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# Enantio- and diastereoselective Michael additions of *C*-succinimidyl esters to nitro olefins using cinchonine-derived bifunctional organocatalysts

Pavol Jakubec [a], Dane M. Cockfield [b], Peter S. Hynes [b], Ed Cleator [c], Darren J. Dixon [a,*]

[a] *The Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, UK*
[b] *School of Chemistry, The University of Manchester, Oxford Road, Manchester M13 9PL, UK*
[c] *Merck Sharp Dohme Research Laboratories, Global Process Research, Hoddesdon, Hertfordshire EN11 9BU, UK*

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ABSTRACT

A novel bifunctional organocatalytic Michael addition of a succinimide-derived pronucleophile to nitro olefins is described. The use of a range of nitro olefins afforded Michael adducts containing contiguous quaternary and tertiary stereogenic centres in high enantioselectivities and moderate diastereoselectivities.



## 1. Introduction

Bifunctional Brønsted base, hydrogen-bond donor organocatalysts based on the 9-amino(9-deoxy) epicinchona scaffold, introduced by our group and others, have recently emerged as highly selective catalysts for numerous addition reactions of carbon- and heteroatom-centred pronucleophiles to reactive electrophiles, such as electron deficient C–C multiple bonds, carbonyl compounds and imines.[1,2] In our original work describing the highly enantioselective Michael addition of malonate pronucleophiles to nitro olefins, a library of bifunctional organocatalysts derived from 9-amino(9-deoxy) epicinchonine was synthesized and screening of this library allowed the identification of thiourea catalyst **1a** (Fig. 1) as the optimum catalyst for this reagent combination. Subsequent reports by our group and others have revealed that **1a**, although outstanding in many reactions, is not necessarily the optimal catalyst for all reagent combinations.[3,4]

In continuation of our work in the field of bifunctional organocatalysed Michael additions to nitro olefins, we were interested in identifying other synthetically relevant pronucleophiles, specifically prochiral pronucleophiles, which would afford adducts with two adjacent stereogenic centres. Accordingly, issues of both relative and absolute stereocontrol in the screening of our catalyst library would arise.

Although the commercially available cyclic β-ketoesters have been extensively studied in the stereoselective Michael addition to nitro olefins,[5] to date *C*-succinimidyl esters have not been reported as pronucleophiles despite their high functional group density and potential synthetic utility. The use of such pronucleophiles would indeed give rise to adducts containing contiguous

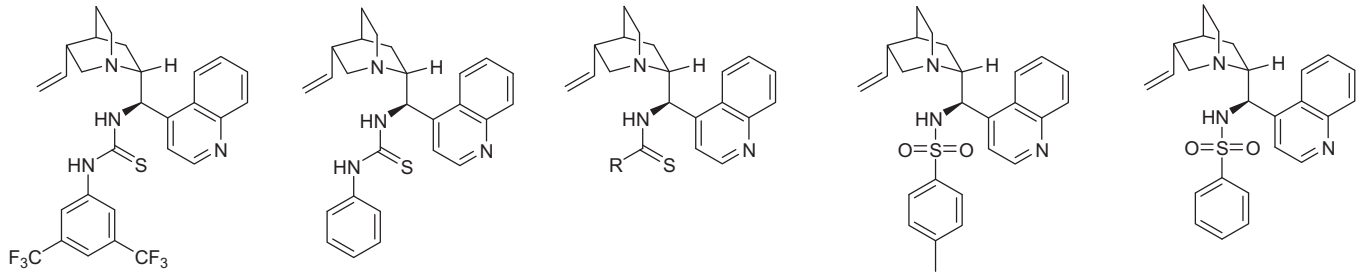


**Figure 1.** Cinchona derived organocatalysts.

* Corresponding author.
*E-mail address:* Darren.dixon@chem.ox.ac.uk (D.J. Dixon).

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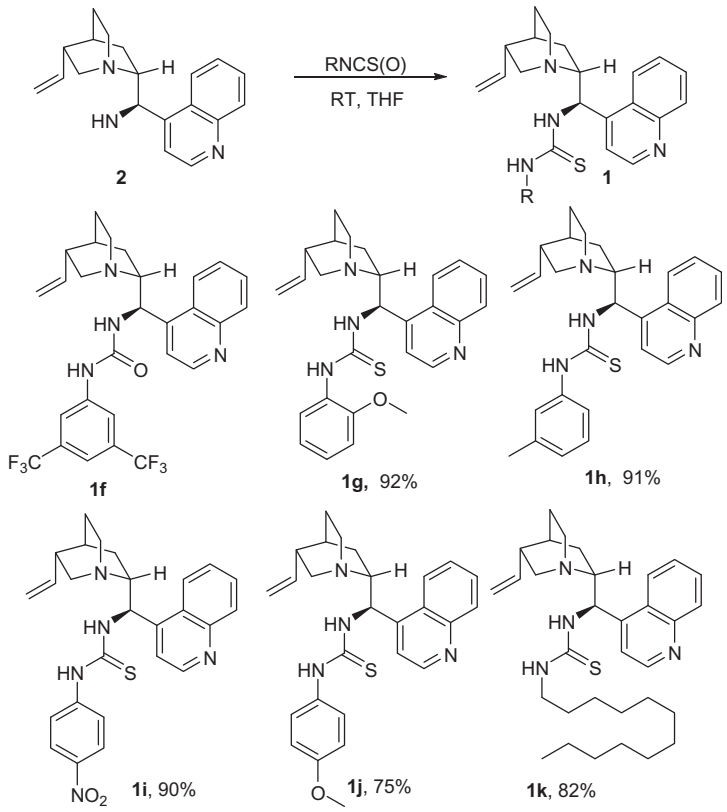



**Scheme 1.** Synthesis of cinchonine derived organocatalysts.

quaternary and tertiary stereogenic centres and, accordingly, issues of both relative and absolute stereocontrol would arise in the screening of our catalyst library. Herein we report our findings.

## 2. Results and discussion

A representative succinimide-derived pronucleophile **4** was synthesized in two steps from commercially available succinimide. The *n*-butyl group was arbitrarily chosen as a blocking group for the acidic NH. Initial feasibility and catalyst identification studies were performed on nitro olefin **3a** (Scheme 2) catalysed by a range of cinchonine derived organocatalysts **1**, prepared by reaction of 9-*epi*-aminocinchonine (9-EACN) **2** with an iso(thio)cyanide or sulfonylchloride (Scheme 1 and Section 4).

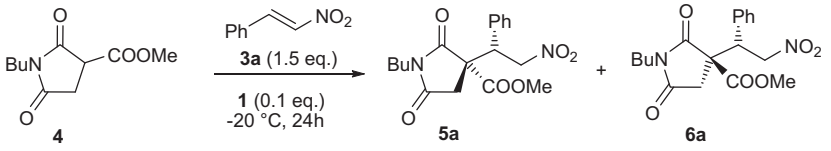
In a series of experiments, the starting materials were dissolved in dichloromethane, cooled to −20 °C and the solid catalysts **1a–k** added directly in one portion. After 24 h the chilled reaction mixture was passed through a plug of silica gel to remove the catalyst, and on concentrating in vacuo, the reaction conversion was measured by $^1$H NMR analysis. Following the chromatographic separation of the diastereoisomers, the enantiomeric excess of the major diastereoisomer was measured by HPLC analysis. The results are presented in Table 1.

At first glance, all of the catalysts, with the exception of the $C_2$-symmetric dimeric catalyst **1c**, performed well in relation to the diastereoselectivity, conversion and enantiocontrol. On closer inspection, the (thio)urea catalysts bearing an *N*-aryl group generally outperformed the sulfonamide catalysts **1d** and **1e** on the basis of reactivity. However the reaction diastereoselectivity was notably higher (10:1 dr) with catalysts **1d** and **1e** compared to ~3:1 dr with the thiourea catalysts **1a–c** and **1g–k** (although the two

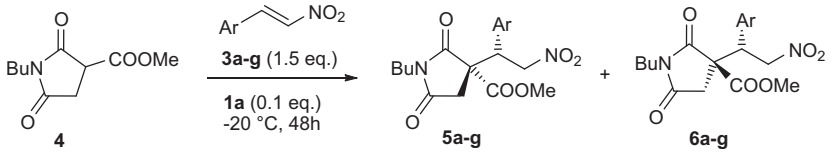
**Table 1**
Catalyst screen for the Michael addition of *C*-succinidyl ester **4** to nitrostyrene **3a**

| Entry | Catalyst | Conv [a,b] (%) | dr[b] | ee[c] (%) |
|---|---|---|---|---|
| 1 | **1a** | >95 | 3:1 | 93 |
| 2 | **1b** | >95 | 2.5:1 | 86 |
| 3 | **1c** | 43 | 2.6:1 | 50 |
| 4 | **1d** | 71 | 10:1 | 92 |
| 5 | **1e** | 69 | 10:1 | 90 |
| 6 | **1f** | >95 | 5:1 | 85 |
| 7 | **1g** | 86 | 3.2:1 | 78 |
| 8 | **1h** | 95 | 2.7:1 | 92 |
| 9 | **1i** | >95 | 3:1 | 86 |
| 10 | **1j** | 94 | 2.7:1 | 93 |
| 11 | **1k** | >95 | 4:1 | 85 |

[a] Reaction was carried out with **4** (1.0 equiv), **3a** (1.5 equiv) and **1a–k** (0.1 equiv) in $CH_2Cl_2$ (0.16 M in **4**).
[b] Determined by $^1$H NMR after 24 h.
[c] ee of major diastereoisomer determined **5a** by HPLC analysis.




**Scheme 2.**




**Scheme 3.**

**Table 2**
Scope of the Michael addition of *C*-succinimidyl ester **4** to nitrostyrenes **3a–g**

| Entry | Adducts | Ar | Time[a] (h) | Yield[b] (%) | dr[c] | ee[d] maj (%) | ee[d] min (%) |
|---|---|---|---|---|---|---|---|
| 1 | **5a**, **6a** | Ph | 48 | 81 | 1.9:1 | 94 | 89 |
| 2 | **5b**, **6b** | 2-Br-Ph | 48 | 88 | 4.1:1 | 95 | 90 |
| 3 | **5c**, **6c** | 2-Cl-Ph | 48 | 85 | 4.5:1 | 96 | 87 |
| 4 | **5d**, **6d** | 4-Tolyl | 48 | 84 | 2.2:1 | 91 | 84 |
| 5 | **5e**, **6e** | 3-MeO-Ph | 48 | 78 | 3.5:1 | 96 | 91 |
| 6 | **5f**, **6f** | 2-Furyl | 48 | 90 | 1.5:1 | 94 | 91 |
| 7 | **5g**, **6g** | 2-Naphthyl | 48 | 96 | 2.1:1 | 95 | 90 |

[a] Reactions were carried out with **4** (1.0 equiv), **3a–g** (1.5 equiv) and **1a** (0.1 equiv) in $CH_2Cl_2$ (0.16 M in **4**).
[b] Isolated yield.
[c] Determined from the amount of separated **5** and **6** after column chromatography.
[d] Determined by HPLC analysis.

diastereoisomers were easily separable by silica gel chromatography). The highest enantioselectivity of 93% was obtained with thioureas **1a** and **1j**. On the basis of the highest reactivity and enantiocontrol, catalyst **1a**, already shown to be optimal for the addition of dimethyl malonate Michael additions[3a] and also for Mannich reactions,[1b] was selected as the champion. Next, the scope of the reaction with **4** was investigated by probing changes to the Michael acceptor **3** (Scheme 3, Table 2).

For a range of aromatic and heteroaromatic nitro olefins **3a–g**, high enantioselectivities (91–96% ee for the major diastereoisomer, 84–91% ee for the minor diastereoisomer), high yields and moderate diastereoselectivities (dr 2.2:1–4.25:1) were obtained after 48 h at −20 °C. In all cases the diastereoisomers were easily separated by flash column chromatography.

The absolute and relative stereochemical configuration of these adducts was established by single crystal X-ray diffraction of the two diastereoisomeric adducts **5b** and **6b** (Fig. 2). The major enantiomer of the major diastereoisomer was found to be (*S*,*R*)-**5b**, the major enantiomer of the minor diastereoisomer (*R*,*R*)-**6b**. The stereochemistry of the all other adducts **5** and **6** were assigned by analogy.

Epimeric at the quaternary, but not the tertiary stereogenic centre, these structural data imply that the thiourea organocatalyst provides excellent control to the *Re*-face of the nitro olefin on addition of the enolised pronucleophile. Furthermore, the chiral pocket offered by the catalyst is of sufficient size to preferentially envelope one enantiomer of both diastereoisomers and thus similar levels of enantioselectivity are observed in both diastereoisomers.

The relatively high reactivity of *C*-succinimidyl ester **4** as a pronucleophile prompted us to investigate the level of catalyst loading that could be tolerated. In a one off experiment the reaction of **4** and **3a** catalysed by 1 mol % of **1a** was performed. The reaction was complete after 4 days at −20 °C and afforded **5a** and **6a** as a 3.4:1 mixture of diastereoisomers in 79% yield. The enantiomeric excess of the major diastereoisomer was 97% and that of the minor diastereoisomer was 91%. These data are similar to those obtained when the reaction was performed at 10 mol % catalysts loading.

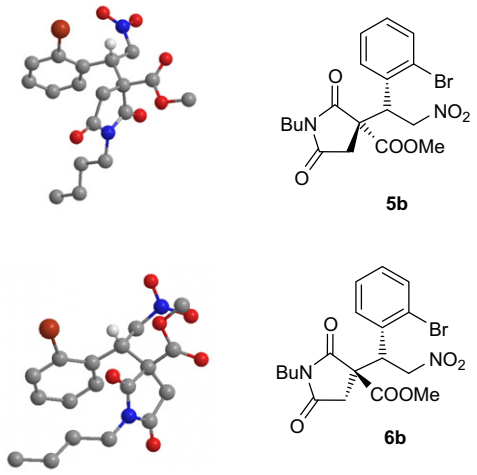



**Figure 2.** Single crystal X-ray determination of absolute and relative stereochemical configurations of **5b** and **6b**.

## 3. Conclusion

In conclusion, we have successfully demonstrated that a prochiral pronucleophile derived from *N*-butyl *C*-succinimidyl ester **4** can be employed in highly stereoselective organocatalysed Michael addition reactions with a range of nitro olefins, affording adducts bearing contiguous quaternary and tertiary stereocentres. The screening of a library of catalysts based on the 9-amino(9-deoxy) epicinchonine scaffold allowed the identification of the best catalyst, thiourea **1a** (although a number of those screened performed nearly as well). The synthetic utility of the generated adducts, their further manipulation and the application of these reactions in natural product synthesis is ongoing.

## 4. Experimental

All reactions conducted under anhydrous conditions glassware was dried in an oven at 100 °C and carried out under a nitrogen atmosphere, unless otherwise stated.

Bulk solutions were evaporated under reduced pressure using a Büchi rotary evaporator. Reagents used were obtained from commercial suppliers or purified according to standard procedures. Petrol refers to distilled light petroleum of fraction (40–65 °C).

Anhydrous tetrahydrofuran and diethyl ether were freshly distilled from sodium-benzophenone.

Flash column chromatography was performed with commercial solvents using Merck Kieselgel 60 silica gel (200–400 mesh). Thin layer chromatography (TLC) was performed on aluminium or glass plates pre-coated with Merck Kieselgel 60 F254 and visualised by ultra-violet radiation or by staining with either aqueous basic potassium permanganate or vanillin. Enantiomeric excesses were determined using high performance liquid chromatography (HPLC) performed on a Hewlett-Packard Series 1050 series system (column conditions are given with the compound).

Melting points were recorded on a Gallenkamp melting point apparatus with the sample contained in a thin glass tube at ambient pressure and are uncorrected.

Optical rotations were recorded using an Optical Activity AA-1000 polarimeter; specific rotations ($[\alpha]_D$) are reported in $10^{-1}$ deg cm$^2$ g$^{-1}$; concentrations ($c$) are quoted in g (100 mL)$^{-1}$; $D$ refers to the D-line of sodium (589 nm); temperatures ($T$) are given in degrees Celsius (°C).

Infrared spectra were recorded on a Perkin Elmer Spectrum RX1 FTIR spectrometer (thin film deposited onto a sodium chloride plate). Only selected absorbencies ($\nu_{max}$) are reported.

$^1$H, $^{13}$C, DEPT, COSY and HMQC NMR spectra were recorded on Bruker 500 MHz and Varian 300 MHz spectrometers. Chemical shifts ($\delta_H$) are quoted in parts per million (ppm ± 0.01 ppm) downfield of tetramethylsilane, relative to the residual protiosolvent ($\delta_H$ ($CHCl_3$) = 7.26 ppm) against an internal deuterium lock. Coupling constants ($J$) are given in Hertz (Hz ± 0.1 Hz). The $^1$H NMR spectra are reported as follows: $\delta$/ppm (multiplicity, number of protons, coupling constants $J$/Hz, assignment). DEPT and two-dimensional NMR spectroscopy (COSY and HMQC) were used where appropriate to assist the assignment of the signals in the $^1$H NMR and $^{13}$C NMR spectra.

Low resolution mass spectrometry (electron impact/chemical ionisation) was recorded on a Micromass Trio 2000 quadropole mass spectrometer and (electrospray) on a Micromass Platform II spectrometer. High resolution mass spectra (accurate mass) were recorded on a Thermo Finnigan Mat95XP mass spectrometer.

*N*-Butylsuccinimide and nitro olefins **3a**, **3f** are commercially available, compounds **1a** (Mp 186–189 °C), **1b–d**[3a] were prepared according to literature procedures.

### 4.1. *N*-[(9*R*)-Cinchonan-9-yl]benzenesulfonamide 1e

9-Amino(9-deoxy) epicinchonine[2a,2p] (703 mg, 2.4 mmol) and $Et_3N$ (668 μL, 4.8 mmol) were dissolved in dry DCM (30 mL) and cooled to 0 °C. Benzenesulfonyl chloride (458 μL, 3.6 mmol) in dry DCM (15 mL) was added. The reaction mixture was allowed to warm to rt and stirred for 20 h until analysis by TLC indicated that all of the amine had been consumed. Purification by flash column chromatography [EtOAc/MeOH/$Et_3N$ (300:5:1) afforded catalyst **1e** as a colourless solid (659 mg, 63% yield). Mp 139–144 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 3629 (H), 3070, 2937, 2863 (CH), 1166 ($SO_2$); $^1$H NMR (400 MHz, $CD_3OD$) $\delta_H$ ppm: 8.59–8.50 (m, 1H, Ar-*H*), 8.04 (d, 1H, $J$ = 6.6, Ar-*H*), 7.88 (d, 1H, $J$ = 8.4, Ar-*H*), 7.72–7.63 (m, 1H, Ar-*H*), 7.62–7.53 (m, 1H, Ar-*H*), 7.50–7.33 (m, 3H, Ar-*H*), 7.28 (t, 1H, $J$ = 7.5, Ar-*H*), 7.18–7.07 (m, 2H, Ar-*H*), 5.74–5.63 (m, 1H, $CH_2$ = C*H*), 5.06–4.74 (m, 3H, C*H*$_2$ = CH and C*H*NH), 2.97–2.75 (m, 3H, quinuclidine-*H*), 2.75–2.63 (m, 1H, quinuclidine-*H*), 2.50–2.38 (m, 1H, quinuclidine-*H*), 2.13 (d, 1H, $J$ = 6.1, quinuclidine-*H*), 1.50–1.30 (m, 3H, quinuclidine-*H*), 1.00–0.86 (m, 1H, quinuclidine-*H*), 0.70–0.60 (m, 1H, quinuclidine-*H*); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta_C$ 149.9, 148.9, 145.0, 140.1, 139.1, 132.7, 130.5, 129.1, 128.6, 128.1, 127.7, 127.4, 127.3, 126.8, 122.2, 120.1, 114.7, 61.6, 52.0, 49.0, 46.0, 38.6, 27.1, 26.4, 24.1; MS $m/z$ (ES+) 434 (100%, MH$^+$). [HR-MS (ES+): MH$^+$, 434.1906. $[C_{25}H_{28}N_3O_2S]^+$ requires 434.1897]; $[\alpha]_D^{20}$ = +67 ($c$ 1.00, $CHCl_3$).

### 4.2. 1-(3,5-Bis(trifluoromethyl)phenyl)-3-[(*R*)-(quinolin-4-yl)((2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl]urea 1f

A solution of 9-amino(9-deoxy) epicinchonine[2a,2p] (448 mg, 1.53 mmol) in dry THF (1 mL/0.17 mmol) was added slowly to bis(trifluoromethyl)isocyanate (291 μL, 1.68 mmol) in dry THF (1 mL/0.19 mmol) at 0 °C. The reaction mixture was allowed to warm to rt and stirred for 3 h until analysis by TLC indicated that all of the amine had been consumed. Purification by flash column chromatography [EtOAc/MeOH/$Et_3N$ (100:2:3–100:10:3) afforded catalyst **1h** as a colourless solid (629 mg, 75% yield). Mp 200–204 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2937 (N–H), 1678 (C=O), 1594 and 1551 (C=C); $^1$H NMR (500 MHz, $CD_3OD$) $\delta_H$ 8.83 (d, 1H, $J$ = 4.7, Ar-*H*), 8.50 (d, 1H, $J$ = 8.4, Ar-*H*), 8.06 (d, 1H, $J$ = 7.9, Ar-*H*), 7.89 (s, 2H, Ar-*H*), 7.76 (t, 1H, $J$ = 7.6, Ar-*H*), 7.68 (t, 1H, $J$ = 7.6, Ar-*H*), 7.62 (d, 1H, $J$ = 4.7, Ar-*H*), 7.41 (s, 1H, Ar-*H*), 5.89 (ddd, 1H, $J$ = 17.1, 10.5, 6.4, $CH_2$=C*H*), 5.62 (br s, 1H, NH–C*H*), 5.15–5.11 (m, 2H, C*H*$_2$=CH), 3.21 (dd, 1H, $J$ = 18.5, 9.0, C*H*–N), 3.12 (dd, 1H, $J$ = 13.5, 7.5, C*H*–N), 3.05–2.95 (m, 3H, C*H*–N), 2.29 (dd, 1H, $J$ = 15.8, 7.7, quinuclidine-*H*), 1.58–1.53 (m, 3H, quinuclidine-*H*), 1.21–1.17 (m, 1H, quinuclidine-*H*), 0.96–0.93 (m, 1H, quinuclidine-*H*); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta_C$ 156.7, 151.0, 149.1, 143.2, 141.5, 133.1 (q, $J$ = 33, 2× Ar), 131.0, 130.1, 128.8, 128.2, 125.5 (q, $J$ = 272, 2 × $CF_3$), 125.0, 119.0, 119.0, 115.5 (br q, $J$ = 4, 3 × Ar), 115.3, 61.3, 61.2, 50.2, 48.1, 40.5, 28.9, 27.4, 26.4; MS $m/z$ (ES+) 549 (98%, MH$^+$). [HR-MS (ES+): MH$^+$, 549.2097. $[C_{28}H_{27}N_4OF_6]^+$ requires 549.2089]; $[\alpha]_D^{20}$ = +134.0 ($c$ 1.00, $CHCl_3$).

### 4.3. General method A for the synthesis of catalysts 1g–k

A solution of amine **2** in dry THF (1 mL/0.17 mmol) was added slowly to the isothiocyanate (1.1 equiv) in dry THF (1 mL/0.19 mmol) at 0 °C. The reaction mixture was allowed to warm to rt and stirred until analysis by TLC indicated that all of the amine had been consumed. Purification by flash column chromatography on silica gel [EtOAc/MeOH/$Et_3N$ (100:2:3–100:10:3) or $Et_2O$/MeOH/$Et_3N$ (100:10:0–90:10:10)] afforded the title organocatalyst **1g–k**.

### 4.4. 1-[(9*R*)-Cinchonan-9-yl]-3-(2-methoxyphenyl)thiourea 1g

Following general method A using amine **2** (340 mg, 1.2 mmol) and 2-methoxyphenyl isothiocyanate (232 mg, 194 μL, 1.4 mmol), the title compound **1g** (488 mg, 92% yield) was obtained as a white solid. Mp 105–109 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2938, 2872, 1509; $^1$H NMR (500 MHz, $CD_3OD$) $\delta_H$ 8.72 (d, 1H, $J$ = 4.7, Ar-*H*), 8.61 (d, 1H, $J$ = 8.5, Ar-*H*), 8.02 (dd, 1H, $J$ = 8.5, 0.6, Ar-*H*), 7.82 (br d, 1H, $J$ = 7.9, Ar-*H*), 7.75–7.72 (m, 1H, Ar-*H*), 7.65–7.62 (m, 1H, Ar-*H*), 7.49 (d, 1H, $J$ = 4.7, Ar-*H*), 7.09 (td, 1H, $J$ = 7.9, 1.6, Ar-*H*), 6.93–6.92 (m, 1H, Ar-*H*), 6.85 (td, 1H, $J$ = 7.7, 1.3, Ar-*H*), 6.19 (br d, 1H, $J$ = 10.1, NH–C*H*), 5.90 (ddd, 1H, $J$ = 17.2, 10.6, 6.3, $CH_2$=C*H*), 5.18–5.14 (m, 2H, C*H*$_2$=CH), 3.67 (s, 3H, C*H*$_3$O), 3.16–3.10 (m, 2H, C*H*–N), 2.95–2.78 (m, 3H, C*H*–N), 2.27 ('q', 1H, $J$ = 7.8, quinuclidine-*H*), 1.49–1.40 (m, 3H, quinuclidine-*H*), 1.22–1.17 (m, 1H, quinuclidine-*H*), 0.76–0.71 (m, 1 H, quinuclidine-*H*); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta_C$ 182.2, 153.4, 151.0, 150.6, 148.9, 141.7, 131.0, 129.9, 129.2, 128.6, 127,9, 127.4, 126.3, 126.2, 121.4, 121.1, 115.4, 112.4, 61.9, 56.3, 56.3, 50.0, 48.4, 40.5, 28.9, 27.4, 26.2; MS $m/z$ (ES+) 459 (100%, MH$^+$). [HR-MS (ES+): MH$^+$, 459.2193. $[C_{27}H_{31}ON_4S]^+$ requires 459.2213]; $[\alpha]_D^{25}$ = +322.5 ($c$ 0.08, $CHCl_3$).

### 4.5. 1-[(9*R*)-Cinchonan-9-yl]-3-(3-methylphenyl)thiourea 1h

Following general method A using amine **2** (220 mg, 0.75 mmol) and 3-methylphenyl isothiocyanate (123 mg, 112 μL, 0.82 mmol), the title compound **1h** (301 mg, 91% yield) was obtained as a white solid. Mp 102–106 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2938, 2870, 1509 $^1$H NMR (500 MHz, $CD_3OD$) $\delta_H$ 8.74 (d, 1H, *J* = 4.7, Ar-*H*), 8.61 (d, 1H, *J* = 8.5, Ar-*H*), 8.03 (dd, 1H, *J* = 8.5, 0.6, Ar-*H*), 7.75 (dt, 1H, *J* = 7.7, 1.3, Ar-*H*), 7.66–7.63 (m, 1H, Ar-*H*), 7.51 (d, 1H, *J* = 4.7, Ar-*H*), 7.19–7.14 (m, 2H, Ar-*H*), 7.09 (br d, 1H *J* = 7.6, Ar-*H*), 6.96 (d, 1H, *J* = 7.6, Ar-*H*), 6.19 (br d, 1H, *J* = 10.4, NH–C*H*), 5.97–5.90 (m, 1H, $CH_2$=C*H*), 5.20–5.16 (m, 2H, $CH_2$=CH), 3.16–3.13 (m, 2H, C*H*–N), 3.00–2.86 (m, 3H, C*H*–N), 2.32–2.27 (m, 1H, quinuclidine-*H*), 2.27 (s, 3H, $CH_3$Ar), 1.52–1.42 (m, 3H, quinuclidine-*H*), 1.26–1.22 (m, 1H, quinuclidine-*H*), 0.81–0.75 (m, 1H, quinuclidine-*H*); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta_C$ 182.1, 151.0, 150.5, 149.0, 141.7, 140.3, 139.7, 131.0, 130.1, 129.9, 129.1, 127.9, 127.4, 126.1, 125.7, 122.2, 121.1, 115.5, 61.9, 56.5, 50.0, 48.4, 40.5, 29.0, 27.4, 26.2, 21.7; MS *m*/*z* (ES+) 443 (100%, MH$^+$). [HR-MS (ES+): MH$^+$, 443.2257. $[C_{27}H_{31}N_4S]^+$ requires 443.2264]; $[\alpha]_D^{25} = +317.0$ (*c* 0.11, $CHCl_3$).

### 4.6. 1-[(9*R*)-Cinchonan-9-yl]-3-(4-nitrophenyl)thiourea 1i

Following general method A using amine **2** (430 mg, 1.47 mmol), the title compound **1i** (624 mg, 90% yield) was obtained as an orange solid. Mp 148–154 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2936 (N-H), 1596 and 1549 (C=C), 1507 and 1328 (N–O and C=S); $^1$H NMR (500 MHz, $CD_3OD$) $\delta_H$ 8.78 (d, 1H, *J* = 4.7, Ar-*H*), 8.59 (d, 1H, *J* = 8.4, Ar-*H*), 8.14–8.07 (m, 2H, Ar-*H*), 8.01 (dd, *J* = 8.5, 0.9, 1H, Ar-*H*), 7.77–7.72 (m, 3H, Ar-*H*), 7.65 (ddd, 1H, *J* = 8.3, 6.9, 1.2, Ar-*H*), 7.57 (d, 1H, *J* = 4.7, Ar-*H*), 6.22 (br d, 1H, *J* = 9.4, NH–C*H*), 5.92 (ddd, 1H, *J* = 17.1, 10.6, 6.3, $CH_2$=C*H*), 5.20–5.13 (m, 2H, $CH_2$=CH), 3.25–3.23 (m, 1H, C*H*–N), 3.14 (br dd, 1H, *J* = 13.8, 7.0, C*H*–N), 2.99–2.96 (m, 3H, C*H*–N), 2.33 (br d, 1H, *J* = 15.7, 7.8, quinuclidine-*H*), 1.57–1.52 (m, 3H, quinuclidine-*H*), 1.27–1.20 (m, 1H, quinuclidine-*H*), 0.89–0.82 (m, 1H, quinuclidine-*H*); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta_C$ 181.9, 150.9, 149.9, 148.9, 147.3, 144.2, 141.5, 131.0, 129.9, 129.0, 127.9, 125.9, 125.3 (2 × C), 122.0 (2 × C), 120.9, 115.4, 61.9, 61.5, 50.0, 48.4, 40.4, 28.8, 27.3, 26.1; MS *m*/*z* (ES+) 474 (100%, MH$^+$). [HR-MS (ES+): MH$^+$, 474.1964. $[C_{26}H_{28}O_2N_5S]^+$ requires 474.1958]; $[\alpha]_D^{20} = +216.7$ (*c* 1.00, $CHCl_3$).

### 4.7. 1-[(9*R*)-Cinchonan-9-yl]-3-(4-methoxyphenyl)thiourea 1j

Following general method A using amine **2** (346 mg, 1.18 mmol), the title compound **1j** (406 mg, 75% yield) was obtained as a colourless solid. Mp 117–119 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2938, 1595, 1532, 1509; $^1$H NMR (500 MHz, $CD_3OD$) $\delta_H$ 8.71 (d, 1H, *J* = 4.6, Ar-*H*), 8.56 (d, 1H, *J* = 8.3, Ar-*H*), 7.97 (d, 1H, *J* = 8.3, Ar-*H*), 7.71 (t, 1H, *J* = 7.6, Ar-*H*), 7.60 (t, 1H, *J* = 7.6, Ar-*H*), 7.47 (d, 1H, *J* = 4.6, Ar-*H*), 7.13 (d, 2H, *J* = 8.9, Ar-*H*), 6.82 (d, 2H, *J* = 8.9, Ar-*H*), 6.14 (br d, 1H, *J* = 10.5, NH–C*H*), 5.89 (ddd, 1H, *J* = 17.1, 10.5, 6.3, $CH_2$=C*H*), 5.17–5.09 (m, 2H, $CH_2$=CH), 3.71 (s, 3H, Ar-$OCH_3$), 3.14–3.06 (m, 2H, C*H*–N), 2.91 (dd, 1H, *J* = 14.2, 10.1, C*H*–N), 2.85 (br t, 2H, *J* = 7.1, C*H*–N), 2.26 (br dd, 1H, *J* = 15.7, 7.6, quinuclidine-*H*), 1.54–1.39 (m, 3H, quinuclidine-*H*), 1.23–1.15 (m, 1H, quinuclidine-*H*), 0.79–0.72 (m, 1H, quinuclidine-*H*); $^{13}$C NMR (75 MHz, $CD_3OD$) $\delta_C$ 182.5, 159.2, 150.9, 150.4, 148.8, 141.6, 132.2, 130.8, 129.8, 128.9, 127.8, 127.6 (2× C), 126.0, 125.8, 121.0, 115.3 (2 × C), 61.7, 56.3, 56.0, 49.9, 48.2, 40.4, 28.8, 27.3, 26.1; MS *m*/*z* (ES+) 459 (100%, MH$^+$). [HR-MS (ES+): MH$^+$, 459.2214. $[C_{27}H_{31}ON_4S]^+$ requires 459.2213]; $[\alpha]_D^{24} = +303.4$ (*c* 1.30, $CHCl_3$).

### 4.8. 1-[(9*R*)-Cinchonan-9-yl]-3-dodecylthiourea 1k

Following general method A using amine **2** (220 mg, 0.75 mmol) and dodecyl isothiocyanate (207 mg (90% pure), 0.82 mmol), the title compound **1k** (273 mg, 82% yield) was obtained as an white solid solid. Mp 57–60 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2923, 2853, 1509; $^1$H NMR (500 MHz, $CD_3OD$) $\delta_H$ 8.77 (d, 1H, *J* = 4.8, Ar-*H*), 8.66 (d, 1H, *J* = 8.1, Ar-*H*), 8.03 (dd, 1H, *J* = 8.5, 0.9, Ar-H), 7.74 (td, 1H, *J* = 7.6, 1.0, Ar-*H*), 7.66–7.62 (m, 1H, Ar-*H*), 7.54 (br s, 1H, Ar-*H*), 6.21 (br s, 1H, *C–*H*), 5.91 (ddd, 1H, *J* = 17.2, 10.6, 6.3, $CH_2$=C*H*), 5.21–5.14 (m, 2H, $CH_2$=CH), 3.36–3.25 (m. 2H, NH$CH_2CH_2$), 3.21–3.05 (m, 2H, C*H*–N), 2.99–2.85 (m, 3H, C*H*–N), 2.28 ('q', 1H, *J* = 7.6, quinuclidine-*H*), 1.51–1.39 (m, 5H, 3H of quinuclidine-*H*, 1 × $CH_2$ of $NHCH_2(CH_2)_{10}CH_3$), 1.31–1.20 (m, 19H, 1H of quinuclidine-*H*, 9 × $CH_2$ of $NHCH_2(CH_2)_{10}CH_3$)), 0.88 (t, 3H, *J* = 7.0, $CH_2CH_3$), 0.79–0.74 (m, 1H, quinuclidine-*H*); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta_C$ 182.2, 150.9, 150.9, 149.0, 141.6, 131.9, 129.9, 129.1, 127.9, 126.3, 121.1, 115.5, 61.9, 56.0, 50.1, 48.4, 45.5, 40.5, 33.2, 30.9, 30.9, 30.8, 30.8, 30.6, 30.6, 30.2, 29.0, 28.1, 27.4, 26.3, 23.9, 14.7; MS *m*/*z* (ES+) 521 (100%, MH$^+$). [HR-MS (ES+): MH$^+$, 521.3672. $[C_{26}H_{28}O_2N_5S]^+$ requires 521.3655]; $[\alpha]_D^{25} = +195.1$ (*c* 0.12, $CHCl_3$).

### 4.9. General method B for the synthesis of nitro olefins 3b–e, g

According to the modified literature procedure.[6] To a stirred solution of the aryl aldehyde and nitromethane (10 equiv) was added ammonium acetate (1.1 equiv). The solution was heated at reflux for 24 h. The reaction mixture was concentrated in vacuo and then dissolved in $CH_2Cl_2/H_2O$ (1:1), the organics were extracted into $CH_2Cl_2$ (3×), then washed with brine, dried (magnesium sulfate), filtered and concentrated in vacuo. Purification by flash column chromatography on silica gel [EtOAc/petroleum ether] afforded the title nitro olefin.

### 4.10. 1-Bromo-2-[(*E*)-2-nitroethenyl]benzene 3b

Following general method B, the title compound **3b** (1.49 g, 47% yield) was obtained as a yellow solid after flash column chromatography on silica gel [EtOAc/petroleum ether (1:8–1:2)]. Mp 82–87 °C, lit.[7a] 88–91 °C; lit.[7b] 86 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 1632 (C=C), 1561 and 1339 (N–O), 970 (C=C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 8.43 (d, 1H, *J* = 13.6, C*H*=$CHNO_2$), 7.72 (dd, 1H, *J* = 7.8, 1.3, Ar-*H*), 7.60 (dd, 1H, *J* = 7.8, 1.8, Ar-*H*), 7.57 (d, 1H, *J* = 13.6, =C*H*–$NO_2$), 7.42 (dt, 1H, *J* = 7.6, 1.3, Ar-*H*), 7.37 (dt, 1H, *J* = 7.6, 1.8, Ar-*H*); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 139.2 (CH=$CHNO_2$), 138.0 (CH=$CHNO_2$), 134.4 (Ar:$C_{quat}$), 133.4 (Ar), 130.8 (Ar), 128.9 (Ar), 128.5 (Ar), 126.8 (Ar:$C_{ortho}$-Br); MS *m*/*z* (CI+) 245 (100%, $MNH_4^+$), 247 (100%, $MNH_4^+$). [HR-MS (ES+): $MNH_4^+$, 244.9915. $[C_8H_{10}BrN_2O_2]^+$ requires 244.9920].

### 4.11. 1-Chloro-2-[(*E*)-2-nitroethenyl]benzene 3c

Following general method B, the title compound **3c** (936 mg, 73% yield) was obtained as a yellow solid after flash chromatography [EtOAc/petroleum ether (1:6–1:3). Mp 45–48 °C, lit.[8a] 48 °C, lit.[8b] 42–43 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 1630 (C=C), 1529 and 1375 (N–O), 963 (C=C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 8.44 (d, 1H, *J* = 13.7, C*H*=$CHNO_2$), 7.63 (d, 1H, *J* = 13.7, =C*H*–$NO_2$), 7.62 (dd, 1H, *J* = 7.7, 1.7, Ar-*H*), 7.53 (dd, 1H, *J* = 8.0, 1.0, Ar-*H*), 7.46 (dt, 1H, *J* = 7.7, 1.7, Ar-*H*), 7.37 (ddd, 1H, *J* = 8.0, 7.7, 1.0, Ar-*H*); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 139.2 (CH=$CHNO_2$), 136.5 (CH=$CHNO_2$), 135.5 (Ar:$C_{quat}$), 133.3 (Ar-CH), 131.2 (Ar:$C_{ortho}$-Cl), 129.0, 128.9, 127.9 (Ar-C); MS *m*/*z* (CI+) 201 (37%, $MNH_4^+$), 203 (12%, $MNH_4^+$). [HR-MS (ES+): $MNH_4^+$, 201.0430. $[C_8H_{10}ClN_2O_2]^+$ requires 201.0425].

### 4.12. 1-Methyl-4-[(*E*)-2-nitroethenyl]benzene 3d

Following general method B, the title compound **3d** (1.79 g, 78% yield) was obtained as a yellow solid after flash column chromatography on silica gel [EtOAc/petroleum ether (1:8–1:4)]. Mp 106–109 °C, lit.[8a] 101–102 °C, lit.[9] 104.5–105 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 1630 (C=C), 1560 and 1377 (N–O), 963 (C=C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.90 (d, 1H, $J$ = 13.6, C*H*=CHNO$_2$), 7.49 (d, 1H, $J$ = 13.6, =C*H*–NO$_2$), 7.36 (d, 2H, $J$ = 8.1, Ar-*H*), 7.18 (d, 2H, $J$ = 8.1, Ar-*H*), 2.33 (s, 3H, Ar-C*H*$_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 143.6 (Ar:C$_{para}$–CH$_3$), 139.7 (CH=CHNO$_2$), 136.7 (CH=CHNO$_2$), 130.6 (Ar:C$_{quat}$), 129.6 (2 × Ar), 127.7 (2 × Ar-C), 22.1 (Ar-CH$_3$); MS $m/z$ (CI+) 181 (100%, MNH$_4^+$); [HR-MS (ES+): M$^+$,163.0630. [C$_9$H$_9$NO$_2$]$^+$ requires 163.0628].

### 4.13. 1-Methoxy-3-[(*E*)-2-nitroethenyl]benzene 3e

Following general method B, the title compound **3e** (2.57 g, 99% yield) was obtained as a yellow solid after flash silica gel chromatography [EtOAc/petroleum ether (1:4–1:1)]. Mp 89–91 °C, lit.[8b] 89–9 l °C, lit.[10] 91–92 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 1638 (C=C), 1577 and 1377 (N–O), 962 (C=C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 8.01 (d, 1H, $J$ = 13.7, C*H*=CHNO$_2$), 7.60 (d, 1H, $J$ = 13.7, =C*H*–NO$_2$), 7.40 (dd, 1H, $J$ = 9.0, 7.7, Ar-*H*), 7.18 (d, 1H, $J$ = 7.7, Ar-*H*), 7.12–7.06 (m, 2H, Ar-*H*), 3.88 (s, 3H, OC*H*$_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 160.5 (Ar:C$_{meta}$–OCH$_3$), 139.5 (CH=CHNO$_2$), 137.8 (CH=CHNO$_2$), 131.7 (Ar:C$_{quat}$), 130.9, 122.2, 118.4, 114.4 (Ar-C), 55.9 (Ar-OCH$_3$); MS $m/z$ (CI+) 197 (78%, MNH$_4^+$). [HR-MS (ES+): MNH$_4^+$, 197.0926. [C$_9$H$_{13}$N$_2$O$_3$]$^+$ requires 197.0921].

### 4.14. 2-[(*E*)-2-Nitroethenyl]naphthalene 3g

Following general method B, the title compound **3g** (2.07 g, 74% yield) was obtained as a yellow solid after flash column chromatography on silica gel [EtOAc/petroleum ether (1:4–1:3)]. Mp 128–131 °C, lit.[11] 120–121 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 1629 (C=C), 1535 and 1377 (N–O), 964 (C=C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 8.21 (d, 1H, $J$ = 13.6, C*H*=CHNO$_2$), 8.06 (s, 1H, Ar-*H*), 7.93–7.91 (m, 3H, Ar-*H*), 7.74 (d, 1H, $J$ = 13.6, =C*H*–NO$_2$), 7.65–7.62 (m, 3H, Ar-*H*); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 139.7 (Ar), 137.6 (Ar), 135.3 (Ar:C$_{quat}$), 133.6 (Ar:C$_{quat}$), 132.7, 129.8, 129.3, 128.8, 128.4 (Ar-C), 128.0 (Ar:C$_{quat}$), 127.7, 123.7 (Ar-C); MS $m/z$ (CI+) 217 (100%, MNH$_4^+$). [HR-MS (ES+): M$^+$, 199.0625. [C$_{12}$H$_9$NO$_2$]$^+$ requires 199.0628].

### 4.15. Preparation of (*rac*)-methyl 1-butyl-2,5-dioxopyrrolidine-3-carboxylate 4

To a solution of *n*-butylsuccinimide (1.98 g, 12.77 mmol) in THF (40 mL) at −78 °C was added lithium hexamethyldisilazide (25.5 mmol) dropwise as a 1 M solution (THF (25.5 mL)). The solution was warmed to 0 °C for 30 min before being cooled to −78 °C. Methyl chloroformate (0.997 mL, 12.77 mmol) was then added rapidly and the solution was stirred for 15 minutes at −78 °C before being quenched with saturated ammonium chloride solution. The reaction mixture was warmed to room temperature, extracted into $Et_2O$ and washed with brine After extraction the organics were dried using $MgSO_4$ and the crude product purified by flash column chromatography [$Et_2O$/petroleum ether (1:1)] to yield succinimide **3** as a colourless oil (1.05 g, 40%); IR $\nu_{max}$(film) 2958 (CH) 1744 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 3.82 (s, 3H, OC*H*$_3$), 3.77 (dd, 1 H, $J$ = 9.4, 4.7), 3.5 (m, 2 H, C*H*$_2$N), 3.1 (dd, 1 H, $J$ = 18.2, 4.7), 2.89 (dd, 1 H, $J$ = 18.2, 9.4), 1.60–1.51 (m, 2 H, C*H*$_2$CH$_2$N), 1.30 (qd, 2 H, $J$ = 14.8, 7.4, C*H*$_2$CH$_3$), 0.92 (t, 3 H, $J$ = 7.4, C*H*$_3$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 174.8 (*C*=O), 171.9 (*C*=O), 167.9 (*C*=O), 53.1 (CH$_3$O), 45.9 (*C*H$_2$N), 39.0 (*C*HC(O)N), 31.9 (*C*H$_2$CH$_2$N), 29.3 (*C*H$_2$C(O)N), 19.7 (CH$_3$*C*H$_2$), 13.3 (*C*H$_3$CH$_2$); MS $m/z$ (ES+) 227 (30%, MNH$_4^+$); [HR-MS (EI+): M, 213.0989. [C$_{10}$H$_{15}$NO$_4$]$^+$ requires 213.0996].

### 4.16. General method C for the organocatalysed Michael addition of succinimide 4 to nitro olefins 3

To a stirred solution of nitro olefin **3** (0.493 mmol) and succinimide **4** (70 mg, 0.329 mmol) in dry $CH_2Cl_2$ (2.0 mL) was added catalyst **1** (0.0329 mmol). The reaction was stirred at −20 °C until analysis by TLC indicated that all of the succinimide had been consumed (48 h). The solution was then filtered through a plug of silica, concentrated, and analysed by $^1$H NMR before purification by flash column chromatography [$Et_2O$/petroleum ether (1:1)] to yield the desired adducts **5** and **6** as chromatographically separable diastereoisomers.

### 4.17. (*S*)-Methyl 1-butyl-3-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-3-carboxylate 4a and (*R*)-methyl 1-butyl-3-((*S*)-2-nitro-1-phenylethyl)-2,5-dioxopyrrolidine-3-carboxylate 5a

Following the general method C, the title compounds **5a** (63 mg, 53% yield) and **6a** (33 mg, 28% yield) were obtained after 48 h as colourless solids in 94% ee (**5a**) [Chiralpak 1B, Hexane/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 11.7 min, $t$ (minor) = 16 min]) and 89% ee (**6a**) [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 16.3 min, $t$ (minor) = 21.3 min] as determined by HPLC analysis.

*Data for* **5a**: Mp 83–86 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2958 (CH), 1743 (C=O), 1705 (C=O), 1557 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.30 (m, 3H, Ar-*H*), 7.15 (m, 2H, Ar-*H*), 5.29 (dd, 1H, $J$ = 13.9, 10.9, C*H*$_A$H$_B$–NO$_2$), 5.11 (dd, 1H, $J$ = 13.9, 3.38, CH$_A$*H*$_B$-NO$_2$), 4.25 (dd, 1H, $J$ = 10.9, 3.38, Ar-*C*H), 3.81 (s, 3H, C*H*$_3$O), 3.44 (m, 2H, C*H*$_2$N), 2.82 (d, 1H, $J$ = 18.3, C*H*$_2$C(O)N), 2.64 (d, 1H, $J$ = 18.3, C*H*$_2$C(O)N), 1.53–1.39 (m, 2H, C*H*$_2$CH$_2$N), 1.21 (m, 2H, CH$_3$C*H*$_2$CH$_2$), 0.90 (t, 3H, $J$ = 7.4, 7.4, C*H*$_3$CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 174.1 (*C*=O), 173.4 (*C*=O), 168.7 (*C*=O), 139.3, 130.3, 130.2, 129.0 (Ar-*C*), 76.1 (*C*H$_2$NO$_2$), 57.9 (quaternary *C*), 54.2 (OCH$_3$), 45.6 (*C*H$_2$N), 39.5 (NO$_2$CH$_2$*C*H), 35.3 (*C*H$_2$C(O)N), 29.3 (*C*H$_2$CH$_2$N), 19.9 (CH$_3$*C*H$_2$), 13.8 (*C*H$_3$CH$_2$); MS $m/z$ (CI+) 380 (40%, MNH$_4^+$). [HR-MS (ES+): MNH$_4^+$, 380.1814. [C$_{18}$H$_{26}$O$_6$N$_3$]$^+$ requires 380.1816]; $[\alpha]_D^{25} = +89$ ($c$ 0.7, CHCl$_3$).

*Data for* **6a**: Mp 84–88 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2958 (CH), 1744 (C=O), 1706 (C=O), 1557 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.32–7.28 (m, 3H, Ar-*H*), 7.25–7.22 (m, 2H, Ar-*H*), 5.13 (dd, 1H, $J$ = 13.4, 4.3, C*H*$_A$H$_B$-NO$_2$), 4.95 (dd, 1H, $J$ = 13.4, 10.6, CH$_A$*H*$_B$-NO$_2$), 4.51 (dd, 1H, $J$ = 10.6, 4.3, Ar-*C*H), 3.84 (s, 3H, C*H*$_3$O), 3.27 (t, 2H, $J$ = 7.5, C*H*$_2$N), 3.18 (d, 1H, $J$ = 18.3, C*H*$_2$C(O)N), 2.83 (d, 1H, $J$ = 18.2, C*H*$_2$C(O)N), 1.13 (m, 2H, C*H*$_2$CH$_2$N), 1.06–0.90 (m, 2H, CH$_3$C*H*$_2$CH$_2$), 0.79 (t, 3H, $J$ = 7.3, C*H*$_3$CH$_2$) $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 173.8 (*C*=O), 173.2 (*C*=O), 168.5 (*C*=O), 133.4, 129.3, 129.2, 128.9 (Ar-*C*), 75.8 (*C*H$_2$NO$_2$) 57.6 (quaternary *C*), 54.0 (C=O)OCH$_3$), 45.8 (*C*H$_2$N), 39.3 (NO$_2$CH$_2$*C*H), 35.2 (*C*H$_2$C(O)N), 29.1 (*C*H$_2$CH$_2$N), 19.7 (CH$_3$*C*H$_2$), 13.6 (*C*H$_3$CH$_2$); MS $m/z$ (ES) 385 (100%, MNa$^+$). [HR-MS (ES+): MNa$^+$, 385.1380. [C$_{18}$H$_{22}$O$_6$N$_2$Na]$^+$ requires 385.1370]; $[\alpha]_D^{25} = -55$ ($c$ 0.3, CHCl$_3$).

### 4.18. (*S*)-Methyl 3-((*R*)-1-(2-bromophenyl)-2-nitroethyl)-1-butyl-2,5-dioxopyrrolidine-3-carboxylate 5b and (*R*)-methyl 3-((*R*)-1-(2-bromophenyl)-2-nitroethyl)-1-butyl-2,5-dioxopyrrolidine-3-carboxylate 6b

Following general method C, the title compounds **5b** (94 mg, 70% yield) and **6b** (23 mg, 18% yield) were obtained after 48 h as

colourless crystals in 95% ee **5b** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 18.5 min, $t$ (minor) = 9.9 min] and 90% ee **6b** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 18.8 min, $t$ (minor) = 15.1 min] as determined by HPLC analysis.

*Data for* **5b**: Mp 106–109 °C; IR $\upsilon_{max}$(film)/cm$^{-1}$ 2959 (CH), 1783 (C=O), 1746 (C=O), 1706 (C=O), 1556; $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.56 (dd, 1H, $J$ = 8.3, 1.3, Ar-*H*), 7.18 (m, 1H, Ar-*H*), 7.10 (m, 2H, Ar-*H*), 5.25 (dd, 1H, $J$ = 14.2, 10.9, C$H_A$H$_B$-NO$_2$), 5.12 (dd, 1H, $J$ = 14.2, 3.4, CH$_A$$H_B$–NO$_2$), 5.04 (dd, 1H, $J$ = 10.9, 3.4, Ar-*C*H), 3.78 (s, 3H, C$H_3$O), 3.39 (t, 2H, $J$ = 7.4, C$H_2$N), 2.81 (d, 1H, $J$ = 18.5, C$H_2$C(O)N), 2.60 (d, 1H, $J$ = 18.6, C$H_2$C(O)N), 1.41 (m, 2H, C$H_2$CH$_2$N), 1.15 (m, 2H, CH$_3$C$H_2$CH$_2$), 0.84 (t, 3H, $J$ = 7.4, C$H_3$CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 174.6 (*C*=O), 173.4 (*C*=O), 169.4 (*C*=O), 134.2, 133.6, 130.5, 128.4, 127.7, 127.6 (Ar-*C*), 76.4 ($CH_2NO_2$), 56.4 (quaternary *C*), 54.0 (O$CH_3$), 43.4 ($CH_2$N), 39.3 (NO$_2$CH$_2$CH), 37.5 ($CH_2$C(O)N), 29.2 ($CH_2CH_2$N), 19.8 ($CH_3CH_2$), 13.5 ($CH_3CH_2$); MS $m/z$ (CI+) 458 (Br$_{78}$) (40%, MNH$_4^+$) 461 (Br$_{81}$) (50%, MNH$_4^+$). [HR-MS (ES+): MNH$_4^+$, 458.0910. [C$_{18}$H$_{21}$BrN$_2$O$_6$]$^+$ requires 458.0921]; $[\alpha]_D^{25}$ = +93.3 (99% ee) ($c$ 0.3, $CHCl_3$).

*Data for* **6b**: Mp 72–74 °C; IR $\upsilon_{max}$(film)/cm$^{-1}$ 2958 (CH), 1743 (C=O), 1704 (C=O), 1557; $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.61 (m, 2H, Ar-*H*), 7.34 (dt, 1H, $J$ = 7.7, 1.3, Ar-*H*), 7.19 (ddd, 1H, $J$ = 8.0, 7.5, 1.7, Ar-*H*), 5.59 (dd, 1H, $J$ = 14.1, 3.3, C$H_A$H$_B$-NO$_2$), 5.30 (dd, 1H, $J$ = 14.2, 10.2, CH$_A$$H_B$-NO$_2$), 4.77 (dd, 1H, $J$ = 10.2, 3.4, Ar-*C*H), 3.81 (s, 3H, C$H_3$O) 3.54 (t, 2H, $J$ = 7.3, C$H_2$N), 2.94 (d, 1H, $J$ = 18.4, C$H_2$C(O)N), 2.76 (d, 1H, $J$ = 18.4, C$H_2$C(O)N), 1.51 (m, 2H, C$H_2$CH$_2$N) 1.30 (m, 2H, CH$_3$C$H_2$CH$_2$), 0.93 (m, 3H, C$H_3$CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$); $\delta_C$ 173.8 (*C*=O), 173.7 (*C*=O), 168.5 (*C*=O), 135.3, 134.0, 130.3, 128.8, 128.7 (Ar-*C*), 77.0 ($CH_2NO_2$), 57.2 (quaternary *C*), 53.8 (O$CH_3$), 44.5 ($CH_2$N), 39.4 (NO$_2$CH$_2$CH), 37.6 ($CH_2$C(O)N), 29.3 ($CH_2CH_2$N), 19.8 ($CH_3CH_2$), 13.6 ($CH_3CH_2$); MS $m/z$ (CI+) 458 (Br$_{78}$) (10%, MNH$_4^+$) 461 (Br$_{81}$) (20%, MNH$_4^+$). [HR-MS (ES+): MNH$_4^+$ 458.0921. [C$_{18}$H$_{21}$BrN$_2$O$_6$]$^+$ requires 458.0921]; $[\alpha]_D^{25}$ = +68.8 (99% ee) ($c$ 0.5, $CHCl_3$).

### 4.19. (*S*)-Methyl 1-butyl-3-((*R*)-1-(2-chlorophenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-carboxylate 5c and (*R*)-methyl 1-butyl-3-((*R*)-1-(2-chlorophenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-carboxylate 6c

Following general method C, the title compounds **5c** (90 mg, 69% yield) and **6c** (20 mg, 16% yield) were obtained after 48 h as colourless solids in 96% ee **5c** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 13.6 min, $t$ (minor) = 8.4 min] and 87% ee **6c** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, t (major) = 14.6 min, t (minor) = 12.1 min] as determined by HPLC analysis.

*Data for* **5c**: Mp 84–87 °C; IR $\upsilon_{max}$(film)/cm$^{-1}$ 2959 (CH), 1746 (C=O), 1703 (C=O), 1556; $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.45 (dd, 1H, $J$ = 8.0, 1.1, Ar-*H*), 7.27 (m, 1H, Ar-*H*), 7.20 (m, 2H, Ar-*H*), 5.33 (dd, 1H, $J$ = 14.2, 11.0, C$H_A$H$_B$–NO$_2$), 5.20 (dd, 1H, $J$ = 14.2, 3.4, CH$_A$$H_B$–NO$_2$), 5.11 (dd, 1H, $J$ = 10.9, 3.4, Ar-*C*H), 3.85 (s, 3H, C$H_3$O), 3.46 (m, 2H, C$H_2$N), 2.88 (d, 1H, $J$ = 18.6, C$H_2$C(O)N) 2.64 (d, 1H, $J$ = 18.6, C$H_2$C(O)N) 1.49 (m, 2H, C$H_2$CH$_2$N) 1.22 (m, 2H, CH$_3$C$H_2$CH$_2$) 0.91 (t, 3H, $J$ = 7.3, C$H_3$CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$) 174.6 (*C*=O), 173.5 (*C*=O), 169.5 (*C*=O), 136.2, 131.9, 130.9, 130.3, 127.9, 127.7 (Ar-*C*), 76.2 ($CH_2NO_2$), 56.3 (quaternary *C*), 54.0 (O$CH_3$), 40.7 ($CH_2$N), 39.3 (NO$_2$CH$_2$CH), 37.5 ($CH_2$C(O)N), 29.3 ($CH_2CH_2$N), 19.9 ($CH_3CH_2$), 13.5 ($CH_3CH_2$); MS $m/z$ (CI+) 414 (20%, MNH$_4^+$). [HR-MS (ES+): MNH$_4^+$, 414.1433. [C$_{18}$H$_{25}$N$_3$O$_6$Cl]$^+$ requires 414.1426]; $[\alpha]_D^{24}$ = +49 ($c$ 1, $CHCl_3$).

*Data for* **6c**: Mp 74–76 °C; $\upsilon_{max}$(film)/cm$^{-1}$ 2958, 2874 (CH), 1800, 1751, 1715 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ ppm 7.43 (dd, 1H, $J$ = 8.0, 1.1, Ar-*H*)) 7.25 (m, 1H, Ar-*H*)) 7.19 (m, 2H, Ar-*H*)) 5.31 (dd, 1H, $J$ = 14.2, 11.0, C$H_A$H$_B$-NO$_2$) 5.18 (dd, 1H, $J$ = 14.2, 3.4, CH$_A$$H_B$–NO$_2$), 5.10 (dd, 1H, $J$ = 10.9, 3.4, Ar-*C*H), 3.83 (s, 3H, C$H_3$O), 3.44 (m, 2H, C$H_2$N), 2.86 (d, 1H, $J$ = 18.6, C$H_2$C(O)N), 2.62 (d, 1H, $J$ = 18.6, C$H_2$C(O)N), 1.46 (m, 2H, C$H_2$CH$_2$N), 1.22 (m, 2H, CH$_3$C$H_2$CH$_2$), 0.90 (t, 3H, $J$ = 7.3, C$H_3$CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 174.4 (*C*=O), 173.3 (*C*=O), 169.3 (*C*=O), 133.0, 130.8, 130.7, 128.0, (Ar-*C*), 76.1 ($CH_2NO_2$), 57.2 (quaternary *C*), 53.8 (O$CH_3$), 40.5 ($CH_2$N), 39.1 (NO$_2$CH$_2$CH), 37.3 ($CH_2$C(O)N), 29.1 ($CH_2CH_2$N), 19.7 ($CH_3CH_2$), 13.3 ($CH_3CH_2$); $m/z$ (CI+) 414 (10%, MNH$_4^+$); [HR-MS (ES+): MNH$_4^+$, 414.1434. [C$_{18}$H$_{25}$N$_3$O$_6$Cl]$^+$ requires 414.1426]; $[\alpha]_D^{24}$ = +31 ($c$ 4, $CHCl_3$).

### 4.20. (*S*)-Methyl 1-butyl-3-((*S*)-2-nitro-1-p-tolylethyl)-2,5-dioxopyrrolidine-3-carboxylate 5d and (*R*)-methyl 1-butyl-3-((*S*)-2-nitro-1-p-tolylethyl)-2,5-dioxopyrrolidine-3-carboxylate 6d

Following general method C, the title compounds **5d** (71 mg, 58% yield) and **6d** (32 mg, 26% yield) were obtained after 48 h as colourless solids in 91% ee **5d** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 14.5 min, $t$ (minor) = 11 min] and 84% ee **6d** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 19.9 min, $t$ (minor) = 16.6 min] as determined by HPLC analysis.

*Data for* **5d**: Mp 72–77 °C; IR $\upsilon_{max}$(film)/cm$^{-1}$ 2959 (CH), 1745 (C=O), 1702 (C=O), 1556; $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.10 (d, 2H, $J$ = 8.0, Ar-*H*), 7.04 (d, 2H, $J$ = 8.2, Ar-*H*), 5.26 (m, 1H, C$H_A$H$_B$–NO$_2$), 5.10 (dd, 1H, $J$ = 13.7, 3.4, CH$_A$$H_B$–NO$_2$), 4.22 (dd, 1H, $J$ = 10.9, 3.4, Ar-*C*H), 3.82 (s, 3H, C$H_3$O), 3.45 (t, 2H, $J$ = 7.2, C$H_2$N), 2.82 (d, 1H, $J$ = 18.3, C$H_2$C(O)N), 2.66 (m, 1H, C$H_2$C(O)N), 2.29 (s, 3H, Ar-C$H_3$), 1.47 (m, 2H, C$H_2$CH$_2$N), 1.23 (m, 2H, CH$_3$C$H_2$CH$_2$), 0.92 (t, 3H, $J$ = 7.3); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 174.7 (C=O), 173.6 (*C*=O), 169.8 (*C*=O), 139.2, 130.4, 130.2, 128.8 (Ar-*C*), 76.9 ($CH_2NO_2$), 56.3 (quaternary *C*), 53.9 (O$CH_3$), 46.2 ($CH_2$N), 39.3 (NO$_2$CH$_2$CH), 38.2 ($CH_2$C(O)N), 29.2 ($CH_2CH_2$N), 21.1 ($CH_3$Ar), 19.9 ($CH_3CH_2$), 13.6 ($CH_3CH_2$); $m/z$ (ES$^+$) 399 (100%, MNa$^+$); [HR-MS (ES+): MNa$^+$, 399.1530. [C$_{19}$H$_{24}$N$_2$O$_6$Na]$^+$ requires 399.1527]; $[\alpha]_D^{21}$ = +60 ($c$ 0.5, $CHCl_3$).

*Data for* **6d**: MP: 65–68C; IR $\upsilon_{max}$(film)/cm$^{-1}$ 2959 (CH), 1744 (C=O), 1702 (C=O), 1556 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.11 (s, 4H, Ar-*H*), 5.09 (dd, 1H, $J$ = 13.3, 4.4, C$H_A$H$_B$-NO$_2$), 4.91 (dd, 1H, $J$ = 13.3, 10.6, CH$_A$$H_B$–NO$_2$), 4.47 (dd, 1 H, $J$ = 10.6, 4.4, Ar-*C*H), 3.84 (s, 3H, C$H_3$O), 3.28 (t, 2H, $J$ = 7.0, C$H_2$N), 3.17 (d, 1H, $J$ = 18.2, C$H_2$C(O)N), 2.82 (d, 1H, $J$ = 18.2, C$H_2$C(O)N), 2.29 (s, 3H, Ar-C$H_3$), 1.13 (m, 2H, C$H_2$CH$_2$N), 0.98 (m, 2H, CH$_3$C$H_2$CH$_2$), 0.80 (t, 3H, $J$ = 7.3, C$H_3$CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta_C$ 172.8, 172.2, 167.5 (*C*=O), 138.0, 129.1, 128.9, 127.7 (Ar-*C*), 74.9 ($CH_2NO_2$), 56.6 (quaternary *C*), 52.9 (O$CH_3$), 44.4 ($CH_2$N), 38.3 (NO$_2$CH$_2$CH), 34.0 ($CH_2$C(O)N), 28.1 ($CH_2CH_2$N), 20.0 ($CH_3$Ar), 18.6 ($CH_3CH_2$), 12.5 ($CH_3CH_2$); $m/z$ (ES$^+$) 394 (100%, MNH$_4^+$); [HR-MS (ES+): MNH$_4^+$, 394.1982. [C$_{19}$H$_{28}$N$_3$O$_6$]$^+$ requires 394.1973]; $[\alpha]_D^{21}$ = −32.4 ($c$ 0.5, $CHCl_3$).

### 4.21. (*S*)-Methyl 1-butyl-3-((*S*)-1-(3-methoxyphenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-carboxylate 5e and (*R*)-methyl 1-butyl-3-((*S*)-1-(3-methoxyphenyl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-carboxylate 6e

Following general method C, the title compounds **5e** (74 mg, 57% yield) and **6e** (21 mg, 16% yield) were obtained after 48 h as colourless oils in 96% ee **5e** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 17.5 min, $t$ (minor) = 15.3 min] and 91% ee **6e** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, $t$ (major) = 29.4 min, $t$ (minor) = 22.1 min] as determined by HPLC analysis.

*Data for* **5e**: IR $\upsilon_{max}$(film)/cm$^{-1}$ 2959 (CH), 1745 (C=O), 1702 (C=O), 1556 (C=O); $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ 7.15 (m, 1H,

Ar-*H*), 6.76 (m, 1H, Ar-*H*), 6.67 (m, 1H, Ar-*H*), 6.62 (m, 1H, Ar-*H*), 5.20 (dd, 1H, *J* = 13.9, 10.8, C*H*$_A$H$_B$-NO$_2$), 5.04 (dd, 1H, *J* = 13.9, 3.4, CH$_A$*H*$_B$-NO$_2$), 4.16 (dd, 1H, *J* = 10.8, 3.4, Ar-*C*H), 3.76 (s, 3H, C*H*$_3$O), 3.69 (s, 3H, ArOC*H*$_3$), 3.39 (t, 2H, *J* = 7.4, C*H*$_2$N), 2.75 (d, 1H, *J* = 18.3, C*H*$_2$C(O)N), 2.62 (d, 1H, *J* = 18.3, C*H*$_2$C(O)N), 1.40 (m, 2H, C*H*$_2$CH$_2$N), 1.16 (m, 2H, CH$_3$C*H*$_2$CH$_2$), 0.85 (t, 3H, *J* = 7.4, C*H*$_3$CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_C$ 174.5 (*C*=O), 173.4 (*C*=O), 169.6 (*C*=O), 159.9, 135.0, 130.4, 120.8, 115.3, 113.7 (Ar-*C*), 76.8 (*C*H$_2$NO$_2$), 56.0 (quaternary *C*), 55.0 (ArO*C*H$_3$), 53.7 (O*C*H$_3$), 46.3 (*C*H$_2$N), 39.2 (NO$_2$CH$_2$*C*H), 38.0 (*C*H$_2$C(O)N), 29.1 (*C*H$_2$CH$_2$N), 19.7 (CH$_3$*C*H$_2$), 13.4 (*C*H$_3$CH$_2$); *m*/*z* (CI+) 410 (30%, MNH$_4^+$); [HR-MS (ES+): MNH$_4^+$, 410.1914, [C$_{19}$H$_{28}$N$_3$O$_7$]$^+$ requires 410.1922]; $[\alpha]_D^{24} = +48$ (*c* 1, CHCl$_3$).

*Data for* **6e**: IR $\nu_{max}$(film)/cm$^{-1}$ 2959 (CH), 1747 (C=O), 1702 (C=O), 1555 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$ 7.22 (t, 1H, *J* = 8.0 Hz,, Ar-*H*), 6.80 (m, 3H, Ar-*H*), 5.12 (dd, 1H, *J* = 13.5, 4.3, C*H*$_A$H$_B$-NO$_2$), 4.93 (dd, 1H, *J* = 13.5, 10.5, CH$_A$*H*$_B$–NO$_2$), 4.46 (dd, 1H, *J* = 10.5, 4.3, Ar-*C*H), 3.84 (s, 3H, C*H*$_3$O), 3.77 (s, 3H, ArOC*H*$_3$), 3.30 (t, 2H, *J* = 7.1, C*H*$_2$N), 3.17 (d, 1H, *J* = 18.2, C*H*$_2$C(O)N), 2.82 (d, 1H, *J* = 18.2, C*H*$_2$C(O)N), 1.30 (m, 2H, C*H*$_2$CH$_2$N), 1.03 (m, 2H CH$_3$C*H*$_2$CH$_2$), 0.81 (t, 3H, *J* = 7.3); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_C$ 173.7 (*C*=O), 173.2 (*C*=O), 168.4 (*C*=O), 160.0, 134.8, 130.3, 120.4, 115.3, 114.2 (Ar-*C*), 75.8 (*C*H$_2$NO$_2$), 57.6 (quaternary *C*), 55.2 (ArO*C*H$_3$), 54.0 (O*C*H$_3$), 45.7 (*C*H$_2$N), 39.3 (NO$_2$CH$_2$*C*H), 35.2 (*C*H$_2$C(O)N), 29.1 (*C*H$_2$CH$_2$N), 19.6 (CH$_3$*C*H$_2$), 13.5 (*C*H$_3$CH$_2$); *m*/*z* (CI+) 410 (40%, MNH$_4^+$); [HR-MS (ES+): MNH$_4^+$, 410.1923. [C$_{19}$H$_{24}$N$_2$O$_7$]$^+$ requires 410.1922]; $[\alpha]_D^{24} = -35$ (*c* 0.7, CHCl$_3$).

### 4.22. (*S*)-Methyl 1-butyl-3-((*S*)-1-(furan-2-yl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-carboxylate 5f and (*R*)-methyl 1-butyl-3-((*S*)-1-(furan-2-yl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-car boxylate 6f

Following general method C, the title compounds **5f** (63 mg, 54% yield) **6f** (42 mg, 36% yield) were obtained after 48 h as colourless oils in 94% ee **5f** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, *t* (major) = 16.8 min, *t* (minor) = 10.5 min] and 91% ee **6f** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, *t* (major) = 16.5 min, *t* (minor) = 13.9 min] as determined by HPLC analysis.

*Data for* **5f**: IR $\nu_{max}$(film)/cm$^{-1}$ 2959 (CH); 1745 (C=O), 1707 (C=O); 1557 (C=O); *m*/*z* (ES+) 370 (30%, MNH$_4^+$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$ ppm 7.31 (m, 1H, Ar-*H*) 6.33 (m, 2H, Ar-*H*), 5.14 (dd, 1H, *J* = 13.8, 10.6, C*H*$_A$H$_B$-NO$_2$), 5.03 (dd, 1H, *J* = 13.8, 3.3, CH$_A$*H*$_B$–NO$_2$), 4.50 (dd, 1H, *J* = 10.6, 3.2, Het-*C*H), 3.84 (s, 3H, C*H*$_3$O), 3.51 (t, 2H, *J* = 7.4, C*H*$_2$N), 2.93 (d, 1H, *J* = 18.3, C*H*$_2$C(O)N), 2.75 (d, 1H, *J* = 18.4, C*H*$_2$C(O)N), 1.53 (m, 2H, C*H*$_2$CH$_2$N), 1.31 (m, 2H, CH$_3$C*H*$_2$CH$_2$), 0.95 (t, 3H, *J* = 7.3, C*H*$_3$CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_C$ 173.9 (*C*=O), 173.5 (*C*=O), 169.2 (*C*=O), 147.7, 143.6, 111.3, 110.9 (Het-*C*), 75.1 (*C*H$_2$NO$_2$), 55.5 (quaternary *C*), 54.0 (O*C*H$_3$), 40.6 (NO$_2$CH$_2$*C*H), 39.4 (*C*H$_2$C(O)N), 38.3 (*C*H$_2$N), 29.2 (*C*H$_2$CH$_2$N), 19.9 (CH$_3$*C*H$_2$), 13.6 (*C*H$_3$CH$_2$); MS *m*/*z* (ES+) 375 (100%, MNa$^+$); [HR-MS (ES+): 370.1609, C$_{16}$H$_{24}$N$_3$O$_7$ requires 370.1609]; $[\alpha]_D^{25} = +27.6$ (*c* 3.7, CHCl$_3$).

*Data for* **6f**: IR $\nu_{max}$(film)/cm$^{-1}$ 2959 (CH), 1745 (C=O), 1709 (C=O), 1559 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$ 7.32 (s, 1H, Ar-*H*), 6.29 (d, 2H, *J* = 1.3, Ar-*H*), 4.93 (dd, 1H, *J* = 13.2, 4.3, C*H*$_A$H$_B$–NO$_2$), 4.86 (dd, 1H, *J* = 13.1, 9.9, CH$_A$*H*$_B$-NO$_2$), 4.71 (dd, 1H, *J* = 9.9, 4.3, Het-*C*H), 3.83 (s, 3H, C*H*$_3$O), 3.36 (dt, 2H, *J* = 7.5, 1.6, C*H*$_2$N), 3.19 (d, 1H, *J* = 18.1, C*H*$_2$C(O)N), 3.01 (d, 1H, *J* = 18.1, C*H*$_2$C(O)N), 1.29 (m, 2H, C*H*$_2$CH$_2$N), 1.13 (m, 2H, CH$_3$C*H*$_2$CH$_2$), 0.84 (t, 3H, *J* = 7.3, C*H*$_3$CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_C$ 173.7 (*C*=O), 172.7 (*C*=O), 167.8 (*C*=O), 147.2, 143.3, 110.9, 110.6 (Het-*C*), 74.1 (*C*H$_2$NO$_2$), 57.0 (Het-*C*), 53.8 (O*C*H$_3$), 39.5 (NO$_2$CH$_2$*C*H), 39.1 (*C*H$_2$C(O)N), 35.0 (*C*H$_2$N), 29.0 (*C*H$_2$CH$_2$N), 19.5 (CH$_3$*C*H$_2$), 13.2 (*C*H$_3$CH$_2$); *m*/*z* (ES+) 370 (40%, MNH$_4^+$); [HR-MS (ES+): MNH$_4^+$, 370.1602. [C$_{16}$H$_{24}$N$_3$O$_7$]$^+$ requires 370.1609]; $[\alpha]_D^{24} = -42$ (*c* 1, CHCl$_3$).

### 4.23. (*S*)-Methyl 1-butyl-3-((*S*)-1-(naphthalen-2-yl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-carboxylate 5g and (*R*)-methyl 1-butyl-3-((*S*)-1-(naphthalen-2-yl)-2-nitroethyl)-2,5-dioxopyrrolidine-3-carboxylate 6g

Following general method C, the title compounds **5g** (87 mg, 64% yield) and **6g** (43 mg, 32% yield) were obtained after 48 h as colourless solids in 95% ee **5g** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, *t* (major) = 16.3 min, *t* (minor) = 24 min] and 90% ee **6g** [Chiralpak IB, Hexanes/IPA 85:15, 1.0 mL/min, $\lambda$ 215 nm, *t* (major) = 25.1 min, *t* (minor) = 52 min] as determined by HPLC analysis.

*Data for* **5g**: Mp 94–97 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2959 (CH), 1745 (C=O), 1703 (C=O), 1556 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$ 7.78 (m, 3H, Ar-*H*), 7.66 (d, 1H, *J* = 1.6, Ar-*H*), 7.50 (m, 2H, Ar-*H*), 7.25 (dd, 1H, *J* = 8.5, 1.9, Ar-*H*), 5.43 (dd, 1H, *J* = 13.9, 10.9, C*H*$_A$H$_B$–NO$_2$), 5.21 (dd, 1H, *J* = 13.9, 3.4, CH$_A$*H*$_B$-NO$_2$), 4.45 (dd, 1H, *J* = 10.9, 3.3, Ar-*C*H), 3.83 (m, 3H, C*H*$_3$O), 3.45 (dt, 2H, *J* = 8.0, 6.9, 2.8, C*H*$_2$N), 2.86 (d, 1H, *J* = 18.3, C*H*$_2$C(O)N), 2.72 (d, 1H, *J* = 18.3, C*H*$_2$C(O)N), 1.52 (m, 2H, C*H*$_2$CH$_2$N), 1.39 (m, 2H, C*H*$_2$CH$_2$N), 1.20 (m, 2H, CH$_3$C*H*$_2$CH$_2$), 0.88 (t, 3H, *J* = 7.4, C*H*$_3$CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_C$ 174.6 (*C*=O), 173.2 (*C*=O), 169.6 (*C*=O), 133.1, 133.0, 130.8, 129.4, 128.7, 127.7, 127.6, 126.8, 126.8, 125.5 (Ar-*C*), 76.7 (*C*H$_2$NO$_2$), 56.2 (quaternary *C*), 53.8 (O*C*H$_3$), 46.5 (*C*H$_2$N), 39.2 (NO$_2$CH$_2$*C*H), 38.0 (*C*H$_2$C(O)N), 29.1 (*C*H$_2$CH$_2$N), 19.7 (CH$_3$*C*H$_2$), 13.4 (*C*H$_3$CH$_2$); *m*/*z* (CI+) 430 (20%, MNH$_4^+$); [HR-MS (ES+): MNH$_4^+$, 430.1966. [C$_{22}$H$_{28}$N$_3$O$_6$]$^+$ requires 430.1967]; $[\alpha]_D^{23} = +2.0$ (*c* 0.4, CHCl$_3$).

*Data for* **6g**: Mp 121–124 °C; IR $\nu_{max}$(film)/cm$^{-1}$ 2958 (CH), 1743 (C=O), 1705 (C=O), 1557 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta_H$ 7.81 (m, 3H, Ar-*H*), 7.71 (d, 1H, *J* = 1.6, Ar-*H*), 7.50 (m, 2H, Ar-*H*), 7.34 (dd, 1H, *J* = 8.6, 1.9, Ar-*H*), 5.22 (dd, 1H, *J* = 13.4, 4.3, C*H*$_A$H$_B$–NO$_2$), 5.08 (dd, 1H, *J* = 13.4, 10.5, CH$_A$*H*$_B$–NO$_2$), 4.67 (dd, 1H, *J* = 10.5, 4.3, Ar-*C*H), 3.87 (s, 3H, C*H*$_3$O), 3.23 (m, 3H, C*H*$_2$C(O)N, C*H*$_2$N), 2.93 (d, 1H, *J* = 18.2, C*H*$_2$C(O)N), 0.94 (m, 2H, C*H*$_2$CH$_2$N), 0.80 (m, 2H, CH$_3$C*H*$_2$CH$_2$), 0.54 (t, 3H, *J* = 7.2, C*H*$_3$CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_C$ 173.5 (*C*=O), 173.0 (*C*=O), 168.3 (*C*=O), 133.0, 132.9, 130.5, 129.1, 128.7, 127.9, 127.4, 126.8, 126.7, 125.4 (Ar-*C*), 75.7 (*C*H$_2$NO$_2$), 57.5 (quaternary *C*), 53.9 (O*C*H$_3$), 45.7 (*C*H$_2$N), 39.1 (NO$_2$CH$_2$*C*H), 35.1 (*C*H$_2$C(O)N), 28.8 (*C*H$_2$CH$_2$N), 19.3 (CH$_3$*C*H$_2$), 13.1 (*C*H$_3$CH$_2$); *m*/*z* (ES+) 430 (30%, MNH$_4^+$); [HR-MS (ES+): MNH$_4^+$, 430.1977. [C$_{22}$H$_{28}$N$_3$O$_6$]$^+$ requires 430.1967]; $[\alpha]_D$ = +30.0 (*c* 0.2, CHCl$_3$).

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