{12}-H)^-$ requires *m*/*z* 615.1939, found *m*/*z* 615.1959; enantiomeric excess: 89%, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 7.507 min (major), t_R = 6.713 min (minor).

4.3.4. (2*S*,5*R*)-Diethyl-2,5-bis(4-cyanophenyl)-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)imidazolidine-4,4-dicarboxylate 3da

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 81%; >20:1 dr; colorless solid; $[\alpha]_D^{20} = -29$ (*c* 0.24, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.71–7.62 (m, 4H), 5.69 (s, 1H), 5.37 (d, *J* = 7.0 Hz, 1H), 4.46–4.38 (m, 1H), 4.36–4.27 (m, 1H), 3.99 (s, 1H), 3.93–3.91 (m, 1H), 3.90–3.84 (m, 1H), 3.83–3.79 (m, 1H), 3.79–3.73 (m, 2H), 3.54 (d, *J* = 8.7 Hz, 1H), 3.41–3.36 (m, 1H), 1.33 (t, *J* = 5.7 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.85 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 167.6, 166.1, 165.9, 144.4, 143.0, 132.5, 131.7, 129.1, 118.5, 118.4, 113.3, 111.9, 67.4, 62.7, 62.6, 62.0, 61.6, 61.5, 55.0, 13.9, 13.8, 13.7, 13.4; IR (KBr): 3235, 2963, 1737, 1637, 1617, 1384, 1326, 1261, 1098, 1019, 803, 617 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{32}N_4O_{8-}-H)^-$ requires *m*/*z* 575.2143, found *m*/*z* 575.2093; enantiomeric excess: 85%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 25.700 min (major), t_R = 21.570 min (minor).

4.3.5. (2*S*,5*R*)-Diethyl-2,5-bis(3-cyanophenyl)-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)imidazolidine-4,4-dicarboxylate 3ea

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 68%; > 20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = +36$ (*c* 0.39, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 6.8 Hz, 2H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.4 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 1H), 5.65 (s, 1H), 5.36 (s, 1H), 4.51 (s, 1H), 4.48–4.42 (m, 1H), 4.27–4.22 (m, 1H), 3.99 (s, 1H), 3.93–3.72 (m, 5H), 3.48–3.41 (m, 1H), 1.33 (t, *J* = 6.9 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 167.7, 166.1, 165.9, 140.4, 139.4, 133.1, 132.8, 132.2, 131.8, 129.7, 129.0, 118.4, 118.4, 112.8, 112.1, 67.1, 62.7, 62.6, 61.8, 61.7, 61.6, 13.9, 13.8, 13.7, 13.4; IR (KBr): 3230, 2988, 1736, 1629, 1504, 1285, 1100, 1007, 995, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{32}N_4O_8+-Na)^+$ requires *m*/*z* 599.2118, found *m*/*z* 599.2111; enantiomeric excess: 82%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 7.827 min (major), t_R = 4.887 min (minor).

4.3.6. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-bis(4-(methoxycarbonyl)phenyl)imidazolidine-4,4-dicarboxylate 3fa

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 61%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = -15$ (*c* 0.27, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.1 Hz, 2H), 8.01 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 7.7 Hz, 2H), 5.71 (s, 1H), 5.36 (d, *J* = 8.8 Hz, 1H), 4.47–4.39 (m, 1H), 4.37–4.23 (m, 1H), 4.02 (s, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.91–3.80 (m, 2H), 3.79–3.73 (m, 1H), 3.69 (q, *J* = 7.1 Hz, 2H), 3.61 (d, *J* = 9.3 Hz, 1H), 3.34–3.13 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H), 0.82 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 167.8, 166.8, 166.7, 166.3, 166.1, 144.3, 142.8, 131.1, 129.9, 129.8, 129.1, 128.4, 67.4, 62.5, 62.4, 62.0, 61.4, 61.3, 352.2,

52.1, 13.9, 13.8, 13.7, 13.3; IR (KBr): 3238, 2996, 1733, 1630, 1614, 1390, 1318, 1044, 868, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{38}N_2O_{12}+Na)^+$ requires *m*/*z* 665.2317, found *m*/*z* 665.2355; enantiomeric excess: 47%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 15.263 min (major), t_R = 13.583 min (minor).

4.3.7. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-bis(4-(trifluoromethyl)phenyl)imidazolidine-4,4-dicarboxylate 3ga

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 36%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20}$ = −13 (*c* 0.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.0 Hz, 2H), 7.75–7.68 (m, 4H), 7.61 (d, J = 8.1 Hz, 2H), 5.71 (s, 1H), 5.40 (d, J = 9.5 Hz, 1H), 4.47–4.39 (m, 1H), 4.37–4.27 (m, 1H), 4.03 (s, 1H), 3.95–3.86 (m, 1H), 3.85–3.81 (m, 1H), 3.80–3.69 (m, 3H), 3.59 (d, J = 10.0 Hz, 1H), 3.40–3.29 (m, 1H), 1.32 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H), 1.07 (t, J = 6.4 Hz, 3H), 0.79 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 167.9, 166.3, 166.1, 143.0, 141.9, 131.7, 131.4, 130.5, 130.2, 129.1, 128.9, 125.6, 125.6, 125.3, 125.2, 124.8, 124.8, 122.6, 122.5, 67.4, 62.5, 62.0, 61.4, 58.4, 55.0, 53.4, 13.9, 13.7, 13.6, 13.1; IR (KBr): 3274, 2986, 1733, 1630, 1617, 1384, 1318, 1047, 868, 717 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{32}F_6N_2O_8+Na)^+$ requires *m*/*z* 685.1955, found *m*/*z* 685.1993; enantiomeric excess: 44%, determined by HPLC (Daicel Chirapak IA, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.683 min (major), t_R = 4.537 min (minor).

4.3.8. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-bis(4-fluorophenyl)imidazolidine-4,4-dicarboxylate 3ha

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 49%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20}$ = −49 (*c* 0.12, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.67 (m, 2H), 7.58–7.51 (m, 2H), 7.12 (t, J = 8.5 Hz, 2H), 7.03 (t, J = 8.4 Hz, 2H), 5.60 (s, 1H), 5.29 (d, J = 9.6 Hz, 1H), 4.46–4.39 (m, 1H), 4.32–4.23 (m, 1H), 4.03 (s, 1H), 3.95–3.88 (m, 1H), 3.87–3.75 (m, 4H), 3.54 (d, J = 10.4 Hz, 1H), 3.48–3.35 (m, 1H), 1.31 (t, J = 4.8 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H), 0.86 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 168.3, 166.5, 166.4, 134.3, 133.6, 130.2, 115.6, 115.4, 114.9, 114.6, 97.4, 67.0, 62.3, 61.9, 61.3, 61.2, 55.0, 18.4, 13.9, 13.8, 13.7, 13.4; IR (KBr): 3273, 2963, 1734, 1629, 1509, 1370, 1261, 1096, 1021, 801 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{32}F_6N_2O_8+Na)^+$ requires *m*/*z* 585.2019, found *m*/*z* 585.2025; enantiomeric excess: 87%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 9.197 min (major), t_R = 6.190 min (minor).

4.3.9. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-5-(2-fluorophenyl)-2-(o-tolyl)imidazolidine-4,4-dicarboxylate 3ia

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 45%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20}$ = −20 (*c* 0.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.75 (s, 1H), 7.38–7.30 (m, 1H), 7.24–7.16 (m, 2H), 7.12–7.08 (m, 2H), 7.05–6.95 (m, 1H), 6.09 (s, 1H), 5.59 (d, J = 11.0 Hz, 1H), 4.51–4.45 (m, 1H), 4.40–4.24 (m, 1H), 4.10–3.94 (m, 3H), 3.89–3.56 (m, 4H), 3.44 (s, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 1.08 (t, J = 7.1 Hz, 3H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 166.54, 163.3, 160.8, 130.8, 130.7, 129.6, 129.3, 129.0, 124.6, 124.5, 123.7, 115.9, 97.4, 62.4, 62.3, 61.3, 55.0, 53.4, 31.6, 22.6, 14.1, 13.9, 13.8, 13.5, 13.3; IR (KBr): 3275, 2960, 1738, 1632, 1500, 1374, 1260, 1095, 1022, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{32}F_6N_2O_8+Na)^+$ requires *m*/*z* 585.2019, found *m*/*z* 585.1976; enantiomeric excess: 41%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 8.103 min (major), t_R = 7.433 min (minor).

4.3.10. (2*S*,5*R*)-Diethyl-2,5-bis(3-cyano-4-fluorophenyl)-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)imidazolidine-4,4-dicarboxylate 3ja

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 51%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20}$ = +21 (*c* 0.11, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26–8.08 (m, 1H), 8.04–7.90 (m, 1H), 7.87–7.74 (m, 1H), 7.45 (t, J = 8.4 Hz, 1H), 7.41–7.30 (m, 1H), 7.27–7.18 (m, 1H), 5.58 (s, 1H), 5.33 (d, J = 5.3 Hz, 1H), 4.53–4.40 (m, 1H), 4.29–4.19 (m, 4H), 3.96–3.83 (m, 2H), 3.82–3.71 (m, 1H), 3.60–3.49 (m, 1H), 3.47–3.40 (m, 1H), 1.29 (t, J = 7.1, 3H), 1.21 (t, J = 7.1, 3H), 1.16 (t, J = 7.1 Hz, 3H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 167.7, 165.8, 161.5, 135.6, 135.2, 135.1, 133.7, 132.3, 117.1, 116.9, 116.3, 113.5, 101.7, 101.2, 97.4, 93.7, 90.4, 66.5, 62.8, 62.4, 62.0, 61.8, 6, 58.4, 55.0, 18.4, 14.5, 13.9, 13.8, 13.5; IR (KBr): 3316, 2965, 1738, 1630, 1585, 1500, 1447, 1260, 1095, 1027, 948 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{30}F_2N_4O_8+Na)^+$ requires *m*/*z* 635.1930, found *m*/*z* 635.1960; enantiomeric excess: 87%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 80:20, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 13.420 min (major), t_R = 14.597 min (minor).

4.3.11. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-diphenylimidazolidine-4,4-dicarboxylate 3ka

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 51%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20}$ = +108 (*c* 0.08, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.5 Hz, 2H), 7.57 (d, J = 7.0 Hz, 2H), 7.47–7.38 (m, 3H), 7.32 (t, J = 7.4 Hz, 2H), 7.25 (d, J = 6.9 Hz, 1H), 5.65 (s, 1H), 5.31 (s, 1H), 4.47–4.39 (m, 1H), 4.34–4.22 (m, 1H), 4.09 (s, 1H), 3.94–3.85 (m, 1H), 3.83–3.81 (m, 1H), 3.80–3.72 (m, 1H), 3.73–3.57 (m, 3H), 3.33–3.29 (m, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H), 1.07 (t, J = 7.1 Hz, 3H), 0.80 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 168.3, 166.7, 166.6, 138.8, 137.9, 129.2, 128.5, 128.50, 127.9, 127.8, 67.6, 62.2, 62.1, 62.0, 61.1, 55.0, 13.9, 13.8, 13.7, 13.3; IR (KBr): 3236, 2980, 1734, 1629, 1285, 1007, 986, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{34}N_2O_8+Na)^+$ requires *m*/*z* 549.2207, found *m*/*z* 549.2259; enantiomeric excess: 27%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.847 min (major), t_R = 5.913 min (minor).

4.3.12. (2*S*,5*R*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-bis(4-methoxyphenyl)imidazolidine-4,4-dicarboxylate 3la

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 62%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20}$ = +5 (*c* 0.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 7.6 Hz, 2H), 6.94 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.4 H z, 2H), 5.55 (s, 1H), 5.24 (s, 1H), 4.45–4.39 (m, 1H), 4.33–4.17 (m, 1H), 4.06 (s, 1H), 3.93–3.87 (m, 2H), 3.84 (s, 3H), 3.80 (s, 3H), 3.79–3.71 (m, 3H), 3.55 (s, 1H), 3.40–3.29 (m, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H), 0.85 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 169.5, 166.4, 162.0, 132.0, 130.7, 130.6, 129.9, 114.3, 113.9, 113.2, 67.0, 62.1, 62.1, 62.0, 61.9, 61.0, 58.5, 55.4, 14.05 13.9, 13.8, 13.7, 13.4; IR (KBr): 3233, 2984, 1735, 1629, 1509, 1283, 1109, 1007, 994, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{38}N_2O_{10}+Na)^+$ requires *m*/*z* 609.2416, found *m*/*z* 609.2416; enantiomeric excess: 23%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 11.140 -min (major), t_R = 7.263 min (minor).

4.3.13. (2*S*,5*S*)-Diethyl-1-(1,3-diethoxy-1,3-dioxopropan-2-yl)-2,5-di(thiophen-2-yl)imidazolidine-4,4-dicarboxylate 3ma

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 38%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = -39$ (*c* 0.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.32 (dd, *J* = 3.5, 0.8 Hz, 1H), 7.22 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.06 (d, *J* = 3.1 Hz, 1H), 7.03 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.95 (dd, *J* = 5.0, 3.5 Hz, 1H), 5.91 (s, 1H), 5.48 (s, 1H), 4.52–4.45 (m, 1H), 4.39–4.33 (m, 1H), 4.29 (s, 1H), 4.18–4.09 (m, 1H), 4.08–4.00 (m, 1H), 3.93–3.86 (m, 1H), 3.81–3.74 (m, 2H), 3.72–3.65 (m, 2H), 1.36 (t, *J* = 5.8 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 166.7, 166.6, 166.2, 145.1, 142.5, 127.9, 126.7, 126.6, 126.3, 125.9, 125.0, 74.6, 63.4, 62.4, 61.4, 14.13, 14.0, 13.9, 13.6, 13.5; IR (KBr): 3235, 1738, 1625, 1505, 1286, 1111, 1002, 996, 745 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{30}N_2O_8S_2+Na)^+$ requires *m*/*z* 561.1336, found *m*/*z* 561.1332; enantiomeric excess: 37%, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 4.723 min (major), t_R = 4.107 min (minor).

4.3.14. (2*S*,5*R*)-Dimethyl-1-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-2,5-bis(4-nitrophenyl)imidazolidine-4,4-dicarboxylate 3ab

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 72%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = -34$ (*c* 0.43, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.4 Hz, 2H), 8.24 (d, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 5.74 (s, 1H), 5.42 (s, 1H), 4.13–4.00 (m, 2H), 3.95 (s, 3H), 3.55 (s, 3H), 3.34 (s, 3H), 3.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 167.6, 166.5, 166.2, 148.7, 147.7, 146.2, 144.5, 129.3, 124.0, 123.1, 67.3, 61.7, 53.9, 53.4, 53.1, 52.5, 52.3; IR (KBr): 3233, 2956, 1740, 1637, 1615, 1519, 1439, 1349, 1216, 1093, 796, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{24}N_4O_{12}+Na)^+$ requires *m*/*z* 583.1283, found *m*/*z* 583.1305; enantiomeric excess: 84%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 28.860 min (major), t_R = 23.523 min (minor).

4.3.15. (2*S*,5*R*)-Dimethyl-1-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-2,5-bis(3-nitrophenyl)imidazolidine-4,4-dicarboxylate 3bb

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 75%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = -63$ (*c* 0.42, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.38 (s, 1H), 8.27 (d, *J* = 8.1 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 5.67 (s, 1H), 5.36 (s, 1H), 4.11–4.02 (m, 2H), 3.90 (s, 3H), 3.52 (s, 3H), 3.30 (s, 3H), 3.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 167.6, 166.6, 166.2, 148.4, 147.9, 141.1, 139.8, 134.2, 134.1, 130.1, 129.0, 124.5, 123.6, 123.4, 123.2, 67.1, 64.3, 61.6, 53.8, 53.1, 52.5, 52.3; IR (KBr): 3236, 2985, 1737, 1629, 1500, 1384, 1261, 1059, 800, 767 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{24}N_4O_{12}+Na)^+$ requires *m*/*z* 583.1283, found *m*/*z* 583.1255; enantiomeric excess: 83%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 9.767 -min (major), t_R = 7.030 min (minor).

4.3.16. (2*S*,5*R*)-Dimethyl-1-(1,3-dimethoxy-1,3-dioxopropan-2-yl)-2,5-bis(2-nitrophenyl)imidazolidine-4,4-dicarboxylate 3cb

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 45%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = -48$ (*c* 0.19, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.7 Hz, 1H), 8.14 (t, *J* = 7.8 Hz, 1H), 7.99 (t, *J* = 7.7 Hz, 1H), 7.89–7.85 (m, 1H), 7.84–7.75 (m, 1H), 7.69–7.62 (m, 1H), 7.62–7.53 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 6.34 (s, 1H), 5.68 (s, 1H), 4.24–4.12 (m, 2H), 3.97 (s, 3H), 3.66 (s, 3H), 3.33 (s, 3H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 167.2, 166.1, 163.0, 148.1, 147.5, 141.4, 139.9, 134.7, 134.1, 130.0, 129.2, 124.8, 123.6, 123.4, 123.0, 67.0, 64.5, 61.8, 53.8, 53.2, 52.5, 52.1; IR (KBr): 3237, 2966, 1735, 1620, 1519, 1384, 1369, 1260, 1099, 808, 767 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{24}N_4O_{12}+Na)^+$ requires *m*/*z* 583.1283, found *m*/*z* 583.1245; enantiomeric excess: 93%, determined by HPLC (Daicel Chirapak IA, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 10.033 min (major), t_R = 8.847 min (minor).

4.3.17. (2*S*,5*R*)-Dimethyl-2,5-bis(4-cyanophenyl)-1-(1,3-dimethoxy- 1,3-dioxopropan-2-yl)imidazolidine-4,4-dicarboxylate 3db

(Flash column chromatography eluent, petroleum ether/ethyl acetate = 6:1); reaction time = 24 h; yield = 77%; >20:1 dr; colorless sticky oil; $[\alpha]_D^{20} = +17$ (*c* 0.39, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.8 Hz, 4H), 5.67 (s, 1H), 5.35 (s, 1H), 4.04 (d, *J* = 5.5 Hz, 2H), 3.92 (s, 3H), 3.52 (s, 3H), 3.33 (s, 3H), 3.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 167.8, 166.5, 166.2, 144.2, 142.7, 132.9, 132.7, 131.7, 129.9, 129.2, 129.0, 118.4, 118.3, 113.4, 112.0, 97.4, 67.5, 61.6, 55.0, 53.8, 53.1, 52.4, 52.2; IR (KBr): 3269, 2989, 1733, 1629, 1556, 1384, 1436, 1021, 996, 808, 760 cm^{-1}; ESI FTMS exact mass calcd for $(C_{26}H_{24}N_4O_8+Na)^+$ requires *m*/*z* 543.1486, found *m*/*z* 543.1478; enantiomeric excess: 80%, determined by HPLC (Daicel Chirapak IC, hexane/isopropanol = 70:30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 40.620 min (major), t_R = 34.337 min (minor).

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