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General and stereoselective aminoxylation of biradical titanium(IV) enolates with TEMPO: a detailed study on the effect of the chiral auxiliary

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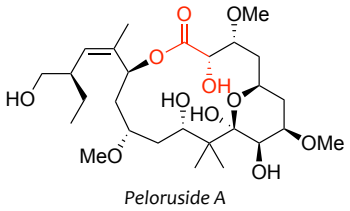
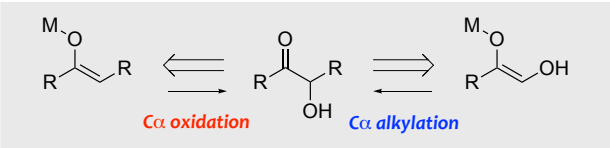
A comprehensive analysis of the influence of the chiral auxiliary on the α-aminoxylation of titanium(IV) enolates with TEMPO indicated that (*S*) 4-*tert*-butyl-1-oxazolidine-2-thione is the most appropriate scaffold to provide a single diastereomer in high yields for a variety of substrates, which converts such a radical reaction into a highly chemo- and stereoselective oxidation.

Introduction

The widespread presence of α-hydroxy carbonylic and carboxylic structures in biologically active natural products has fostered the development of increasingly efficient transformations involving either the asymmetric construction of carbon–carbon or carbon–oxygen bonds from metal enolates to access these structures (Scheme 1).[1]



Peloruside A



Scheme 1 Reactivity of the Cα position of enolates

Particularly, the stereoselective Cα-oxidation of carbonyl bonds has received lasting attention, resulting in a number of procedures based on the treatment of metal enolates with a variety of oxidizing agents like *N*-sulfonyloxaziridines, peroxides, or transition metals.[2,3] Aside from these methods, the emergence of organocatalytic procedures represented a major step forward in the asymmetric synthesis of α-hydroxy carbonylic compounds. Thereby, initial reports on the enantioselective preparation of aminoxylated adducts through addition of aldehydes and activated ketones to nitrosobenzene catalyzed by chiral amines[4] were soon enlarged by the SOMO activation mode concept.[5] This broadly referred to the oxidation of chiral enamines, which provided a cation radical that underwent highly enantioselective reactions. Thus, it presently stands as a milestone in asymmetric transformations involving radical or electronically excited species.[5,6]

Mirroring such achievements, the recognition of the biradical character of titanium(IV) enolates[7] laid the foundations for their use in SOMO-like transformations without the need for a stoichiometric oxidizing reagent. Zakarian proved the feasibility of such a new approach by developing a new photoredox alkylation of titanium(IV) enolates from chiral *N*-acyl oxazolidinones catalyzed by a ruthenium complex.[8] In this context, the commercially available and persistent radical TEMPO was an appealing reagent to trap chiral titanium(IV) biradical enolates and stereoselectively afford the aminoxylated derivatives. TEMPO had been used as precursor of electrophilic reagents for the stereoselective construction of carbon-oxygen bonds.[9] In contrast, its use in radical like reactions was scarce and restricted to non-stereoselective transformations[10] until Zakarian[11] and our group[12] independently developed the asymmetric oxidation of titanium(IV) enolates of a wide range of chiral *N*-acyl oxazolidinones with TEMPO, which provides the corresponding aminoxylated adducts with good yields and diastereoselectivities (Scheme 2).

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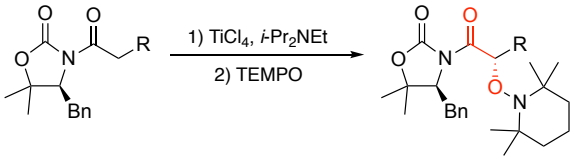
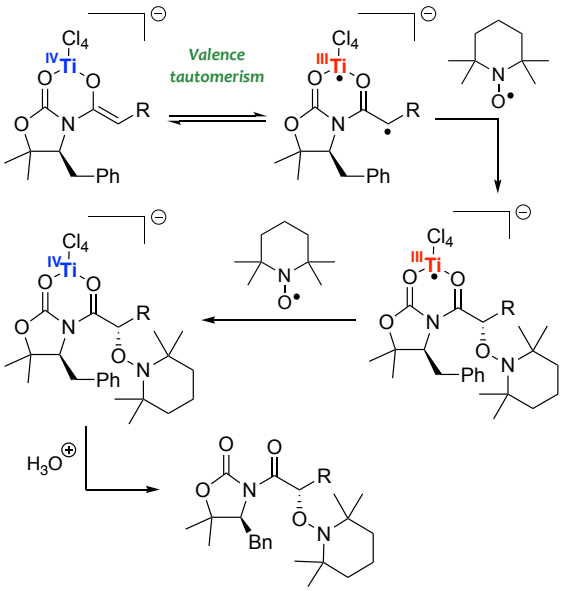
Electronic Supplementary Information (ESI) available: copies of ^{1}H and ^{13}C NMR spectra of compounds described in the Experimental section. See DOI: 10.1039/x0xx00000x



Scheme 2 Stereoselective aminoxylation of titanium(IV) enolates with TEMPO

We have also reported theoretical insights of this TEMPO-mediated oxidation reinforcing the proof of the valence tautomerism and the resulting biradical character of titanium(IV) enolates from *N*-acyl oxazolidinones as well as offering a concise explanation of the entire mechanism.[13] Essentially, the process hinges on the radical attack of a first molecule of TEMPO to the Cα position of the biradical form of the titanium(IV) enolate (Scheme 3). This is then followed by a fast oxidation of the resultant titanium(III) complex by a second molecule of TEMPO. Thereby, the high stereocontrol achieved by such transformations may be explained through a chelated titanium(IV) enolate in which the C4-benzyl group favours the approach of the oxidizing agent to the less sterically hindered π-face of the biradical enolate.



Scheme 3. Mechanism for the stereoselective aminoxylation of titanium(IV) enolates from chiral *N*-acyl oxazolidinones with TEMPO

Thus, considering the key role played by chiral scaffolds in stereoselective reactions,[14,15] we decided to assess its influence on such oxidations with the aim of identifying other chiral auxiliaries which may able to produce a single diastereomer and be easily removed from the resultant aminoxylated adduct leaving enantiopure synthons. Particularly, we focused our attention on chiral oxazolidinones developed by Evans[16,17] and related five membered heterocycles with a long tradition within stereoselective synthesis (Figure 1).[18–21]

Herein, we describe a detailed study of the aminoxylation of titanium(IV) enolates derived from a wide array of chiral auxiliaries possessing different oxygen and sulphur patterns and several side chains as well as a further analysis of the scope of the reaction and the final removal of the chiral scaffold.

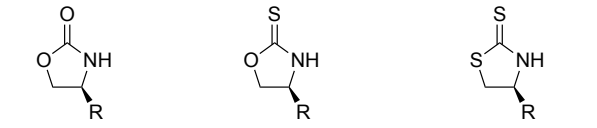


Fig. 1 Five membered cyclic chiral auxiliaries

Results and Discussion

Chiral auxiliary screening.

Taking advantage of our own studies on the aminoxylation of titanium(IV) enolates from *N*-acyl oxazolidinones with TEMPO,[12,13] we initially investigated the influence of chiral auxiliaries **1–6** with various combinations of oxygen and sulphur heteroatoms *exo* and *endo* to the heterocycle and bulky groups at C4 (Figure 2).[22–24] By choosing such a wide range of chiral substrates we envisaged to fully understand the effect both the heteroatoms and the groups at C4 and therefore to find the most effective scaffold for this type of reaction.

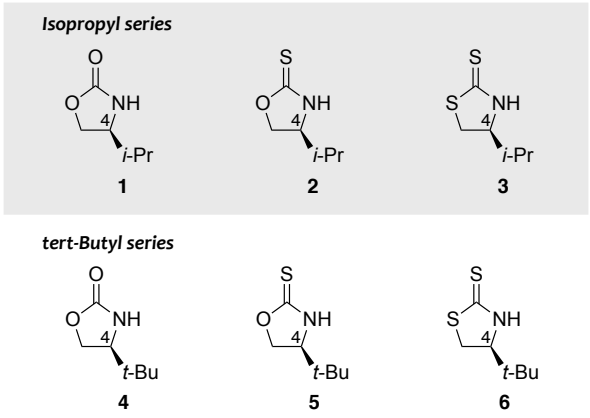


Fig. 2 C4 Substituted five membered cyclic chiral auxiliaries

To best analyse the isolated effects of such parameters we conducted the aminoxylation of *N*-propanoyl derivatives **1a–6a** (Scheme 4), easily prepared from chiral auxiliaries **1–6**, under the same conditions, more specifically the optimised conditions reported in our previous report.[12] The results of this preliminary examination summarised in Scheme 3 showed a clear trend. Indeed, substitution of the exocyclic oxygen by sulphur both in the isopropyl and the *tert*-butyl series produced a significant

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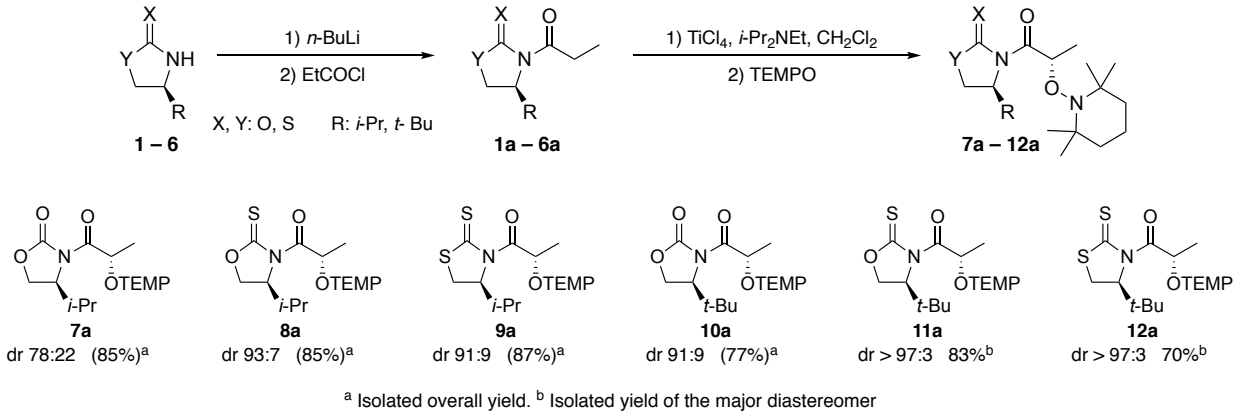

Scheme 4 Stereoselective aminoxylation of titanium(IV) enolates from *N*-propanoyl C4-substituted chiral auxiliaries **1a–6a** with TEMPO

improvement of the diastereoselectivity. Moreover, the bulky *tert*-butyl group turned out to be crucial to obtain a single diastereomer; in all cases moving from isopropyl to *tert*-butyl as the C4 group induced a significant increase in the diastereomeric ratio. Particularly, *tert*-butyl *N*-propanoyl oxazolidinethione **5a** (X: S, Y: O, R: *t*-Bu) and thiazolidinethione **6a** (X, Y: S, R: *t*-Bu) were the most appropriate platforms to carry out a completely stereocontrolled oxidation in high yields.

Having identified the crucial role of the exocyclic heteroatom and the C4 alkyl group, we next evaluated the consequences of placing geminal groups at the C5 position. As we had already described the aminoxylation using chiral auxiliary **14**,[12] in which the oxazolidinone possesses a geminal dimethyl moiety at C5, we next evaluated the outcome of parallel reactions from oxazolidinones and oxazolidinethiones **13–16** shown in Figure 3.[25]

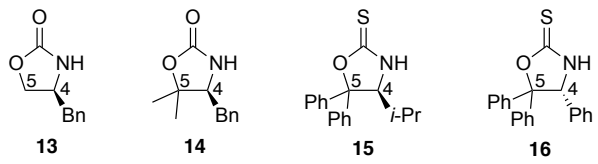

Fig. 3 C4 and C5 Substituted chiral auxiliaries

Thus, *N*-propanoyl derivatives **13a–16a**, easily prepared from chiral auxiliaries **13–16**, were submitted to the previous experimental conditions. The results summarised in Scheme 5 proved the benefit of installing two groups at C5. Indeed, the results from *N*-propanoyl C4 benzyl oxazolidinones **13a** (X: O, R: H) and **14a** (X: O, R: Me) clearly showed that the diastereoselectivity is greatly increased by attaching two geminal methyl groups at C5. Furthermore, the placement of two phenyl groups at this position was also advantageous for the isopropyl oxazolidinethione **15a** (X: S, R: Ph, R^1: *i*-Pr) since just a single diastereomer **19a** was obtained albeit in a moderate yield (compare **8a** and **19a** in Scheme 4 and 5 respectively). Finally, *N*-propanoyl 5,5-disubstituted oxazolidinethione **16a** (X: S, R, R^1: Ph) demonstrates that a C4 substituent larger than Ph group is required to obtain a single diastereomer (compare **19a** and **20a** in Scheme 5).

All together, these results indicate that only three of the ten different chiral auxiliaries evaluated (oxazolidinethiones **5** and **15**, and thiazolidinethione **6**) give complete control of the newly created stereocentre (see **11a** and **12a** in Scheme 4 and **19a** in Scheme 5). Among all the scaffolds, the *tert*-butyl oxazolidinethione **5** emerges as the most appropriate choice. Certainly, it provides marginally lower yields than the *SuperQuat* auxiliary **14**, but it offers the advantage of giving complete stereocontrol and it is also significantly easier to synthesise starting from readily available *tert*-leucine.[§]

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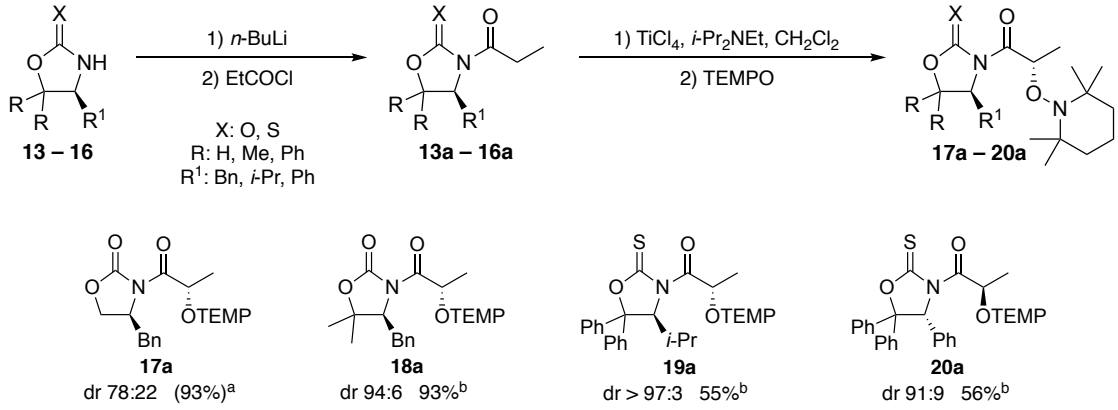

[a] Isolated overall yield. [b] Isolated yield of the major diastereomer

Scheme 5 Stereoselective aminoxylation of titanium(IV) enolates from *N*-propanoyl C4 and C5-substituted chiral auxiliaries **13a–16a** with TEMPO

Scope of the Aminoxylation Reaction

Since the screening process led us to a new chiral auxiliary, we next reexamined the scope of the radical aminoxylation with TEMPO using this new scaffold. To do this, we varied the acyl group attached to the chiral heterocycle intending to test the impact of sterically hindered R groups as well as others containing various common functional groups. The results summarised in Scheme 6 demonstrated that the simple treatment of titanium(IV) enolates from a wide array of *N*-acyl *tert*-butyl oxazolidinethiones (**5a–g**) with TEMPO afforded a single diastereomer **11** for all the substrates with the exception of α-phenyl derivative **11e**, which was obtained as an equimolecular mixture of two diastereomers in 90% overall yield. Presumably, the higher acidity of the Cα position in *N*-(2-phenylacetyl) oxazolidinethione **5e** precludes its use,[26] in contrast to the high stereocontrol achieved with a parallel reaction from oxazolidinone *SuperQuat* **14**. Importantly, the steric bulk of R nor the presence of a terminal double bond or an ester had a significant influence on the yield. All together, these results highlight the excellent chemo- and diastereoselectivity of the radical-mediated direct oxidation with TEMPO, which permits the obtainment of a single stereoisomer in high yields using straightforward and mild experimental conditions.

In turn, we took advantage of crystalline properties of adduct **11b** to confirm the configuration of the α stereocentre by X-ray analysis (Figure 4).‡

Removal of the chiral auxiliary

We finally proceeded to investigate the removal of the chiral auxiliary from adducts **11a** and **11b** (Scheme 7) using both the most simple propyl chain and also a more complex example. Initially, we employed $NaBH_4$ to obtain the corresponding alcohols **21a** and **21b**. In the case of **11a** the reaction took two hours at 0 °C and yielded 85% of the enantiopure alcohol **21a**. Moving to the more hindered adduct **11b** the reaction required a longer time and at room temperature but also gave an excellent 92% yield of the desired alcohol **21b**. Carboxylic acids **22a** and **22b** were next obtained through common treatment with lithium hydroperoxide in good yields. Methanol was then used to displace the auxiliary and leave an ester. Adducts **11a** and **11b** performed in a similar manner. Both gave excellent yields of methyl esters **23a** and **23b** respectively with **11b** taking longer to complete the reaction. Changing methanol for

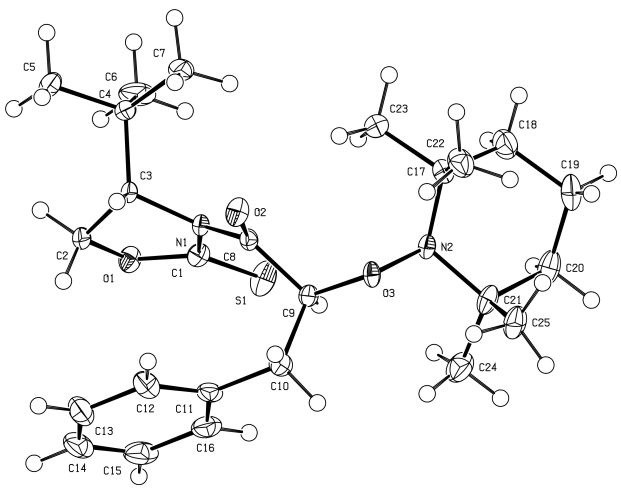

Fig. 4 ORTEP X-ray structure of adduct **11b** (ellipsoid contour probability: 50%).

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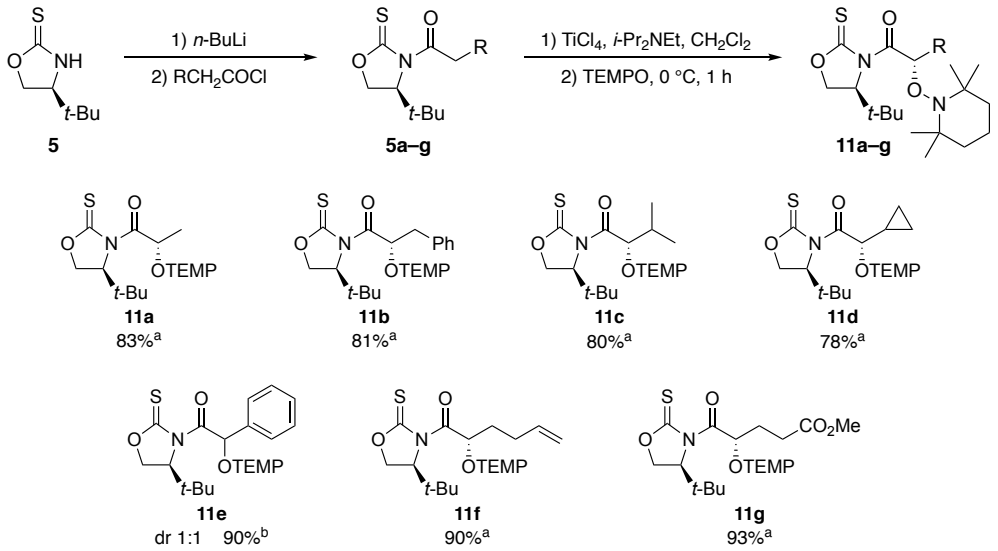
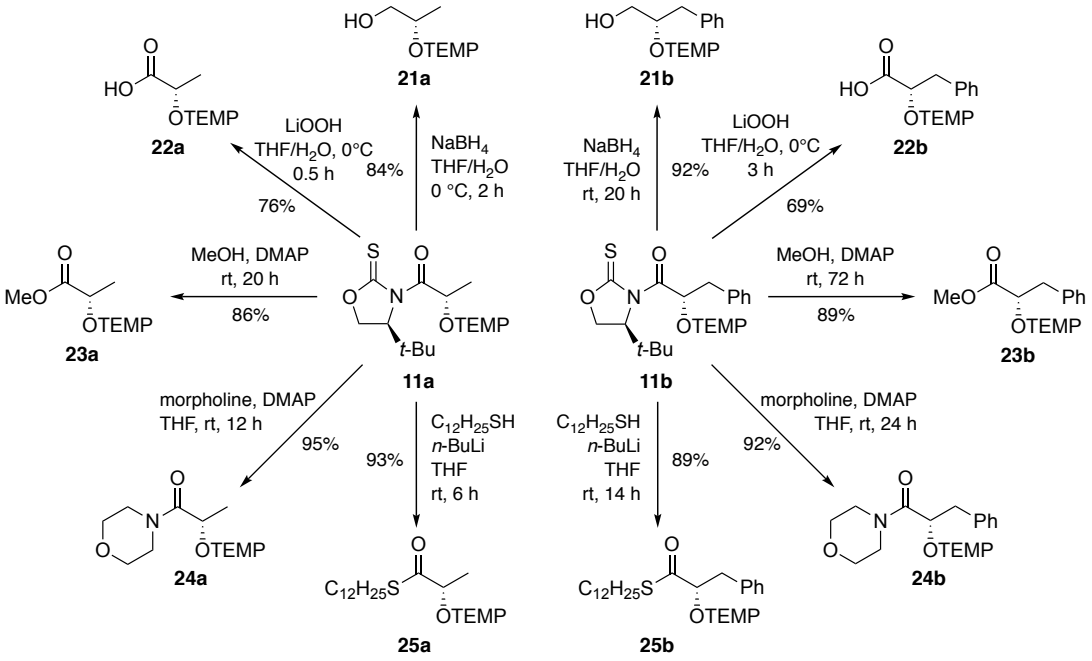


[a] Isolated yield of diastereomerically pure adduct **11**. [b] Overall isolated yield.

Scheme 6 Stereoselective aminoxylation of titanium(IV) enolates from (*S*) *N*-acyl-4-*tert*-butyl-1,3-oxazolidine-2-thiones **5** with TEMPO



Scheme 7 Removal of the chiral auxiliary from α-aminoxylated adducts

morpholine allowed us to form amides **24a** and **24b**, again in excellent yields. Finally, displacement of the chiral auxiliary with a thiol to form thioesters **25a** and **25b** also proceeded smoothly and both derivatives were isolated in excellent yields. Remarkably, the recovery of the auxiliary was excellent in all cases, with the minimum amount being 78% and an average recovery of 89% over the ten different reactions.

Conclusions

In summary, we have comprehensively investigated the role of the chiral auxiliary on the outcome, both in terms of yield and stereocontrol, of the α-aminoxylation of the titanium(IV) enolates from a number of *N*-acylated imide-like derivatives with TEMPO. The 4-*tert*-butyl-1,3-oxazolidine-2-thione auxiliary has been identified as the most appropriate to carry out this reaction since it combines all the favoured characteristics and gives complete control of the newly formed stereocentre with an excellent yield for a wide range of *N*-acylated 4-*tert*-butyl-1,3-oxazolidine-2-thiones. Compared to previous studies that used *SuperQuat,* this is more selective, with a comparable yield and is also much easier to synthesise from commercially available *tert*-leucinol. Finally, straighforward conversion of α-OTEMP adducts affords enantiopure intermediates in excellent yields and with a high recovery of the chiral auxiliary.

Experimental section

General experimental remarks

Unless otherwise stated, reactions were conducted in oven-dried glassware under an inert atmosphere of nitrogen with anhydrous solvents. The solvents and reagents were dried and purified, when necessary, according to standard procedures. All commercial reagents were used as received. Analytical thin-layer chromatographies (TLC) were carried out on Merck silica gel 60 F254 plates and analyzed by UV (254 nm) and stained with phosphomolybdic acid. R_f values are approximate. Column chromatography were carried out under low pressure (*flash*) conditions and performed on SDS silica gel 60 (35-70 μm). Melting points are uncorrected. Specific rotations ([α]) were determined at 589 nm and at 20 °C. IR spectra (Attenuated Total Reflectance, ATR) were recorded on a Nicolet 6700 FT-IR Thermo Scientific spectrometer and only the more representative frequencies (ν) are reported. ^{1}H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded on a Varian Mercury 400 spectrometer. Chemical shifts (δ) are quoted in ppm and referenced to internal TMS (δ 0.00 for ^{1}H NMR) or $CDCl_3$ (δ 77.0 for ^{13}C NMR); data are reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad (and their corresponding combinations) with coupling constants measured in Hz; when necessary, 2D techniques (COSY and HSQC) were also used to assist with structure elucidation. High resolution mass spectra (HRMS) were obtained with an Agilent 1100 spectrometer by the Unitat d'Espectrometria de Masses, Universitat de Barcelona.

Synthesis of (*S*)-4-*tert*-butyl-1,3-oxazolidine-2-thione (5)

Neat CS_2 (8.4 mL, 135 mmol) was added to a solution of *tert*-leucinol (5.27 g, 45 mmol) in EtOH (10 mL) at room temperature under N_2. Then, a 2.6 M solution of KOH (26 mL, 67.5 mmol) in 1:1 EtOH/H_2O was added and the resulting mixture was heated at reflux for two days. The volatiles were removed and the residue was carefully acidified with 2 M HCl until pH 2. The mixture was extracted with CH_2Cl_2 (3 × 100 mL) and the organic layers were dried ($MgSO_4$), and concentrated. The resulting solid was purified by column chromatography (CH_2Cl_2) to give 5.50 g (34.5 mmol, 77% yield) of heterocycle **5** as a white solid. Mp: 155–156 °C [lit.[27] Mp: 155.1–155.3 °C]. R_f = 0.65 (CH_2Cl_2). $[\alpha]_D^{20}$ = –11.0 (*c* 1.0, $CHCl_3$) [lit.[27] $[\alpha]_D^{20}$ = –11.6 (*c* 0.92, $CHCl_3$)]. IR (ATR): 3183, 2997, 2960, 1534, 1183 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (br s, 1H), 4.62 (t, *J* = 9.5 Hz, 1H), 4.46 (dd, *J* = 9.5, 6.3 Hz, 1H), 3.81 (dd, *J* = 9.5, 6.3 Hz, 1H), 0.94 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 189.6, 71.8, 65.8, 33.6, 20.0. HRMS (+ESI): *m/z* calcd. for $C_7H_{14}NOS$ $[M+H]^+$: 160.0791; found: 160.0793.

Acylation of 5: Synthesis of (*S*)-4-*tert*-butyl-*N*-propanoyl-1,3-oxazolidine-2-thione (5a)

A 1.6 M solution of *n*-BuLi in hexanes (2.1 mL, 3.3 mmol) was added dropwise to a solution of **5** (478 mg, 3.0 mmol) in THF (4 mL) at –78 °C under N_2. The reaction mixture was stirred for 10 min and then propanoyl chloride (0.34 mL, 3.9 mmol) was carefully added dropwise. The resulting solution was stirred for 5 min at –78 °C and then allowed to warm to room temperature and stirred for further 1.5 h. The reaction mixture was cooled with an ice-water bath and quenched with sat NH_4Cl (2 mL) and water (5 mL). This mixture was extracted with CH_2Cl_2 (3 × 20 mL), the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. The crude reaction mixture was purified by column chromatography (50:50 CH_2Cl_2/Hexanes) to afford 595 mg (2.8 mmol, 92% yield) of *N*-propanoyl oxazolidinethione **5a** as a colourless oil. R_f =0.4 (50:50 CH_2Cl_2/Hexanes). $[\alpha]_D^{20}$ = +152.2 (*c* 1.1, $CHCl_3$). IR (ATR): 2967, 1708, 1479, 1402, 1362, 1267, 1179, 1048 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.78 (dd, *J* = 7.5, 1.7 Hz, 1H), 4.45 (dd, *J* = 9.5, 1.7 Hz, 1H), 4.34 (dd, *J* = 9.5, 7.5 Hz, 1H), 3.38 (dq, *J* = 18.1, 7.2 Hz, 1H), 3.29 (dq, *J* = 18.1, 7.2 Hz, 1H), 1.21 (t, *J*= 7.2 Hz, 3H), 0.94 (s, 9H). ^{13}C NMR (100.6b MHz, $CDCl_3$): δ 187.0, 174.9, 69.2, 65.1, 36.1, 31.1, 25.8, 8.9. HRMS (+ESI): *m/z* calcd. for $C_{10}H_{18}NO_2S$ $[M+H]^+$: 216.1053; found: 216.1058.

General aminoxylation procedure

Neat $TiCl_4$ (121 μL, 1.1 mmol, 1.1 equiv) was added dropwise to a solution of the acylated chiral auxiliary (1 mmol, 1 equiv) in CH_2Cl_2 (4 mL) at 0 °C under N_2 and the resultant mixture was stirred for 5 min. Then, *i*-Pr_2NEt (192 μL, 1.1 mmol, 1.1 equiv) was added and the mixture was further stirred for 30 min. A solution of TEMPO (328 mg, 2.1 mmol, 2.1 equiv) in CH_2Cl_2 (0.5 mL + 0.5 mL) was added via cannula and the reaction mixture was stirred for 1 h, quenched with sat NH_4Cl (2 mL), and stirred vigorously for 10 min. It was then diluted in water (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was washed with brine (50 mL), dried ($MgSO_4$), and concentrated to yield the crude product. Column chromatography was then conducted to yield the isolated product.

(*S*)-4-*tert*-Butyl-*N*-[(*S*)-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)propanoyl]-1,3-oxazolidine-2-thione (11a). Starting from (*S*) 4-*tert*-butyl-*N*-propanoyl-1,3-oxazolidine-2-thione (**5a**, 215 mg, 1.0

mmol) diastereomerically pure adduct **11a** (308 mg, 0.83 mmol, 83% yield) was isolated as a white solid after chromatographic purification (60:40 CH_2Cl_2/Hexanes). Mp: 130–131 °C. R_f = 0.3 (60:40 CH_2Cl_2/Hexanes). $[\alpha]_D^{20}$ = +84.0 (*c* 1.0, $CHCl_3$). IR (ATR): 2970, 2926, 1717, 1178, 1357, 1138, 943, 800, 601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.57 (q, *J* = 6.8 Hz, 1H), 4.66 (dd, *J* = 7.4, 1.4 Hz, 1H), 4.45 (dd, *J* = 9.5, 1.4 Hz, 1H), 4.28 (dd, *J* = 9.5, 7.4 Hz, 1H), 1.50–1.15 (m, 18H), 1.41 (d, *J* = 6.8 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 186.9, 175.3, 79.4, 69.2, 66.0, 59.6, 40.2, 36.1, 34.0, 26.0, 20.2, 19.3, 17.1. HRMS (ESI): *m/z* calcd. for $C_{19}H_{35}N_2O_3S$ $[M+H]^+$: 371.2363; found: 371.2359.

(*S*)-4-*tert*-Butyl-*N*-[(*S*)-3-phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)propanoyl]-1,3-oxazolidine-2-thione (11b). Starting from (*S*) 4-*tert*-butyl-*N*-(3-phenylpropanoyl)-1,3-oxazolidine-2-thione (**5b**, 291 mg, 1.0 mmol) diastereomerically pure adduct **11b** (361 mg, 0.81 mmol, 81% yield) was isolated as a white solid after chromatographic purification (CH_2Cl_2). Mp: 138–139 °C. R_f = 0.8 (CH_2Cl_2). $[\alpha]_D^{20}$ = +87.0 (*c* 1.0, $CHCl_3$). IR (ATR): 2962, 2922, 2862, 1713, 1479, 1368, 1349, 1308, 1182, 1149 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.29–7.15 (m, 5H), 7.00 (dd, *J* = 10.7, 6.0 Hz, 1H), 3.97–3.91 (m, 2H), 3.47 (dd, *J* = 12.6, 6.0 Hz, 1H), 2.92–2.85 (m, 2H), 1.57–1.13 (m, 18H), 0.85 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 187.3, 175.1, 135.3, 129.6, 128.4, 126.9, 80.8, 68.7, 66.7, 59.9, 40.4, 40.2, 35.9, 34.1, 33.5, 26.1, 20.2, 20.1, 17.2. HRMS (ESI): *m/z* calcd. for $C_{24}H_{39}N_2O_3S$ $[M+H]^+$: 447.2676; found: 447.2682.

(*S*)-4-*tert*-Butyl-*N*-[(*S*)-3-methyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)butanoyl]-1,3-oxazolidine-2-thione (11c). Starting from (*S*) 4-*tert*-butyl-*N*-(3-methylbutanoyl)-1,3-oxazolidine-2-thione (**5c**, 243 mg, 1.0 mmol) diastereomerically pure adduct **11c** (320 mg, 0.80 mmol, 80% yield) was isolated as a white solid after chromatographic purification (CH_2Cl_2). Mp: 111–112 °C. R_f = 0.7 (CH_2Cl_2). $[\alpha]_D^{20}$ = +97.0 (*c* 1.0, $CHCl_3$). IR (ATR): 2962, 2929, 1698, 1468, 1349, 1301, 1171, 1145 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.75 (d, *J* = 5.4 Hz, 1H), 4.62 (dd, *J* = 7.3, 1.3 Hz, 1H), 4.44 (dd, *J* = 9.5, 1.3 Hz, 1H), 4.21 (dd, *J* = 9.5, 7.3 Hz, 1H), 2.49–2.36 (m, 1H), 1.63–1.09 (m, 18H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.99 (s, 9H), 0.90 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 187.6, 173.0, 82.3, 69.2, 66.7, 59.8, 40.4, 36.2, 34.2, 31.7, 26.2, 25.8, 22.4, 22.3, 20.3, 17.9, 17.1, 16.8. HRMS (ESI): *m/z* calcd. for $C_{21}H_{39}N_2O_3S$ $[M+H]^+$: 399.2676; found: 399.2679.

(*S*)-4-*tert*-Butyl-*N*-[(*S*)-2-cyclopropyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)acetyl]-1,3-oxazolidine-2-thione (11d). Starting from (*S*) 4-*tert*-butyl-*N*-(2-cyclopropylacetyl)-1,3-oxazolidine-2-thione (**5d**, 241 mg, 1.0 mmol) diastereomerically pure adduct **11d** (308 mg, 0.78 mmol, 78% yield) was isolated as a white solid after chromatographic purification (95:5 CH_2Cl_2/EtOAc). Mp: 107–108 °C. R_f = 0.4 (CH_2Cl_2). $[\alpha]_D^{20}$ = +112.1 (*c* 1.0, $CHCl_3$). IR (ATR): 2958, 2925, 1716, 1483, 1353, 1316, 1182, 1138, 949 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.64 (d, *J* = 8.4 Hz, 1H), 4.64 (dd, *J* = 7.4, 1.4 Hz, 1H), 4.46 (dd, *J* = 9.5, 1.4 Hz, 1H), 4.26 (dd, *J* = 9.5, 7.4 Hz, 1H), 1.47–1.15 (m, 19H), 0.97 (s, 9H), 0.71–0.56 (m, 2H), 0.54–0.45 (m, 1H), 0.29–0.21 (m, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 187.0, 172.7, 83.1, 69.1 (×2), 66.1, 64.9, 59.7, 42.3, 40.1, 36.0 (×2), 25.9, 25.7, 17.1, 14.6, 6.8, 4.3, 4.2, 1.4. HRMS (ESI): *m/z* calcd. for $C_{21}H_{37}N_2O_3S$ $[M+H]^+$: 397.2519; found: 397.2524.

(*S*)-4-*tert*-Butyl-*N*-[(*S*)-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)-5-hexenoyl]-1,3-oxazolidine-2-thione (11f). Starting from (*S*) 4-*tert*-butyl-*N*-(5-hexenoyl)-1,3-oxazolidine-2-thione (**5f**, 255 mg, 1.0 mmol) diastereomerically pure adduct **11f** (368 mg, 0.90 mmol, 90% yield) was isolated as a white solid after chromatographic purification. Mp: 94–95 °C. R_f = 0.8 (CH_2Cl_2). $[\alpha]_D^{20}$ = +96.9 (c 1.0, $CHCl_3$). IR (ATR): 2966, 2922, 2862, 1716, 1475, 1360, 1327, 1297, 1179, 1134 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.66 (dd, *J* = 7.0, 3.2 Hz, 1H), 5.83–5.71 (m, 1H), 5.02–4.96 (m, 1H), 4.98–4.91 (m, 1H), 4.63 (dd, *J* = 7.3, 1.3 Hz, 1H), 4.45 (dd, *J* = 9.5, 1.3 Hz, 1H), 4.26 (dd, *J* = 9.5, 7.3 Hz, 1H), 2.23–2.11 (m, 2H), 2.02–1.90 (m, 1H), 1.89–1.78 (m, 1H), 1.47 (br s, 6H), 1.18 (s, 6H), 1.16 (s, 6H), 0.99 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 186.9, 173.7, 137.9, 114.7, 81.2, 69.2, 66.5, 40.3, 36.2, 31.1, 27.4, 26.1, 17.1. HRMS (ESI): *m/z* calcd. for $C_{22}H_{39}N_2O_3S$ $[M+H]^+$: 411.2676; found: 411.2680.

(*S*)-4-*tert*-Butyl-*N*-[(*S*)-5-methoxy-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)-5-oxopentanoyl]-1,3-oxazolidine-2-thione (11g). Starting from (*S*) 4-*tert*-butyl-*N*-(5-methoxy-5-oxopentanoyl)-1,3-oxazolidine-2-thione (**5g**, 287 mg, 1.0 mmol) diastereomerically pure adduct **11g** (413 mg, 0.93 mmol, 93% yield) was isolated as a white solid after chromatographic purification (95:5 CH_2Cl_2/EtOAc). Mp: 104–105 °C. R_f = 0.4 (CH_2Cl_2). $[\alpha]_D^{20}$ = +102.5 (*c* 1.0, $CHCl_3$). IR (ATR): 2929, 1731, 1713, 1360, 1320, 1297, 1167, 1142, 934 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.71 (dd, *J* = 6.1, 2.3 Hz, 1H), 4.54–4.48 (m, 1H), 4.50–4.45 (m, 1H), 4.45–4.40 (m, 1H), 3.61 (s, 3H), 2.61–2.51 (m, 1H), 2.41–2.30 (m, 2H), 2.20–2.10 (m, 1H), 1.47 (s, 6H), 1.17 (s, 6H), 1.15 (s, 6H), 0.96 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 187.3, 173.9, 173.1, 80.1, 69.3, 66.4, 51.4, 40.0, 35.8, 26.4, 25.9, 25.6, 16.9. HRMS (ESI): *m/z* calcd. for $C_{22}H_{39}N_2O_5S$ $[M+H]^+$: 443.2574; found: 443.2576.

Removal of the chiral auxiliary

(*S*)-2-(2,2,6,6-Tetramethylpiperidin-1-yloxy)-1-propanol (21a). A solution of **11a** (74 mg, 0.20 mmol) in THF (1.5 mL) was added to a solution of $NaBH_4$ (31 mg, 0.8 mmol, 4 equiv) in 40:1 THF/H_2O (1.4 mL) at 0 °C under N_2 and the resultant mixture was stirred at room temperature for 2 h. The mixture was then diluted with Et_2O (20 mL), washed with 1 M NaOH (3 × 20 mL), water (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$), and concentrated. The crude was purified by column chromatography (90:10 Hexanes/EtOAc) to give 36 mg (0.17 mmol, 84% yield) of pure alcohol **21a** as a colourless oil. The aqueous phase was acidified and extracted with CH_2Cl_2 (3 × 20 mL) to recover 34 mg (90%) of pure auxiliary **5**. R_f = 0.2 (90:10 Hexanes/EtOAc). $[\alpha]_D^{20}$ = –35.6 (*c* 1.0, $CHCl_3$). IR (ATR): 3376 (br), 2972, 2928, 1453, 1375, 1162, 1131, 1043 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.53 (s br, 1H), 4.38 (dqd, *J* = 9.3, 6.3, 2.2 Hz, 1H), 3.90 (dd, *J* = 11.9, 9.3 Hz, 1H), 3.57 (dd, *J* = 11.9, 2.2 Hz, 1H), 1.60–1.25 (m, 6H), 1.32 (s, 3H), 1.30 (s, 3H), 1.15 (s, 3H), 1.11 (s, 3H), 1.01 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100.6 MHz,

$CDCl_3$): δ 76.8, 69.3, 61.1, 59.9, 40.2, 39.9, 34.5, 32.6, 20.4, 20.3, 17.2, 16.0. HRMS (ESI): *m/z* calcd. $C_{12}H_{26}NO_2$ $[M+H]^+$: 216.1958; found: 216.1964.

(*S*)-3-Phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy-1-propanol (21b). A solution of **11b** (58 mg, 0.13 mmol) in THF (1.5 mL) was added to a solution of $NaBH_4$ (31 mg, 0.8 mmol, 6.15 equiv) in 40:1 THF/H_2O (1.4 mL) at 0 °C under N_2 and the resultant mixture was stirred at room temperature for 20 h. The mixture was then diluted with Et_2O (20 mL), washed with 1 M NaOH (3 × 20 mL), water (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated. The crude was purified by column chromatography (95:5 CH_2Cl_2/EtOAc) to give 35 mg (0.12 mmol, 92% yield) of pure alcohol **21b** as colourless oil. The aqueous layer was acidified and extracted with CH_2Cl_2 (3 × 20 mL) to recover 20 mg (95%) of pure auxiliary **5**. R_f = 0.5 (95:5 CH_2Cl_2/EtOAc). $[\alpha]_D^{20}$ = –62.1 (*c* 1.0, $CHCl_3$). IR (ATR): 3303 (br), 2923, 1451, 1359, 1131, 1027, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.18 (m, 5H), 5.67 (br s, 1H), 4.47 (dddd, *J* = 9.4, 7.2, 5.5, 2.0 Hz, 1H), 3.97 (dd, *J* = 11.9, 9.4 Hz, 1H), 3.65 (dd, *J* = 11.9, 2.0 Hz, 1H), 2.72 (dd, *J* = 13.7, 7.2 Hz, 1H), 2.59 (dd, *J* = 13.7, 5.5 Hz, 1H), 1.58–1.42 (m, 6H), 1.47 (s, 3H), 1.30 (s, 3H), 1.12 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 138.3, 129.4, 128.1, 126.1, 81.2, 67.8, 61.5, 60.0, 40.3, 39.9, 37.6, 34.5, 32.4, 29.7, 20.6, 20.2, 17.1. HRMS (ESI): *m/z* calcd. for $C_{18}H_{30}NO_2$ $[M+H]^+$: 292.2271; found: 292.2278.

(*S*)-2-[(2,2,6,6-Tetramethylpiperidin-1-yl)oxy]propanoic acid (22a). A mixture of **11a** (74 mg, 0.20 mmol), 30% H_2O_2 (90 μL, 0.8 mmol, 4 equiv), and LiOH (10 mg, 0.42 mmol, 2 equiv) in 3:1 THF/H_2O (4 mL) was stirred at 0 °C for 30 min. A sat solution of $Na_2S_2O_3$ (2 mL) was added and the volatiles were removed in vacuo. The solution was acidified with 2 M HCl and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude was purified by column chromatography (from CH_2Cl_2 to 65:35 CH_2Cl_2/EtOAc) to give 27 mg (84%) of pure auxiliary **5** and 35 mg (0.15 mmol, 76% yield) of carboxylic acid **22a** as a colourless oil. R_f = 0.3 (65:35 CH_2Cl_2/EtOAc). $[\alpha]_D^{20}$ = – 39.8 (*c* 1.0, $CHCl_3$). IR (ATR): 2974, 2927, 2873, 1720, 1454, 1372, 1359, 1239, 1128, 1077, 935, 783 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.55 (q, *J* = 6.7 Hz, 1H), 1.73–1.63 (m, 5H), 1.54–1.48 (m, 1H), 1.50 (d, *J* = 6.7 Hz, 3H), 1.35 (s, 3H), 1.30 (s, 3H), 1.26 (s, 3H), 1.24 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 174.3, 62.9, 62.5, 39.2, 39.0, 30.9, 30.1, 29.7, 20.9 (×2), 17.0, 16.4. HRMS (ESI): *m/z* calcd. for $C_{12}H_{24}NO_3$ $[M+H]^+$: 230.1751; found: 230.1759.

(*S*)-3-Phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)propanoic acid (22b). A mixture of **11b** (89 mg, 0.20 mmol), 30% H_2O_2 (90 μL, 0.8 mmol, 4 equiv), and LiOH (11 mg, 0.42 mmol, 2 equiv) in 3:1 THF/H_2O (4 mL) was stirred at 0 °C for 3 h. A sat solution of $Na_2S_2O_3$ (2 mL) was added and the volatiles were removed in vacuo. The solution was acidified with 2 M HCl and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude was purified by column chromatography (65:35 CH_2Cl_2/EtOAc) to give 25 mg (78%) of pure auxiliary **5** and 42 mg (0.14 mmol, 69% yield) of carboxylic acid **22b** as a colourless oil. R_f = 0.4 (65:35 CH_2Cl_2/EtOAc). $[\alpha]_D^{20}$ = –68.5 (*c* 1.0, $CHCl_3$). IR (ATR): 2971, 2927, 2870, 1717, 1454, 1372, 1233, 1131, 1027, 751, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.20 (m, 5H), 4.69 (dd, *J* = 8.5, 3.4 Hz, 1H), 3.46 (dd, *J* = 14.6, 8.5 Hz, 1H), 3.14 (dd, *J* = 14.6, 3.4 Hz, 1H), 1.68–1.59 (m, 5H), 1.50–1.44 (m, 1H), 1.28 (s, 3H), 1.18 (s, 3H), 1.12 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 173.1, 137.6, 129.6, 128.2, 126.5, 80.5, 63.1, 62.8, 39.3, 39.2, 37.6, 31.2, 29.9, 21.0, 20.8, 16.3. HRMS (ESI): *m/z* calcd. for $C_{18}H_{28}NO_3$ $[M+H]^+$: 306.2064; found: 306.2070.

Methyl (*S*)-2-[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]propanoate (23a). A solution of **11a** (74 mg, 0.20 mmol) and DMAP (11 mg, 80 μmol) in methanol (5 mL) was stirred for 20 h at room temperature under N_2. The volatiles were removed and the resultant residue was diluted in Et_2O (20 mL), washed with 1 M NaOH (3 × 20 mL), water (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated. The crude was purified by column chromatography (90:10 Hexanes/EtOAc) to give 42 mg (0.17 mmol, 86% yield) of pure ester **23a** as a colourless oil. The aqueous layer was acidified and extracted with CH_2Cl_2 (3 × 20 mL) to recover 28 mg (88%) of pure auxiliary **5**. R_f = 0.4 (90:10 Hexanes/EtOAc). $[\alpha]_D^{20}$ = –56.3 (*c* 1.0, $CHCl_3$). IR (ATR): 2931, 1741, 1452, 1374, 1361, 1262, 1243, 1197, 1131, 1078, 973, 941, 788 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.34 (q, *J* = 6.9 Hz, 1H), 3.71 (s, 3H), 1.49–1.38 (m, 6H), 1.40 (d, *J* = 6.9 Hz, 3H), 1.18 (br s, 3H), 1.12 (br s, 6H), 1.02 (br s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 174.5, 81.6, 60.1, 59.5, 51.4, 40.3, 40.1, 33.6, 32.9, 20.2, 20.0, 18.1, 17.1. HRMS (ESI): *m/z* calcd. for $C_{13}H_{26}NO_3$ $[M+H]^+$: 244.1907; found: 244.1901.

Methyl (*S*)-3-phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)propanoate (23b). A solution of **11b** (89 mg, 0.2 mmol) and DMAP (11 mg, 80 μmol) in methanol (5 mL) was stirred for 72 h at room temperature under N_2. The volatiles were removed and the resultant residue was diluted in Et_2O (20 mL), washed with 1 M NaOH (3 × 20 mL), water (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated. The crude was purified by column chromatography (50:50 CH_2Cl_2/Hexanes) to give 57 mg (0.18 mmol, 89% yield) of pure ester **23b** as a colourless oil. The aqueous layer was acidified and extracted with CH_2Cl_2 (3 × 20 mL) to recover 30 mg (94%) of pure auxiliary **5**. R_f = 0.5 (50:50 CH_2Cl_2/Hexanes). $[\alpha]_D^{20}$ = –17.1 (*c* 1.0, $CHCl_3$). IR (ATR): 2946, 2911, 1736, 1366, 1166, 1043, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.13 (m, 5H), 4.45 (dd, *J* = 10.2, 5.5 Hz, 1H), 3.50 (s, 3H), 3.25 (dd, *J* = 13.2, 5.5 Hz, 1H), 2.99 (dd, *J* = 13.2, 10.2 Hz, 1H), 1.49–0.99 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 173.1, 136.0, 129.4, 128.3, 126.6, 86.6, 60.6, 59.5, 51.1, 40.3, 40.2, 38.5, 33.5, 32.9, 20.3, 20.1, 17.1. HRMS (ESI): *m/z* calcd. for $C_{19}H_{30}NO_3$ $[M+H]^+$: 320.2220; found: 320.2225.

***N*-[2(*S*)-(2,2,6,6-Tetramethylpiperidin-1-yloxy)propanoyl]morpholine (24a).** A solution of **11a** (74 mg, 0.20 mmol), morpholine (69 μL, 0.78 mmol, 3.9 equiv), and DMAP (14 mg, 0.1 mmol) in THF (2 mL) was stirred for 12 h at room

temperature under N_2. The volatiles were then removed and the residue was purified by column chromatography (from CH_2Cl_2 to 90:10 CH_2Cl_2/EtOAc) to afford 57 mg (0.19 mmol, 95% yield) of pure amide **24a** as a white solid and 31 mg (97%) of chiral auxiliary **5**. Mp: 57–58 °C. R_f = 0.3 (90:10 CH_2Cl_2/EtOAc). $[\alpha]_D^{20}$ = –3.0 (*c* 1.0, $CHCl_3$). IR (ATR): 2949, 2851, 1644, 1464, 1429, 1233, 1109, 568 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.61 (q, *J* = 7.1 Hz, 1H), 3.77–3.53 (m, 8H), 1.60–1.05 (m, 18H), 1.44 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 172.3, 83.0, 66.9, 66.6, 59.6, 46.1, 42.1, 40.2, 40.1, 33.9, 33.2, 29.7, 20.6, 20.3, 18.5, 17.0. HRMS (ESI): *m/z* calcd. for $C_{16}H_{31}N_2O_3$ $[M+H]^+$: 299.2329; found: 299.2334.

***N*-[(*S*)-[3-Phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)propanoyl]morpholine** (**24b**). A solution of **11b** (89 mg, 0.20 mmol), morpholine (69 μL, 0.78 mmol, 3.9 equiv), and DMAP (14 mg, 0.1 mmol 0.5 equiv) in THF (2 mL) was stirred for 24 h at room temperature under N_2. The volatiles were then removed and the residue was purified by column chromatography (from CH_2Cl_2 to 80:20 CH_2Cl_2/EtOAc) to afford 69 mg (0.18 mmol, 92% yield) of pure amide **24b** as a white solid and 26 mg (81%) of chiral auxiliary **5**. Mp: 148–149 °C. R_f = 0.7 (90:10 CH_2Cl_2/EtOAc). $[\alpha]_D^{20}$ = –4.7 (*c* 1.0, $CHCl_3$). IR (ATR): 2930, 1632, 1448, 1239, 1109, 1024, 701 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.17 (m, 5H), 4.73 (dd, *J* = 11.0, 4.6 Hz, 1H), 3.64–3.53 (m, 2H), 3.39 (ddd, *J* = 11.5, 5.5, 3.1 Hz, 1H), 3.32–3.21 (m, 4H), 3.10 (dd, *J* = 12.5, 11.0 Hz, 1H) 3.05–3.00 (m, 1H), 2.74 (ddd, *J* = 11.5, 7.8, 2.9 Hz, 1H), 1.62–1.02 (m, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 171.1, 136.5, 129.7, 128.4, 126.7, 82.6, 66.5, 66.1, 60.4, 59.5, 46.0, 41.7 40.5, 40.3, 39.0, 33.9, 33.3 20.4, 20.2, 17.1. HRMS (ESI): *m/z* calcd. for $C_{22}H_{35}N_2O_3$ $[M+H]^+$: 375.2642; found: 375.2651.

***S*-Dodecyl (*S*)-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)propanethioate** (**25a**). A 1.6 M solution of *n*-BuLi in hexanes (38 μL, 60 μmol) was added to a solution of dodecanethiol (145 μL, 0.6 mmol) in THF (2 mL) at 0 °C under N_2 and the resultant solution was stirred for 15 min. Then, a solution of **11a** (74 mg, 0.20 mmol) in THF (2 × 0.75 mL) was added and the reaction mixture was stirred at room temperature for 6 h. It was diluted with Et_2O (20 mL), washed with 1 M NaOH (3 × 20 mL), water (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated. The crude was purified by column chromatography (70:30 Hexanes/CH_2Cl_2) to give 77 mg (0.19 mmol, 93% yield) of pure thioester **25a** as a colourless oil. The aqueous layer was acidified and extracted with CH_2Cl_2 (3 × 20 mL) to recover 30 mg (94%) of pure chiral auxiliary **5**. R_f = 0.2 (70:30 Hexanes/CH_2Cl_2). $[\alpha]_D^{20}$ = –5.8 (*c* 1.0, $CHCl_3$). IR (ATR): 2922, 2852, 1681, 1453, 1361, 1132, 957, 922, 573 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.42 (q, *J* = 6.9 Hz, 1H), 2.85 (t, *J* = 7.4 Hz, 2H), 1.67–0.99 (m, 41H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 203.4, 87.1, 60.5, 59.5, 40.3, 34.4, 33.5, 31.9, 29.6 (× 3), 29.5, 29.4, 29.3, 29.1, 28.9, 28.1, 22.7, 20.3, 19.4, 17.1, 14.1. HRMS (ESI): *m/z* calcd. for $C_{24}H_{48}NO_2S$ $[M+H]^+$: 414.3400; found: 414.3390.

***S*-Dodecyl (*S*)-[3-phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)]propanethioate** (**25b**). A 1.6 M solution of *n*-BuLi in hexanes (38 μL, 60 μmol) was added to a solution of dodecanethiol (145 μL, 0.6 mmol) in THF (2 mL) at 0 °C under N_2 and the resultant solution was stirred for 15 min. Then, a solution of **11b** (89 mg, 0.20 mmol) in THF (2 × 0.75 mL) was added and the reaction mixture was stirred at room temperature for 14 h. It was diluted with Et_2O (20 mL), washed with 1 M NaOH (3 × 20 mL), water (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated. The crude was purified by column chromatography (80:20 Hexanes/CH_2Cl_2) to give 87 mg (0.18 mmol, 89% yield) of pure thioester **25b** as a colourless oil. The aqueous layer was acidified and extracted with CH_2Cl_2 (3 × 20 mL) to recover 28 mg (88%) of pure chiral auxiliary **5**. R_f = 0.4 (80:20 Hexanes/CH_2Cl_2). $[\alpha]_D^{20}$ = +21.1 (*c* 1.0, $CHCl_3$). IR (ATR): 2921, 2850, 1686, 1451, 1362, 1130, 934, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26–7.16 (m, 5H), 4.53 (dd, *J* = 9.2, 5.1 Hz, 1H), 3.30 (dd, *J* = 13.5, 5.1 Hz, 1H), 3.01 (dd, *J* = 13.5, 9.2 Hz, 1H), 2.74 (t, *J* = 7.3 Hz, 2H), 1.54–0.85 (m, 40H), 0.88 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 201.1, 136.4, 129.7, 128.2, 126.5, 91.4, 40.5, 38.8, 31.9, 29.7, 29.6 (× 2), 29.5, 29.4, 29.1, 28.8, 28.4, 22.7, 20.3, 20.2, 17.1, 14.1. HRMS (ESI): *m/z* calcd. for $C_{30}H_{52}NO_2S$ $[M+H]^+$: 490.3713, found: 490.3715.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

‡ Crystallographic data for adduct **11b** has been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1835692. A copy of the data can be obtained free of charge on application to CCDC (E-mail: deposit@ccdc.cam.ac.uk).
§ See Experimental Section

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