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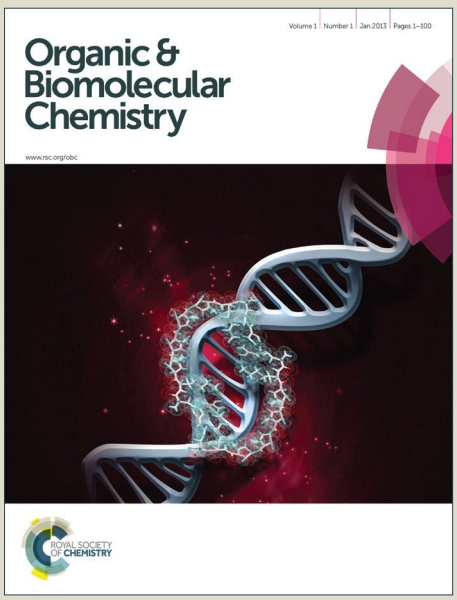

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PAPER

Organocatalytic Asymmetric Michael Addition of α-alkylidene succinimides to Nitrostyrenes

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A bifunctional squaramide-catalyzed asymmetric Michael addition reaction of α-alkylidene succinimides to nitrostyrenes and a nitrodiene has been developed. This organocatalytic asymmetric reaction provides an easy access to functionalized succinimides with two contiguous stereocenters with a broad substrate scope. The desired succinimide derivatives were obtained in good to excellent yields (up to 98%) with high to excellent diastereoselectivities (up to >99:1 dr) and excellent enantioselectivities (up to 99% ee). This protocol provides a straightforward entry to functionalized chiral succinimides derivatives from simple starting materials.

Introduction

The chiral succinimides are present in a variety of natural products and are studied as potential pharmacophores in drug discovery research.[1] For example, the chiral succinimide andrimid **A** and moiramide **B** exhibit potent in vitro antibacterial activity against ethicillin-resistant *Staphylococcus aureus* and a range of other antibiotic-resistant human pathogens,[2] and the hirsutellone **C** display a significant inhibitory activity against *Mycobacterium tuberculosis* H37Ra.[3] In this context, many synthetic strategies have been developed in recent years for the asymmetric synthesis of succinimide derivatives. *N*-maleimides as electrophiles are an important class of substrates that have been successfully used in asymmetric organocatalytic transformations towards chiral succinimides.[4]

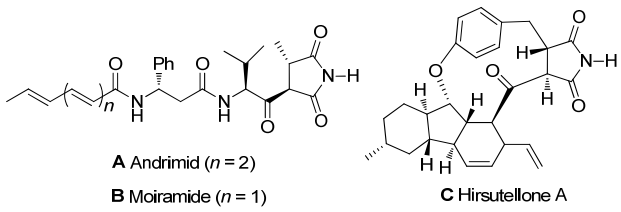

Figure 1 Examples of bioactive chiral succinimide derivatives.

As interesting and useful synthons with multiple functionalization, α-alkylidene succinimides derived from *N*-maleimides, have been introduced to asymmetric synthesis for the assembly of succinimide motifs.[5] For instance, one bicyclic guanidine-catalyzed direct asymmetric allylic addition of *N*-aryl α-alkylidene succinimides to imines was developed in 2010.[5a] Recently, we also disclosed an example of highly enantioselective cascade Michael/Michael reaction of the α-alkylidene succinimides with 3-olefinic oxindoles to synthesize chiral spirooxindoles bearing a disubstituted succinimide unit, in which α-alkylidene succinimides were used as tandem reagents triggering the cascade reaction.[6]

However, the reaction scope of α-alkylidene succinimides used as nucleophiles is still limited due to their low reactivities.[5a] In order to extend the application of α-alkylidene succinimides in asymmetric synthesis of succinimide derivatives, we urgently need to find approaches to enhance the reactivities of α-alkylidene succinimides. We herein will report this approach and present one squaramide-catalyzed asymmetric Michael addition of α-alkylidene succinimides to nitrostyrenes for the synthesis of succinimide derivatives.

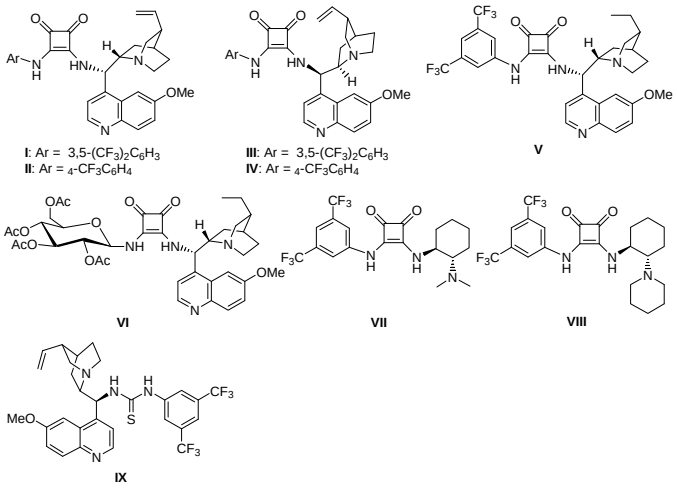

Figure 2 Squaramide and thiourea organocatalysts.

In recent years, squaramide-catalyzed asymmetric Michael addition of various nucleophiles to unsaturated acceptors provide an important route for the synthesis of valuable chiral molecules.[7]

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We have also demonstrated that chiral squaramides are effective catalysts for the asymmetric reactions.[8]

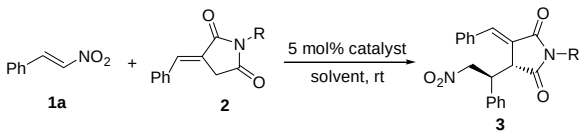
Results and discussion

Our study of the catalytic asymmetric reaction began with the finding more active α-alkylidene succinimides. We initially chose unprotected α-alkylidene succinimide **2a** to test the feasibility of asymmetric Michael addition reaction with nitrostyrene **1a** in the presence of the squaramide **I** (5 mol%) in CH_2Cl_2 at room temperature (Table 1, entry 1). Unfortunately, no reaction was observed, perhaps due to the relatively low reactivity of unprotected α-alkylidene succinimide. When *N*-Ph α-alkylidene succinimide **2b** was used as the nucleophile, we detected a trace amount of product by TLC (Table 1, entry 2). On the other hand, changing the R substituent on the nitrogen of the α-alkylidene succinimide to a *t*-butyloxy carbonyl (Boc) group, the corresponding substrate **2c** reacted smoothly with **1a** under the same conditions to afford **3ac** as the major diastereomer (>99:1 dr) in good yield with excellent enantioselectivity (95% *ee*). The *t*-butyloxy carbonyl group can promote α-alkylidene succinimide transform into anion species. It is worth mentioning that we didn't detect any other products, such as adduct of cascade Michael/Michael reaction, in spite of increasing the catalyst loading and prolonging the reaction time.

With the above result in hand, we evaluated a small library of organocatalysts (Figure 2) for this Michael addition reaction. Quinine-derived squaramide **II** bearing 4-CF_3 group on the aromatic ring gave a slightly lower enantioselectivity (Table 1, entry 4). Squaramides **III** derived from quinidine afforded the desired adduct with better yield but lower enantioselectivity and opposite configuration (Table 1, entry 5). Quinidine-derived squaramide **IV** bearing 4-CF_3 group on the aromatic ring gave a result similar to squaramide **II** with opposite configuration (Table 1, entry 6). A little improvement in yield and enantioselectivity was observed when hydroquinine-derived squaramide **V** was used as the catalyst (Table 1, entry 7). Squaramide **VI** derived from hydroquinine afforded the product in lower yield and enantioselectivity. Squaramides **VII** and **VIII** derived from (1*S*,2*S*)-1,2-diaminocyclohexane were also examined, but lower yield and/or enantioselectivity were observed (Table 1, entries 9 and 10). In addition, for comparison with the used squaramides, the corresponding quinine-derived thiourea **IX** was also evaluated (Table1, entry 11). Unfortunately, no further improvement was observed. At last, we chose hydroquinine-derived squaramide **V** as the optimal catalyst.

In order to improve the Michael addition reaction, further optimization was carried out using squaramide **V**. The effect of solvent, temperature and catalyst loading were evaluated for the optimal reaction conditions (Table1, entries 12–20). The screening of different reaction solvents show that $CHCl_3$ is the optimal solvent (Table1, entry 12), the desired product **3ac** was obtained in higher yield. When the temperature was reduced to 0 °C, an improved outcome was obtained (Table 1, entry 17). When the temperature was further reduced to −10 °C, we were glad to find that the outcome has been further improved slightly (Table 1, entry 18). Considering the reaction time, we didn't continue to lower the temperature. Subsequently, the catalyst loading of reaction was studied. Neither increasing nor reducing the catalyst loading could improve the result obviously (Table 1, entries 19 and 20). So we finally still determined to use 5 mol% catalyst loading.

Table 1 Screening of organocatalysts and optimization of reaction conditions for the asymmetric Michael addition.[a]



Entry	Solvent	R	Catalyst	Yield[b][%]	dr[c]	*ee*[c]
1	CH_2Cl_2	H (**2a**)	**I**	—	—	—
2	CH_2Cl_2	Ph (**2b**)	**I**	trace	—	—
3	CH_2Cl_2	Boc (**2c**)	**I**	89 (**3ac**)	>99:1	95
4	CH_2Cl_2	Boc (**2c**)	**II**	85 (**3ac**)	>99:1	82
5	CH_2Cl_2	Boc (**2c**)	**III**	93 (**3ac**)	>99:1	91[d]
6	CH_2Cl_2	Boc (**2c**)	**IV**	82 (**3ac**)	>99:1	83[d]
7	CH_2Cl_2	Boc (**2c**)	**V**	92 (**3ac**)	>99:1	96
8	CH_2Cl_2	Boc (**2c**)	**VI**	71 (**3ac**)	>99:1	85
9	CH_2Cl_2	Boc (**2c**)	**VII**	90 (**3ac**)	>99:1	82
10	CH_2Cl_2	Boc (**2c**)	**VIII**	73 (**3ac**)	>99:1	65
11	CH_2Cl_2	Boc (**2c**)	**IX**	89 (**3ac**)	>99:1	94
12	$CHCl_3$	Boc (**2c**)	**V**	93 (**3ac**)	>99:1	96
13	PhMe	Boc (**2c**)	**V**	91 (**3ac**)	>99:1	95
14	MeCN	Boc (**2c**)	**V**	80 (**3ac**)	>99:1	87
15	THF	Boc (**2c**)	**V**	92 (**3ac**)	>99:1	88
16	Et_2O	Boc (**2c**)	**V**	73 (**3ac**)	>99:1	98
17[e]	$CHCl_3$	Boc (**2c**)	**V**	95 (**3ac**)	>99:1	98
18[f]	$CHCl_3$	Boc (**2c**)	**V**	98 (**3ac**)	>99:1	98
19[f,g]	$CHCl_3$	Boc (**2c**)	**V**	95 (**3ac**)	>99:1	98
20[f,h]	$CHCl_3$	Boc (**2c**)	**V**	91 (**3ac**)	>99:1	98

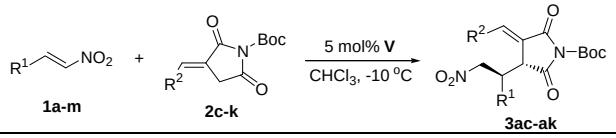
[a] Reaction conditions: **1a** (0.12 mmol), **2** (0.1 mmol) and catalyst (5 mol%) in solvent (0.5 mL) was stirred at room temperature for 3–5 h. [b] Isolated yield. [c] Determined by HPLC analysis. [d] The opposite configuration. [e] The reaction was performed at 0 °C for 10 h. [f] The reaction was performed at −10 °C for 40 h. [g] 10 mol% catalyst was used. [h] 2.5 mol% catalyst was used.

With the optimized conditions in hand, we next examined the substrate scope of the asymmetric Michael addition reaction for the synthesis of chiral succinimides. The results are summarized in Table 2. Firstly, a range of differently substituted nitrostyrenes were examined (entries 1–13). Generally, a wide array of aromatic nitrostyrenes bearing electron-neutral, electron-withdrawing or electron-donating substituents reacted smoothly with α-alkylidene succinimide **2c** to afford the corresponding adducts in good to high yields with high diastereoselectivities and excellent enantioselectivities (90–99% ee) (entries 2–10). These results indicated that the position and the electronic property of the substituent on the aromatic ring had a limited effect on both diastereoselectivity and enantioselectivity. Heteroaromatic nitrostyrenes were also suitable substrates, and the desired

products **3kc** and **3lc** were obtained with excellent enantioselectivities (entries 11 and 12). When nitrostyrene **1m** served as an acceptor, a slightly lower yield (89%) and a decrease in enantioselectivity (87% ee) were obtained (entry 13). In addition, cyclohexane substituted nitrostyrene was also examined, but there is no corresponding product was found.

Then, a variety of α-alkylidene succinimides **2** were tested (entries 14–21). The presence of either electron-withdrawing or electron-donating groups on the aromatic rings of α-alkylidene succinimides is well tolerated (entries 14–20), which indicate that the position and electronic nature of the substituents on the aromatic rings have little influence on this asymmetric Michael addition process. Meanwhile, the enantioselectivity is maintained for the less reactive phenylethyl substituted α-alkylidene succinimide. The corresponding product **3ak** was obtained with longer reaction time at room temperature, but in decreasedyield with lower diastereoselectivity. When isopropyl substituted α-alkylidene succinimide served as donor, only trace amounts of product can be detected by TLC after 72 h at room temperature.

Table 2 Substrate scope of asymmetric Michael addition for synthesis of chiral succinimides.[a]

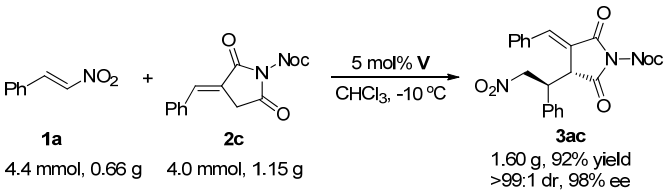


1a-m **2c-k** **3ac-ak**

Entry	R^1	R^2	Product	Yield[b] [%]	dr[c]	ee[c]
1	Ph	Ph	**3ac**	98	>99:1	98
2	4-FC_6H_4	Ph	**3bc**	93	95:5	97
3	2-ClC_6H_4	Ph	**3cc**	82	99:1	92
4	4-ClC_6H_4	Ph	**3dc**	89	94:6	97
5	2-BrC_6H_4	Ph	**3ec**	93	89:11	90
6	2-MeC_6H_4	Ph	**3fc**	92	92:8	97
7	4-MeC_6H_4	Ph	**3gc**	95	92:8	96
8	4-$MeOC_6H_4$	Ph	**3hc**	91	96:4	99
9	3,4-$(MeO)_2C_6H_3$	Ph	**3ic**	82	94:6	99
10	4-$(Me_2NH)C_6H_4$	Ph	**3jc**	76	97:3	95
11	2-furyl	Ph	**3kc**	87	88:12	97
12	2-thienyl	Ph	**3lc**	95	91:9	99
13	4-$MeOC_6H_3CH$=CH	Ph	**3mc**	89	90:10	87
14	Ph	4-ClC_6H_4	**3ad**	93	97:3	99
15	Ph	2-BrC_6H_4	**3ae**	90	>99:1	97
16	4-$MeOC_6H_4$	4-BrC_6H_4	**3hf**	88	99:1	98
17	Ph	4-MeC_6H_4	**3ag**	96	89:11	99
18	Ph	2-$MeOC_6H_4$	**3ah**	86	87:13	98
19	Ph	4-$MeOC_6H_4$	**3ai**	92	>99:1	99
20	Ph	2-naphthyl	**3aj**	89	94:6	98
21[d]	Ph	2-$PhCH_2CH_2$	**3ak**	57	74:26	95

[a]Reaction conditions: **1** (0.24 mmol), **2** (0.2 mmol) and catalyst **V** (5 mol%) in $CHCl_3$ (1.0 mL) was stirred at –10 °C for 20–40 h. [b] Isolated yield. [c] Determined by HPLC analysis. [d] The reaction was performed at room temperature for 60 h.

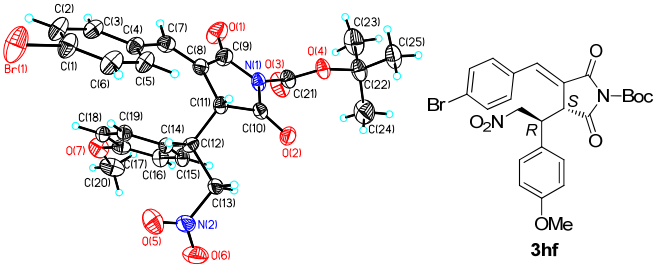
To demonstrate the synthetic potential of this asymmetric Michael addition methodology, a gram-scale synthesis of **3ac** was performed (Scheme 1). The reaction proceeded smoothly affording the corresponding product **3ac** in 92% yield with same diastereo- and enantioselectivity as that of 0.2 mmol-scale reaction.



1a 4.4 mmol, 0.66 g **2c** 4.0 mmol, 1.15 g **3ac** 1.60 g, 92% yield >99:1 dr, 98% ee

Scheme 1. The gram-scale preparation of **3ac**.

The absolute configuration of the product was elucidated by single crystal X-ray diffraction analysis of **3hf**.[9] The absolute configuration of **3hf** was determined as (3*R*, 4*S*) (Figure 3) and those of other products were assigned by analogy.



3hf

Figure 3 X-ray structure of **3hf**.

Conclusions

In summary, we have developed a squaramide-catalyzed highly diastereo- and enantioselective direct Michael addition of α-alkylidene succinimides to nitrostyrenes and a nitrodiene. This catalytic system was very effective to afford the corresponding Michael adducts in high yields (up to 98%) with high diastereoselectivities (up to 97: 3 dr) and excellent enantioselectivities (up to 99% ee). This process provides an easy access to optically active succinimide derivatives. Moreover, the gram-scale preparation can be performed well, demonstrating the synthetic potential of this chiral squaramide organocatalytic system. Further investigations involving the application of α-alkylidene succinimides and this catalytic approach are currently underway in our group and will be reported in due course.

Experimental

General Methods

Commercially available compounds were used without further purification. Solvents were dried according to standard procedures. Column chromatography was performed with silica gel (200–300 mesh). Melting points were determined with an XT–4 melting-point apparatus and were uncorrected. ^{1}H NMR spectra were measured with a Bruker Avance 400 MHz spectrometer. Chemical shifts were reported in δ (ppm) units relative to tetramethylsilane (TMS) as the internal standard. ^{13}C NMR spectra were measured at 100 MHz;

chemical shifts were reported in ppm relative to TMS with the solvent resonance as internal standard. Infrared spectra were obtained with a Perkin Elmer Spectrum One spectrometer. High resolution mass spectra (Electron spray ionization) were measured with a Bruker APEX IV Fourier-Transform mass spectrometer or an Agilent 6520 Accurate-Mass-Q-TOF MS system equipped with an electrospray ionization (*ESI*) source. Enantiomeric excesses were determined by chiral HPLC analysis using an Agilent 1200 LC instrument with a Daicel Chiralpak IA, IB, AS-H or AD-H column.

Materials

Chiral squaramide catalysts **I**, **II**, **III**, **IV**, **VII** and **VIII**,[10] **V**,[11] **VI**[8a] and chiral thiourea catalyst **IX**,[12] nitrostyrenes,[13] α-alkylidene succinimides[6] were prepared according to the reported procedures.

General procedure for asymmetric Michael addition reactions

To a dried small bottle were added **2** (0.2 mmol) and catalyst **V** (6.3 mg, 0.01 mmol, 5 mol %) in $CHCl_3$ (1.0 mL). The reaction mixture was stirred at −10 °C for 15 min, and **1** (0.24 mmol) was then added. After stirring at −10 °C for 20–40 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the desired product **3**.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ac): The title compound **3ac** was obtained according to the general procedure as a white solid (85.3 mg, 98% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 10.4 min, t_{major} = 25.6 min; >99:1 dr, 98% *ee*. M.p. 109–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 1.6 Hz, 1H, =CH), 7.63 (d, J = 7.2 Hz, 2H, ArH), 7.60–7.51 (m, 3H, ArH), 7.25–7.18 (m, 3H, ArH), 6.80 (d, J = 7.2 Hz, 2H, ArH), 5.56 (dd, J_1 = 14.0 Hz, J_2 = 9.6 Hz, 1H, CH_2), 4.79 (dd, J_1 = 14.0 Hz, J_2 = 5.2 Hz, 1H, CH_2), 4.33 (dd, J_1 = 3.4 Hz, J_2 = 2.2 Hz, 1H, CH), 4.13–4.08 (m, 1H, CH), 1.54 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 165.5, 145.8, 138.3, 133.2, 132.8, 131.1, 130.1, 129.5, 128.9, 128.1, 124.7, 86.2, 75.6, 45.2, 41.3, 27.7 ppm; IR (KBr): $\tilde{\nu}$ 3032, 2981, 2928, 1796, 1762, 1717, 1648, 1555, 1371, 1333, 1256, 1170, 1148, 1128, 974, 842, 803, 765, 700, 631 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{25}N_2O_6$ $[M + H]^+$ 437.17071, found 437.17169; calcd. for $C_{24}H_{24}N_2NaO_6$ $[M + Na]^+$ 459.15266, found 459.15391.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-1-(4-fluorophenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3bc): The title compound **3bc** was obtained according to the general procedure as a white solid (84.3 mg, 93% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 10.0 min, t_{major} = 10.9 min; minor diastereomer: t_R = 14.2 min; 95:5 dr, 97% *ee*. M.p. 115–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (S, 1H, =CH), 7.63–7.51 (m, 5H, ArH), 6.90 (t, J = 8.2 Hz, 2H, ArH), 6.80 (d, J = 8.0 Hz, 1H, ArH), 6.79 (d, J = 8.0 Hz, 1H, ArH), 5.50 (dd, J_1 = 14.0 Hz, J_2 = 9.2 Hz, 1H, CH_2), 4.80 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H, CH_2), 4.31 (s, 1H, CH), 4.13–4.08 (m, 1H, CH), 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 165.4, 162.7 (d, $^1J_{C\text{-}F}$ = −247.1 Hz), 145.7, 138.5, 132.7, 131.2, 130.1, 129.8 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.6, 129.1 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 124.5, 115.9 (d, $^2J_{C\text{-}F}$ = 21.6 Hz), 86.4, 75.6, 45.2, 40.5, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 3060, 2984, 2936, 1797, 1763, 1717, 1647, 1606, 1556, 1512, 1450, 1372, 1331, 1256, 1229, 1149, 1109, 974, 865, 839, 766, 738, 694, 630, 571, 519 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{23}FN_2NaO_6$ $[M + Na]^+$ 477.1432, found 477.1434.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-1-(2-chlorophenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3cc): The title compound **3cc** was obtained according to the general procedure as a white solid (77.1 mg, 82% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 10.6 min, t_{major} = 18.0 min; minor diastereomer: t_R = 19.6 min; 99:1 dr, 92% *ee*. M.p. 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66–7.65 (m, 3H, ArH), 7.55–7.48 (m, 3H, ArH), 7.26–7.24 (m, 1H, ArH), 7.20–7.17 (m, 3H, ArH), 5.48 (dd, J_1 = 14.4 Hz, J_2 = 9.6 Hz, 1H, CH_2), 5.06–5.01 (m, 1H, CH), 4.71 (dd, J_1 = 14.4 Hz, J_2 = 5.6 Hz, 1H, CH_2), 4.38 (dd, J_1 = 4.0 Hz, J_2 = 2.0 Hz, 1H, CH), 1.57 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 165.7, 145.8, 139.6, 135.2, 133.1, 131.5, 131.0, 130.5, 130.4, 129.9, 129.2, 127.9, 127.2, 122.8, 86.3, 75.2, 44.6, 37.2, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 3062, 2983, 2935, 1797, 1763, 1716, 1646, 1556, 1478, 1450, 1437, 1372, 1330, 1255, 1171, 1149, 1075, 1037, 975, 842, 763, 737, 691, 633 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{23}ClN_2NaO_6$ $[M + Na]^+$ 493.1137, found 493.1139.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-1-(4-chlorophenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3dc): The title compound **3dc** was obtained according to the general procedure as a white solid (83.7mg, 89% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 10.3 min, t_{major} = 11.5 min; minor diastereomer: t_R = 15.0 min; 94:6 dr, 97% *ee*. M.p. 118–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 2.0 Hz, 1H, =CH), 7.63–7.53 (m, 5H, ArH), 7.18 (d, J = 8.4 Hz, 2H, ArH), 6.74 (d, J = 8.4 Hz, 2H, ArH), 5.49 (dd, J_1 = 14.0 Hz, J_2 = 9.2 Hz, 1H, CH_2), 4.80 (dd, J_1 = 14.2 Hz, J_2 = 5.8 Hz, 1H, CH_2), 4.31 (dd, J_1 = 3.8 Hz, J_2 = 2.2 Hz, 1H, CH), 4.12–4.07 (m, 1H, CH), 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 165.3, 145.7, 138.6, 134.9, 132.7, 131.7, 131.2, 130.1, 129.6, 129.3, 129.1, 124.3, 86.4, 75.4, 45.1, 40.6, 27.7 ppm; IR (KBr): $\tilde{\nu}$ 2983, 2933, 1797, 1763, 1717, 1647, 1598, 1555, 1494, 1450, 1372, 1330, 1255, 1168, 1148, 1126, 1096, 1015, 974, 830, 765, 736, 693, 561 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{23}ClN_2NaO_6$ $[M + Na]^+$ 493.1137, found 493.1140.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-1-(2-bromophenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ec): The title compound **3ec** was obtained according to the general procedure as

a white solid (95.6 mg, 93% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{major} = 10.1 min, t_{minor} = 11.0 min; minor diastereomer: t_R = 16.9, 21.3 min; 89:11 dr, 90% *ee*. M.p. 138–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 7.6 Hz, 2H, ArH), 7.65 (s, 1H, =CH), 7.55–7.48 (m, 3H, ArH), 7.45 (d, *J* = 8.0 Hz, 1H, ArH), 7.24–7.17 (m, 2H, ArH), 7.12–7.08 (m, 1H, ArH), 5.46 (dd, J_1 = 14.4 Hz, J_2 = 9.6 Hz, 1H, CH_2), 5.06–5.02 (m, 1H, CH), 4.68 (dd, J_1 = 14.2 Hz, J_2 = 5.4 Hz, 1H, CH_2), 4.38 (dd, J_1 = 4.4 Hz, J_2 = 2.0 Hz, 1H, CH), 1.58 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 165.7, 145.9, 139.6, 134.0, 133.3, 131.1, 130.7, 130.2, 129.3, 127.9, 126.0, 122.9, 86.3, 75.3, 44.6, 40.2, 27.7 ppm; IR (KBr): $\tilde{\nu}$ 3061, 2982, 2933, 1796, 1763, 1716, 1646, 1555, 1474, 1450, 1431, 1372, 1329, 1255, 1170, 1148, 1126, 1024, 974, 841, 763, 735, 691 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{23}BrN_2NaO_6$ $[M + Na]^+$ 537.0632, found 537.0631.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-2-nitro-1-(*o*-tolyl)ethyl)-2,5-dioxopyrrolidine-1-carboxylate (3fc): The title compound **3fc** was obtained according to the general procedure as a white solid (82.7 mg, 92% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{major} = 9.4 min, t_{minor} = 10.5 min; minor diastereomer: t_R = 16.3 min; 92:8 dr, 97% *ee*. M.p. 135–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 7.2 Hz, 2H, ArH), 7.59 (d, *J* = 1.6 Hz, 1H, =CH), 7.57–7.51 (m, 3H, ArH), 7.14–7.08 (m, 3H, ArH), 7.02 (d, *J* = 6.8 Hz, 1H, ArH), 5.50–5.41 (m, 1H, CH), 4.73–4.64 (m, 2H, CH_2), 4.33 (dd, J_1 = 3.6 Hz, J_2 = 2.0 Hz, 1H, CH), 1.71 (s, 3H, CH_3), 1.58 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 165.8, 145.9, 137.9, 137.2, 132.8, 132.0, 131.5, 131.1, 130.3, 129.5, 128.5, 126.5, 126.2, 124.4, 86.2, 76.2, 45.1, 36.9, 27.7, 19.1 ppm; IR (KBr): $\tilde{\nu}$ 3060, 3028, 2983, 2934, 1797, 1763, 1717, 1647, 1555, 1494, 1451, 1372, 1331, 1293, 1255, 1224, 1149, 974, 842, 765, 735, 692, 634 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{26}N_2NaO_6$ $[M + Na]^+$ 473.1683, found 473.1681.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-2-nitro-1-(*p*-tolyl)ethyl)-2,5-dioxopyrrolidine-1-carboxylate (3gc): The title compound **3gc** was obtained according to the general procedure as a white solid (85.5 mg, 95% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 9.3 min, t_{major} = 9.9 min; minor diastereomer: t_R = 10.9, 11.4 min; 92:8 dr, 96% *ee*. M.p. 126–127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 2.0 Hz, 1H, =CH), 7.62 (d, *J* = 7.2 Hz, 2H, ArH), 7.59–7.50 (m, 3H, ArH), 6.99 (d, *J* = 8.0 Hz, 2H, ArH), 6.68 (d, *J* = 8.0 Hz, 2H, ArH), 5.52 (dd, J_1 = 14.0 Hz, J_2 = 9.6 Hz, 1H, CH_2), 4.76 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H, CH_2), 4.30 (dd, J_1 = 3.6 Hz, J_2 = 2.4 Hz, 1H, CH), 4.09–4.05 (m, 1H, CH), 2.26 (s, 3H, CH_3), 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 165.6, 145.8, 138.6, 138.2, 132.9, 131.0, 130.12, 130.09, 129.6, 129.5, 127.9, 124.8, 86.1, 75.7, 45.2, 41.0, 27.7, 21.0 ppm; IR (KBr): $\tilde{\nu}$ 2980, 2922, 1796, 1762, 1717, 1647, 1554, 1515, 1450, 1371, 1329, 1254, 1168, 1148, 1126, 973, 841, 820, 765, 692, 630, 567 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{26}N_2NaO_6$ $[M + Na]^+$ 473.1683, found 473.1690.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-1-(4-methoxyphenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3hc): The title compound **3hc** was obtained according to the general procedure as a white solid (84.7 mg, 91% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 13.3 min, t_{major} = 14.5 min; minor diastereomer: t_R = 19.2 min; 96:4 dr, 99% *ee*. M.p. 99–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 2.0 Hz, 1H, =CH), 7.62 (d, *J* = 7.2 Hz, 2H, ArH), 7.58–7.49 (m, 3H, ArH), 6.74–6.69 (m, 5H, ArH), 5.49 (dd, J_1 = 14.0 Hz, J_2 = 9.6 Hz, 1H, CH_2), 4.77 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H, CH_2), 4.28 (dd, J_1 = 3.6 Hz, J_2 = 2.4 Hz, 1H, CH), 4.08–4.03 (m, 1H, CH), 3.72 (s, 1H, OCH_3), 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 165.5, 159.7, 145.8, 138.1, 132.8, 131.0, 130.1, 129.4, 129.1, 124.94, 124.85, 114.1, 86.0, 75.8, 55.1, 45.3, 40.6, 27.7 ppm; IR (KBr): $\tilde{\nu}$ 3059, 2982, 2936, 1797, 1762, 1717, 1648, 1611, 1583, 1554, 1515, 1450, 1372, 1329, 1255, 1172, 1149, 1125, 1032, 974, 833, 766, 736, 693, 572 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{26}N_2NaO_7$ $[M + Na]^+$ 489.1632, found 489.1633.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-1-(3,4-dimethoxyphenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ic): The title compound **3ic** was obtained according to the general procedure as a white solid (81.4 mg, 82% yield). HPLC (Daicel Chiralpak IB + AD-H, *n*-hexane/2-propanol = 60:40, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 21.0 min, t_{major} = 23.9 min; minor diastereomer: t_R = 25.4 min; 94:6 dr, 99% *ee*. M.p. 115–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H, =CH), 7.63–7.52 (m, 5H, ArH), 6.65 (d, *J* = 8.0 Hz, 1H, ArH), 6.30 (d, *J* = 7.2 Hz, 1H, ArH), 6.29 (s, 1H, ArH), 5.51 (dd, J_1 = 14.2 Hz, J_2 = 9.4 Hz, 1H, CH_2), 4.79 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H, CH_2), 4.31 (s, 1H, CH), 4.10–4.05 (m, 1H, CH), 3.80 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 165.5, 149.1, 148.9, 145.8, 138.0, 132.8, 130.9, 129.9, 129.4, 125.4, 124.8, 120.6, 111.0, 110.4, 86.2, 75.7, 55.6, 45.1, 40.6, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 3060, 2980, 2937, 2838, 1796, 1762, 1716, 1648, 1554, 1519, 1465, 1451, 1372, 1330, 1256, 1172, 1148, 1026, 977, 843, 766, 735, 694, 646 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{28}N_2NaO_8$ $[M + Na]^+$ 519.1738, found 519.1746.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*S*)-1-(4-(dimethylamino)phenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3jc): The title compound **3jc** was obtained according to the general procedure as a white solid (72.8 mg, 76% yield). HPLC (Daicel Chiralpak IB+AD-H, *n*-hexane/2-propanol = 60:40, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 16.6 min, t_{major} = 20.6 min; minor diastereomer: t_R = 22.2 min; 97:3 dr, 95% *ee*. M.p. 131–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 2.0 Hz, 1H, =CH), 7.62 (d, *J* = 7.2 Hz, 2H, ArH), 7.56 (t, *J* = 7.2 Hz, 2H, ArH), 7.51 (d, *J* = 7.2 Hz, 1H, ArH), 6.64 (d, *J* = 8.8 Hz, 2H, ArH), 6.47 (d, *J* = 8.8 Hz, 2H, ArH), 5.48 (dd, J_1 = 14.0 Hz, J_2 = 9.6 Hz, 1H, CH_2), 4.72 (dd, J_1 = 13.8 Hz, J_2 =

5.4 Hz, 1H, CH_2), 4.23 (dd, J_1 = 3.4 Hz, J_2 = 2.2 Hz, 1H, CH), 4.03–3.98 (m, 1H, CH), 2.87 (s, 6H, $N(CH_3)_2$), 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 165.7, 150.3, 145.9, 137.8, 132.9, 130.8, 130.1, 129.3, 128.6, 125.1, 119.8, 112.1, 85.7, 75.9, 45.3, 40.6, 40.0, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 2982, 2934, 2808, 1796, 1762, 1716, 1647, 1614, 1553, 1525, 1449, 1370, 1352, 1329, 1255, 1168, 1149, 1064, 974, 843, 820, 765, 736, 693, 568 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{26}H_{30}N_3O_6$ $[M + H]^+$ 480.2129, found 480.2135.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*R*)-1-(furan-2-yl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3kc): The title compound **3kc** was obtained according to the general procedure as a colorless solid (74.7 mg, 87% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 14.5 min, t_{major} = 22.8 min; minor diastereomer: t_R = 15.9 min; 88:12 dr, 97% *ee*. M.p. 55–56 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H, =CH), 7.59–7.47 (m, 5H, ArH), 7.26 (d, *J* = 8.4 Hz, 1H, ArH), 6.21 (dd, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H, ArH), 5.90 (d, *J* = 3.2 Hz, 1H, ArH), 5.42 (dd, J_1 = 14.2 Hz, J_2 = 8.6 Hz, 1H, CH_2), 4.76 (dd, J_1 = 14.6 Hz, J_2 = 5.0 Hz, 1H, CH_2), 4.28–4.24 (m, 2H, CH), 1.58 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 165.6, 147.1, 146.0, 143.1, 138.3, 132.7, 130.9, 129.9, 129.3, 124.6, 110.4, 109.4, 86.1, 74.3, 44.0, 35.8, 27.7 ppm; IR (KBr): $\tilde{\nu}$ 2984, 2936, 1798, 1764, 1718, 1648, 1557, 1373, 1332, 1256, 1225, 1172, 1149, 1015, 977, 842, 766, 741, 694, 598 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{22}H_{22}N_2NaO_7$ $[M + Na]^+$ 449.1319, found 449.1319.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*R*)-2-nitro-1-(thiophen-2-yl)ethyl)-2,5-dioxopyrrolidine-1-carboxylate (3lc): The title compound **3lc** was obtained according to the general procedure as a white solid (84.0 mg, 95% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 15.6 min, t_{major} = 27.1 min; minor diastereomer: t_R = 23.3, 24.3 min; 91:9 dr, 99% *ee*. M.p. 112–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 2.0 Hz, 1H, =CH), 7.61–7.49 (m, 5H, ArH), 7.15 (d, *J* = 5.2 Hz, 1H, ArH), 6.86 (dd, J_1 = 4.8 Hz, J_2 = 3.6 Hz, 1H, ArH), 6.63 (d, *J* = 3.2 Hz, 1H, ArH), 5.50 (dd, J_1 = 14.2 Hz, J_2 = 9.4 Hz, 1H, CH_2), 4.77 (dd, J_1 = 14.2 Hz, J_2 = 5.4 Hz, 1H, CH_2), 4.41–4.36 (m, 1H, CH), 4.31 (t, *J* = 3.0 Hz, 1H, CH), 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 165.5, 145.8, 138.7, 134.3, 132.6, 131.0, 130.0, 129.4, 127.0, 126.6, 125.7, 124.6, 86.2, 75.9, 45.2, 36.6, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 2982, 2935, 1797, 1763, 1717, 1647, 1556, 1371, 1332, 1255, 1174, 1148, 973, 840, 765, 736, 695, 633 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{22}H_{22}N_2NaO_6S$ $[M + Na]^+$ 465.1091, found 465.1093.

(*R*,*E*)-*tert*-butyl 3-benzylidene-4-((*R*,*E*)-4-(4-methoxyphenyl)-1-nitrobut-3-en-2-yl)-2,5-dioxopyrrolidine-1-carboxylate (3mc): The title compound **3mc** was obtained according to the general procedure as a colorless solid (87.5 mg, 89% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 11.0 min, t_{major} = 16.9 min; minor diastereomer: t_R = 13.7, 29.4 min; 90:10 dr, 87% *ee*. M.p. 58–59 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 2.0 Hz, 1H, =CH), 7.54–7.47 (m, 5H, ArH), 7.11 (d, *J* = 8.4 Hz, 2H, ArH), 6.77 (d, *J* = 8.4 Hz, 2H, ArH), 6.13 (d, *J* = 15.6 Hz, 1H, =CH), 5.56 (dd, J_1 = 15.6 Hz, J_2 = 9.6 Hz, 1H, =CH), 5.17 (dd, J_1 = 13.6 Hz, J_2 = 8.8 Hz, 1H, CH_2), 4.65 (dd, J_1 = 13.4 Hz, J_2 = 6.2 Hz, 1H, CH_2), 4.14 (t, *J* = 2.4 Hz, 1H, CH), 3.76 (s, 1H, OCH_3), 3.65–3.58 (m, 1H, CH), 1.57 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 165.8, 159.8, 146.1, 138.2, 136.5, 132.6, 130.9, 130.1, 129.3, 128.1, 127.8, 124.8, 117.2, 113.9, 86.4, 76.1, 55.2, 44.7, 40.3, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 2982, 2936, 2838, 1797, 1762, 1718, 1648, 1607, 1553, 1513, 1450, 1372, 1331, 1253, 1176, 1148, 1032, 970, 840, 796, 765, 738, 694 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{27}H_{28}N_2NaO_7$ $[M + Na]^+$ 515.1789, found 515.1789.

(*R*,*E*)-*tert*-butyl 3-(4-chlorobenzylidene)-4-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ad): The title compound **3ad** was obtained according to the general procedure as a white solid (87.3 mg, 93% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 90:10, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{major} = 19.9 min, t_{minor} = 21.6 min; minor diastereomer: t_R = 15.9 min; 97:3 dr, 99% *ee*. M.p. 117–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 1.6 Hz, 1H, =CH), 7.60 (d, *J* = 8.8 Hz, 2H, ArH), 7.55 (d, *J* = 8.8 Hz, 2H, ArH), 7.27–7.19 (m, 3H, ArH), 6.80 (d, *J* = 7.2 Hz, 2H, ArH), 5.57 (dd, J_1 = 14.4 Hz, J_2 = 10.0 Hz, 1H, CH_2), 4.78 (dd, J_1 = 14.4 Hz, J_2 = 5.2 Hz, 1H, CH_2), 4.29 (dd, J_1 = 3.4 Hz, J_2 = 2.2 Hz, 1H, CH), 4.09–4.05 (m, 1H, CH), 1.53 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 165.3, 145.6, 137.1, 136.7, 132.9, 131.3, 131.1, 129.7, 128.9, 128.8, 127.9, 125.1, 86.1, 75.3, 44.9, 41.1, 27.5 ppm; IR (KBr): $\tilde{\nu}$ 3064, 3034, 2983, 2935, 1797, 1764, 1717, 1649, 1590, 1555, 1492, 1456, 1372, 1334, 1255, 1224, 1166, 1149, 1094, 1013, 975, 841, 823, 773, 738, 701, 651, 626, 548 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{24}H_{23}ClN_2NaO_6$ $[M + Na]^+$ 493.1137, found 493.1141.

(*R*,*E*)-*tert*-butyl 3-(2-bromobenzylidene)-4-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ae): The title compound **3ae** was obtained according to the general procedure as a white solid (92.4 mg, 90% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 11.7 min, t_{major} = 15.5 min; >99:1 dr, 97% *ee*. M.p. 113–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 2.4 Hz, 1H, =CH), 7.78 (d, *J* = 8.0 Hz, 1H, ArH), 7.59 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H, ArH), 7.54 (t, *J* = 7.6 Hz, 1H, ArH), 7.41–7.39 (m, 1H, ArH), 7.24 (d, *J* = 7.2 Hz, 3H, ArH), 6.84 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 2H, ArH), 5.51 (dd, J_1 = 14.2 Hz, J_2 = 9.8 Hz, 1H, CH_2), 4.67 (dd, J_1 = 14.4 Hz, J_2 = 5.2 Hz, 1H, CH_2), 4.32 (dd, J_1 = 3.8 Hz, J_2 = 2.6 Hz, 1H, CH), 3.75–3.70 (m, 1H, CH), 1.54 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 164.6, 145.6, 137.5, 133.7, 133.1, 132.9, 131.9, 129.4, 129.0, 128.9, 128.18, 128.15, 127.0, 125.1, 86.3, 75.5, 44.4, 41.7, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 3064, 3034, 2983, 2933, 1798, 1764, 1719, 1656, 1555, 1467, 1456, 1428, 1372, 1332, 1255, 1221, 1172,

1148, 1028, 975, 841, 758, 738, 701, 660, 630, 575 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{24}H_{23}BrN_2NaO_6$ $[M + Na]^+$ 537.0632, found 537.0634.

(*R*,*E*)-*tert*-butyl 3-(4-bromobenzylidene)-4-((*S*)-1-(4-methoxyphenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-1-carboxylate (3hf): The title compound **3hf** was obtained according to the general procedure as a white solid (95.6 mg, 88% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 12.5 min, t_{major} = 17.1 min; minor diastereomer: t_R = 21.6 min; 99:1 dr, 98% *ee*. M.p. 128–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.8 Hz, 2H, ArH), 7.64 (d, *J* = 2.0 Hz, 1H, =CH), 7.52 (d, *J* = 8.4 Hz, 2H, ArH), 6.72 (s, 4H, ArH), 5.55 (dd, J_1 = 14.2 Hz, J_2 = 10.2 Hz, 1H, CH_2), 4.73 (dd, J_1 = 14.4 Hz, J_2 = 5.2 Hz, 1H, CH_2), 4.24 (dd, J_1 = 3.8 Hz, J_2 = 2.2 Hz, 1H, CH), 4.05–4.00 (m, 1H, CH), 3.74 (s, 3H, OCH_3) , 1.55 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 165.4, 159.7, 145.7, 136.8, 132.7, 131.6, 131.5, 129.1, 125.6, 125.4, 124.7, 114.2, 86.2, 75.5, 55.1, 45.0, 40.4, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 2980, 1797, 1763, 1716, 1648, 1611, 1585, 1553, 1514, 1488, 1371, 1330, 1254, 1168, 1148, 1073, 1032, 1009, 975, 832, 812, 767, 619 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{25}H_{29}BrN_3O_7$ $[M + NH_4]^+$ 562.1183, found 562.1182.

(*R*,*E*)-*tert*-butyl 3-(4-methylbenzylidene)-4-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ag): The title compound **3ag** was obtained according to the general procedure as a white solid (86.3 mg, 96% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 230 nm): major diastereomer: t_{minor} = 9.6 min, t_{major} = 26.3 min; minor diastereomer: t_R = 13.7, 16.4 min; 89:11 dr, 99% *ee*. M.p. 133–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 1H, =CH), 7.53 (d, *J* = 8.4 Hz, 2H, ArH), 7.37 (d, *J* = 8.0 Hz, 2H, ArH), 7.24–7.17 (m, 3H, ArH), 6.81 (d, *J* = 7.2 Hz, 2H, ArH), 5.54 (dd, J_1 = 14.0 Hz, J_2 = 9.6 Hz, 1H, CH_2), 4.83 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H, CH_2), 4.27 (d, *J* = 1.2 Hz, 1H, CH), 4.17–4.13 (m, 1H, CH), 2.45 (s, 3H, CH_3) , 1.53 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 165.6, 145.8, 141.8, 138.2, 133.1, 130.3, 130.2, 129.9, 128.7, 128.0, 123.3, 85.9, 75.5, 45.1, 41.0, 27.6, 21.5 ppm; IR (KBr): $\tilde{\nu}$ 3063, 3033, 2983, 2933, 1796, 1762, 1717, 1646, 1607, 1555, 1513, 1456, 1371, 1332, 1256, 1208, 1168, 1149, 975, 842, 812, 739, 702, 629 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{25}H_{26}N_2NaO_6$ $[M + Na]^+$ 473.1683, found 473.1689.

(*R*,*E*)-*tert*-butyl 3-(2-methoxybenzylidene)-4-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ah): The title compound **3ah** was obtained according to the general procedure as a white solid (80.2 mg, 86% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 230 nm): major diastereomer: t_{minor} = 9.4 min, t_{major} = 15.5 min; minor diastereomer: t_R = 14.4 min; 87:13 dr, 98% *ee*. M.p. 113–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 2.4 Hz, 1H, =CH), 7.48 (d, *J* = 8.4 Hz, 2H, ArH), 7.24–7.16 (m, 3H, ArH), 7.13 (t, *J* = 7.4 Hz, 1H, ArH), 7.06 (d, *J* = 8.4 Hz, 1H, ArH), 6.78 (d, *J* = 6.8 Hz, 2H, ArH), 5.44 (dd, J_1 = 13.6 Hz, J_2 = 9.2 Hz, 1H, CH_2), 4.77 (dd, J_1 = 13.4 Hz, J_2 = 5.8 Hz, 1H, CH_2), 4.25 (dd, J_1 = 3.6 Hz, J_2 = 2.4 Hz, 1H, CH), 3.94 (s, 3H, OCH_3), 3.85–3.80 (m, 1H, CH), 1.54 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 165.4, 157.9, 145.9, 134.7, 133.5, 132.4, 130.0, 128.7, 128.5, 127.9, 124.8, 121.8, 120.9, 111.4, 85.8, 76.1, 55.5, 45.8, 41.5, 27.5 ppm; IR (KBr): $\tilde{\nu}$ 3064, 3033, 2982, 2938, 2842, 1796, 1762, 1717, 1647, 1599, 1555, 1488, 1465, 1438, 1371, 1333, 1291, 1255, 1212, 1181, 1149, 1024, 976, 841, 792, 756, 737, 702, 632, 590 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{25}H_{26}N_2NaO_7$ $[M + Na]^+$ 489.1632, found 489.1636.

(*R*,*E*)-*tert*-butyl 3-(4-methoxybenzylidene)-4-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-1-carboxylate (3ai): The title compound **3ai** was obtained according to the general procedure as a colorless solid (85.8 mg, 92% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 12.3 min, t_{major} = 37.7 min; >99:1 dr, 99% *ee*. M.p. 65–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 1.2 Hz, 1H, =CH), 7.60 (d, *J* = 8.8 Hz, 2H, ArH), 7.24–7.17 (m, 3H, ArH), 7.08 (d, *J* = 8.8 Hz, 2H, ArH), 6.82 (d, *J* = 6.8 Hz, 2H, ArH), 5.57 (dd, J_1 = 14.2 Hz, J_2 = 9.4 Hz, 1H, CH_2), 4.84 (dd, J_1 = 14.2 Hz, J_2 = 5.4 Hz, 1H, CH_2), 4.23 (d, *J* = 1.6 Hz,1H, CH), 4.21–4.16 (m, 1H, CH), 3.89 (s, 3H, OCH_3), 1.53 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 165.7, 161.8, 145.8, 137.9, 133.1, 132.4, 128.7, 128.0, 125.2, 121.5, 114.9, 85.8, 75.5, 55.4, 45.2, 40.9, 27.5 ppm; IR (KBr): $\tilde{\nu}$ 3063, 3034, 2982, 2937, 2841, 1795, 1761, 1714, 1642, 1602, 1555, 1514, 1457, 1426, 1371, 1334, 1307, 1257, 1166, 1149, 1028, 975, 833, 792, 737, 702, 628, 549 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{25}H_{26}N_2NaO_7$ $[M + Na]^+$ 489.1632, found 489.1634.

(*R*,*E*)-*tert*-butyl 3-(naphthalen-1-ylmethylene)-4-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-1-carboxylate (3aj): The title compound **3aj** was obtained according to the general procedure as a colorless solid (86.4 mg, 89% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 230 nm): major diastereomer: t_{minor} = 8.0 min, t_{major} = 9.1 min; minor diastereomer: t_R = 9.9 min; 94:6 dr, 98% *ee*. M.p. 72–73 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, =CH), 8.01 (d, *J* = 8.0 Hz, 1H, ArH), 7.98–7.94 (m, 2H, ArH), 7.71 (d, *J* = 7.2 Hz, 1H, ArH), 7.66–7.61 (m, 3H, ArH), 7.18 (d, *J* = 7.6 Hz, 1H, ArH), 7.10 (t, *J* = 7.6 Hz, 2H, ArH), 6.62 (d, *J* = 7.2 Hz, 2H, ArH), 5.42 (dd, J_1 = 14.2 Hz, J_2 = 9.8 Hz, 1H, CH_2), 4.59 (dd, J_1 = 14.2 Hz, J_2 = 5.4 Hz, 1H, CH_2), 4.37 (t, *J* = 3.0 Hz, 1H, CH), 3.72–3.67 (m, 1H, CH), 1.57 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 165.0, 145.8, 136.4, 133.6, 133.2, 131.2, 129.7, 129.0, 128.7, 128.6, 128.1, 127.3, 126.8, 126.7, 126.5, 125.5, 123.7, 86.2, 75.6, 44.7, 41.1, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 3062, 3035, 2983, 2935, 1798, 1763, 1717, 1649, 1555, 1497, 1456, 1426, 1396, 1372, 1335, 1256, 1216, 1178, 1149, 1126, 968, 842, 800, 777, 737, 702, 627, 595, 531 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{28}H_{26}N_2NaO_6$ $[M + Na]^+$ 509.1683, found 509.1687.

(*R*,*E*)-*tert*-butyl 3-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxo-4-(3-phenylpropylidene)pyrrolidine-1-carboxylate (3ak): The title

compound **3ak** was obtained according to the general procedure at room temperature for 60 h, and the obtained adduct was a colorless solid (52.8 mg, 57% yield). HPLC (Daicel Chiralpak AS-H, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{major} = 12.2 min, t_{minor} = 21.6 min; minor diastereomer: t_R = 10.5, 29.1 min; 74:26 dr, 95% *ee*. M.p. 48–49 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 7.2 Hz, 3H, ArH), 7.24 (d, *J* = 8.0 Hz, 3H, ArH), 7.20 (d, *J* = 7.4 Hz, 2H, ArH), 6.95 (t, *J* = 7.6 Hz, 1H, ArH), 6.77 (d, *J* = 7.6 Hz, 2H, ArH), 5.39 (dd, J_1 = 14.4 Hz, J_2 = 9.2 Hz, 1H, CH_2), 4.83 (dd, J_1 = 14.4 Hz, J_2 = 5.6 Hz, 1H, CH_2), 3.92–3.86 (m, 1H, CH), 3.47 (s, 1H, CH), 2.96–2.92 (m, 2H, CH_2), 2.86–2.73 (m, 2H, CH_2), 1.47 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 164.3, 145.6, 141.9, 139.9, 132.6, 129.4, 128.9, 128.8, 128.5, 128.0, 127.0, 126.7, 85.8, 75.6, 44.8, 44.6, 34.4, 31.4, 27.6 ppm; IR (KBr): $\tilde{\nu}$ 3063, 3030, 2983, 2934, 1797, 1763, 1718, 1673, 1554, 1496, 1455, 1371, 1327, 1255, 1148, 841, 739, 701, 631 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{26}H_{28}N_2NaO_6$ $[M + Na]^+$ 487.1840, found 487.1847.

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