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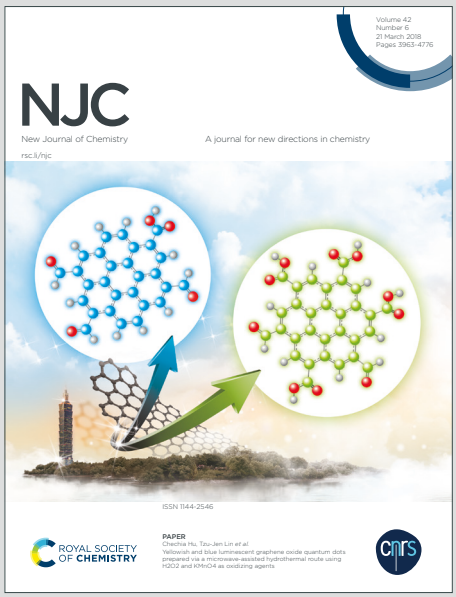

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PAPER

β-C(sp2)–H Alkylation of enamides using xanthate chemistry

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An access to the γ-amino-β,γ-unsaturated acyl scaffold was developed by applying xanthate chemistry to enamides. This original β-C(sp2)-H alkylation is regioselective and exhibits broad substrate scope and good functional group tolerance. The large availability of xanthates is advantageous to the scope of the reaction which combines a radical process and a polar reaction.

Introduction

Due to the importance of electron-rich C(sp3)–H bonds found in many biologically active natural products and pharmaceuticals,[1] the development of methods that allow the coupling of sp3 centers represents a great challenge in organic synthesis. Recent advances have permitted significant progress in sp3–sp2 cross coupling particularly in those involving single-electron pathways.[2,3]

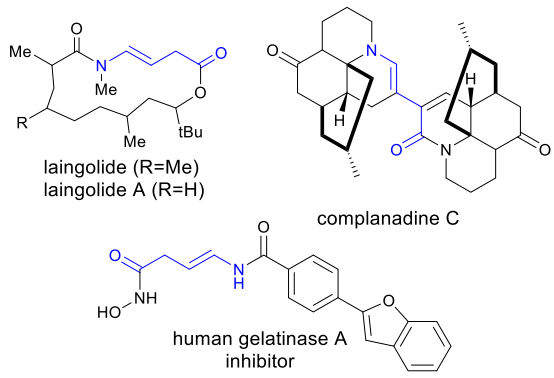
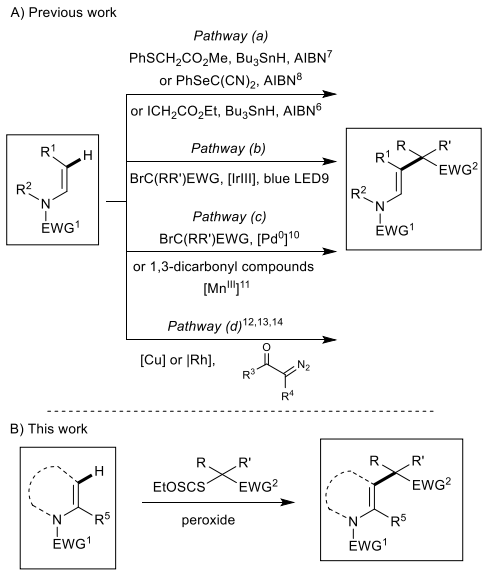


Figure 1. Representative bioactive compounds containing the γ-amino-β,γ-unsaturated acyl scaffold.

The β-C(sp2)–H alkylation of electron-rich olefins such as enamides has attracted particular attention, as the γ-amino-β,γ-unsaturated acyl moiety is a unique structural framework of biological interest and a polyvalent building block that can be readily derivatized under a variety of conditions (Figure 1).[4] As a result, a series of interesting methods on the direct intermolecular β-C(sp2)–H alkylation of enamides has been reported (Scheme 1).[3a-b,5] Most of them were triggered by the addition of an alkyl radical which is mainly generated by direct radical initiation[6] or a single electron-transfer (SET) process. Renaud and Schubert studied the stereocontrolled addition of sulfonylmethyl radicals to chiral enamines followed by H-atom transfers (*path. (a)*).[7] Curran *et al.* described the addition of methyl malononitrile radicals to *N*-vinylpyrrolidinones as part of a broader study of phenylselenenyl group transfer additions to electron-rich alkene acceptors.[8] Friestad reported an unusual non-reductive coupling of *N*-vinyloxazolidinones with α-haloesters and iodoacetonitrile in presence of tri-*n*-butylstannane and AIBN as radical precursor.[6] Visible-light iridium photoredox-catalysis was highlighted by Yu and co-workers using electron-deficient bromides as alkylating agents (*path. (b)*).[9]



Scheme 1. Strategies for direct intermolecular β-C(sp2)-H alkylation of enamide and access to the γ-amino-β,γ-unsaturated systems.

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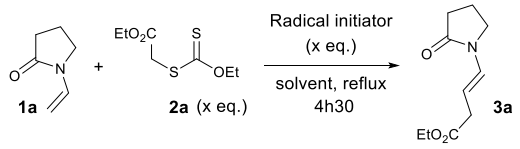
Loh's group elegantly described a palladium-catalyzed strategy for the branch-selective alkylation of enamides (*path. (c)*).[10] Li and co-workers developed an efficient Mn^{III}-mediated cross dehydrogenation coupling reaction between enamides and 1,3-dicarbonyl compounds.[11] Another approach involved α-diazo compounds as reported by Maas and Muller[12] or Yan[13] through a Cu^{II}-catalyzed process and more recently upon Rh^{II}-catalysis by Musaev and France.[5b] Although some of these methods show high efficiency and good functional group tolerance, there is still great room for improvement with the perspective of developing an efficient, generally applicable method.

Complementarily, xanthates[14] have emerged as attractive feedstocks in radical coupling reactions and in promoting the direct alkylation of olefins, as elegantly developed by Zard,[15] Miranda[16] or Landais.[17] It has been demonstrated that xanthates display an inherent advantage in the oxidative radical substitution of het(aryl) compounds. Zard reported the C-2 alkylation of *t*-butyl 3-indolecarboxylate[15a] using such a strategy. The oxidative direct intermolecular alkylation of several heteroaromatic systems (i.e. indoles, pyrroles, furans, and thiophenes) was observed by Miranda.[16b] Furthermore, the same group demonstrated that xanthate-based radical chemistry could be used for the intermolecular alkylation of 1,3-dimethyluracil.[16] Of particular interest, the addition of a radical species derived from xanthate was highlighted by Zard on azetines,[15b] also once on the *N*-vinylpyrolidone[15c], and by Landais[17] in the carbo-alkenylation of enamides. Apart from these examples, and to the best of our knowledge, no study has showcased to date the applicability of xanthate in the direct intermolecular C(sp2)–H alkylation of electron-rich olefins such as enamides. Following our interest in radical processes to promote the selective functionalization of nitrogen-containing heterocycles, we report here the application of xanthate chemistry to the β-C(sp2)–H alkylation of a range of non-aromatic enamides to synthesize new γ-amino-β,γ-unsaturated systems which are envisioned to be useful for further elaboration.

Results and discussion

At the outset of our study, we chose the commercially available *N*-vinylpyrrolidinone **1a** and xanthate of ethyl acetate **2a** as the coupling partner for our model reaction (Table 1). By applying Zard's guidelines,[15] we began the optimization conditions by performing the reaction with enamide **1a** (1 equiv.) and **2a** (2 equiv.) in 1,2-dichloroethane (1,2-DCE) using readily biodegradable lauroyl peroxide (DLP, 1.2 equiv.) as the radical precursor. The reaction mixture was refluxed until the starting material **1a** had been consumed (TLC monitoring). The related γ-amino-β,γ-unsaturated ester **3a** was obtained in good yield (e.g., 62%, entry 1) after 4h30. The *E* geometry of **3a** was assigned on the basis of NMR data.[18] Other radical initiators such as di-*tert*-butyl peroxide (DTBP), azobisisobutyronitrile (AIBN), iodobenzene diacetate or *tert*-butyl hydroperoxide were next studied. In most instances, the reaction did not proceed or a dramatic decrease in yield was observed (entries 2–5). The yield of **3a** was affected by the amount of DLP (entries 8-9) but little by the stoichiometry of the xanthate derivative (entries 6-7), demonstrating that 2 equiv. of **2** and 1.2 equiv. of DLP was mandatory. The decomposition half-life for a given radical precursor at an operating temperature is often of great significance. Lastly, portionwise (a portion every 90 min) addition of the DLP initiator was compared with its addition in a single portion (entry 10). As expected, the direct addition of DLP proved to be the optimum choice. Polar effects in radical mediated processes are much less important than in ionic processes, allowing a much wider choice of solvents. The next step was therefore to screen common solvents for radical reactions. Of note, less polar aprotic solvents such as 1,4-dioxane (entry 11) or the bio-renewable 2-Me-THF (entry 12) were capable of performing the transformation, albeit with lower efficiencies, whereas with ethyl acetate (entry 13) the addition proceeded well and product **3a** was isolated with the same yield as previously observed with 1,2-DCE. We avoided using 1,2-DCE for environmental reasons. Acetonitrile proved less effective (44%, entry 14). In addition, it is noteworthy that degradation was observed when conventional heating was replaced by microwave heating.

Table 1. Optimization of the β-C(sp2)-H alkylation of enamide **1a** using xanthate **2a**.



Entry	Radical initiator	Equiv.	Solvent	Yield [%] of **3a**[b]
1	DLP	1.2	1,2-DCE	62
2	DTBP	1.2	1,2-DCE	0
3	AIBN	1.2	1,2-DCE	0
4	$PhI(OAc)_2$	1.2	1,2-DCE	10
5	*t*-BuOOH [5M]	1.2	1,2-DCE	0
6[c]	DLP	1.2	AcOEt	58
7[d]	DLP	1.2	AcOEt	62
8	DLP	0.5	1,2-DCE	30
9	DLP	1	1,2-DCE	50
10[e]	DLP	1.2	1,2-DCE	35
11	DLP	1.2	1,4-Dioxane	32
12	DLP	1.2	2-Me-THF	31
13	DLP	1.2	AcOEt	62
14	DLP	1.2	MeCN	44

[a] Typical reaction conditions: Argon-free oxygen atmosphere, compound **1a** (56 mg, 1 equiv.), xanthate **2a** (2 equiv.), radical initiator (1.2 equiv.), solvent (1.5 mL), heating under reflux for 4h30. [b] Isolated yield after purification by column chromatography (SiO_2, petroleum ether/EtOAc). [c] 1.5 equiv. of xanthate **2a** was used. [d] 2.5 equiv. of xanthate **2a** was used. [e] A portion (0.4 equiv.) of the radical initiator was added every 90 min.

On the basis of literature precedent, the following mechanism can be proposed (Figure 2). The thermal decomposition of lauroyl peroxide (DLP) initiates first the radical addition of enamide **1** by the electrophilic alkyl radical **A** to provide the amido radical **B**. As observed with (het)aromatic systems and the uracil system,[16] lauroyl peroxide induces the oxidation of

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the latter into the corresponding cation **C** and its resonance structure **D**. A proton elimination generated the enamide **3**. The transfer-xanthate product resulting from the trapping of the amido radical **B** by the xanthate was not observed. However, in some specific cases with more electron-rich enamides, the iminium species **D** can be trapped by a nucleophile (i.e. the released carboxylate $C_{11}H_{23}CO_2^-$) leading to the difunctionalized adduct **4**, isolated as a mixture of cis-trans diastereoisomers. This mechanism demonstrated the need for a stoechiometric amount of lauryl peroxide for the reaction to succeed.

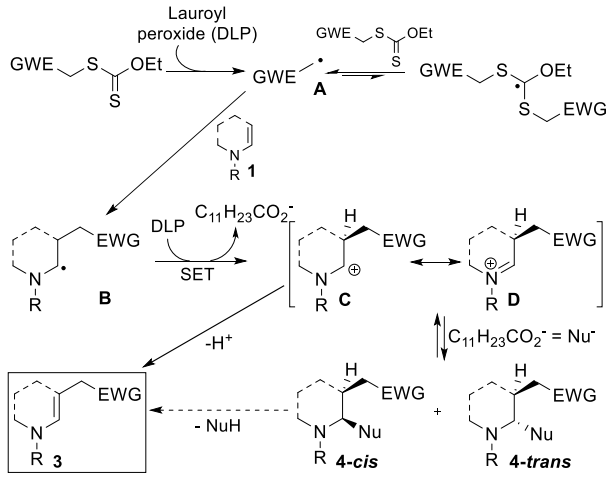
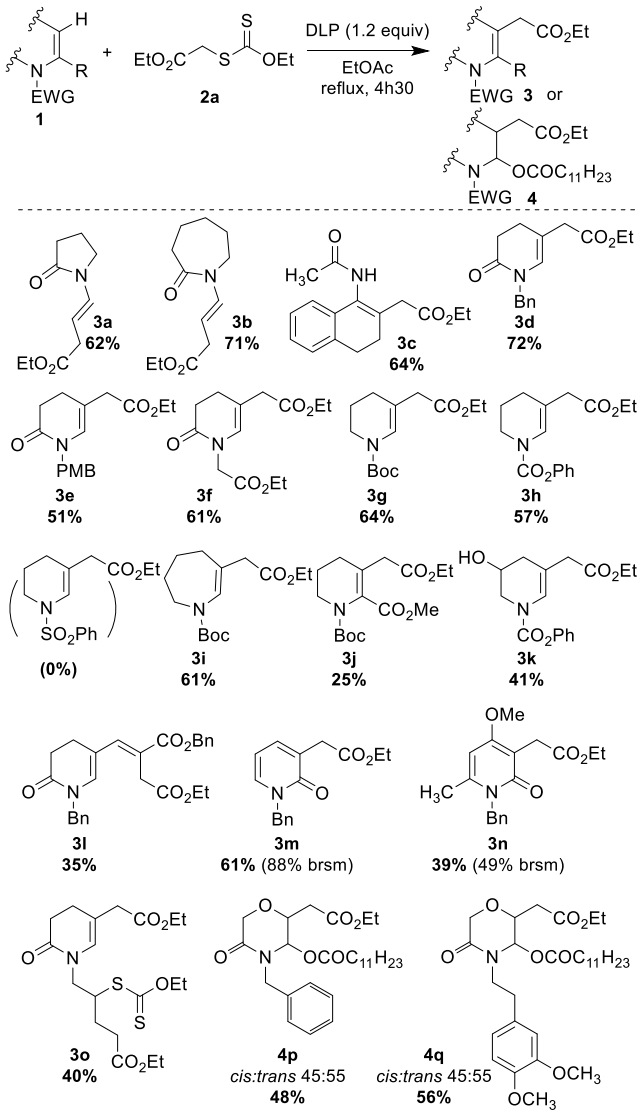


Figure 2. Proposed mechanism.

With the optimized conditions in hand, we next examined the β-C(sp2)–H alkylation of various enamides **1a-q** with **2a** (Scheme 2). To our delight, a series of cyclic and acyclic enamides **1** were successfully converted to the corresponding β-alkylated enamides **3**. Monosubstituted 5- or 7-membered ring tertiary enamides **1a**–**b** worked well, giving the new alkylated product **3a**–**b** as a unique *E* stereoisomer.[18] The secondary enamide **1c** was also suitable for this alkylation reaction and provided **3c** in good yield. Cyclic (i.e. 6- or 7-membered rings) di-substituted enamides **1d**–**i** bearing various electron-withdrawing *N*-protecting groups were also good substrates in this reaction and led to the desired alkylated products **3d**–**i** with moderate to good yields. It is worth noting that no alkylated product was observed in the case of the corresponding ene-sulfonamide.[19] The alkylation of **3j** bearing an ester group at the C-2 position, which could serve as a valuable synthetic intermediate was tolerated. Furthermore, the reaction turned out to be compatible with other functional groups such as a hydroxyl group (**3k**), which was amenable to further useful transformations. Notably, the vinylogous β-alkylester enamide **3l** and pyridones **3m**–**n** were isolated in moderate yields accompanied, in the case of **3m,** with unreacted starting material. It is noteworthy that functionalized pyridones are useful partners in Diels-Alder cycloadditions.[20] Interestingly, no chemoselectivity was observed starting from the *N*-allyl enamide **1o**; a xanthate transfer was indeed additionally observed onto the allylic olefin allowing the implementation of a potential second radical sequence (**3o**). The observed low yields are due mainly to a slight degradation of the reaction mixture. As previously observed by us,[21] when more electron-rich enamides were used, the di-functionalized morpholin-2-ones **4p**–**q** were originally isolated as a *cis*:*trans* isomer mixture (45:55 ratio). In this case, we assume that no elimination step occurred as the electron donor property of the oxygen atom lowers the acidity of the nearby proton in **4p**–**q**. The latter two examples illustrate in an interesting way the oxyalkylation reaction of enamides.[22]



Scheme 2. β-C(sp2)-H Alkylation of diverse enamides **1a-q** using xanthate **2a.** Reaction conditions: Argon-free oxygen atmosphere, enamide **1** (1 equiv., 0.33 M), xanthate **2a** (2 equiv.), DLP (1.2 equiv.), AcOEt, heating under reflux for 4h30. brsm: based on recovered starting material.

To ascertain the scope of this reaction, various xanthates **2b**–**f** (Scheme 3) were prepared by substitution of the corresponding halo derivative with commercially available potassium ethyl xanthogenate.[23] Remarkably, a variety of electron-deficient primary and secondary alkyl groups successfully underwent this transformation to give a range of new substituted acyclic enamides **3ab**–**af** bearing an γ-ester or γ-nitrile function in moderate to good yields (39–72%).

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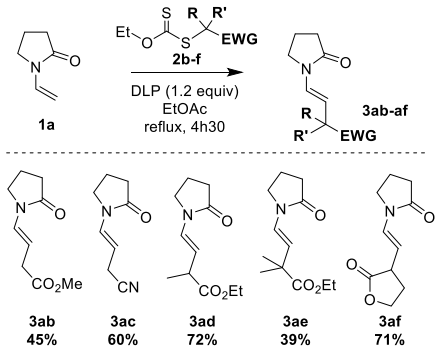
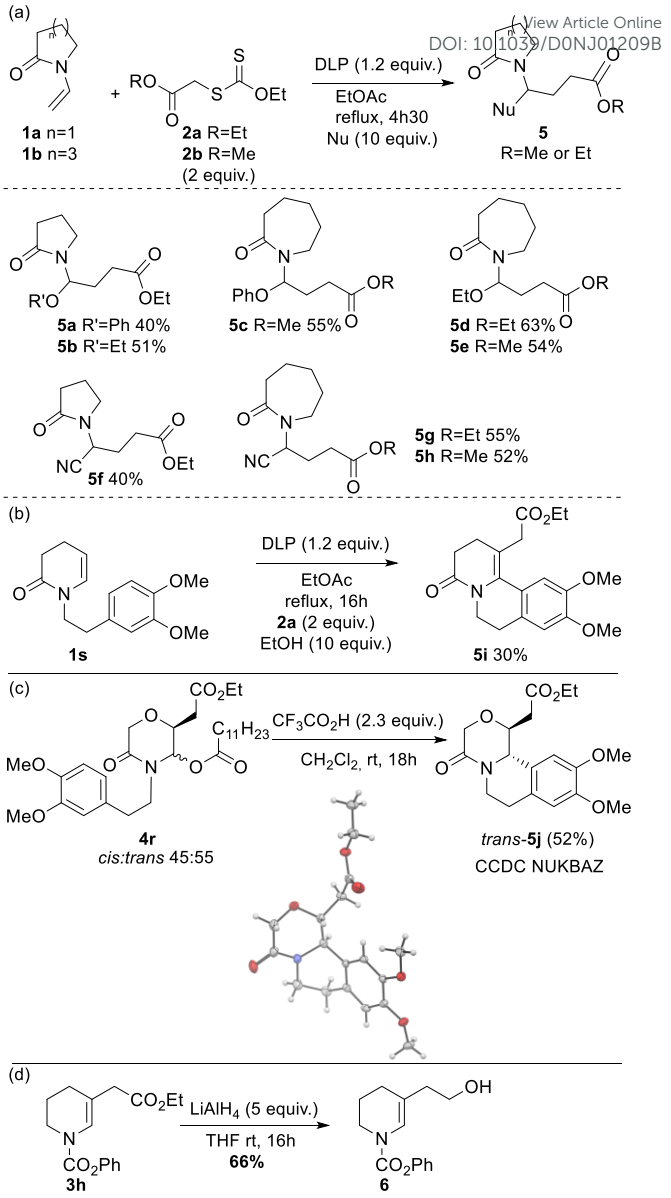
With the objective of increasing the molecular diversity, and based on the proposed mechanism depicted in Figure 2, we next envisaged that a nucleophile introduced into the reaction mixture could be trapped by the iminium species of type **D** (Figure 2), leading to enamides **5** in good yields. Intra- and intermolecular processes can be envisioned (Scheme 4, (a) and (b)). The tandem difunctionalization of enamides involving the simultaneous formation of C(sp3)–C(sp3) and C–O or C–CN bonds has proven to be a powerful tool for the synthesis of various motifs.[24,25a] Firstly, starting from 5- or 7-membered exocyclic enamides **1a**–**b** and through a sequential one-pot reaction, 10 equivalents of ethanol or phenol were used to intermolecularly trap the iminium ion intermediate leading to **5a**–**h** in good yields. In addition to this oxyalkylation reaction, cyanoalkylation was observed using TMSCN as the nucleophile.[25]



Scheme 3. Alkylation reactions of enamide **1a** with diverse xanthates **2b-f**. Reaction conditions: Argon-free oxygen atmosphere, enamide **1a** (1 equiv., 0.33 M), xanthate **2b–f** (2 equiv.), DLP (1.2 equiv.), AcOEt, heating under reflux for 4h30.

A large array of transformations can thus be envisaged to introduce further diversity and complexity into the structures. Starting from the enamide **1s** bearing a chain with a pendant dimethoxyphenyl group as the nucleophile, spontaneous cyclization occurred, leading directly to the new tricyclic enamide **5i** with an overall yield of 30% for the three-step sequence. As the limiting step is the intramolecular addition of the nucleophilic aryl moiety onto the iminium ion intermediate, conducting the reaction in the absence of ethanol resulted in the degradation of the reaction mixture. Additionally, a two-step sequence can be achieved by taking advantage of the iminium ion intermediate reactivity in acidic media (Scheme 4, (c)) from **4r** allowing the formation of the original tricyclic and diversely substituted morpholine derivative **5j**. The compound **5j** was isolated as a unique *trans* diastereoisomer; The relative stereochemistry was unambiguously confirmed by X-ray crystallography.[26] Furthermore, the γ-ester function in the enamide **3h** was reduced with good yields in the corresponding primary alcohol **6** in presence of $LiAlH_4$. This approach thus illustrated the potential of this strategy to provide access to a wide range of nitrogen containing heterocycles decorated with various functional groups.



Scheme 4. (a) and (b) Difunctionalization of enamide **1a** or **1b** with xanthate **2a** or **2b** in presence of nucleophiles. Reaction conditions: Argon-free oxygen atmosphere, enamide**1a** or **1b** (1 equiv., 0.33 M), xanthate **2a** or **2b** (2 equiv.), DLP (1.2 equiv.), related nucleophile (10 equiv.), AcOEt, heating under reflux for 4h30 to 18h. (c) Cyclization of **4r** to **5j** in presence of trifluoroacetic acid. Ortep view of the crystal structure **5j** (CCDC NUKBAZ). Displacement ellipsoids are drawn at the 30% probability level and hydrogen atoms with an arbitrary radius size. (d) Reduction of the γ-amino-β,γ-unsaturated ester **3h** to the primary alcohol **6**.

Conclusions

In summary, we have developed a mild, simple and efficient access to the γ-amino-β,γ-unsaturated acyl scaffold by applying xanthate chemistry to enamide. This original reaction is totally regioselective and exhibits broad substrate scope, good functional group tolerance and thus demonstrates its potent application in the synthesis of versatile *N*-containing building blocks. The large availability of xanthates is advantageous to the scope of the reaction which combines a radical process and a

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polar reaction. Further applications based on this chemistry are in progress in our laboratory.

Experimental

General information

Unless otherwise noted, all reagents and solvents were purchased from commercial sources and used as received. All manipulations were conducted under argon. The reactions were monitored by thin-layer chromatography (TLC) using silica gel (60 F254) plates. Compounds were visualized using a UV lamp (254 nm) and/or by potassium permanganate stain. Flash column chromatography was carried out on silica gel 60 (230-400 mesh, 0.040-0.063 mm). Melting points (mp [°C]) were taken on samples in open capillary tubes and are uncorrected. The infrared spectra of compounds were recorded on a Thermo Scientific Nicolet iS10. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a spectrometer at 250 MHz (^{13}C, 62.9 MHz) or 400 MHz (^{13}C, 100 MHz; ^{19}F: 376 MHz CPD). High-resolution accurate mass measurements (HRAM) were recorded with a Maxis Bruker 4G instrument and were performed in positive mode with an ESI source on a Q-TOF mass spectrometer with an accuracy tolerance of 2 ppm by the "Fédération de Recherche" ICOA/CBM (FR2708) platform.

General Procedure for the Synthesis of Enamides 1d–i, 1k, 1l and 1o–1q (G.P. A). An oven-dried single-necked round-bottomed flask under argon atmosphere was charged with dry toluene, the related imide **1** (1.0 equiv., 0.49 M) and a magnetic stir bar. The reaction vessel was cooled to –78 °C (dry ice/acetone bath) and a 1 M solution of $LiEt_3BH$ in THF (1.1 equiv.) was then added dropwise. The mixture was stirred further at –78 °C for 1 h. Next, *N,N*-Diisopropylethylamine (DIPEA, 5.7 equiv.) and a catalytic amount of 4-Dimethylaminopyridine (DMAP, 0.03 equiv.) were added, followed by the dropwise addition of Trifluoroacetic anhydride (TFAA, 1.2 equiv.) and the reaction mixture was allowed to warm up to room temperature (ca. 20 °C). The mixture was stirred for 3 h at the same temperature and it was quenched by the addition of water. The aqueous phase was then extracted twice with EtOAc, combined organic phases were washed (sat. aq. NaCl), dried over $MgSO_4$ and filtered through a cotton plug. The solvents were evaporated under reduced pressure and the resulting crude enamide derivative was purified by column chromatography (SiO_2).

General Procedure for the Direct Oxidative Radical β-C(sp2)–H Monoalkylation of Enamides (G.P. B). An oven-dried 2–5 mL microwave vial under argon atmosphere was charged with the enamide substrate (1.0 equiv., 0.33 M), ethyl acetate, corresponding xanthate (2.0 equiv., 0.66 M) and a magnetic stir bar. The solution was degassed 3 times (vacuum/argon cycles), the reaction vessel was capped and it was placed in a pre-heated oil bath for 5 min at 90 °C. Next, the vial was uncapped and dilauroyl peroxide (DLP, 1.2 equiv.) was added. The vessel was sealed and the reaction mixture was heated at 78 °C for 4.5 h under argon atmosphere. After cooling to rt (ca. 20 °C), the solvent was concentrated under reduced pressure. The residue was taken up in dichloromethane and dry silica was added (approximately 10 times the mass of the sample). The solvents were evaporated *in vacuo* until the silica is dry and free-flowing and the coated support was packed on top of a silica gel column. The crude product was purified (SiO_2) to give the desired monoalkylated enamide derivative in moderate to good yield.

General Procedure for the Radical Difunctionalisation of Enamides With Xanthates in Presence of a Nucleophile (G.P. C). An oven-dried 2–5 mL microwave vial under argon atmosphere was charged with the enamide substrate (1.0 equiv., 0.33 M), related xanthate derivative (2.0 equiv., 0.66 M), ethyl acetate and a magnetic stir bar. The solution was degassed 3 times (vacuum/argon cycles), the reaction vessel was capped and it was placed in a pre-heated oil bath for 5 min at 90 °C. Next, the vial was uncapped and DLP (1.2 equiv.) followed by corresponding nucleophile (10 equiv.) were added. The vessel was sealed and the reaction mixture was heated at 78 °C for 4.5 h under argon atmosphere. After cooling to rt (ca. 20 °C), the solvent was concentrated under reduced pressure. The residue was taken up in dichloromethane and dry silica was added (approximately 10 times the mass of the sample). The solvents were evaporated *in vacuo* until the silica is dry and free-flowing and the coated support was packed on top of a silica gel column. The crude product was purified (SiO_2) to give the desired dialkylated enamide compound in moderate to good yield.

General procedure D (G.P. D). Alternatively, after solvent concentration in **G.P. B** and **G.P. C**, addition of cold acetonitrile could be performed at 0 °C, leaving decomposition products from DLP undissolved. The precipitate was filtered through a sintered glass Büchner funnel and the mother liquor was recovered. Then, the acetonitrile was removed by rotary evaporation and the product residue was purified further by flash SiO_2–column chromatography.

4-(3,4-Dimethoxyphenethyl)-1,4-oxazin-3-one (1q). The titled compound was obtained following **G.P. A**. Purification by flash chromatography using petroleum ether/EtOAc (8:2, v/v) gave **1q** as a yellow oil (632.0 mg, 48%). R_f 0.1 (SiO_2, petroleum ether/EtOAc 8:2, v/v). M.p. < 40 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80 (d, J = 8.0 Hz, 1 H, H_{Ar}), 6.77–6.70 (po, 2 H, H_{Ar}), 6.11 (d, J = 4.3 Hz, 1 H, H-6), 5.46 (d, J = 4.3 Hz, 1 H, H-5), 4.39 (s, 2 H, H-2), 3.87 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.68 (t, J = 7.4 Hz, 2 H, NCH_2), 2.83 (t, J = 7.4 Hz, 2 H, NCH_2CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.5 (C, C-3), 149.1 (C, C_{Ar}), 147.9 (C, C_{Ar}), 130.7 (C, C_{Ar}), 130.5 (CH, C-6), 120.9 (CH, CH_{Ar}), 112.2 (CH, CH_{Ar}), 111.5 (CH, CH_{Ar}), 111.0 (CH, C-5), 67.7 (CH_2, C-2), 56.0 (CH_3, OCH_3), 56.0 (CH_3, OCH_3), 47.3 (CH_2, NCH_2), 34.1 (CH_2, NCH_2CH_2) ppm. HRMS (ESI): m/z calcd. for $C_{14}H_{18}NO_4$ $[M + H]^+$ 264.123034, found 264.123098.

Ethyl (*E*)-4-(2-oxopyrrolidin-1-yl)but-3-enoate (3a). According to **G.P. B**, the reaction was performed with enamide **1a** (56 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg,

1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 75:25 to 70:30, v/v) to afford **3a** as a colourless oil (61 mg, 62%). R_f 0.2 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 6.97 (d, J = 14.6 Hz, 1 H, H-4), 5.03 (dt, J = 14.6, 7.3 Hz, 1 H, H-3), 4.15 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.54 (t, J = 7.2 Hz, 2 H, H-5'), 3.10 (d, J = 7.3 Hz, 2 H, H-2), 2.48 (t, J = 8.1 Hz, 2 H, H-3'), 2.18–2.04 (m, 2 H, H-4'), 1.27 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.2 (C, *C*O), 172.1 (C, *C*O), 126.6 (CH, C-4), 103.6 (CH, C-3), 60.9 (CH$_2$, O*C*H$_2$CH$_3$), 45.3 (CH$_2$, C-5'), 35.7 (CH$_2$, C-2), 31.3 (CH$_2$, C-3'), 17.6 (CH$_2$, C-4'), 14.3 (OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1728 (C=O), 1653 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{10}H_{16}NO_3$ $[M + H]^+$ 198.112470, found 198.112227.

Ethyl (*E*)-4-(2-oxoazepan-1-yl)but-3-enoate (3b). According to **G.P. B**, the reaction was performed with enamide **1b** (70 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 85:15 to 75:25, v/v) to afford **3b** as a colourless oil (80 mg, 71%). R_f 0.14 (SiO_2, petroleum ether/EtOAc 75:25, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.24 (d, J = 14.6 Hz, 1 H, H-4), 5.13 (dt, J = 14.6, 7.2 Hz, 1 H, H-3), 4.14 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.63–3.56 (m, 2 H, H-7'), 3.10 (dd, J = 7.2, 1.2 Hz, 2 H, H-2), 2.65–2.58 (m, 2 H, H-3'), 1.79–1.60 (po, 6 H, H-6' + H-5' + H-4'), 1.26 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.3 (C, *C*O), 172.4 (C, *C*O), 129.6 (CH, C-4), 102.4 (CH, C-3), 60.8 (CH$_2$, O*C*H$_2$CH$_3$), 45.5 (CH$_2$, C-7'), 37.2 (CH$_2$, C-3'), 35.8 (CH$_2$, C-2), 29.5 (CH$_2$, C-6'), 27.4 (CH$_2$, C-5'), 23.5 (CH$_2$, C-4'), 14.3 (CH$_3$, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1690 (C=O), 1652 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{12}H_{20}NO_3$ $[M + H]^+$ 226.143770 found, 226.143888.

Ethyl 2-(1-acetamido-3,4-dihydronaphthalen-2-yl)acetate (3c). Compound **3c** was prepared according to **G.P. B**, using enamide **1c** (94 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by passage though SiO_2–column chromatography (petroleum ether/EtOAc 70/30 to 50/50 v/v) and was obtained in moderate yield (87 mg, 64%) as a mixture of rotamers (ca. 65:35). R_f 0.16 (SiO_2, petroleum ether/EtOAc 5:5, v/v). M.p. 107–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.06 (po, 4 H, H$_{Ar}$ *maj.* + H$_{Ar}$ *min.*), 6.71 (s, 0.35 H, N*H* *min.*), 4.16 (po, 2 H, OCH_2CH$_3$ *min.* + OCH_2CH$_3$ *maj.*), 3.36 (s, 0.75 H, H-2 *min.*), 3.27 (s, 1.25 H, H-2 *maj.*), 2.85 (t, J = 8.0 Hz, 2 H, H-3' *maj.* + H-3' *min.* or H-4' *maj.* + H-4' *min.*), 2.46 (t, J = 8.0 Hz, 2 H, H-4' *maj.* + H-4' *min.* or H-3' *maj.* + H-3' *min.*), 2.20 (s, 1.87 H, CH_3CO *maj.*), 1.83 (s, 1.13 H, CH_3CO *min.*), 1.27 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3 *maj.* + OCH$_2$CH_3 *min.*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0 (C, *C*O *min.*), 171.5 (C, *C*O *maj.*), 170.4 (C, *C*O *min.*), 169.3 (C, *C*O *maj.*), 135.8 (C, C$_{Ar}$ *min.*), 135.7 (C, C$_{Ar}$ *maj.*), 133.1 (C, C^{IV} *min.*), 132.2 (C, C^{IV} *maj.*), 131.7 (C, C^{IV} *min.*), 131.0 (C, C^{IV} *min.*), 130.2 (C, C^{IV} *maj.*), 129.2 (C, C^{IV} *min.*), 128.0 (CH, CH$_{Ar}$ *min.*), 127.7 (CH, CH$_{Ar}$ *min.*), 127.6 (CH, CH$_{Ar}$ *maj.*), 127.5 (CH, CH$_{Ar}$ *maj.*), 127.0 (CH, CH$_{Ar}$ *min.*), 126.6 (CH, CH$_{Ar}$ *maj.*), 122.7 (CH, CH$_{Ar}$ *min.*), 122.6 (CH, CH$_{Ar}$ *maj.*), 61.3 (CH$_2$, OCH$_2$CH$_3$ *min.*), 61.2 (CH$_2$, OCH$_2$CH$_3$ *maj.*), 39.3 (CH$_2$, C-2 *maj.*), 38.5 (CH$_2$, C-2 *min.*), 28.6 (CH$_2$, C-3' *maj.*), 28.2 (CH$_2$, C-3' *min.*), 27.7 (CH$_2$, C-4' *maj.*), 27.5 (CH$_2$, C-4' *min.*), 23.4 (CH$_3$, CH$_3$*C*O *maj.*), 20.3 (CH$_3$, CH$_3$*C*O *min.*), 14.3 (CH$_3$, OCH$_2$*C*H$_3$ *maj.* + OCH$_2$*C*H$_3$ *min.*) ppm. IR (neat): $\tilde{\nu}$ = 3244 (N–H), 1725 (C=O), 1641 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{16}H_{20}NO_3$ $[M + H]^+$ 274.143770 found, 274.143607.

Ethyl 2-(1-benzyl-2-oxo-3,4-dihydropyridin-3-yl)acetate (3d). According to **G.P. B**, the reaction was performed with enamide **1d** (94 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 85:15 to 80:20, v/v) to give **3d** as a colourless oil (98 mg, 72%). R_f 0.1 (SiO_2, petroleum ether/EtOAc 75:25, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.37–7.09 (po, 5 H, H$_{Ar}$), 5.97–5.88 (m, 1 H, H-6'), 4.67 (s, 2 H, CH_2Ph), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2), 2.99 (s, 2 H, H-2), 2.62 (dd, J = 8.8, 7.2 Hz, 2 H, H-3'), 2.38 (t, J = 8.1 Hz, 2 H, H-4'), 1.24 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 171.0 (C, C-1), 168.9 (CH$_2$, C-2'), 137.0 (C, C$_{Ar}$), 128.6 (CH, CH$_{Ar}$), 127.5 (CH, CH$_{Ar}$), 127.4 (CH, CH$_{Ar}$), 127.2 (CH, C-6'), 112.9 (C, C-5'), 60.7 (CH$_2$, O*C*H$_2$), 48.8 (CH$_2$, N*C*H$_2$Ph), 39.0 (CH$_2$, C-2), 31.0 (CH$_2$, C-3'), 24.2 (CH$_2$, C-4'), 14.1 (CH$_3$, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 2926 (C-H), 1732 (C=O), 1643 (C=O), 1563 (C=C) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{16}H_{20}NO_3$ $[M + H]^+$ 274.143770, found 274.143849.

Ethyl 2-[1-[(4-methoxyphenyl)methyl]-2-oxo-3,4-dihydropyridin-5-yl]acetate (3e). According to **G.P. B**, the reaction was performed with enamide **1e** (109 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 85:15 to 75:25, v/v) to afford **3e** as a colourless oil (77 mg, 51%). R_f 0.14 (SiO_2, petroleum ether/EtOAc 75:25, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, J = 8.7 Hz, 2 H, H$_{Ar}$), 6.85 (d, J = 8.7 Hz, 2 H, H$_{Ar}$), 5.92 (s, 1 H, H-6'), 4.60 (s, 2 H, NCH_2Ph), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.79 (s, 3 H, OCH$_3$), 2.98 (s, 2 H, H-2), 2.60 (t, J = 8.0 Hz, 2 H, H-3'), 2.36 (t, J = 8.1 Hz, 2 H, H-4'), 1.24 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$/TMS): δ 171.1 (C, *C*O), 168.8 (C, *C*O), 159.0 (C, C$_{Ar}$), 129.2 (C, C$_{Ar}$), 129.1 (CH, CH$_{Ar}$), 127.1 (CH, C-6'), 114.0 (CH, CH$_{Ar}$), 112.7 (C, C-5'), 60.8 (CH$_2$, O*C*H$_2$CH$_3$), 55.2 (CH$_3$, O*C*H$_3$), 48.3 (CH$_2$, N*C*H$_2$), 39.1 (CH$_2$, C-2), 31.1 (CH$_2$, C-3'), 24.3 (CH$_2$, C-4'), 14.2 (CH$_3$, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1724 (C=O), 1659 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{17}H_{22}NO_4$ $[M + H]^+$ 304.154335, found 304.154465.

Ethyl 2-[1-(2-ethoxy-2-oxoethyl)-2-oxo-3,4-dihydropyridin-5-yl]acetate (3f). The titled compound was synthesized according to **G.P. B**, using enamide **1f** (92 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30 v/v) to provide **3f** as a colourless oil (82 mg, 61%). R_f 0.07 (SiO_2, petroleum ether/EtOAc 75:25, v/v).

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^{1}H NMR (400 MHz, $CDCl_3$): δ 5.91 (s, 1 H, H-6'), 4.25–4.10 (po, 6 H, CH_2N + 2 × OCH_2CH$_3$), 3.03 (s, 2 H, H-2), 2.65–2.55 (m, 2 H, H-3'), 2.39 (t, J = 7.9 Hz, 2 H, H-4'), 1.26 (t, J = 7.2 Hz, 3 H, OCH$_2$CH_3), 1.25 (t, J = 7.2 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.1 (C, *C*O), 169.3 (C, *C*O), 168.8 (C, *C*O), 127.9 (CH, C-6'), 113.0 (C, C-5'), 61.5 (CH$_2$, O*C*H$_2$CH$_3$), 61.0 (CH$_2$, O*C*H$_2$CH$_3$), 47.4 (CH$_2$, N*C*H$_2$), 39.2 (CH$_2$, C-2), 30.8 (CH$_2$, C-3'), 24.3 (CH$_2$, C-4'), 14.3 (CH$_3$, OCH$_2$*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1732 (C=O), 1672 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{13}H_{20}NO_5$ [M + H]$^+$ 270.133599 found, 270.133791.

***tert*-Butyl 5-(2-ethoxy-2-oxoethyl)-3,4-dihydro-2*H*-pyridine-1-carboxylate (3g)**. According to **G.P. B**, the reaction was performed with enamide **1g** (93 mg, 0.51 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 98:2 to 97:3, v/v) to afford **3g** as a colourless oil (88 mg, 64%). Mixture of rotamers ca. 6:4. R_f 0.6 (SiO_2, petroleum ether/EtOAc 75:25, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 6.80 (br s, 0.4 H, H-6 *min.*), 6.65 (br s, 0.6 H, H-6 *maj.*) 4.23–4.06 (m, 2 H, CH$_2$, OCH_2CH$_3$ *maj.* + OCH_2CH$_3$ *min.*), 3.58–3.43 (m, 2 H, H-2 *maj.* + H-2 *min.*), 2.95 (s, 2 H, H-1' *maj.* + H-1' *min.*), 2.04 (t, J = 6.1 Hz, 2 H, H-4 *maj.* + H-4 *min.*), 1.88–1.77 (m, 2 H, H-3 *maj.* + H-3 *min.*), 1.46 (s, 9 H, C(CH_3)$_3$ *maj.* + C(CH_3)$_3$ *min.*), 1.33–1.21 (m, 3 H, OCH$_2$CH_3 *maj.* + OCH$_2$CH_3 *min.*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.0 (C, C-2' *maj.* + C-2' *min.*), 152.8 (C, N*C*O *min.*), 152.3 (C, N*C*O *maj.*), 124.1 (CH, C-6 *maj.*), 123.8 (CH, C-6 *min.*), 111.1 (C, C-5 *min.*), 110.5 (C, C-5 *maj.*), 80.8 (C, *C*(CH$_3$)$_3$ *maj.*), 80.6(C, *C*(CH$_3$)$_3$ *min.*), 60.7 (CH$_2$, O*C*H$_2$CH$_3$ *maj.*), 60.6 (CH$_2$, O*C*H$_2$CH$_3$ *min.*), 42.1 (CH$_2$, C-2 *min.*), 41.1 (CH$_2$, C-1' *min.*), 41.0 (CH$_2$, C-2 *maj.*), 41.0 (CH$_2$, C-1' *maj.*), 28.4 (CH$_3$, C(*C*H$_3$)$_3$ *maj.* + C(*C*H$_3$)$_3$ *min.*), 25.4 (CH$_2$, C-4 *maj.*), 25.2 (CH$_2$, C-4 *min.*), 21.8 (CH$_2$, C-3 *min.*), 21.6 (CH$_2$, C-3 *maj.*), 14.3 (CH$_3$, OCH$_2$*C*H$_3$ *maj.* + OCH$_2$*C*H$_3$ *min.*) ppm. HRMS (ESI): m/z calcd. for $C_{14}H_{24}NO_4$ [M + H]$^+$ 270.169985 found, 270.170411.

Phenyl 5-(2-ethoxy-2-oxoethyl)-3,4-dihydro-2*H*-pyridine-1-carboxylate (3h). The reaction was performed according to **G.P. B**, using enamide **1h** (102 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude titled product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 95:5 to 90:10 v/v) to afford **3h** as a colourless oil (82 mg, 57%). Mixture of rotamers ca. 6:4. R_f 0.2 (SiO_2, petroleum ether/EtOAc 85:15, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (br t, J = 7.7 Hz, 2 H, H$_{Ar}$), 7.21 (t, J = 7.4 Hz, 1 H, H$_{Ar}$), 7.12 (d, J = 7.7 Hz, 2 H, H$_{Ar}$), 6.94 (br s, 0.6 H, H-6 *maj.*), 6.87 (br s, 0.4 H, H-6 *min.*), 4.17 (m, 2 H, OCH_2CH$_3$ *maj.* + OCH_2CH$_3$ *min.*), 3.81–3.74 (m, 0.8 H, H-2 *min.*), 3.71–3.64 (m, 1.2 H, H-2 *maj.*), 3.03 (s, 2 H, H-1' *maj.* + H-1' *min.*), 2.15 (t, J = 6.1 Hz, 2 H, H-4 *maj.* + H-4 *min.*), 1.99–1.88 (m, 2 H, H-3 *maj.* + H-3 *min.*), 1.30–1.21 (m, 3 H, OCH$_2$CH_3 *maj.* + OCH$_2$CH_3 *min.*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.5 (C, C-2' *maj.*), 171.6 (C, C-2' *min.*), 152.0 (C, N*C*O *min.*), 151.5 (C, N*C*O *maj.*), 151.1 (C, C$_{Ar}$ *maj.*), 151.0 (C, C$_{Ar}$ *min.*), 129.3 (CH, CH$_{Ar}$ *maj.* + CH$_{Ar}$ *min.*), 125.5 (CH, CH$_{Ar}$ *maj.* + CH$_{Ar}$ *min.*), 123.5 (CH, C-6 *min.*), 123.2 (CH, C-6 *maj.*), 121.7 (CH, CH$_{Ar}$ *maj.*), 121.6 (CH, CH$_{Ar}$ *min.*), 113.4 (C, C-5 *min.*), 112.8 (C, C-5 *maj.*), 60.7 (CH$_2$, O*C*H$_2$CH$_3$ *maj.*), 60.6 (CH$_2$, O*C*H$_2$CH$_3$ *min.*), 42.4 (CH$_2$, C-2 *min.*), 41.9 (CH$_2$, C-2 *maj.*), 40.8 (CH$_2$, C-1' *maj.*), 40.7 (CH$_2$, C-1' *min.*), 25.3 (CH$_2$, C-4 *maj.*), 25.0 (CH$_2$, C-4 *min.*), 21.6 (CH$_2$, C-3 *min.*), 21.4 (CH$_2$, C-3 *maj.*), 14.2 (CH$_3$, OCH$_2$*C*H$_3$ *maj.* + OCH$_2$*C*H$_3$ *min.*) ppm. IR (neat): $\tilde{\nu}$ = 1716 (C=O), 1674 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{16}H_{20}NO_4$ [M + H]$^+$ 290.138685 found, 290.138613.

***tert*-Butyl 6-(2-ethoxy-2-oxoethyl)-2,3,4,5-tetrahydroazepine-1-carboxylate (3i)**. The titled compound was synthesized according to **G.P. B**, using enamide **1i** (198 mg, 1.0 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (420 mg, 2.0 mmol), DLP (478 mg, 1.2 mmol) and EtOAc (3.0 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 97:3 to 95:5 v/v) to give **3i** as a colourless oil (173 mg, 61%). Mixture of rotamers ca. 6:4. R_f 0.3 (SiO_2, petroleum ether/EtOAc 85:15, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.50 (br s, 0.4 H, H-7 *min.*), 6.37 (br s, 0.6 H, H-7 *maj.*), 4.14 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$ *maj.* + OCH_2CH$_3$ *min.*), 3.68–3.59 (br m, 2 H, H-2 *maj.* + H-2 *min.*), 2.97 (br s, 2 H, H-1' *maj.* + H-1' *min.*), 2.31–2.18 (br m, 2 H, H-5 *maj.* + H-5 *min.*), 1.84–1.67 (po, 4 H, H-3 *maj.* + H-4 *maj.* + H-3 *min.* + H-4 *min.*), 1.47 (s, 9 H, C(CH_3)$_3$ *maj.* + C(CH_3)$_3$ *min.*), 1.26 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3 *maj.* + OCH$_2$CH_3 *min.*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.1 (C, C-2' *maj.* + C-2' *min.*), 153.8 (C, N*C*O *maj.* + N*C*O *min.*), 129.9 (CH, C-7 *maj.* + C-7 *min.*), 121.0 (C, C-6 *maj.* + C-6 *min.*), 80.5 (C, *C*(CH$_3$)$_3$ *maj.* + *C*(CH$_3$)$_3$ *min.*), 60.7 (CH$_2$, O*C*H$_2$CH$_3$ *maj.* + CH$_2$, O*C*H$_2$CH$_3$ *min.*), 47.9 (CH$_2$, C-2 *min.*), 47.0 (CH$_2$, C-2 *maj.*), 42.9 (C, C-1' *maj.* + C-1' *min.*), 31.0 (CH$_2$, C-5 *maj.*), 30.7 (CH$_2$, C-5 *min.*), 28.2 (CH$_3$, C(*C*H$_3$)$_3$ *maj.* + C(*C*H$_3$)$_3$ *min.*), 28.1 (CH$_2$, C-3 *maj.* + C-3 *min.*), 24.3 (CH$_2$, C-4 *maj.* + C-4 *min.*), 14.4 (CH$_3$, OCH$_2$*C*H$_3$ *maj.* + OCH$_2$*C*H$_3$ *min.*) ppm. IR (neat): $\tilde{\nu}$ = 1762 (C=O), 1682 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{15}H_{26}NO_4$ [M + H]$^+$ 284.185635 found, 284.185824.

1-*O*-*tert*-Butyl 6-*O*-methyl 5-(2-ethoxy-2-oxoethyl)-3,4-dihydro-2*H*-pyridine-1,6-dicarboxylate (3j). The titled compound was synthesized according to **G.P. B**, using enamide **1j** (121 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 93:7 to 95:5 v/v) to give **3j** as a colourless oil (41 mg, 25%). R_f 0.17 (SiO_2, petroleum ether/EtOAc 85:15, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.14 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.75 (s, 3 H, OCH_3), 3.60–3.50 (m, 2 H, H-2), 3.32 (s, 2 H, H-1'), 2.23 (t, J = 6.7 Hz, 2 H, H-4), 1.86–1.79 (m, 2 H, H-3), 1.43 (s, 9 H, C(CH_3)$_3$), 1.24 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. IR (neat): $\tilde{\nu}$ = 1731 (C=O), 1702 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{16}H_{26}NO_6$ [M + H]$^+$ 328.175464 found, 328.176091.

(*rac*)-Phenyl 5-(2-ethoxy-2-oxoethyl)-3-hydroxy-3,4-dihydro-2*H*-pyridine-1-carboxylate (3k). Compound **3k** was prepared according to **G.P. B**, using enamide **1k** (110 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product

was purified by column chromatography (SiO_2, petroleum ether/EtOAc 85/15 to 75/25 v/v) to provide **3k** as a colourless oil (63 mg, 41%) and a mixture of rotamers (ca. 55:45). R_f 0.2 (SiO_2, petroleum ether/EtOAc 6:4, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.33 (m, 2 H, H_{Ar} *maj.* + H_{Ar} *min.*), 7.25–7.20 (m, 1 H, H_{Ar} *maj.* + H_{Ar} *min.*), 7.16–7.10 (m, 2 H, H_{Ar} *maj.* + H_{Ar} *min.*), 6.99 (br s, 0.55 H, H-6 *maj.*), 6.93 (br s, 0.45 H, H-6 *min.*), 4.27 (br s, 1 H, H-3 *maj.* + H-3 *min.*), 4.21–4.11 (m, 2 H, OCH_2CH_3 *maj.* + OCH_2CH_3 *min.*), 3.95 (dd, *J* = 12.7, 4.1 Hz, 0.45 H, H-2a *min.*), 3.81 (dd, *J* = 12.7, 4.8 Hz, 0.55 H, H-2a *maj.*), 3.63 (br d, *J* = 12.5 Hz, 0.45 H, H-2b *min.*), 3.56 (br d, *J* = 12.7 Hz, 0.55 H, H-2b *maj.*), 3.06 (s, 2 H, H-1' *maj.* + H-1' *min.*), 2.48 (br dd, *J* = 17.0, 4.0 Hz, 1 H, H-4a *maj.* + H-4a *min.*), 2.41 (br s, 0.45 H, OH *min.*), 2.30 (br s, 0.55 H, OH *maj.*), 2.22–2.13 (m, 1 H, H-4b *maj.* + H-4b *min.*), 1.28 (td, *J* = 7.2, 2.4 Hz, 3 H OCH_2CH_3 *maj.* + OCH_2CH_3 *min.*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.9 (C, C-2' *maj.*), 171.8 (C, C-2' *min.*), 152.7 (C, NCO *maj.*), 152.1 (C, NCO *min.*), 151.1 (C, C_{Ar} *maj.*), 151.0 (C, C_{Ar} *min.*), 129.5 (CH, CH_{Ar} *maj.* + CH_{Ar} *min.*), 125.8 (CH, CH_{Ar} *maj.* + CH_{Ar} *min.*), 123.9 (CH, C-6 *min.*), 123.4 (CH, C-6 *maj.*), 121.8 (CH, CH_{Ar} *maj.*), 121.5 (CH, CH_{Ar} *min.*), 109.2 (C, C-5 *maj.* + C-5 *min.*), 63.0 (CH, C-3 *maj.* + C-3 *min.*), 61.1 (CH_2, OCH_2CH_3 *maj.* + OCH_2CH_3 *min.*), 48.4 (CH_2, C-2 *min.*), 47.8 (CH_2, C-2 *maj.*), 40.3 (CH_2, C-1' *maj.*), 40.1 (CH_2, C-1' *min.*), 33.9 (CH_2, C-4 *maj.*), 33.7 (CH_2, C-4 *min.*), 14.3 (CH_3, OCH_2CH_3 *maj.* + OCH_2CH_3 *min.*) ppm. IR (neat): $\tilde{\nu}$ = 1716 (C=O), 1070 (C–OH), 1563 cm^{-1}. HRMS (ESI): m/z calcd. for $C_{16}H_{20}NO_5$ $[M + H]^+$ 306.133599 found, 306.133786.

1-*O*-Benzyl 4-*O*-ethyl (2*E*)-2-[(1-benzyl-2-oxo-3,4-dihydropyridin-5-yl)methylene]butanedioate (3l). Compound **3l** was synthesized according to **G.P. B**, using enamide **1l** (348 mg, 1.0 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (420 mg, 2.0 mmol), DLP (478 mg, 1.2 mmol) and EtOAc (3.0 mL). The crude product was obtained as a single diastereomer. It was purified by column chromatography (SiO_2, petroleum ether/EtOAc 85/15 to 75/25 v/v) to give **3l** as a colourless oil (152 mg, 35%). R_f 0.5 (SiO_2, petroleum ether/EtOAc 6:4, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.41–7.11 (po, 11 H, H_{Ar} + H-6'), 6.50 (s, 1 H, C-5'–C*H*), 5.18 (s, 2 H, OCH_2Ph), 4.71 (s, 2 H, NCH_2Ph), 4.08 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 3.46 (s, 2 H, H-3), 2.64 (s, 4 H, H-3' + H-4'), 1.18 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.3 (C, C-4), 168.8 (C, C-2'), 167.6 (C, C-1), 140.6 (CH, C-6'), 136.6 (C, C_{Ar}), 136.3 (CH, C-5'–*C*H), 136.2 (C, C_{Ar}), 129.0 (CH, CH_{Ar}), 128.6 (CH, CH_{Ar}), 128.3 (CH, CH_{Ar}), 128.2 (CH, CH_{Ar}), 128.0 (CH, CH_{Ar}), 127.9 (CH, CH_{Ar}), 120.6 (C, C-2), 115.9 (C, C-5'), 66.9 (CH_2, OCH_2Ph), 61.1 (CH_2, OCH_2CH_3), 49.6 (CH_2, NCH_2Ph), 33.8 (CH_2, C-3), 31.0 (CH_2, C-3'), 23.4 (CH_2, C-4'), 14.2 (CH_3, OCH_2CH_3) ppm. IR (neat): $\tilde{\nu}$ = 1732 (C=O), 1682 (C=O), 1619 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{26}H_{28}NO_5$ $[M + H]^+$ 434.196199 found, 434.196219.

Ethyl 2-(1-benzyl-2-oxo-3-pyridyl)acetate (3m). Compound **3m** was synthesized according to **G.P. B**, using pyridone **1n** (93 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 75/25 to 40/60 v/v) to give **3m** as a colourless oil (83 mg, 61%, (88% brsm)). R_f 0.4 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.36–7.26 (po, 6 H, H_{Ar} + H-6'), 7.22 (dd, *J* = 6.8, 2.0 Hz, 1 H, H-4'), 6.13 (t, *J* = 6.8 Hz, 1 H, H-5'), 5.15 (s, 2 H, NCH_2Ph), 4.18 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 3.56 (s, 2 H, H-2), 1.26 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.3 (C, C-1), 162.3 (C, C-2'), 138.4 (CH, C-6'), 136.5 (C, C_{Ar}), 136.2 (CH, C-4'), 129.0 (CH, CH_{Ar}), 128.3 (CH, CH_{Ar}), 128.1 (CH, CH_{Ar}), 126.9 (C, C-3'), 105.9 (CH, C-5'), 61.0 (CH_2, OCH_2CH_3), 52.4 (CH_2, NCH_2Ph), 36.5 (CH_2, C-2), 14.3 (CH_3, OCH_2CH_3) ppm. IR (neat): $\tilde{\nu}$ = 1730 (C=O), 1651 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{16}H_{18}NO_3$ $[M + H]^+$ 272.128120 found, 272.128007.

Ethyl 2-(1-benzyl-4-methoxy-6-methyl-2-oxo-3-pyridyl)acetate (3n). Compound **3n** was prepared according to **G.P. B**, using pyridone **1n** (150 mg, 0.654 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (271 mg, 1.30 mmol), DLP (311 mg, 0.78 mmol) and EtOAc (2.2 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 75/25 to 40/60 v/v) to give **3n** as a colourless oil (80 mg, 39% (49% brsm)). R_f 0.25 (SiO_2, petroleum ether/EtOAc 5:5, v/v). M.p. 94–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.32–7.22 (po, 3 H, H_{Ar}), 7.13 (d, *J* = 7.1 Hz, 2 H, H_{Ar}), 5.94 (s, 1 H, H-5'), 5.34 (s, 2 H, NCH_2Ph), 4.15 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 3.83 (s, 3 H, OCH_3), 3.61 (s, 2 H, H-2), 2.28 (s, 3 H, CH_3), 1.24 (d, *J* = 7.1 Hz, 3 H, OCH_2CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.9 (C, C-1), 164.1 (C, C-2' or C-4'), 163.9 (C, C-4' or C-2'), 146.0 (C, C-6')), 136.7 (C, C_{Ar}), 128.7 (CH, CH_{Ar}), 127.2 (CH, CH_{Ar}), 126.4 (CH, CH_{Ar}), 105.1 (C, C-3'), 95.5 (C, C-5'), 60.4 (CH_2, OCH_2CH_3), 55.7 (CH_3, OCH_3), 47.2 (CH_2, NCH_2Ph), 29.6 (CH_2, C-2), 21.0 (CH_3, CH_3), 14.2 (CH_3, OCH_2CH_3) ppm. IR (neat): $\tilde{\nu}$ = 2930 (C–H), 1732 (C=O), 1672 (C=O), 1644 (C=C), 1563 cm^{-1}. HRMS (ESI): m/z calcd. for $C_{18}H_{22}NO_4$ $[M + H]^+$ 316.154335 found, 316.154606.

Ethyl 4-ethoxycarbothioylsulfanyl-5-[5-(2-ethoxy-2-oxoethyl)-2-oxo-3,4-dihydropyridin-1-yl]pentanoate (3o). Compound **3o** was prepared according to **G.P. B**, using *N*-allyl enamide **1o** (69 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by passage though SiO_2–column chromatography (petroleum ether/EtOAc 85/15 to 75/25 v/v) and was obtained in moderate yield (86 mg, 40%). R_f 0.44 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.10 (s, 1 H, H-6'), 4.64 (d, *J* = 7.0 Hz, 2 H, $SCOCH_2CH_3$), 4.20–4.07 (po, 4 H, 2 × OCH_2CH_3), 4.02–3.93 (po, 2 H, H-4 + H-5a), 3.50–3.41 (m, 1 H, H-5b), 3.05 (s, 2 H, H-1"), 2.60–2.50 (po, 3 H, H-3' + H-2a), 2.48–2.40 (m, 1 H, H-2b), 2.40–2.30 (m, 2 H, H-4'), 2.15–2.04 (m, 1 H, H-3a), 1.89–1.76 (m, 1 H, H-3b), 1.43 (t, *J* = 7.1 Hz, 3 H, $SCOCH_2CH_3$), 1.26 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.26 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 213.4 (C, *C*S), 172.7 (C, C-1), 171.2 (C, C-2"), 169.3 (C, C-2'), 127.7 (CH, C-6'), 112.9 (C, C-5'), 70.4 (CH_2, $SCOCH_2CH_3$), 61.0 (CH_2, OCH_2CH_3), 60.7 (CH_2, OCH_2CH_3), 49.6 (CH, C-4), 48.9 (CH_2, C-5), 39.3 (CH_2, C-1"), 31.6 (CH_2, C-2), 31.2 (CH_2, C-3'), 26.2 (CH_2, C-3), 24.2 (CH_2, C-4'), 14.3 (CH_3, OCH_2CH_3), 14.3 (CH_3, OCH_2CH_3), 13.9 (CH_3, $SCOCH_2CH_3$) ppm. IR (neat): $\tilde{\nu}$ = 2923 (C–H), 1763

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(C=O), 1683 (C=O), 1663 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{19}H_{30}NO_6S_2$ $[M + H]^+$ 432.150906 found, 432.151189.

***Cis*- and *trans*-[4-benzyl-2-(2-ethoxy-2-oxoethyl)-5-oxo-morpholin-3-yl] dodecanoate (4p)**. Prepared following **G.P. B**, using enamide **1p** (189 mg, 1.0 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (420 mg, 2.0 mmol), DLP (478 mg, 1.2 mmol) and EtOAc (3.0 mL). The crude product was obtained as a mixture of diastereomers (*trans*:*cis* 55:45). It was purified by SiO_2–column chromatography (petroleum ether/EtOAc 90:10 to 85:15 v/v) to give 2,3-*cis*-**4p** (105 mg, 22%) and 2,3-*trans*-**4p** (124 mg, 26%).

2,3-*cis*-**4p**. Colourless oil. R_f 0.3 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.35–7.25 (po, 5 H, H_{Ar}), 6.05 (d, J = 1.2 Hz, 1 H, H-3), 4.94 (d, J = 14.8 Hz, 1 H, 0.5 × NCH_2Ph), 4.44 (d, J = 16.9 Hz, 1 H, H-6a), 4.30 (d, J = 16.9 Hz, 1 H, H-6b), 4.28–4.21 (po, 2 H, H-2 + 0.5 × NCH_2Ph), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 2.51 (dd, J = 16.4, 8.2 Hz, 1 H, H-1'a), 2.40 (dd, J = 16.4, 5.0 Hz, 1 H, H-1'b), 2.30–2.10 (m, 2 H, CH_2(CO)O), 1.60–1.49 (m, 2 H, CH_2CH$_2$(CO)O), 1.27 (s, 16 H, (CH_2)$_8$), 1.22 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3), 0.88 (t, J = 6.8 Hz, 3 H, (CH$_2$)$_8$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.4 (C, *C*O), 169.5 (C, *C*O), 167.0 (C, *C*O), 136.3 (C, C_{Ar}), 128.8 (CH, CH_{Ar}), 128.5 (CH, CH_{Ar}), 128.0 (CH, CH_{Ar}), 77.7 (CH, C-3), 72.6 (CH, C-2), 68.2 (CH$_2$, C-6), 61.3 (CH$_2$, O*C*H$_2$CH$_3$), 47.8 (CH$_2$, N*C*H$_2$Ph), 35.8 (CH$_2$, C-1'), 33.9 (CH$_2$, *C*H$_2$(CO)O), 32.0 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.6 (CH$_2$, (*C*H$_2$)$_8$), 29.4 (CH$_2$, (*C*H$_2$)$_8$), 29.3 (CH$_2$, (*C*H$_2$)$_8$), 29.2 (CH$_2$, (*C*H$_2$)$_8$), 24.7 (CH$_2$, *C*H$_2$CH$_2$(CO)O), 22.8 (CH$_2$, (*C*H$_2$)$_8$), 14.2 (CH$_3$, (CH$_2$)$_8$*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 2922 (C–H), 2852 (C–H), 1735 (C=O), 1672 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{27}H_{41}NNaO_6$ $[M + Na]^+$ 498.282609 found, 498.282760.

2,3-*trans*-**4p**. Colourless oil. R_f 0.4 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.38–7.21 (po, 5 H, H_{Ar}), 5.93 (d, J = 3.7 Hz, 1 H, H-3), 4.99 (d, J = 14.8 Hz, 1 H, 0.5 × NCH_2Ph), 4.36–4.27 (po, 2 H, H-6a + H-6b), 4.26–4.20 (po, 2 H, H-2 + 0.5 × NCH_2Ph), 4.15–4.07 (m, 2 H, OCH_2CH$_3$), 2.57 (dd, J = 15.7, 8.6 Hz, 1 H, H-1'a), 2.38 (dd, J = 15.7, 5.1 Hz, 1 H, H-1'b), 2.27–2.08 (m, 2 H, CH_2(CO)O), 1.59–1.49 (m, 2 H, CH_2CH$_2$(CO)O), 1.26 (br s, 16 H, (CH_2)$_8$), 1.22 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3), 0.88 (t, J = 6.8 Hz, 3 H, (CH$_2$)$_8$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.1 (C, *C*O), 169.4 (C, *C*O), 167.7 (C, *C*O), 136.2 (C, C_{Ar}), 128.9 (CH, CH_{Ar}), 128.5 (CH, CH_{Ar}), 128.0 (CH, CH_{Ar}), 79.2 (CH, C-3), 72.5 (CH, C-2), 65.0 (CH$_2$, C-6), 61.3 (CH$_2$, O*C*H$_2$CH$_3$), 47.2 (CH$_2$, N*C*H$_2$Ph), 35.4 (CH$_2$, C-1'), 34.1 (CH$_2$, *C*H$_2$(CO)O), 32.0 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.6 (CH$_2$, (*C*H$_2$)$_8$), 29.5 (CH$_2$, (*C*H$_2$)$_8$), 29.3 (CH$_2$, (*C*H$_2$)$_8$), 29.2 (CH$_2$, (*C*H$_2$)$_8$), 24.7 (CH$_2$, *C*H$_2$CH$_2$(CO)O), 22.8 (CH$_2$, (*C*H$_2$)$_8$), 14.2 (CH$_3$, (CH$_2$)$_8$*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$). IR (neat): $\tilde{\nu}$ = 2922 (C–H), 2852 (C–H), 1735 (C=O), 1672 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{27}H_{41}NNaO_6$ $[M + Na]^+$ 498.282609 found, 498.282760.

***Cis*- and *trans* [4-(3,4-dimethoxyphenethyl)-2-(2-ethoxy-2-oxoethyl)-5-oxo-morpholin-3-yl] dodecanoate (4q)**. Prepared following **G.P. B**, using enamide **1q** (158 mg, 0.60 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (253 mg, 1.2 mmol), DLP (287 mg, 0.72 mmol) and EtOAc (2.0 mL). The crude product was purified by passage though SiO_2–column chromatography (petroleum ether/EtOAc 85:15 to 75:25 v/v) and was obtained in moderate yield (184 mg, 56%) as a mixture of diastereomers (*trans*:*cis* 55:45).

2,3-*cis*-**4q**. R_f 0.27 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.84–6.71 (po, 3 H, H_{Ar}), 5.88 (d, J = 1.5 Hz, 1 H, H-3), 4.37–4.11 (po, 5 H, H-2 + H-6 + OCH_2CH$_3$), 4.02–3.93 (m, 1 H, 0.5 × NCH_2), 3.89 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.25–3.14 (m, 1 H, 0.5 × NCH_2), 2.97–2.86 (m, 1 H, 0.5 × CH_2Ph), 2.85–2.72 (m, 1 H, 0.5 × CH_2Ph), 2.52 (dd, J = 16.3, 7.8 Hz, 1 H, H-1'a), 2.41–2.35 (po, 3 H, H-1'b + CH_2(CO)O), 1.75–1.53 (m, 2 H, CH_2CH$_2$(CO)O), 1.37–1.15 (po, 19 H, OCH$_2$CH_3 + (CH_2)$_8$), 0.88 (t, J = 6.7 Hz, 3 H, (CH$_2$)$_8$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.6 (C, *C*O), 169.5 (C, *C*O), 167.0 (C, *C*O), 149.2 (C, C_{Ar}), 147.9 (C, C_{Ar}), 130.7 (C, C_{Ar}), 121.0 (CH, CH_{Ar}), 112.1 (CH, CH_{Ar}), 111.4 (CH, CH_{Ar}), 78.3 (CH, C-3), 72.4 (CH, C-2), 68.2 (CH, C-6), 61.3 (CH$_2$, O*C*H$_2$CH$_3$), 56.0 (CH$_3$, O*C*H$_3$), 56.0 (CH$_3$, O*C*H$_3$), 46.9 (CH$_2$, N*C*H$_2$), 35.9 (CH$_2$, C-1'), 34.4 (CH$_2$, *C*H$_2$(CO)O), 33.6 (CH$_2$, *C*H$_2$Ph), 32.0 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.6 (CH$_2$, (*C*H$_2$)$_8$), 29.5 (CH$_2$, (*C*H$_2$)$_8$), 29.3 (CH$_2$, (*C*H$_2$)$_8$), 29.3 (CH$_2$, (*C*H$_2$)$_8$), 25.0 (CH$_2$, *C*H$_2$CH$_2$(CO)O), 22.8 (CH$_2$, (*C*H$_2$)$_8$), 14.2 (CH$_3$, (CH$_2$)$_8$*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 2924 (C–H), 2864 (C–H), 1736 (C=O), 1680 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{30}H_{47}NNaO_8$ $[M + Na]^+$ 572.319388 found, 572.318643.

2,3-*trans*-**4q**. R_f 0.34 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.85–6.69 (po, 3 H, H_{Ar}), 5.90 (d, J = 3.7 Hz, 1 H, H-3), 4.25–4.11 (po, 5 H, H-2 + H-6 + OCH_2CH$_3$), 4.08–3.95 (m, 1 H, 0.5 × NCH_2), 3.88 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.23–3.12 (m, 1 H, 0.5 × NCH_2), 2.95–2.87 (m, 1 H, 0.5 × CH_2Ph), 2.83–2.73 (m, 1 H, 0.5 × CH_2Ph), 2.53 (dd, J = 15.7, 8.6 Hz, 1 H, H-1'a), 2.41–2.29 (po, 3 H, H-1'b + CH_2(CO)O), 1.68–1.59 (m, 2 H, CH_2CH$_2$(CO)O), 1.36–1.20 (po, 19 H, OCH$_2$CH_3 + (CH_2)$_8$), 0.88 (t, J = 6.7 Hz, 3 H, (CH$_2$)$_8$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.4 (C, *C*O), 169.5 (C, *C*O), 167.8 (C, *C*O), 149.2 (C, C_{Ar}), 147.9 (C, C_{Ar}), 130.6 (C, C_{Ar}), 121.0 (CH, CH_{Ar}), 112.0 (CH, CH_{Ar}), 111.4 (CH, CH_{Ar}), 80.1 (CH, C-3), 72.4 (CH, C-2), 64.9 (CH$_2$, C-6), 61.3 (CH$_2$, O*C*H$_2$CH$_3$), 56.0 (CH$_3$, O*C*H$_3$), 56.0 (CH$_3$, O*C*H$_3$), 45.6 (CH$_2$, N*C*H$_2$), 35.5 (CH$_2$, C-1'), 34.3 (CH$_2$, *C*H$_2$(CO)O), 33.4 (CH$_2$, *C*H$_2$Ph), 32.0 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.7 (CH$_2$, (*C*H$_2$)$_8$), 29.6 (CH$_2$, (*C*H$_2$)$_8$), 29.4 (CH$_2$, (*C*H$_2$)$_8$), 29.3 (CH$_2$, (*C*H$_2$)$_8$), 29.2 (CH$_2$, (*C*H$_2$)$_8$), 24.9 (CH$_2$, *C*H$_2$CH$_2$(CO)O), 22.8 (CH$_2$, (*C*H$_2$)$_8$), 14.2 (CH$_3$, (CH$_2$)$_8$*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 2924 (C–H), 2864 (C–H), 1736 (C=O), 1680 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{30}H_{47}NNaO_8$ $[M + Na]^+$ 572.319388 found, 572.318643.

Methyl (*E*)-4-(2-oxopyrrolidinyl)but-3-enoate (3ab). Compound **3ab** was prepared according to **G.P. B**, using enamide **1a** (56 mg, 0.50 mmol), methyl 2-ethoxycarbothioylsulfanylacetate **2b** (198 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by passage though SiO_2–column chromatography (petroleum ether/EtOAc 75/25 to 60/40 v/v) and was obtained as colourless oil (41 mg, 45%). R_f 0.1 (SiO_2, petroleum

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ether/EtOAc 6:4, v/v). M.p. < 40 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, J = 14.5 Hz, 1 H, H-4), 5.02 (dt, J = 14.5, 7.3 Hz, 1 H, H-3), 3.69 (s, 3 H, OCH_3), 3.54 (d, J = 7.2 Hz, 2 H, H-5'), 3.11 (dd, J = 7.3, 1.1 Hz, 2 H, H-2), 2.48 (t, J = 8.1 Hz, 2H, H-3'), 2.18–2.06 (m, 2 H, H-4') ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.3 (C, *C*O), 172.5 (C, *C*O), 126.8 (CH, C-4), 103.4 (CH, C-3), 52.1 (CH_3, O*C*H$_3$), 45.3 (CH_2, C-5'), 35.4 (CH_2, C-2), 31.3 (CH_2, C-3'), 17.6 (CH_2, C-4') ppm. IR (neat): $\tilde{\nu}$ = 2952 (C–H), 1724 (C=O), 1686 (C=O), 1661 (C=C) cm^{-1}. HRMS (ESI): m/z calcd. for $C_9H_{14}NO_3$ $[M + H]^+$ 184.096820 found, 184.096651.

(*E*)-4-(2-oxopyrrolidinyl)but-3-enenitrile (3ac). According to **G.P. B**, the reaction was performed, using *N*-vinylpyrrolidone **1a** (56 mg, 0.50 mmol), *O*-ethyl cyanomethylsulfanylmethanethioate **2c** (162 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by passage though SiO_2–column chromatography (petroleum ether/EtOAc 60/40 to 40/60 v/v) and was isolated as a beige solid (45 mg, 60%). R_f 0.03 (SiO_2, petroleum ether/EtOAc 6:4, v/v). M.p. 75–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (br d, J = 14.2 Hz, 1 H, H-4), 4.83 (dt, J = 14.2, 6.6 Hz, 1 H, H-3), 3.51 (t, J = 7.2 Hz, 2 H, H-5'), 3.15 (dd, J = 6.6, 1.2 Hz, 2 H, H-2), 2.50 (t, J = 8.2 Hz, 2 H, H-3'), 2.19–2.07 (m, 2 H, H-4') ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.5 (C, C-2'), 128.3 (CH, C-4), 117.9 (C, C-1), 98.9 (CH, C-3), 45.2 (CH_2, C-5'), 31.1 (CH_2, C-3'), 18.6 (CH_2, C-2 or C-4'), 17.6 (CH_2, C-4' or C-2) ppm. IR (neat): $\tilde{\nu}$ = 2954 (C–H), 2240 (C≡N), 1690 (C=O), 1652 (C=C) cm^{-1}. HRMS (ESI): m/z calcd. for $C_8H_{11}N_2O$ $[M + H]^+$ 151.086589 found, 151.086535.

Ethyl (*E*)-2-methyl-4-(2-oxopyrrolidinyl)but-3-enoate (3ad). Following **G.P. B**, the reaction was performed with enamide **1a** (56 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanylpropanoate **2d** (222 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by passage though SiO_2–column chromatography (petroleum ether/EtOAc 75/25 to 65/35 v/v) and was obtained as a colourless oil (79 mg, 72%). R_f 0.24 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 6.99 (d, J = 14.5 Hz, 1 H, H-4), 5.02 (dd, J = 14.5, 8.4 Hz, 1 H , H-3), 4.13 (qd, J = 7.1, 1.5 Hz, 2 H, OCH_2CH$_3$), 3.52 (t, J = 7.2 Hz, 2 H, H-5'), 3.22–3.11 (m, 1 H, H-2), 2.48 (t, J = 8.1 Hz, 2 H, H-3'), 2.14–2.05 (m, 2 H, H-4'), 1.30 (d, J = 7.1 Hz, 3 H, CH_3), 1.26 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 175.0 (C, *C*O), 173.3 (C, *C*O), 125.0 (CH, C-4), 111.0 (CH, C-3), 60.8 (CH_2, O*C*H$_2$CH$_3$), 45.3 (CH_2, C-5'), 41.0 (CH, C-2), 31.3 (CH_2, C-3'), 18.3 (CH_3), 17.6 (CH_2, C-4'), 14.3 (CH_3, OCH$_2$*C*H$_3$) ppm. HRMS (ESI): m/z calcd. for $C_{11}H_{18}NO_3$ $[M + H]^+$ 212.128120 found, 212.128116.

Ethyl (*E*)-2,2-dimethyl-4-(2-oxopyrrolidinyl)but-3-enoate (3ae). Following **G.P. B**, the reaction was performed with enamide **1a** (56 mg, 0.50 mmol), ethyl 2-ethoxycarbothioylsulfanyl-2-methyl-propanoate **2e** (236 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude residue was purified though SiO_2–column chromatography (petroleum ether/EtOAc 75/25 to 65/35 v/v) to afford compound **3ae** (42 mg, 39%). R_f 0.14 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 6.97 (d, J = 14.8 Hz, 1 H, H-4), 5.17 (d, J = 14.8 Hz, 1 H, H-3), 4.12 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.52 (t, J = 7.2 Hz, 2 H, H-5'), 2.49 (t, J = 8.1 Hz, 2 H, H-3'), 2.17–2.01 (m, 2 H, H-4'), 1.35 (s, 6 H, 2 × CH_3), 1.25 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.6 (C, *C*O), 173.3 (C, *C*O), 123.1 (CH, C-4), 116.9 (CH, C-3), 60.9 (CH_2, O*C*H$_2$CH$_3$), 45.3 (CH_2, C-5'), 43.0 (C, C-2), 31.4 (CH_2, C-3'), 25.6 (CH_3), 25.6 (CH_3), 17.5 (CH_2, C-4'), 14.2 (CH_3, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 2926 (C–H), 1731 (C=O), 1683 (C=O), 1515 (C=C) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{12}H_{20}NO_3$ $[M + H]^+$ 226.143770 found, 226.143487.

1-[(*E*)-2-(2-oxotetrahydrofuran-3-yl)vinyl]pyrrolidin-2-one (3af). The reaction was performed according to **G.P. B**, using *N*-vinylpyrrolidone **1a** (56 mg, 0.50 mmol), *O*-ethyl (2-oxotetrahydrofuran-3-yl)sulfanylmethanethioate **2f** (207 mg, 1.0 mmol), DLP (239 mg, 0.60 mmol) and EtOAc (1.5 mL). The crude product was purified by passage though SiO_2–column chromatography (petroleum ether/EtOAc 50/50 to 25/75 v/v) and was isolated as a colourless oil (70 mg, 71%). R_f 0.1 (SiO_2, petroleum ether/EtOAc 1:3, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 (d, J = 14.5 Hz, 1 H, H-3'), 5.01 (dd, J = 14.5, 6.9 Hz, 1 H, H-2'), 4.41 (td, J = 8.7, 2.4 Hz, 1 H, 0.5 × OCH_2), 4.24 (ddd, J = 10.3, 9.1, 6.3 Hz, 1 H, 0.5 × OCH_2), 3.59–3.46 (m, 2 H, H-5), 3.36–3.23 (m, 1 H, H-1'), 2.56–2.45 (po, 3 H, H-3 + 0.5 × OCH$_2$CH_2), 2.27–2.14 (m, 1 H, 0.5 × OCH$_2$CH_2), 2.16–2.08 (m, 2 H, H-4) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.8 (C, *C*O(O)), 173.4 (C, C-2), 127.0 (CH, C-3'), 105.9 (CH, C-2'), 66.7 (CH_2, O*C*H$_2$), 45.2 (CH_2, C-5), 40.9 (CH, C-1'), 31.2 (CH_2, C-3), 29.7 (CH_2, OCH$_2$*C*H$_2$), 17.6 (CH_2, C-4) ppm. IR (neat): $\tilde{\nu}$ = 2919 (C–H), 1762 (C=O), 1683 (C=O), 1661 (C=C) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{10}H_{14}NO_3$ $[M + H]^+$ 196.096820 found: 196.096790.

Ethyl 4-(2-oxopyrrolidinyl)-4-phenoxy-butanoate (5a). According to **G.P. C**, the reaction was performed with enamide **1a** (56 mg, 0.5 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1 mmol), DLP (239 mg, 0.6 mmol), phenol (470 mg, 5 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to give **5a** as a yellow oil (60 mg, 40%). R_f 0.27 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.26 (t, J = 7.8 Hz, 2 H, H_{Ar}), 6.99–6.94 (po, 3 H, H_{Ar}), 6.04 (t, J = 6.5 Hz, 1 H, H-4), 4.14 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.45–3.39 (m, 1H, H-5'a), 3.32–3.27 (m, 1 H, H-5'b), 2.55–2.25 (po, 5 H, H-3' + H-3a + H-2), 2.15–1.80 (po, 3 H, H-4' + H-3b), 1.26 (t, J = 6.5 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 175.6 (C, *C*O), 172.7 (C, *C*O), 155.9 (C, C_{Ar}), 129.8 (CH, CH_{Ar}), 121.9 (CH, CH_{Ar}), 115.7 (CH, CH_{Ar}), 78.3 (CH, C-4), 60.8 (CH_2, O*C*H$_2$CH$_3$), 41.3 (CH_2, C-5'), 31.3 (CH_2, C-2), 29.9 (CH_2, C-3'), 28.0 (CH_2, C-3), 18.1 (CH_2, C-4'), 14.2 (CH_3, OCH$_2$*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1740 (C=O), 1603 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{16}H_{21}NNaO_4$ $[M + Na]^+$ 314.135680 found, 314.136279.

Ethyl 4-ethoxy-4-(2-oxopyrrolidinyl)butanoate (5b). According to **G.P. C**, the reaction was performed with enamide **1a** (56 mg,

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0.5 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1 mmol), DLP (239 mg, 0.6 mmol), EtOH (300 µl, 5 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 70:30 to 60:40, v/v) to provide **5b** as a yellow oil (26 mg, 51%). R_f 0.2 (SiO_2, petroleum ether/EtOAc 5:5, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.30–5.21 (br t, J = 6.8 Hz, 1 H, H-4), 4.13 (q, J = 7.1 Hz, 2 H, (OC)OCH_2CH$_3$), 3.46–3.27 (po, 4 H, OCH_2CH$_3$ + H-5'), 2.48–2.37 (po, 3 H, H-2a + H-3'), 2.33–2.22 (m, 1 H, H-2b), 2.12–1.94 (po, 3 H, H-4' + H-3a), 1.88–1.77 (m, 1 H, H-3b), 1.24 (t, J = 7.1 Hz, 3 H, (OC)OCH$_2$CH_3), 1.17 (t, J = 7.0 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.0 (C, C-2'), 172.9 (C, C-1), 80.4 (CH, C-4), 63.6 (CH$_2$, OCH$_2$CH$_3$), 60.6 (CH$_2$, (OC)OCH$_2$CH$_3$) 41.2(CH$_2$, C-5'), 31.7 (CH$_2$, C-3'), 30.3 (CH$_2$, C-2), 28.1 (CH$_2$, C-3),18.4 (CH$_2$, C-4'), 15.0 (CH$_3$, (OC)OCH$_2$CH$_3$), 14.3 (CH$_3$, OCH$_2$CH$_3$) ppm. HRMS (ESI): m/z calcd. for $C_{12}H_{21}NNaO_4$ [M + Na]$^+$ 266.136279 found, 266.136185.

Methyl 4-(2-oxoazepanyl)-4-phenoxy-butanoate (5c). According to **G.P. C**, the reaction was performed with enamide **1b** (100 mg, 0.71 mmol), methyl 2-ethoxycarbothioylsulfanylacetate (277 mg, 1.42 mmol), DLP (342 mg, 0.86 mmol), phenol (671 mg, 7.2 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to provide **5c** as a yellow oil (120 mg, 55%). R_f 0.25 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.26 (t, J = 7.4 Hz, 2 H, H_{Ar}), 6.96 (t, J = 7.4 Hz, 1 H, H_{Ar}), 6.91 (br d, J = 8.1 Hz, 2 H, H_{Ar}), 6.46 (t, J = 6.7 Hz, 1 H, H-4), 3.68 (s, 3 H, OCH_3), 3.40–3.20 (m, 2 H, H-7'), 2.58–2.45 (po, 3 H, H-2a + H-3'), 2.45–2.35 (m, 1 H, H-2b), 2.30–2.20 (m, 1 H, H-3a), 2.06–1.97 (m, 1 H, H-3b), 1.70–1.50 (po, 5 H, H-4' + H-5' + H-6'a), 1.31–1.21 (m, 1 H, H-6'b) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.4 (C, CO), 173.3 (C, CO), 156.3 (C, C_{Ar}), 129.7 (CH, CH_{Ar}), 121.7 (CH, CH_{Ar}), 115.3 (CH, CH_{Ar}), 79.6 (CH, C-4), 51.9 (CH$_3$, OCH$_3$), 41.9 (CH$_2$, C-7'), 37.8 (CH$_2$, C-3'), 30.1 (CH$_2$, C-5'), 29.9 (CH$_2$, C-2), 28.9 (CH$_2$, C-6'), 28.6 (CH$_2$, C-3), 23.4 (CH$_2$, C-4') ppm. IR (neat): $\tilde{\nu}$ = 1739 (C=O), 1645 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{17}H_{24}NO_4$ [M + H]$^+$ 306.169896 found, 306.169985; m/z calcd. for $C_{17}H_{23}NNaO_4$ [M + Na]$^+$ 328.151955 found 328.151929.

Ethyl 4-ethoxy-4-(2-oxoazepanyl)butanoate (5d). According to **G.P. C**, the reaction was performed with enamide **1b** (100 mg, 0.71 mmol)), ethyl 2-ethoxycarbothioylsulfanylacetate (300 mg, 1.44 mmol), DLP (342 mg, 0.86 mmol), EtOH (41 µl, 7.2 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to afford **5d** as a yellow oil (121 mg, 63%). R_f 0.25 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.70–5.65 (dd, J = 7.5, 6.0 Hz, 1 H, H-4), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.55–3.15 (po, 4 H, OCH_2CH$_3$ + H-7'), 2.63–2.20 (po, 4 H, H-3' + H-2), 2.05–1.90 (m, 1 H, H-3a), 1.90–1.50 (po, 7 H, H-4' + H-5' + H-6'+H-3b), 1.25 (t, J = 7.1 Hz, 3 H, OCH_2CH$_3$), 1.15 (t, J = 7.0 Hz, 3 H, OCH_2CH$_3$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.0 (C, CO), 173.1 (C, CO), 81.4 (CH, C-4), 63.7 (CH$_2$, OCH$_2$CH$_3$), 60.6 (CH$_2$, OCH$_2$CH$_3$), 41.5 (CH$_2$, C-7'), 38.0 (CH$_2$, C-3'), 30.5 (CH$_2$, C-2), 30.3 (CH$_2$, C-5' or C-6'), 29.4 (CH$_2$, C-6' or C-5'), 28.6 (CH$_2$, C-3), 23.8 (CH$_2$, C-4'), 15.1 (CH$_3$, OCH$_2$CH$_3$), 14.3 (CH$_3$, OCH$_2$CH$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1735 (C=O), 1645 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{14}H_{26}NO_4$ [M + H]$^+$ 272.185396 found, 272.185635; m/z calcd. for $C_{14}H_{25}NNaO_4$ [M + Na]$^+$ 294.167609 found, 294.167579.

Methyl 4-ethoxy-4-(2-oxoazepanyl)butanoate (5e). According to **G.P. C**, the reaction was performed with enamide **1b** (100 mg, 0.71 mmol), methyl 2-ethoxycarbothioylsulfanylacetate (277 mg, 1.42 mmol), DLP (342 mg, 0.86 mmol), EtOH (400 µL, 7.2 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to provide **5e** as a yellow oil (100 mg, 54%). R_f 0.3 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.69–5.65 (m, 1 H, H-4), 3.66 (s, 3 H, OCH_3), 3.48–3.16 (po, 4 H, H-7' + OCH_2CH$_3$), 2.62–2.36 (m, 3 H, H-3' + H-2a), 2.36–2.21 (m, 1 H, H-2b), 2.04–1.90 (m, 1 H, H-3a), 1.99–1.48 (m, 7 H, H-4' + H-5' + H-6' + H-3b), 1.15 (t, J = 7.0, 1.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.0 (C, CO), 173.6 (C, CO), 82.4 (CH, C-4), 63.7 (CH$_2$, OCH$_2$CH$_3$), 51.8 (CH$_3$, OCH$_3$), 41.4 (CH$_2$, C-7'), 37.9 (CH$_2$, C-3'), 30.3 (CH$_2$, C-2), 30.3 (CH$_2$, C-6' or C-5') 29.4 (CH$_2$, C-5' or C-6'), 28.7 (CH$_2$, C-3), 23.8 (CH$_2$, C-4'), 15.1 (CH$_3$, OCH$_2$CH$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1727 (C=O), 1688 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{13}H_{24}NO_4$ [M + H]$^+$ 258.169826 found, 258.169985; m/z calcd. for $C_{13}H_{23}NaNO_4$ [M + Na]$^+$ 280.151725 found 280.151929.

Ethyl 4-cyano-4-(2-oxopyrrolidinyl)butanoate (5f). According to **G.P. C**, the reaction was performed with enamide **1a** (56 mg, 0.5 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (210 mg, 1 mmol), DLP (239 mg, 0.6 mmol), TMSCN (625 µl, 5 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to provide **5f** as a yellow oil (50 mg, 40%). R_f 0.3 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.18 (t, J = 8.0 Hz, 1 H, H-4), 4.16 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.54–3.37 (m, 2 H, H-5'), 2.46–2.25 (po, 4 H, H-2 + H-3'), 2.25–1.90 (po, 4 H, H-4' + H-3), 1.27 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.8 (C, CO), 171.3 (C, CO), 116.4 (C, CN), 61.9 (CH$_2$, OCH$_2$CH$_3$), 43.4 (CH, C-4), 42.1 (CH$_2$, C-5'), 30.2 (CH$_2$ C-3' or C-2), 29.9 (CH$_2$, C-2 or C-3'), 26.3 (CH$_2$, C-3), 17.7 (CH$_2$, C-4'), 14.1 (CH$_3$, OCH$_2$CH$_3$) ppm. IR (neat): $\tilde{\nu}$ = 1750 (C=O), 1640 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{11}H_{17}N_2O_3$ [M + H]$^+$ 225.123214 found, 225.123369; m/z calcd. for $C_{11}H_{16}N_2NaO_3$ [M + Na]$^+$ 247.12105210 found, 247.12105313.

Ethyl 4-cyano-4-(2-oxoazepan-1-yl)butanoate (5g). According to **G.P. C**, the reaction was performed with enamide **1b** (100 mg, 0.71 mmol)), ethyl 2-ethoxycarbothioylsulfanylacetate (300 mg, 1.44 mmol), DLP (342 mg, 0.86 mmol), TMSCN (900 µL, 7.2 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to give **5g** as a yellow oil (100 mg, 55%). R_f 0.2 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.66 (t, J = 8.0 Hz, 1 H, H-4), 4.16 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.47 (t, J = 9.1 Hz, 2 H, H-7'), 2.65–2.49 (m, 2 H, H-3'), 2.49–2.31

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(m, 2 H, H-2), 2.23–2.11 (m, 1 H, H-3a), 2.10–1.98 (m, 1 H, H-3b), 1.90–1.62 (po, 6 H, H-4' + H-5'+ H-6'), 1.27 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 175.6 (C, *C*O), 171.7 (C, *C*O), 117.7 (C, *C*N), 61.1 (CH_2, OCH_2CH_3), 46.1 (CH_2, C-7'), 45.0 (CH, C-4), 36.9 (CH_2, C-3'), 30.3 (CH_2, C-2), 29.9 (CH_2, C-6' or C-5'), 28.8 (CH_2, C-5' or C-6'), 27.0 (CH_2, C-3), 23.2 (CH_2, C-4'), 14.3 (CH_3, OCH_2CH_3) ppm. IR (neat): ṽ = 1739 (C=O), 1654 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{13}H_{21}N_2O_3$ $[M + H]^+$ 253.154708 found, 253.154669; m/z calcd. for $C_{13}H_{20}N_2NaO_3$ $[M + Na]^+$ 275.136713 found, 275.1376613.

Methyl 4-cyano-4-(2-oxoazepanyl)butanoate (5h). According to **G.P. C**, the reaction was performed with enamide **1b** (100 mg, 0.71 mmol), methyl 2-ethoxycarbothioylsulfanylacetate (277 mg, 1.42 mmol), DLP (342 mg, 0.86 mmol), TMSCN (900 µL, 7.2 mmol) and EtOAc (1.5 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to provide **5h** as a yellow oil (90 mg, 52%). R_f 0.25 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^1H NMR (400 MHz, $CDCl_3$): *δ* 5.63 (t, *J* = 7.9 Hz, 1 H, H-4), 3.70 (s, 3 H, OCH_3), 3.48 (m, 2 H, H-7'), 2.62–2.47 (m, 2 H, H-3'), 2.46–2.28 (m, 2 H, H-2), 2.21–2.10 (m, 1 H, H-3a), 2.09–1.97 (m, 1 H, H-3b), 1.81 (po, 6 H, H-4' + H-5' + H-6') ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 175.6 (C, *C*O), 172.1 (C, *C*O), 117.6 (C, *C*N), 52.1 (CH_3, OCH_3), 46.0 (CH_2, C-7'), 44.9 (CH, C-4), 36.8(CH_2, C-3'), 29.9 (CH_2, C-5' or C-2), 29.8 (CH_2, C-2 or C-5'), 28.7 (CH_2, C-6'), 27.0 (CH_2, C-3), 23.2 (CH_2, C-4') ppm. IR (neat): ṽ = 1735 (C=O), 1652 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{12}H_{19}N_2O_3$ $[M + H]^+$ 239.138817 found, 239.139019; m/z calcd. for $C_{12}H_{18}N_2NaO_3$ $[M + Na]^+$ 261.120838 found, 261.120963.

Ethyl 2-(9,10-dimethoxy-4-oxo-2,3,6,7-tetrahydrobenzo[*a*]quinolizinyl)acetate (5i). The titled compound was prepared according to **G.P. C**, using enamide **1r** (500 mg, 1.8 mmol), ethyl 2-ethoxycarbothioylsulfanylacetate (749mg, 3.6 mmol), DLP (861 mg, 2.16 mmol), EtOH (1.04 mL, 18.0 mmol) and EtOAc (3.6 mL). The crude product was purified by column chromatography (SiO_2, petroleum ether/EtOAc 80:20 to 70:30, v/v) to provide **5i** as a yellow oil (186 mg, 30%). R_f 0.6 (SiO_2, petroleum ether/EtOAc 8:2, v/v). ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.62 (s, 1 H, H_{Ar}), 6.68 (s, 1 H, H_{Ar}), 4.15 (q, *J* = 7.1, 2 H, OCH_2CH_3), 3.90–3.85 (t, 2 H, *J* = 6.2 Hz, H-6'), 3.95 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 3.37 (t, *J* = 6.4 Hz, 2 H, H-3'), 2.93 (t, *J* = 6.2 Hz, 2 H, H-7'), 2.75–2.66 (t, *J* = 6.4 Hz, 2 H, H-2'), 1.28–1.23 (m, 5 H, H-2 + OCH_2CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 175.6 (C, *C*O), 173.0 (C, *C*O), 165.7 (C, C=C), 153.6 (C, C^{IV}), 148.6 (C, C^{IV}), 134.9 (C, C^{IV}), 121.4 (C, C_{Ar}), 111.2 (CH, CH_{Ar}), 109.4 (CH, CH_{Ar}), 60.7 (CH_2, OCH_2CH_3), 56.3 (CH_3, OCH_3), 56.3 (CH_3, OCH_3), 42.4 (CH_2, C-6'), 34.7 (CH_2, C-3'), 29.7 (CH_2, C-2'), 29.7 (CH_2, C-2), 28.0 (CH_2, C-7'), 14.4 (CH_3, OCH_2CH_3) ppm. IR (neat): ṽ = 1726 (C=O), 1688 (C=O) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{17}H_{22}NO_6$ $[M - C_2H_5 + H_3O^+ + H]^+$ 336.144391 found, 336.1444164; m/z calcd. for $C_{17}H_{21}NNaO_6$ $[M - C_2H_5 + H_3O^+ + Na]^+$ 358.126130 found, 358.126108.

***Trans*- Ethyl 2-(9,10-dimethoxy-4-oxo-1,6,7,11b-tetrahydro-[1,4]oxazino[3,4-*a*]isoquinolinyl)acetate (5j).** An oven-dried round-bottomed flask under argon atmosphere was charged with compound **4q** (33 mg, 0.060 mmol, *cis*:*trans* 45:55), dry CH_2Cl_2 (1.0 mL) and a magnetic stir bar. Trifluoroacetic acid (10 µL, 0.14 mmol) was then added and the solution mixture was stirred at rt for 18 h. Next, the solution was diluted (CH_2Cl_2) and the organic phase was washed with aqueous $NaHCO_3$ and brine. The organic phase was dried ($MgSO_4$), filtered through a cotton plug and evaporated under reduced pressure. The crude product was obtained as a single diastereomer; purification of which (SiO_2, petroleum ether/EtOAc 85/15 to 75/25) afforded *trans*-**5j** as a white solid (11 mg, 52%). R_f 0.2 (SiO_2, petroleum ether/EtOAc 3:7, v/v). M.p. 110–112 °C. ^1H NMR (400 MHz, $CDCl_3$): *δ* 6.75 (s, 1 H, H_{Ar}), 6.70 (s, 1 H, H_{Ar}), 4.66 (d, *J* = 8.4 Hz, 1 H, H-11'b), 4.48–4.42 (m, 1 H, H-6'a), 4.38 (d, *J* = 16.7 Hz, 1 H, H-3'a), 4.25–4.16 (po, 4 H, H-1' + H-3'b+ OCH_2CH_3), 3.88 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.09–2.99 (m, 1 H, H-6'b), 2.95–2.87 (po, 2 H, H-7'a + H-2a), 2.79 (dd, *J* = 15.6, 7.9 Hz, 1 H, H-2b), 2.76–2.67 (dt, *J* = 15.8, 4.8 Hz, 1 H, H-7'b), 1.28 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 170.5 (C, *C*O), 166.7 (C, *C*O), 148.7 (C, C_{Ar}), 147.7 (C, C_{Ar}), 130.1 (C, C_{Ar}), 124.2 (C, C_{Ar}), 112.0 (CH, CH_{Ar}), 109.6 (CH, CH_{Ar}), 75.1 (CH, C-1'), 67.5 (CH_2, C-3'), 61.3 (CH_2, OCH_2CH_3), 58.2 (CH, C-11'b), 56.3 (CH_3, OCH_3), 56.1 (CH_3, OCH_3), 40.5 (CH_2, C-6'), 38.8 (CH_2, C-2), 28.9 (CH_2, C-7'), 14.3 (CH_3, OCH_2CH_3) ppm. IR (neat): ṽ = 2979 (C–H), 2939 (C–H), 1717 (C=O), 1636 (C=O), 1522 (C=C) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{18}H_{24}NO_6$ $[M + H]^+$ 350.159814 found, 350.160181.

Phenyl 5-(2-hydroxyethyl)-3,4-dihydro-2*H*-pyridine-1-carboxylate (6).
An oven-dried roundbottomed flask under argon atmosphere was charged with ester **3h** (55 mg, 0.19 mmol), anhydrous THF (1.5 mL) and a magnetic stir bar. The solution was cooled to 0 °C (ice-water bath) and $LiAlH_4$ (80 mg, 11 equiv) was added portionwise. The mixture was stirred at rt for 16 h and then heated under reflux for 3 h (reaction monitored by TLC using EP/EtOAc 5/5 as eluent). After cooling at 0 °C (ice-water bath), the mixture was then hydrolysed (H_2O, 0.5 mL), the suspension was filtered through a pad of celite® and the cake rinsed with CH_2Cl_2. Next, the aqueous phase was discarded, the organic layer was dried ($MgSO_4$), filtered through a cotton plug and evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel (petroleum ether/EtOAc: 50/50) to give **6** as a 6:4 mixture of rotamers (colourless oil, 31 mg, 66%). R_f 0.36 (SiO_2, petroleum ether/EtOAc 6:4, v/v). ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.37 (t, *J* = 7.9 Hz, 2 H, H_{Ar} *maj.* + H_{Ar} *min.*), 7.21 (t, *J* = 7.4 Hz, 1 H, H_{Ar} *maj.* + H_{Ar} *min.*), 7.13 (br s, 0.56 H, H_{Ar} *maj.* + H_{Ar} *min.*), 6.89 (br s, 0.6 H, H-6 *maj.*), 6.82 (br s, 0.4 H, H-6 *min.*), 3.85–3.60 (m, 4 H, H-2 *maj.* + H-2 *min.* + H-2' *maj.* + H-2' *min.*), 2.30 (t, *J* = 6.2 Hz, 2 H, H-1' *maj.* + H-1' *min.*), 2.09 (t, *J* = 6.0 Hz, 2 H, H-4 *maj.* + H-4 *min.*), 1.93 (p, *J* = 6.0 Hz, 2 H, H-3 *maj.* + H-3 *min.*), 1.55 (br s, 1 H, O*H maj.* + O*H min.*) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 152.2 (C, *CO min.*), 151.7 (C, *CO maj.*), 151.3 (C, C_{Ar} *maj.*), 151.2 (C, C_{Ar} *min.*), 129.5 (CH, CH_{Ar} *maj.* + CH_{Ar} *min.*), 125.6 (CH, CH_{Ar} *maj.* + CH_{Ar} *min.*), 122.3 (CH, C-6 *min.*), 122.0 (CH, C-6 *maj.*), 121.8 (CH, CH_{Ar} *maj.*) 121.8 (CH, CH_{Ar} *min.*), 116.7 (C, C-5 *min.*), 116.1 (C, C-

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5 *maj.*), 60.7 (CH_2, C-2' *min.*), 60.6 (CH_2, C-2' *maj.*), 42.7 (CH_2, C-2 *min.*), 42.2 (CH_2, C-2 *maj.*), 38.7 (CH_2, C-1' *maj.*), 38.6 (CH_2, C-1' *min.*), 25.0 (CH_2, C-4 *maj.*), 24.9 (CH_2, C-4 *min.*), 21.9 (CH_2, C-3 *min.*), 21.7 (CH_2, C-3 *maj.*) ppm. IR (neat): $\tilde{\nu}$ = 3112 (br, O–H), 2933 (C–H), 1715 (C=O), 1260 (O–H), 1043 (C–OH) cm^{-1}. HRMS (ESI): m/z calcd. for $C_{14}H_{18}NO_3$ $[M + H]^+$ 248.128120 found, 248.127933.

Conflicts of interest

There are no conflicts of interest to declare.

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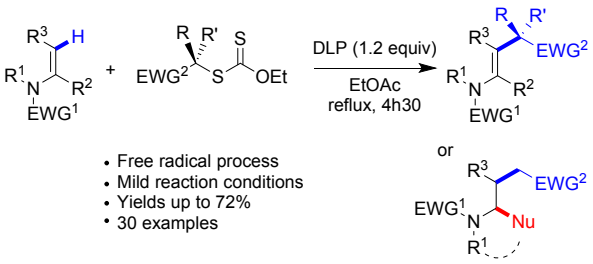

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