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Synthesis of substituted 3-arylpiperidines and 3-arylpyrrolidines by radical 1,4 and 1,2-aryl migrations

Alexandru Gheorghe, Béatrice Quiclet-Sire, Xavier Vila and Samir Z. Zard*

Laboratoire de Synthèse Organique associé au C. N. R. S., Département de Chimie, Ecole Polytechnique, F-91128 Palaiseau, France

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This paper is dedicated with respect to the memory of our friend, Dr Jean-Pierre Finet

Abstract—A route to 3-arylpiperidines and 3-arylpyrrolidines involving radical 1,4- and 1,2-aryl migrations has been explored. For the piperidines, the first route requires a xanthate addition to an *N*-allylarylsulfonamide, followed by acetylation and treatment with lauroyl peroxide to give the corresponding 1,4-aryl transfer product. This compound can be converted into the desired piperidine derivative following acidic hydrolysis. For the second approach to piperidines, addition of an α-keto xanthate to olefins of type **14** causes 1,2-aryl migration leading to an α,β-unsaturated ester, which can be converted into a piperidine by the action of ammonia or a primary amine and sodium cyanoborohydride. Substituted 3-arylpyrrolidines can be obtained by simply starting with an α-amido substituted xanthate.

1. Introduction

Aryl-substituted heterocycles, particularly arylpiperidines and arylpyrrolidines, have attracted the attention of medicinal chemists since the early 1980s because of their varied pharmacological activities, especially those related to the central nervous system. In the case of 3-arylpiperidines, a wide range of biological properties have been uncovered, perhaps the most important targeting is the dopaminergic neurotransmission. The main drug affecting this system is preclamol (Fig. 1), a selective D2 autoreceptor agonist, of which many analogues have been prepared in the search of new drug candidates against diseases such as psychosis, Parkinson's disease, drug addiction or depression.[1] Some members of this family are antagonists of neurokinin receptors (responsible for neurological inflammation, pain transmission and broncho constriction),[2] antagonists of the corticotropin-releasing factor (a peptide playing an important role in response to stress),[3] inhibitors of steroid 5α-reductase (potential therapeutic agents for the treatment of benign prostatic hyperplasia and some prostatic cancers),[4] or ligands for the σ-1 receptor, which modulates the synthesis and release of certain neurotransmitters, displays opioid analgesia, and is related to neuroprotective and anti-amnesic activity.[5]

Figure 1.

Substituted arylpyrrolidines are also important structures. They are sometimes part of the framework of diverse alkaloid families, or subunits in compounds with interesting antidepressant, antinociceptive and anticonvulsant activities.[6] Epibatidine (Fig. 1), a bicyclic 3-arylpyrrolidine alkaloid isolated from the skin of a poison frog, has proved to be a powerful non-opioid analgesic, with 200–500 times the potency of morphine, and one of the most powerful nicotinic agonists ever found.[7]

Despite their interesting and promising properties, only a few synthetic routes to 3-arylpiperidines have been described so far. The majority relies on pyridine-aryl cross-couplings mediated by transition metals,[8] and especially the Suzuki reaction,[9] or Heck cross-couplings with cyclic olefins, e.g., tetrahydropyridines,[10] as shown in Scheme 1. The substituted pyridine or tetrahydropyridine thus formed is then reduced to the corresponding piperidine. These methods are limited to molecules possessing functional groups compatible with Grignard reagents or palladium catalysts and reductive conditions, and are often constrained by a lack of starting materials with suitably diverse substituents.[11]

* Corresponding author. Tel.: +33 169334872; fax: +33 169333851; e-mail: zard@poly.polytechnique.fr

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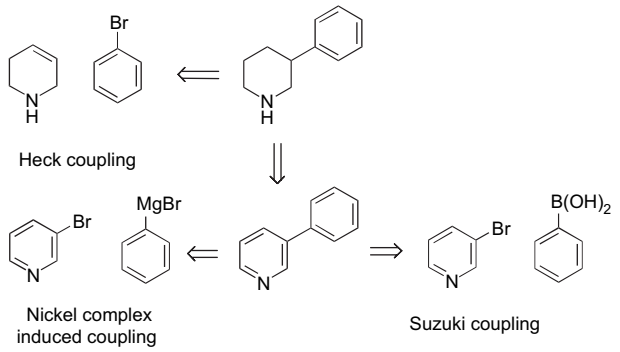
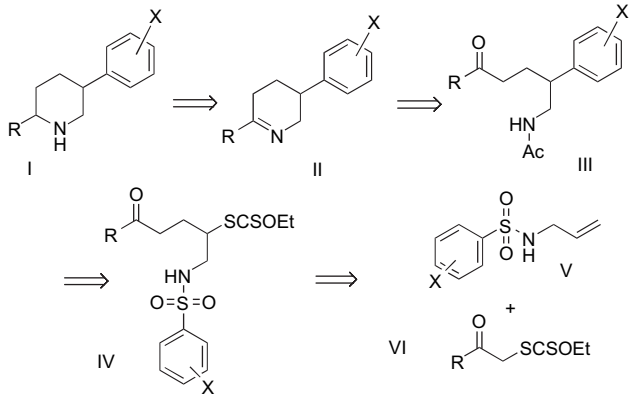


Scheme 1.

2. Results and discussion

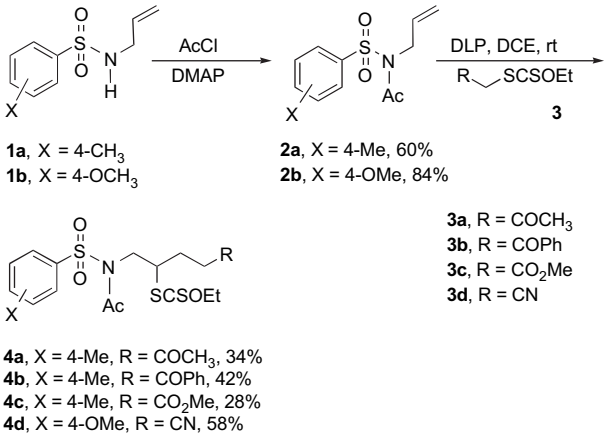
In continuation of a previous work involving a radical synthesis of 2-aryl[12] and 4-arylpiperidines,[13] we describe a new, straightforward synthesis of 6-substituted 3-arylpiperidines and their corresponding pyridines and piperidones obtained via a key step involving a radical 1,4-aryl transfer, as well as the synthesis of 2,6-disubstituted 3-arylpiperidines and 2,5-disubstituted 3-arylpyrrolidines via a radical sequence involving a neophyl rearrangement. The preliminary results of this study were recently disclosed in a communication.[14] We now give a full account of our work, aiming at exploring the scope of this new method, and its extension to the synthesis of fluorinated arylpiperidines and pyrrolidines.

The envisaged retrosynthetic pathway is depicted in Scheme 2 and is based on the rich radical chemistry of xanthates.[15] As outlined in Scheme 2, the desired piperidines **I** would be constructed by reduction of imines **II**, which in turn would be prepared by acid-mediated internal condensation of amidoketones **III**. The latter would be derived by a radical 1,4-aryl transfer of sulfonamides **IV**, obtained by a radical addition of xanthates **VI** onto conveniently substituted *N*-allylsulfonamides **V**.



Scheme 2.

Olefins **1** were easily made in good yield using the Schotten–Baumann procedure from substituted arenesulfonyl chlorides and allylamine (Scheme 3). They were further acetylated on the nitrogen using acetyl chloride into *N*-acetyl sulfonamides **2**, which were then subjected to the radical addition of xanthates **3a–d**. The expected xanthate transfer indeed took place, but the yield of the adducts was rather modest. Later, we found that the radical addition onto non-acetylated arylsulfonamides **1** resulted in much higher yields of the corresponding adducts **6**, in the 70–90% range in most of the cases (Scheme 4). A polarity mismatch between the radical derived from the xanthate and olefins **2a**,**b** could be the cause for the somewhat sluggish reaction and modest yields.



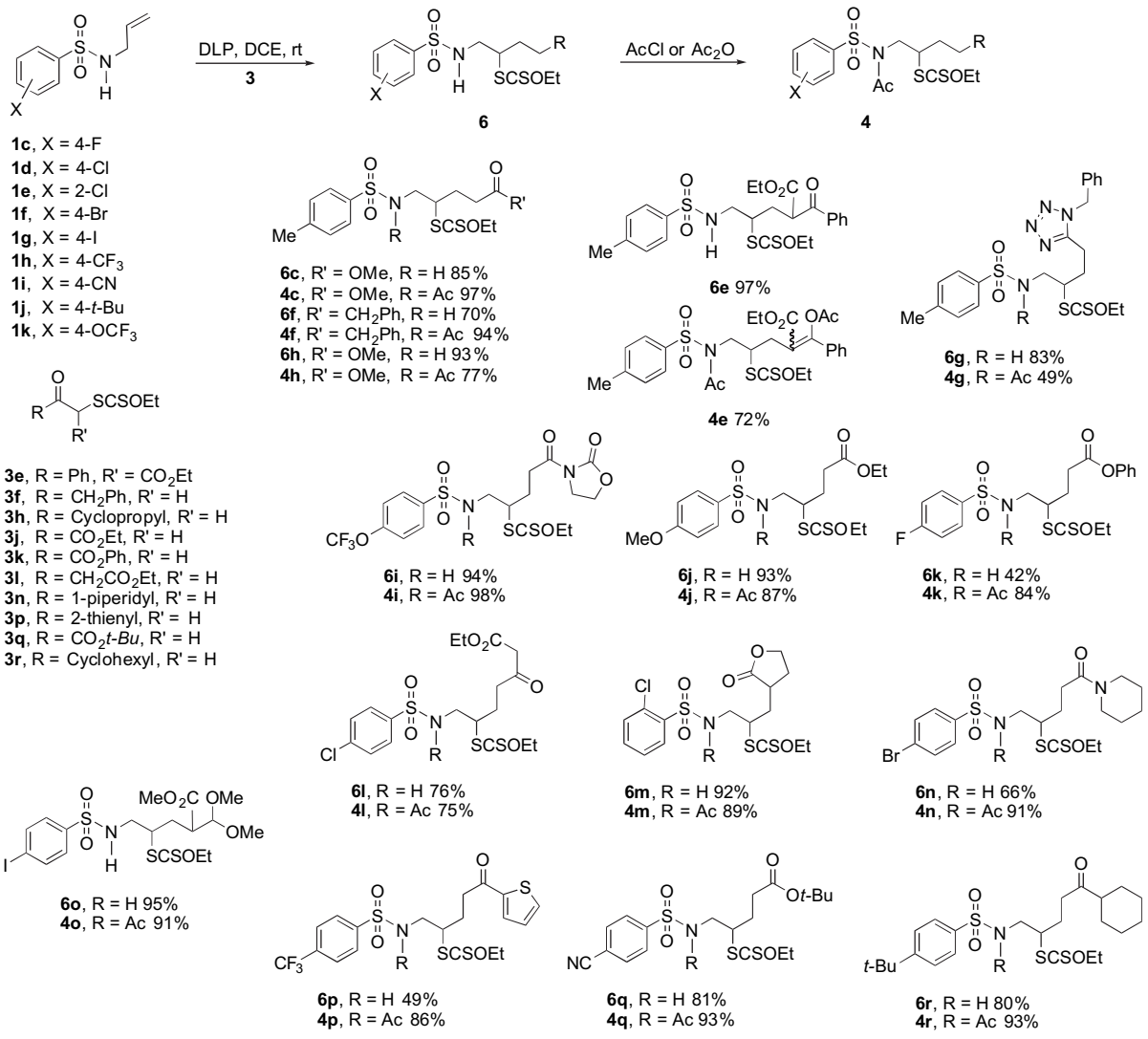
Scheme 3.

From that point onwards, as shown in Scheme 4, the radical addition was carried out using non-acetylated olefins, and acetylation of the nitrogen was performed on the adducts in the next step using acetyl chloride or acetic anhydride. The acetylation is needed to allow the ultimate formation of a reactive amidyl radical capable of abstracting a hydrogen from the solvent (see Scheme 5). In the absence of an acetyl or equivalent group, an unreactive aminyl radical would be formed causing the sequence to fail.

The radical addition was successful with a broad variety of xanthates, including alkyl, aryl, esters, heterocyclic xanthates, as summarised in Scheme 4. The acetylated sulfonamides **4** were converted into β-arylacetamides **5**, precursors of the desired 3-arylpiperidines, by a radical 1,4-aryl transfer promoted by lauroyl peroxide.

Since the discovery of the aryl migration almost a century ago,[16] many examples have appeared in the literature. The most extensively investigated is the 1,2-aryl migration (neophyl rearrangement),[17] but 1,4- and 1,5-aryl migrations have also been observed and studied.[18] Aryl migrations can take place between two carbon atoms, but also between a carbon and a heteroatom, or between two heteroatoms. In our case, the aryl transfer would be between the sulfur of the sulfonamide and a carbon. In this type of rearrangement, first described by Speckamp in 1972,[19] it is possible to transfer both electron-rich and electron-poor arenes. In the examples reported, the yields are sometimes low because of premature reduction prior to migration and/or competing *ortho*-cyclisation to the aromatic ring.[20]

The proposed mechanism for our sequence is displayed in Scheme 5. Treatment of sulfonamide **4** with lauroyl peroxide (DLP) generates radical **I**, which adds to the aryl ring in a 5-*exo* fashion leading to radical **II**. Fragmentation of the latter



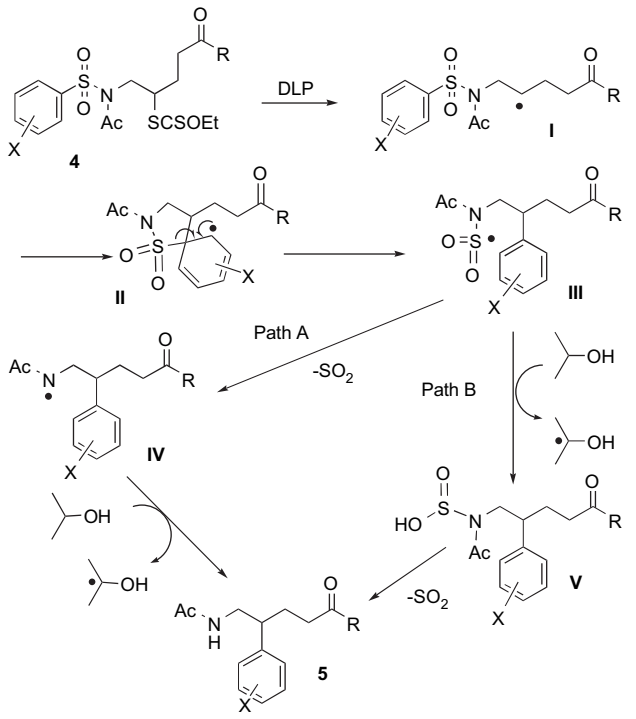
Scheme 4.

furnishes sulfonyl radical **III** and regenerates the aromaticity of the aryl ring. Even though isopropanol is capable of hydrogen atom transfer to radical **I**, thus prematurely reducing it and stopping the desired transformation, this process is relatively slow and does not compete efficiently with the *ipso* substitution. From radical **III**, two different paths can lead to the final product **5**. In path A, extrusion of sulfur dioxide gives a highly reactive electrophilic amidyl radical **IV**, which is rapidly reduced by the isopropanol. Hence the need for the acetylation step: in the absence of the acetyl group, the sequence would have furnished a much less reactive aminyl radical. The ketyl radical, arising from the isopropanol, is oxidised into acetone by the peroxide, which must therefore be used in stoichiometric amounts. In path B, hydrogen abstraction takes place at the level of radical **III**. Such amidosulfonyl radicals are electrophilic and loss of sulfur dioxide may be too slow to compete with the hydrogen abstraction.[21] Either or both pathways may be operating but this has no consequence as far as the preparative aspects are concerned.

We first tried to establish the best conditions to carry out the radical transfer, and also to ascertain that isopropanol was indeed the best hydrogen atom donating solvent. Thus to a solution of xanthate **4a** (Table 1, entry 1) in toluene was added 15% DLP every 90 min, until disappearance of the starting material. The transfer product **5a** was obtained in a 22% yield, much lower than the yield (66%) observed when the reaction was carried out in *i*-PrOH. Another assay using isopropyl acetate as a solvent instead of isopropanol in the case of compound **4c** again showed the superiority of the latter (38% vs 71% yield, respectively; entries 3 and 4).

For some derivatives, the same conditions using isopropanol were not so effective. For instance, compound **4m**, submitted to the same reaction conditions, produced rearranged amide in only 25% yield (entry 5). By diluting the reaction medium 10-fold and increasing the amount of DLP to ensure complete consumption of the starting material, the yield of amide **5m** could be increased to 50% yield (entry 6).

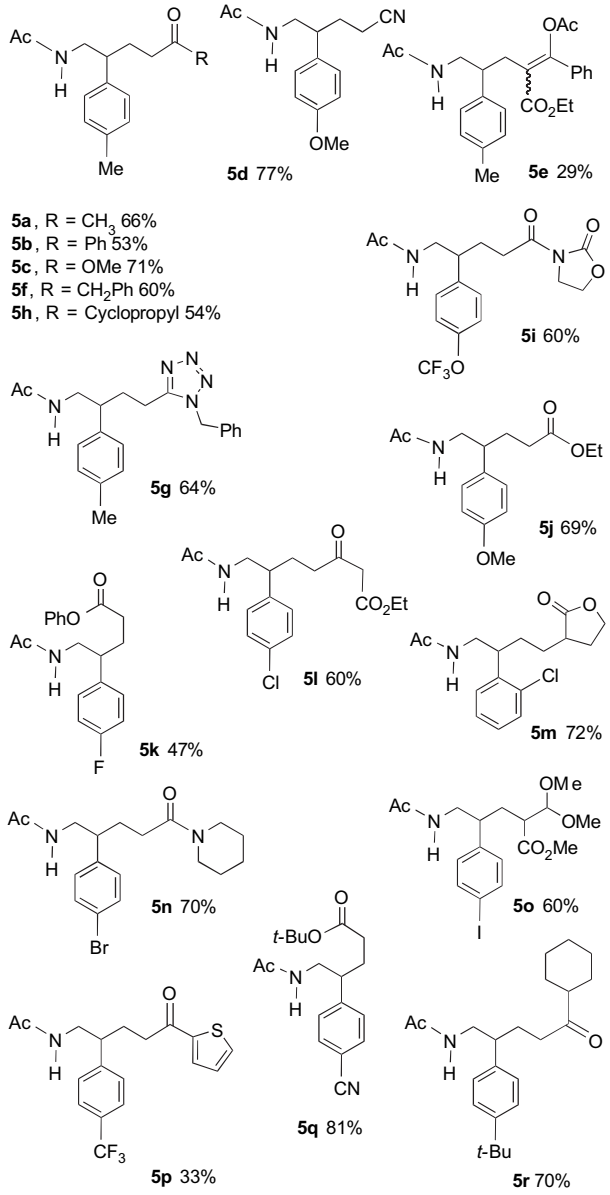
Similarly, applying the standard transfer conditions to compound **4j** resulted in a 34% yield of migration product **5j** (entry 7). Using a greater excess of DLP improved the yield to 45% (entry 8). Other solvents (entries 9–12) such as cyclohexane, *sec*-butanol or isopropyl ether were either less effective or failed completely. The best results were obtained



Scheme 5.

using a 1:1 mixture of 1,2-dichloroethane and isopropanol and a higher dilution (entries 13 and 14). These last conditions were used in cases were isopropanol alone was not sufficiently effective.

The best results for the radical aryl migration are summarised in Scheme 6. As shown, the nature of substituent X on the aromatic ring does not seem to affect greatly the course of the reaction. The yields were similar for both series of electron donating and electron withdrawing substituents. As for the R motif on the xanthate, many groups appear to be tolerated: ketones, esters, lactones, nitriles or amides. In the case of compounds **5b** (R=PhCO–) and **5p** (R=2-thiophenylCO–) the yields (53% and 33%, respectively) were lowered by the competing *ortho*-cyclisation onto the aromatic ring to form a tetralone. In compound **5e**, the presence of a double bond appears to be a source of complications and the yield was consequently rather poor (29%). One possible side reaction is a *5-exo*-ring closure onto the double bond by the intermediate amidyl radical leading to an unreactive tertiary benzylic radical.



Scheme 6.

Table 1. Conditions used to optimise the aryl transfer

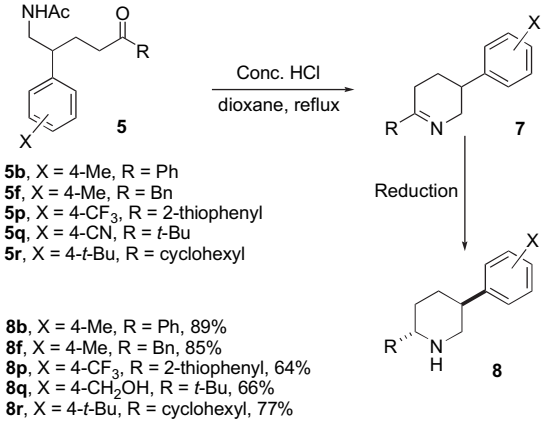
Entry	Substrate **4**	Solvent	Concentration (M)	DLP (equiv)	Product (yield)
1	**4a**	Toluene	0.25	1.00	**5a** (22%)
2	**4a**	*i*-PrOH	0.25	1.50	**5a** (66%)
3	**4c**	Isopropyl acetate	0.25	1.05	**5c** (38%)
4	**4c**	*i*-PrOH	0.25	1.35	**5c** (71%)
5	**4m**	*i*-PrOH	0.25	1.20	**5m** (25%), **4m** (30%)
6	**4m**	*i*-PrOH	0.025	2.20	**5m** (50%)
7	**4j**	*i*-PrOH	0.25	1.20	**5j** (34%)
8	**4j**	*i*-PrOH	0.25	2.70	**5j** (45%)
9	**4j**	Cyclohexane	0.25	0.70	**5j** (27%), **4j** (22%)
10	**4j**	*i*-PrOH/cyclohexane 1:1	0.25	1.25	**5j** (32%), **4j** (20%)
11	**4j**	*s*-BuOH	0.25	1.50	**5j** (0%)
12	**4j**	*i*-Pr_2O	0.03	1.50	**5j** (0%)
13	**4j**	*i*-PrOH/DCE 1:1	0.03	1.50	**5j** (43%), **4j** (34%)
14	**4j**	*i*-PrOH/DCE 1:1	0.02	2.00	**5j** (60%)

Table 2. Influence of the protecting group (PG)

6	PG	4	Transfer product (yield)
6c	Ac	**4c**	**5c** (71%)
6c	CO_2Me	**4c2**	**5c2** (34%), reduced **4c2** (36%)
6c	*t*-Boc	**4c3**	**5c3** (37%), reduced **4c3** (43%)
6j	$COCF_3$	**4j2**	**5j2** (40%), **6j** (15%), reduced **6j** (11%)

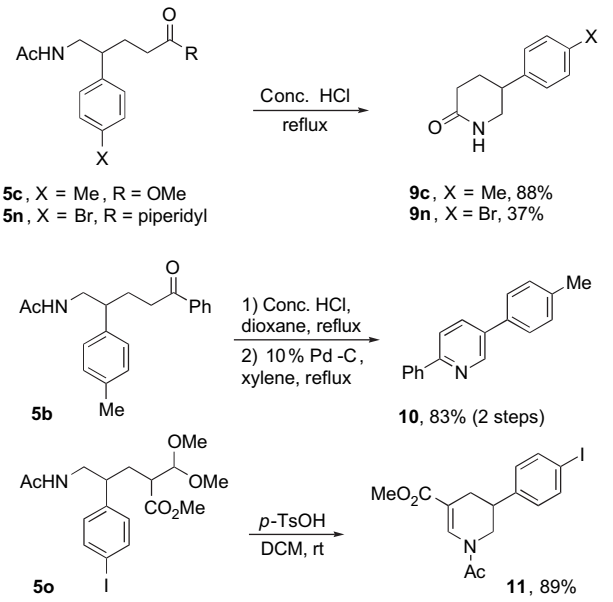
We also examined the aryl migration in the case of sulfonamides **4** with other acyl groups besides acetyl, but the results were less satisfactory. For reasons that are not yet clear, the acetyl initially chosen proved to be the best group. With carbamoyl groups, such as *tert*-butoxycarbonyl and methoxycarbonyl, or trifluoroacetyl, significant amounts of reduced starting material were observed (Table 2).

Once the transfer products were in hand, hydrolysis of the acetamide was carried out under acidic conditions. This induced concomitant cyclisation to the imine or to the lactam, depending on whether a ketone or an ester was present. Thus, as shown in Scheme 7, treatment of amides **5** with concentrated HCl in dioxane at reflux temperature afforded the intermediate imines **7**, which were generally not purified but reduced with $NaBH_3CN$ to afford the desired amines in good yield and as single diastereoisomers. In the case of amide **5q**, the acid treatment also resulted in the hydrolysis of the nitrile group to the corresponding carboxylic acid. The last reduction step was therefore performed with $LiAlH_4$, in order to reduce the carboxylic acid to the alcohol and make the purification easier.



Scheme 7.

Depending on the nature of the R substituent, it is possible to obtain other piperidine derivatives. As depicted in Scheme 8, acid hydrolysis of amide-ester **5c** yielded lactam **9** in good yield and cyclisation of double amide **5n** afforded piperidone **9n** in moderate yield. Pyridines can also be obtained if, in the last step, the imine is subjected to oxidising conditions. In that case, amide **5b** was cleaved by acid hydrolysis, and the intermediate imine **7b** was heated with palladium in xylene at reflux under air to furnish pyridine **10** in good yield. Acid hydrolysis of dimethyl acetal **5o** and acid-mediated cyclisation yielded *N*-acyl piperidine **11**, which possesses a different substitution pattern and can be viewed as a nicotinic acid derivative. The presence of the double bond and the iodine atom allows numerous further transformations.

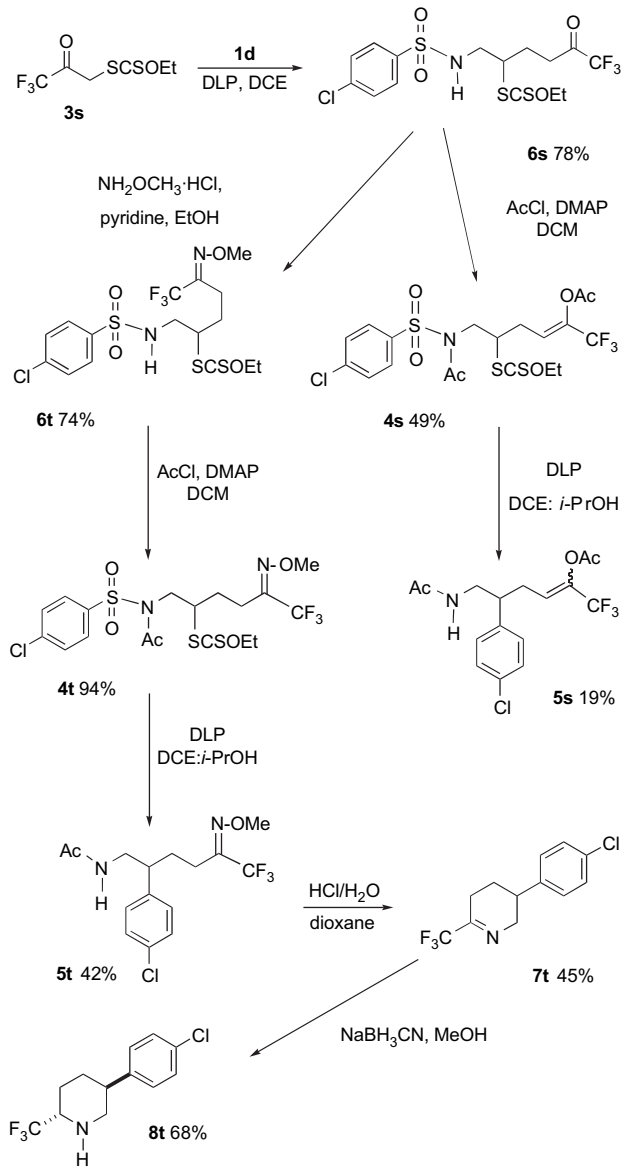


Scheme 8.

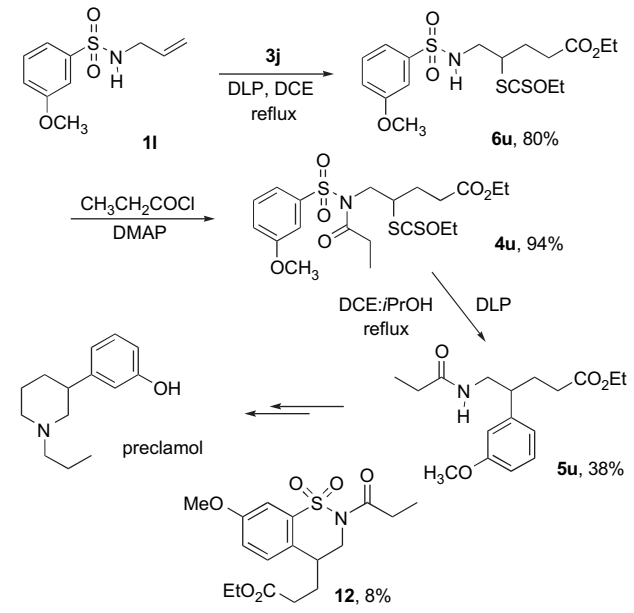
We were also interested in applying the same approach to access fluorinated piperidines, as the introduction of fluorinated groups in organic compounds is well known to modify significantly the chemical, physical and, most importantly, the biological properties, largely as a result of the strong electronegativity of the fluorine atom and the enhanced lipophilic character of fluorine containing derivatives.[22] The introduction of fluorinated motifs into heterocyclic structures is seldom straightforward and relies generally on two strategies, namely the direct fluorination of an existing heterocyclic ring[23] or the construction of the heterocyclic ring using fluorinated synthons.[24,25]

Syntheses of trifluoromethyl piperidines, for instance, are scarce in the literature due to the difficulty of introducing the trifluoromethyl group.[26] By using xanthate **3s**, derived from commercially available 3-bromo-1,1,1-trifluoroacetone, it should be possible to introduce a trifluoromethyl group into the final piperidine structure as indicated in Scheme 9. Radical addition of xanthate **3s** to sulfonamide **1d** afforded indeed the corresponding adduct **6s** in good yield. However, attempts to protect the sulfonamide failed, due to the competing enol acetate formation. Even lowering the amount of acetyl chloride to 1 equiv resulted in mixtures of mono- and diacetylated products along with starting material. Having encountered the previous example (Scheme 6, compound **5e**) where the radical transfer of a diacetylated product proceeded in low yield, we considered protecting the carbonyl group prior to acetylation of the sulfonamide nitrogen. Initial attempts to form the acetal failed, so the carbonyl was eventually protected as *O*-methyloxime **6t**. Acetylation of this compound was accomplished in good yield, but then the radical transfer proceeded in only a moderate yield of 42%. Finally, cyclisation under strong acidic conditions followed by imine reduction yielded the desired 2-trifluoromethyl-5-arylpiperidine in good yield.

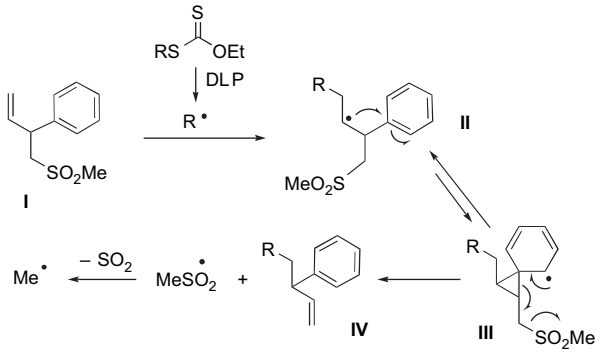
Our methodology could in principle be adapted to the synthesis of preclamol (Fig. 1), starting from the appropriate



Scheme 9.



Scheme 10.



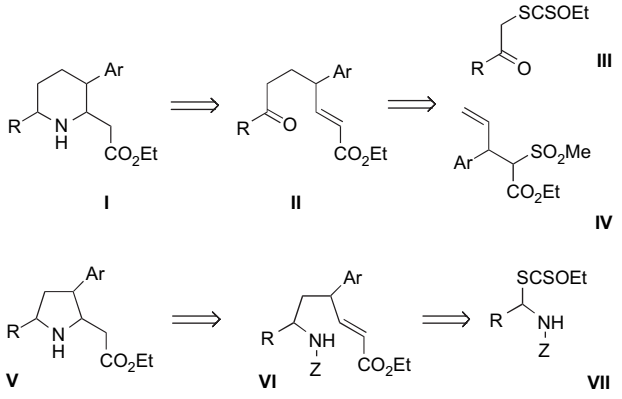
Scheme 11.

meta-substituted aromatic ring (Scheme 10). Thus, addition of xanthate **3j** to sulfonamide **1l** afforded adduct **6u** smoothly. Protection with propionyl chloride (preclamol features an *N*-propyl substituent) was conducted in good yield. Surprisingly, the radical migration occurred in low yield and the product of *ortho*-cyclisation, which had not been observed before when the aromatic ring was substituted in the *ortho*- or *para*-position, was produced concomitantly. In principle, compound **5u** could be converted into preclamol by reduction of the amide and ester groups and ring closure through a Mitsunobu-type reaction, but this has not yet been accomplished.

In parallel to these studies, we examined another equally powerful route to 3-aryl piperidine derivatives hinging on a 1,2-aryl migration, which we recently described.[27] As outlined in Scheme 11, radical addition of a xanthate onto an alkene such as **I** leads directly to the α,β-unsaturated ester by means of a 1,2-aryl shift, which is made irreversible by the β-elimination of a methylsulfonyl radical. The latter extrudes sulfur dioxide to give a methyl radical, an entity that is sufficiently reactive to propagate the chain. The neophyl 1,2-aryl shift is a relatively slow process and has therefore found only rare applications in organic synthesis.[28] The decisive advantage of the xanthate transfer process is that the intermediate radicals have comparatively long lifetimes, because the exchange of a xanthate group is a reversible process. Thus, even though radical **II** can (and does) react with the various xanthates in the medium, it is only irreversibly consumed through the neophyl shift, which now has ample time to take place. The now efficient aryl shift can be applied to the synthesis of nitrogenated heterocycles provided there is a correct functionalisation in both the R and the alkenyl extremities of compound **IV** in order to effect ring closure.

The retrosynthetic analysis for the formation of aryl-substituted heterocycles, including five-membered heterocycles, depending on the nature of the starting xanthate, is displayed in Scheme 12. The radical addition to olefin **IV** leads to α,β-unsaturated esters **II** and **VI**, which can undergo classical conjugate addition, through reaction with a suitable amine in the first case and by basic treatment in the second,

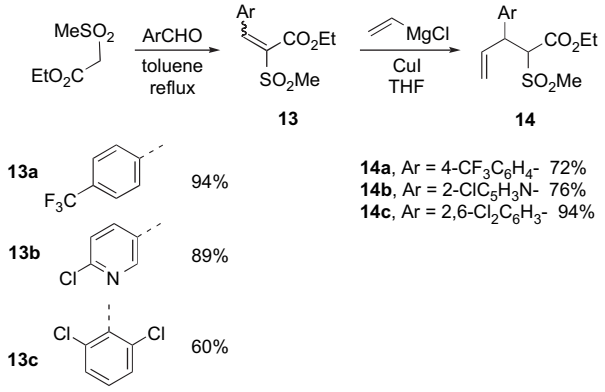
to furnish the desired heterocycles. Indeed, this approach affords heterocycles substituted not only in position 3, but also in the 2,6 positions in the case of piperidines and in the 2,5 positions in the case of pyrrolidines.[29]



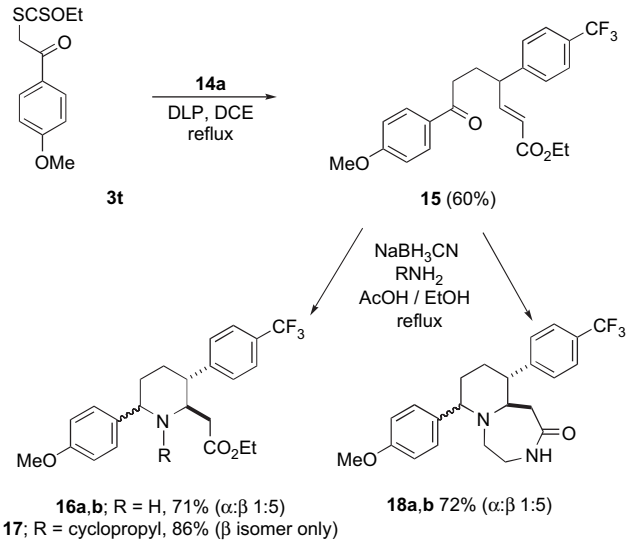
Scheme 12.

Our synthetic approach requires olefins of structure **14**. These were very easily prepared by conjugate addition of vinylmagnesium cuprate onto α,β-unsaturated esters **13** (Scheme 13), themselves readily accessible by a Knoevenagel condensation between ethyl methanesulfonylacetate and the corresponding arenecarboxaldehyde. For the synthesis of 3-aryl-2,6-disubstituted piperidines, reaction between xanthate **3t** and olefin **14a** in the presence of DLP in refluxing DCE resulted in the obtention of ketone **15** in 60% yield (Scheme 14). Upon treatment with different amines and sodium cyanoborohydride, this compound furnished the desired heterocycles in good yield and as a mixture of diastereomers in some cases. With ethylenediamine, bicyclo derivative **18** was obtained in good yield and as a mixture of two diastereomers. The use of cyanoborohydride is to reduce the intermediate enamine, but this operation can be omitted if more oxidised (ultimately pyridines) derivatives are desired. Thus, modification of the xanthate, the olefin and the amine components can lead expeditiously to a vast number of aryl-substituted piperidines and related derivatives that would be otherwise laborious to obtain.

Reaction of olefin **14b** with xanthate **3s** furnished adducts **19a**,**b** as a separable 1.3:1 mixture of diastereoisomers in 57% yield (Scheme 15). The ring closure was induced with *tert*-butoxide in THF to give pyrrolidines **21a**,**b** in



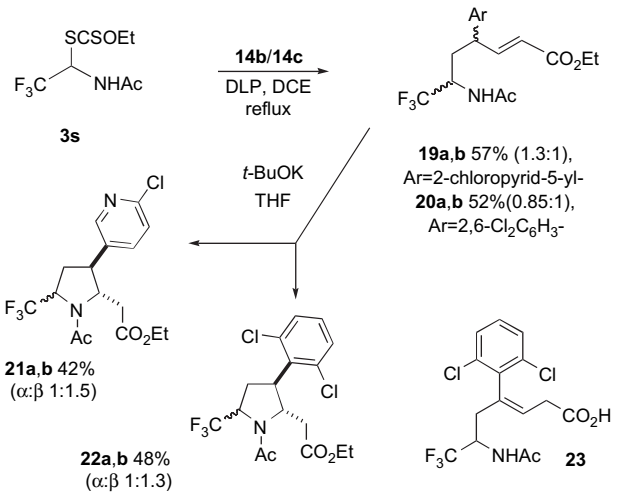
Scheme 13.



Scheme 14.

42% and could be performed with each diastereoisomer separately, thus allowing the determination of the relative configuration of each of the precursors **19a** and **19b**. Interestingly, pyrrolidines **21a**,**b** may be viewed as open-chain analogues of epibatidine and underscore the possibility of introducing heteroaromatic rings through the neophylic rearrangement in addition to a trifluoromethyl group initially present in xanthate **3s**.[30] In the case of olefin **14c**, the radical addition with xanthate **3s** proceeded in slightly lower yield (43%) and the esters **20** were obtained as a 1.2:1 mixture of two diastereomers, which could also be separated by column chromatography. Again the *t*-BuOK mediated cyclisation afforded the desired pyrrolidines **22a**,**b** as a 1:1.3 mixture of two diastereomers in 48% yield, which in this case could not be separated. Nevertheless, from 2D NMR and NOESY experiments, the relative configuration of both diastereomers could be easily deduced. We noted when the cyclisation was attempted with each diastereomer **20** separately, that a mixture of both diastereoisomers **22** was formed in each case, indicating that during the course of the cyclisation, epimerisation at the carbon γ- to the ester group had occurred. This was confirmed by the detection of small amounts of β,γ-unsaturated acid **23**, which can only arise from the extended enolate of the unsaturated ester group.

The literature routes to 3-arylpiperidines have been briefly discussed in Section 1. As for substituted 3-arylpyrrolidines, their synthesis has hitherto relied mostly on 1,3-dipolar cycloadditions between azomethine ylides and monosubstituted olefins conjugated to an aromatic ring.[31] Other strategies exploiting intramolecular cyclisations have also been reported.[32] The present two radical based approaches to highly substituted 3-arylpiperidines and 3-arylpyrrolidines complement previous routes. They are flexible, employ cheap and readily available starting materials, and bring to the fore the synthetic potential of the radical 1,4- and 1,2-aryl migrations. New scaffolds containing pharmacologically interesting structural motifs and functional groups that allow robotised construction of diverse libraries can be rapidly assembled in a highly convergent manner.



Scheme 15.

3. Experimental

3.1. General conditions

All reactions were carried out under an inert atmosphere. Commercial reagents were used as received without further purification. All products were purified by using silica gel (SDS, Silice 60 ACC 40–63 μm) or by crystallisation. Analytical TLC was carried out on Merck silica gel plates using short wave (254 nm) UV light, 1% aqueous $KMnO_4$ solution to visualise components. NMR spectra were recorded in $CDCl_3$ using a Bruker AMX400 operating at 400 MHz for ^1H and 100 MHz for ^{13}C. The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform. ^1H NMR data are reported as follows: δ, chemical shift; multiplicity (recorded as s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quadruplet; qt, quintuplet; ht, heptuplet; dd, double doublet; ddd, double double doublet; dddd, double double double doublet; dt, double triplet; ddt, double double triplet; dq, double quadruplet; tt, triple triplet; td, triple doublet; tdd, triple double doublet; m, multiplet), coupling constants (J are given in hertz, Hz) and integration. Infrared absorption spectra were recorded as a solution in CCl_4 with a Perkin–Elmer 1600 Fourier Transform Spectrophotometer. Mass spectra were recorded with an HP 5989B mass spectrometer via direct introduction for chemical positive ionisation (CI) using ammonia as the reagent gas. Melting points were determined by Reichert microscope apparatus and were uncorrected. HRMS were performed on JEOL JMS-GcMate II, GC–MS system spectrometer. Microanalyses were performed by the Service de Microanalyse, Institut de Chimie des Substantces Naturelles, CNRS, F-91198, Gif-sur-Yvette.

3.1.1. General procedure for the synthesis of *N*-allylbenzenesulfonamides 1. To a solution of NaOH (1.2 equiv) in water (0.5 mL/mmol allylamine) and Et_2O (0.5 mL/mmol allylamine) were added allylamine (1 equiv) and the arenesulfonyl chloride (1.1 equiv) at room temperature. After 5 h, the reaction mixture was extracted with CH_2Cl_2. The organic extracts were dried and evaporated, and the residue was purified by the corresponding method.

3.1.1.1. *N*-Allyl-4-methoxybenzenesulfonamide 1b. Purified by crystallisation (EtOH), white solid, 73%; ν_{max}/cm^{-1} 3394, 3276 (NH), 3079 (Ar), 2839 (=CH_2), 1598 (C=C), 1498 (NH), 1335, 1258, 1159 (SO_2); δ_H 3.57–3.60 (m, 2H, CH_2N), 3.88 (s, 3H, OCH_3), 4.65 (br s, 1H, NH), 5.09–5.20 (dd, 2H, =CH_2), 5.69–5.76 (m, 1H, CH=), 7.81–7.83 (m, 5H, ArH); δ_C 45.9 (CH_2N), 55.7 (OCH_3), 117.9 (=CH_2), 114.3 (CH Ar), 129.2 (CH Ar), 129.4 (CH Ar), 131.5 (CH Ar), 133.0 (C Ar), 134.9 (CH=), 136.8 (C Ar); m/z 228 (MH^+), 245 ($M+NH_4^+$).

3.1.1.2. *N*-Allyl-2-chlorobenzenesulfonamide 1e. Purified by flash column chromatography (petrol/EtOAc 9:1), white solid, 55%; mp 67–70 °C; ν_{max}/cm^{-1} 3392, 1572 (NH), 1352, 1172 (SO_2); δ_H 3.58 (t, J=6 Hz, 2H, H-1′), 5.07 (d, J=10.4 Hz, 1H, H-3′), 5.10 (br s, 1H, NH), 5.16 (d, J=16.8 Hz, 1H, H-3′), 5.69 (ddt, J=6, 10.4, 16.8 Hz, 1H, H-2′), 7.41 (ddd, J=2.5, 5.7, 7.9 Hz, 1H, ArH), 7.45–7.55 (m, 2H, ArH), 8.08 (d, J=7.2 Hz, 1H, ArH); δ_C 45.9 (C-1′), 118.0 (C-3′), 127.2 (CH Ar), 131.26 (CH Ar), 131.33 (CH Ar), 131.5 (CH Ar), 132.5 (C-2), 133.7 (CH Ar), 137.4 (C-*ipso*), m/z 232 (MH^+), 249 ($M+NH_4^+$).

3.1.1.3. *N*-Allyl-4-trifluoromethylbenzenesulfonamide 1h. Purified by flash column chromatography (petrol/EtOAc 9:1), white solid, 73%; mp 100–102 °C; ν_{max}/cm^{-1} 3399 (NH), 1323, 1174 (SO_2); δ_H 3.65 (d, J=5.6 Hz, 2H, H-1′), 4.68 (br s, 1H, NH), 5.13 (dd, J=0.8, 10.4 Hz, 1H, H-3′), 5.18 (dd, J=0.8, 16.8 Hz, 1H, H-3′), 5.72 (ddt, J=6, 10.4, 16.8 Hz, 1H, H-2′), 7.80 (d, J=8.4 Hz, 2H, ArH), 8.02 (d, J=8 Hz, 2H, ArH); δ_C 45.6 (C-1′), 117.9 (C-3′), 123.1 (q, J=271.4 Hz, CF_3), 126.2 (C-*m*), 127.6 (C-*o*), 132.4 (C-2′), 134.2 (q, J=32.5 Hz, C-*p*), 143.5 (C-*ipso*); m/z 266 (MH^+), 283 ($M+NH_4^+$).

3.1.1.4. *N*-Allyl-4-cyanobenzenesulfonamide 1i. Purified by flash column chromatography (petrol/EtOAc 7:3), white solid, 93%; mp 80–81 °C; ν_{max}/cm^{-1} 3400, 3263 (NH), 2233 (CN), 1350, 1165 (SO_2); δ_H 3.65 (t, J=5.4 Hz, 2H, H-1′), 4.93 (t, J=5.4 Hz, 2H, NH), 5.11 (d, J=10.4 Hz, 1H, H-3′), 5.16 (d, J=17.2 Hz, 1H, H-3′), 5.69 (ddt, J=5.6, 11.2, 16.8 Hz, 1H, H-2′), 7.82 (d, J=8.4 Hz, 2H, ArH), 7.99 (d, J=8.4 Hz, 2H, 2H, ArH); δ_C 45.7 (C-1′), 116.4 (C-*p*), 117.2 (CN), 118.2 (C-3′), 127.6 (CH Ar), 132.4 (C-2′), 132.9 (CH Ar), 144.5 (C-*ipso*); m/z 223 (MH^+), 240 ($M+NH_4^+$).

3.1.1.5. *N*-Allyl-4-*tert*-butylbenzenesulfonamide 1j. Purified by flash column chromatography (petrol/EtOAc 7:3), white solid, 85%; mp 65–68 °C; ν_{max}/cm^{-1} 3395, 3276, 1596 (NH), 1343, 1167 (SO_2); δ_H 1.34 (s, 9H, CH_3), 3.59 (t, J=5.6 Hz, 2H, H-1′), 4.75 (t, J=5.8 Hz, 1H, NH), 5.09 (d, J=10.4 Hz, 1H, H-3′), 5.17 (d, J=17.2 Hz, 1H, H-3′), 5.67–5.80 (m, 1H, H-2′), 7.52 (d, J=8 Hz, 2H, ArH), 7.79 (d, J=8 Hz, 2H, ArH); δ_C 31.1 (CH_3), 35.1 (C), 45.7 (C-1), 117.6 (C-3′), 126.0 (CH Ar), 126.9 (CH Ar), 133.1 (C-2), 136.9 (C-*ipso*), 156.4 (C-*p*); m/z 254 (MH^+), 271 ($M+NH_4^+$).

3.1.1.6. *N*-Allyl-4-trifluoromethoxybenzenesulfonamide 1k. Purified by crystallisation (petrol/EtOAc), white crystals, 94%; mp 73–74 °C; δ_C 3.64 (t, J=6 Hz, 2H, H-1′), 4.67 (br s, 1H, NH), 5.16 (dd, J=13.5, 21.4 Hz, 2H, H-3′), 5.73 (m, 1H, H-2′), 7.36 (d, J=8.6 Hz, 2H, ArH),

7.93 (d, J=8.6 Hz, 2H, ArH); δ_C 45.8 (C-1′), 118.0 (C-3′), 120.3 (q, J=259 Hz, OCF_3), 138.4 (C Ar), 152.2 (C Ar), 121.1, 129.4, 132.7 (2CH Ar and C-2′); m/z 282 (MH^+), 299 ($M+NH_4^+$); Elem. Anal. Calcd for $C_{10}H_{10}F_3NO_3S$: C, 42.70; H, 3.58; found: C, 42.85; H, 3.67.

3.1.1.7. *N*-Allyl-3-methoxybenzenesulfonamide 1l. Purified by flash column chromatography (petrol/EtOAc 8:2), transparent oil, 100%; ν_{max}/cm^{-1} 3278 (NH), 1599 (NH), 1321 (SO_2), 1161 (SO_2); δ_H 3.55 (tt, J=1.6, 6 Hz, 2H, NCH_2), 3.81 (s, 3H, OCH_3), 5.04 (ddd, J=1.2, 2.4, 10 Hz, 1H, CH=), 5.14 (ddd, J=1.6, 2.8, 17.2 Hz, 1H, CH=), 5.27 (t, J=6.2 Hz, 1H, NH), 5.68 (ddt, J=6, 10, 17.2 Hz, 1H, CH=), 7.07 (ddd, J=1.2, 2.4, 8.8 Hz, 1H, CH Ar), 7.35–7.40 (m, 2H, ArH), 7.42 (dt, J=1.2, 8 Hz, 1H, ArH); δ_C 45.6 (NCH_2), 55.5 (OCH_3), 111.6 (CH Ar), 117.4 (CH_2=), 119.0 (CH Ar), 119.1 (CH Ar), 130.0 (CH Ar), 132.8 (CH=), 140.8 (C Ar), 159.8 (C Ar); m/z 228 (MH^+), 245 ($M+NH_4^+$).

3.1.2. General procedure for the synthesis of sulfonamides 2. To a solution of benzenesulfonamide **1** (1 equiv) in toluene (2 mL/mmol) was added AcCl (15 equiv) and heated to reflux temperature for 2 days. After that time, the reaction mixture was filtered and the residue was purified by the method indicated.

3.1.2.1. *N*-Acetyl-*N*-allyl-4-methylbenzenesulfonamide 2a. Purified by crystallisation (EtOH), white solid, 60%; ν_{max}/cm^{-1} 3086, 2985, 1704 (CO), 1592 (C=C), 1367, 1172 (SO_2); δ_H 2.34 (s, 3H, CH_3), 2.46 (s, 3H, CH_3 Ar), 4.47 (d, J=5.2 Hz, 2H, CH_2N), 5.27 (m, 2H, =CH_2), 5.84–5.94 (m, 1H, CH=), 7.34 (d, J=8 Hz, 2H, CH Ar), 7.82 (d, J=8 Hz, 2H, CH Ar); δ_C 21.3 (CH_3 acetyl), 24.4 (CH_3 Ar), 48.5 (CH_2N), 117.9 (=CH_2), 127.6 (CH Ar), 127.7 (CH Ar), 129.4 (CH Ar), 130.0 (C Ar), 131.2 (CH Ar), 132.8 (C Ar), 134.9 (CH=), 170.6 (CO); m/z 254 (MH^+), 271 ($M+NH_4^+$).

3.1.2.2. *N*-Acetyl-*N*-allyl-4-methoxybenzenesulfonamide 2b. Purified by crystallisation (EtOH), white solid, 84%; ν_{max}/cm^{-1} 3083, 2840, 1703 (CO), 1596 (C=C), 1360 (SO_2), 1311, 1267, 1163, 1091 (SO_2); δ_H 2.30 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 4.47 (d, J=5.2 Hz, 2H, CH_2N), 5.24–5.31 (m, 2H, =CH_2), 5.85–5.95 (m, 1H, CH=), 7.34 (d, 2H, J=8 Hz, CH Ar), 7.82 (d, 2H, J=8 Hz, CH Ar); δ_C 24.4 (CH_3), 48.5 (CH_2N), 55.6 (OCH_3), 114.3 (2CH Ar), 118.2 (=CH_2), 130.4 (2CH Ar), 131.0 (C Ar), 132.8 (CH=), 163.8 (C Ar), 170.6 (CO); m/z 270 (MH^+), 287 ($M+NH_4^+$).

3.1.2.3. Dithiocarbonic acid *O*-ethyl ester *S*-(2-oxo-3-phenylpropyl)ester 3f. To a solution of phenylacetone (10 mL, 74.8 mmol) in glacial AcOH (25 mL) were added concentrated HBr (12.5 mL) and a solution of Br_2 (8.5 mL, 165 mmol) in glacial AcOH (41 mL), and the resulting mixture was stirred at room temperature for 6 h. Acetone (132 mL) was then added, and stirring continued for a further 18 h. The reaction mixture was then concentrated and extracted with CH_2Cl_2. The organic extracts were dried and concentrated. The residue was purified by flash column chromatography (petroleum ether/AcOEt 95:5), which afforded 1-bromo-3-phenylacetone as a dark yellow oil, as well as other minor isomers due to non-regioselective bromination. A mixture of the intermediate bromide and potassium *O*-ethyl xanthate (15.6 g, 97.2 mmol) in acetone (375 mL) was stirred at room temperature for 4 h. The reaction mixture was then concentrated, the residue taken up in Et_2O and filtrated through Celite™. The solvent was evaporated, and the residue was purified by flash column chromatography (petroleum ether/AcOEt 9:1), and the desired xanthate was obtained as a brown solid (16.9 g, 89%, two steps); mp 55–57 °C, ν_{max}/cm^{-1} 1730 (CO), 1224 (COS), 1052 (CS); δ_H 1.39 (t, J=7.2 Hz, 3H, CH_3), 3.90 (s, 2H, CH_2), 4.00 (s, 2H, CH_2), 4.60 (q, J=7.2 Hz, 2H, OCH_2), 7.20–7.40 (m, 5H, ArH); δ_C 13.6 (CH_3), 44.8 (CH_2), 44.9 (CH_2), 70.8 (OCH_2), 127.2, 128.7, 129.5 (CH Ar), 133.2 (C-*ipso*), 200.6 (CO), 213.0 (CS); m/z 255 (MH^+), 272 ($M+NH_4^+$).

3.1.2.4. Dithiocarbonic acid *O*-ethyl ester *S*-phenoxycarbonylmethyl ester 3k. To a chilled (0 °C) solution of phenol (5.0 g, 53.1 mmol) and triethylamine (7.46 mL, 53.1 mmol) in Et_2O (53 mL) was added chloroacetyl chloride (4.23 mL, 53.1 mmol) and stirred at room temperature for 1 h. After that time, Et_2O (100 mL) was added and the reaction mixture was washed successively with 1 M HCl, aqueous saturated $NaHCO_3$ solution and aqueous saturated NaCl solution. The organic layer was dried and evaporated, and the residue was purified by flash column chromatography (petroleum ether/AcOEt 9:1), and phenyl chloroacetate was obtained as white crystals (6.57 g, 73%).

Phenyl chloroacetate (6.57 g, 38.5 mmol) was dissolved in acetone (193 mL), potassium *O*-ethyl xanthate (8.03 g, 50.1 mmol) was added, and stirred at room temperature for 1 h. After that time, the reaction mixture was concentrated, the residue taken up in Et_2O and filtrated through Celite™. The solvent was evaporated, and the residue was purified by flash column chromatography (petroleum ether/AcOEt 7:3), and it was obtained the desired xanthate as a dark yellow oil (9.55 g, 97%); ν_{max}/cm^{-1} 1759 (CO), 1212 (COS), 1066 (CS); δ_H 1.46 (t, J=7 Hz, 3H, CH_3), 4.15 (s, 2H, CH_2), 4.70 (q, J=7.1 Hz, 2H, OCH_2), 7.14 (d, J=8.4 Hz, 2H, ArH), 7.26 (t, J=6.8 Hz, 1H, ArH), 7.40 (t, J=7.8 Hz, 2H, ArH); δ_C 13.7 (CH_3), 37.9 (CH_2), 70.8 (OCH_2), 121.2, 126.1, 129.5 (C-*o*, C-*m*, C-*p*), 150.6 (C-*ipso*), 166.5 (CO), 212.3 (CS); m/z 257 (MH^+), 274 ($M+NH_4^+$).

3.1.2.5. Dithiocarbonic acid *O*-ethyl ester *S*-(2-oxo-2-piperidin-1-yl-ethyl)ester 3n. To a suspension of K_2CO_3 (55.8 g, 404 mmol) and chloroacetyl chloride (8.1 mL, 101 mmol) in THF (116 mL) was added dropwise a solution of piperidine (10 mL, 101 mmol) in THF (232 mL), and the resulting mixture was stirred at room temperature for 16 h. The reaction mixture was then filtered and concentrated. The residue was purified by flash column chromatography (petroleum ether/AcOEt 7:3), and the desired chloroacetylpiperidine was obtained as a yellow oil (13.1 g, 80%).

To a solution of chloroacetylpiperidine (13.1 g, 81.1 mmol) in acetone (81 mL) at 0 °C was added dropwise a suspension of potassium *O*-ethyl xanthate (14.3 g, 89.2 mmol) in acetone (357 mL), and the resulting mixture was stirred at room temperature for 3 h. The reaction mixture was then concentrated, the residue taken up in Et_2O and filtered through Celite™. The solvent was evaporated, and the residue was purified by flash column chromatography (petroleum

ether/AcOEt 7:3) and the desired xanthate was obtained as a yellow oil (16 g, 80%); ν_{max}/cm^{-1} 1651 (CO), 1220 (COS), 1054 (CS); δ_H 1.41 (t, J=7.2 Hz, 3H, CH_3), 1.50–1.70 (m, 6H), 3.48 (t, J=5.2 Hz, 2H, CH_2N), 3.56 (t, J=5.2 Hz, 2H, CH_2N), 4.11 (s, 2H, CH_2CO), 4.64 (q, J=7.2 Hz, 2H, OCH_2); δ_C 13.7 (CH_3), 24.3, 25.4, 26.5 (CH_2 ring), 39.6 (CH_2CO), 43.4 (CH_2N), 47.3 (CH_2N), 70.4 (OCH_2), 164.7 (CO), 213.9 (CS); m/z 248 (MH^+), 265 ($M+NH_4^+$).

3.1.2.6. Dithiocarbonic acid *O*-ethyl *S*-(2-cyclohexyl-2-oxoethyl)ester 3r. To a solution of cyclohexane carboxylic acid (2.45 g, 19.1 mmol) in THF (143 mL) at 0 °C was added MeLi (48 mL, 1.6 M solution in cyclohexane, 76.3 mmol) and the reaction mixture stirred at that temperature for 2 h. TMSCl (48.5 mL, 382 mmol) was then added, and the ice bath was removed. 1 M aqueous HCl (7.5 mL) was then added, and the reaction mixture was stirred for 30 min. The two layers were then separated, and the aqueous phase was further extracted with Et_2O. The organic extracts were dried and evaporated. The residue was purified by flash column chromatography (petroleum ether/AcOEt 9:1), and acetylcyclohexane was obtained as a yellow oil (1.20 g, 50%).

Acetylcyclohexane (1.2 g, 9.52 mmol) was dissolved in MeOH (7.5 mL), cooled to 0 °C, and a single portion Br_2 (0.5 mL) added, and the resulting mixture stirred at a temperature below 15 °C for 3 h. Water (8 mL) was then added and stirring continued for a further 15 h at room temperature. The reaction mixture was then extracted with AcOEt, and the organic extracts were dried and evaporated. The residue was purified by flash column chromatography (petroleum ether/AcOEt 9:1), and the desired bromoacetylcyclohexane was obtained as a yellow oil (1.35 g, 70%).

To a solution of bromoacetylcyclohexane (1.35 g, 6.59 g) in acetone (33 mL) was added potassium *O*-ethyl xanthate (1.37 g, 8.56 g), and the mixture was stirred at room temperature for 1.5 h. The reaction mixture was then concentrated, the residue taken up in Et_2O, and filtered through Celite™. The solvent was evaporated, and the residue was purified by flash column chromatography (petroleum ether/AcOEt 97:3), and the desired xanthate was obtained as a yellow semi-solid (1.03 g, 64%); ν_{max}/cm^{-1} 1713 (CO), 1224 (COS), 1052 (CS); δ_H 1.25–1.50 (m, 5H), 1.40 (t, J=7.2 Hz, 3H, CH_3), 1.67 (d, J=11.2 Hz, 3H, CH_3), 1.79 (d, J=12.4 Hz, 2H), 1.90 (d, J=12.8 Hz, 2H), 2.59 (tt, J=3.3, 10.9 Hz, 1H, H-1 cyclohexyl), 4.07 (s, 2H, CH_2S), 4.62 (q, J=7.1 Hz, 2H, OCH_2); δ_C 13.7 (CH_3), 25.5 (C-4 cyclohexyl), 25.7 (C-3 and C-5 cyclohexyl), 28.5 (C-2 and C-6 cyclohexyl), 44.5 (CH_2S), 49.8 (C-1 cyclohexyl), 70.6 (OCH_2), 205.7 (CO), 213.5 (CS); m/z 247 (MH^+), 264 ($M+NH_4^+$).

3.1.2.7. Dithiocarbonic acid *O*-ethyl ester *S*-(2-oxo-3,3,3-trifluoropropyl)ester 3s. To a chilled (0 °C) solution of 1-bromo-3,3,3-trifluoroacetone (5.0 g, 26.2 mmol) in acetone (52 mL) was added a suspension of potassium *O*-ethyl xanthate (5.04 g, 31.4 mmol) in acetone (126 mL), and stirred at room temperature for 2 h. After that time, water (100 mL) was added, and the acetone was evaporated. The reaction mixture was extracted with a mixture of 7:3 petroleum ether/Et_2O, and the organic extracts were dried and evaporated. The residue consisted in a ca. 1:1 mixture (estimated by ^1H NMR) of xanthate **3s** and its corresponding hydrate, which was not further purified (yellow oil, 6.77 g); ν_{max}/cm^{-1} 3586 (OH), 1720 (CO), 1050 (CS); δ_H 1.42 (t, J=7 Hz, 3H, CH_3), 1.47 (t, J=7 Hz, 3H, CH_3), 3.74 (s, 2H, 2OH), 3.94 (s, 2H, CH_2S), 4.31 (s, 2H, CH_2S), 4.64 (q, J=7.2 Hz, 2H, OCH_2), 4.71 (q, J=7.2 Hz, 2H, OCH_2); m/z 233 (MH^+).

3.1.3. General procedure for the synthesis of radical precursors 4. For compounds **4c**, **4e**, **4h** and **4i**: To a solution of sulfonamide **6** (1 equiv) in pyridine (53 equiv) was added acetic anhydride (17 equiv), and the reaction mixture stirred until complete consumption of the starting material. The mixture was then evaporated, and CH_2Cl_2 was added. The organic phase was washed with 1 M aqueous HCl, saturated aqueous $NaHCO_3$ solution, brine, dried and evaporated. The residue was purified by flash column chromatography.

For compounds **4f**, **4j**, **4k**, **4l**, **4m**, **4n**, **4o**, **4p**, **4q**, **4r**, **4s** and **4t**: To a solution of sulfonamide **6** (1 equiv) in CH_2Cl_2 (2 mL/mmol) was added DMAP (4 equiv), and the solution was cooled to 0 °C. Acetyl chloride was then added dropwise (3 equiv), and the resulting mixture was stirred at room temperature for 2 h. CH_2Cl_2 was then added, and the organic phase was washed with 1 M aqueous HCl, saturated aqueous $NaHCO_3$ solution, brine, dried and evaporated. The residue was purified by flash column chromatography.

For compound **4c2**: To a solution of sulfonamide **6c** (1 equiv) in CH_2Cl_2 (2 mL/mmol) were added DMAP (2.1 equiv) and methyl chloroformate (2 equiv). The reaction mixture was stirred at room temperature for 12 h, and after that time it was worked up as in the last procedure.

For compound **4c3**: To a solution of sulfonamide **6c** (1 equiv) in CH_2Cl_2 (2 mL/mmol) were added triethylamine (1 equiv), di-*tert*-butyl dicarbonate (2 equiv) and DMAP (1 equiv), and the reaction mixture was stirred at room temperature for 7 h. After that time, the reaction mixture was worked up as in the last procedure.

For compound **4j2**: To a solution of sulfonamide **6e** (1 equiv) in CH_2Cl_2 (2 mL/mmol) cooled at 0 °C were added DMAP (4 equiv) and trifluoroacetic anhydride (3 equiv), and stirred at room temperature for 2 h. After that time, it was worked up as in the last procedure.

Note: compounds **4a–d** were prepared by radical reaction between an olefin **2** and a corresponding xanthate **3**, following the general methodology reported for compounds **6**.

3.1.3.1. Dithiocarbonic acid *O*-ethyl ester *S*-[1-(*N*-acetyl-4-toluenesulfonylaminomethyl)-4-oxopentyl]ester 4a. Prepared from **2a** and **3a**, purified by flash column chromatography (petrol/EtOAc gradient from 8:2 to 1:9), yellow oil, 34%; ν_{max}/cm^{-1} 2925, 1719 (CO), 1495, 1366 (SO_2), 1226 (O–CS), 1169 (SO_2), 1048 (C=S); δ_H 1.46 (t, J=8 Hz, 3H, CH_3 xanthate), 1.80–1.90 (m, 1H, CH), 2.10–2.16 (m, 1H, CH), 2.17 (s, 3H, CH_3CO), 2.36 (s, 3H, CH_3 acetyl), 2.46 (s, 3H, CH_3 Ar), 2.58–2.78 (m, 2H, CH_2CO), 4.10–4.18 (m, 1H, CHS), 4.13–4.14 (m, 2H, CH_2N), 4.66 (q, J=8 Hz, 2H, OCH_2), 7.36 (d, J=8 Hz, 2H, CH Ar), 7.77 (d, J=8 Hz, 2H, CH Ar); δ_C 13.8 (CH_3 xanthate), 21.6 (CH_3CO), 21.8 (CH_2), 25.2 (CH_3 acetyl), 30.1 (CH_3 Ar),

40.6 (CH_2CO), 49.0 (CH_2N), 49.6 (CHS), 70.5 (OCH_2), 127.6 (CH Ar), 127.7 (CH Ar), 130.1 (CH Ar), 136.2 (CH Ar), 136.6 (C Ar), 145.3 (C Ar), 170.6 (CO), 207.4 (CO ketone), 212.9 (CS); *m/z* 432 (MH^+), 449 ($M+NH_4^+$).

3.1.3.2. Dithiocarbonic acid *O*-ethyl ester *S*-[1-(*N*-acetyl-4-toluenesulfonylaminomethyl)-4-oxo-4-phenylbutyl]-ester 4b. Prepared from **2a** and **3b**, purified by flash column chromatography (petrol/EtOAc gradient from 10:0 to 7:3), pale yellow oil, 42%; ν_{max}/cm^{-1} 2926, 1706 (CO), 1691 (CO), 1494, 1448, 1367 (SO2), 1224 (OC–S), 1160 (SO2), 1048 (C═S); δ_H 1.43 (t, *J*=8 Hz, 3H, CH_3 xanthate), 1.98–2.03 (m, 1H, CH), 2.27–2.34 (m, 1H, CH), 2.36 (s, 3H, CH_3 acetyl), 2.46 (s, 3H, CH_3 Ar), 3.18–3.30 (m, 2H, CH_2CO), 4.15–4.23 (m, 2H, NCH_2), 4.24–4.33 (m, 1H, CHS), 4.64 (q, *J*=8 Hz, 2H, OCH_2), 7.35–7.58 (m, 5H, ArH), 7.79 (d, *J*=8 Hz, 2H, CH Ar), 7.88 (d, *J*=8 Hz, 2H, CH Ar); δ_C 13.8 (CH_3 xanthate), 21.7 (CH_3 acetyl), 25.2 (CH_2), 25.7 (CH_3 Ar), 35.7 (CH_2CO), 49.1 (NCH_2), 49.7 (CHS), 70.5 (OCH_2), 127.5–133.2 (9CH Ar), 136.6 (C Ar), 136.7 (C Ar), 145.2 (C Ar), 170.6 (CO), 198.8 (CO), 212.8 (CS); *m/z* 494 (MH^+), 511 ($M+NH_4^+$).

3.1.3.3. Methyl 5-(*N*-acetyl-4-toluenesulfonylamino)-4-ethoxythiocarbonylsulfanyl pentanoate 4c. Prepared from **2a** and **3c**, purified by flash column chromatography (petrol/EtOAc gradient from 10:0 to 7:3), yellow oil; 28%, if prepared from **6c**, 95%; ν_{max}/cm^{-1} 2986, 2951, 1741 (C═O), 1707 (NC═O), 1436, 1366 (SO_2), 1227 (OCS), 1169 (SO_2), 1111, 1051 (C═S); δ_H 1.45 (t, *J*=8 Hz, CH_3 xanthate), 1.85–1.95 (m, 1H, CH), 2.13–2.19 (m, 1H, CH), 2.35 (s, 3H, CH_3CO), 2.46 (s, 3H, CH_3 Ar), 2.51–2.59 (m, 2H, CH_2CO), 3.68 (s, 3H, OCH_3), 4.10–4.15 (m, 2H, CH_2N), 4.18–4.23 (m, 1H, CHS), 4.65 (q, *J*=8 Hz, 2H, OCH_2), 7.36 (d, *J*=8 Hz, 2H, CH Ar), 7.74 (d, *J*=8 Hz, 2H, CH Ar); δ_C 13.8 (CH_3 xanthate), 21.7 (CH_3 acetyl), 25.2 (CH_2), 26.6 (CH_3 Ar), 31.4 (CH_2CO), 49.06 (OCH_3), 49.1 (CH_2N), 49.5 (CHS), 70.5 (OCH_2), 126.3 (CH Ar), 127.6 (CH Ar), 130.2 (CH Ar), 130.3 (CH Ar), 136.6 (C Ar), 145.3 (C Ar), 170.2 (CO), 174.0 (CO ester), 212.8 (CS); *m/z* 448 (MH^+), 465 ($M+NH_4^+$).

3.1.3.4. *O*-ethyl ester *S*-[1-(*N*-acetyl-4-methoxybenzenesulfonylaminomethyl)-3-cyanopropyl]dithiocarbonate 4d. Prepared from **2b** and **3d**, purification by flash column chromatography (petrol/EtOAc gradient from 10:0 to 7:3), 58%, yellow oil; ν_{max}/cm^{-1} 2963, 2942, 2841, 2249 (CN), 1705 (NC═O), 1596, 1498, 1366 (SO_2), 1310, 1263 (O–CS), 1230, 1182, 1163 (SO_2), 1111, 1051 (C═S); δ_H 1.46 (t, *J*=8 Hz, 3H, CH_3 xanthate), 1.95–2.03 (m, 1H, CH), 2.17–2.25 (m, 1H, CH), 2.37 (s, 3H, CH_3 acetyl), 2.50–2.68 (m, 2H, CH_2CN), 3.90 (s, 3H, OCH_3), 4.11–4.15 (m, 2H, CH_2N), 4.17–4.27 (m, 1H, CHS), 4.66 (q, *J*=8 Hz, OCH_2), 7.02 (d, *J*=8 Hz, CH Ar), 7.81 (d, *J*=8 Hz, CH Ar); δ_C 13.8 (CH_3 xanthate), 15.1 (CH_2), 25.1 (CH_3 acetyl), 27.6 (CH_2CN), 48.5 (CHS), 48.8 (CH_2N), 55.9 (OCH_3), 70.9 (OCH_2), 114.8 (2CH Ar), 119.0 (CN), 129.8 (2CH Ar), 130.5 (C Ar), 164.1 (C Ar), 170.6 (CO), 211.5 (CS); *m/z* 431 (MH^+), 448 ($M+NH_4^+$).

3.1.3.5. *N*-Acetyl-*N*-(5-acetoxy-4-ethoxycarbonyl-2-ethoxythiocarbonylsulfanyl-5-phenylpentene-4-enyl)-4-toluenensulfonamide 4e. Purified by flash column chromatography (petrol/EtOAc 78:22), yellow oil, 72%; ν_{max}/cm^{-1} 1772 (CO OAc), 1740 (CO ethyl ester), 1710 (CO amide), 1367, 1170 (SO_2), 1235 (CSO), 1048 (CS); δ_H 0.98 (t, *J*=7.2 Hz, CH_3 ethyl ester), 1.45 (m, 3H, *J*=6.8 Hz, 3H, CH_3 xanthate), 2.22 (s, 3H, CH_3 acetoxy), 2.37 (s, 3H, CH_3 NAc), 2.46 (s, 3H, CH_3 tolyl), 2.88–2.92 (m, 2H, CH_2), 3.98–4.05 (m, 2H, OCH_2 ester), 4.20 (d, *J*=8 Hz, 2H, NCH_2), 4.37–4.45 (m, 1H, CHS), 4.64 (q, *J*=6.8 Hz, 2H, OCH_2 xanthate), 7.32–7.79 (m, 9H, ArH); δ_C 13.7 (CH_3 xanthate), 13.8 (CH_3 ethyl ester), 21.1 (CH_3 OAc), 21.8 (CH_3 tolyl), 25.1 (CH_3 NAc), 30.7 (C-3′), 48.8 (C-1′ and C-2′), 61.1 (OCH_2 ethyl ester), 70.3 (OCH_2 xanthate), 120.9 (C-4′), 127.7–130.1 (9CH Ar), 135.4 (C Ar), 136.3 (C Ar), 145.2 (C-*ipso* tolyl), 155.4 (C-5′), 167.4 (CO acetoxy), 168.1 (CO ethyl ester), 170.6 (CO amide), 212.7 (CS); *m/z* 608 (MH^+), 623 ($M+NH_4^+$).

3.1.3.6. *N*-Acetyl-*N*-[2-ethoxythiocarbonylsulfanyl-5-oxo-6-phenylhexenyl]-4-toluenesulfonamide 4f. Purified by flash column chromatography (petrol/EtOAc 7:3), brown oil, 94%; ν_{max}/cm^{-1} 1759 (CO), 1710 (CO), 1367, 1170 (SO_2), 1224 (COS), 1049 (CS); δ_H 1.42 (t, *J*=7.1 Hz, 3H, CH_3 xanthate), 1.75–1.90 (m, 1H, CH), 2.05–2.15 (m, 1H, CH), 2.33 (s, 3H, CH_3 acetyl), 2.44 (s, 3H, CH_3 tolyl), 2.60–2.75 (m, 2H, CH_2CO), 3.70 (s, 2H, CH_2Ph), 4.00–4.30 (m, 3H, NCH_2 and CHS), 4.63 (q, *J*=7.1 Hz, 2H, OCH_2), 7.20 (d, *J*=7.1 Hz, 2H, ArH), 7.75 (dd, *J*=2.8, 8.1 Hz, 2H, ArH); δ_C 13.7 (CH_3 xanthate), 21.6 (CH_3 tolyl), 25.0 (CH_3 acetyl), 25.1 (CH_2), 38.9 (CH_2CO), 48.9 (NCH_2), 49.4 (CHS), 50.1 (CH_2Ph), 70.3 (OCH_2), 127.4, 128.7, 129.4, 130.0 (CH Ar), 134.0 (C-*ipso* phenyl), 136.6 (C-*p* tolyl), 145.1 (C-*ipso* tolyl), 170.4 (CO acetyl), 206.8 (C-5′), 212.7 (CS); *m/z* 509 (MH^+), 525 ($M+NH_4^+$).

3.1.3.7. *N*-Acetyl-*N*-[2-ethoxythiocarbonylsulfanyl-4-(2-benzyl-1*H*-tetrazole-5-yl)butyl]-4-toluenesulfonamide 4g. Purified by flash column chromatography (petrol/EtOAc 6:4), yellow oil, 49%; ν_{max}/cm^{-1} 1707 (CO), 1366 and 1168 (SO_2), 1228 (COS), 1051 (CS); δ_H 1.37 (t, *J*=6.8 Hz, 3H), 1.95–2.02 (m, 1H, CH), 2.24–2.30 (m, 1H, CH), 2.33 (s, 3H, CH_3 acetyl), 2.45 (s, 3H, CH_3 tolyl), 2.85–2.90 (m, 2H, CH_2CO), 4.07–4.15 (m, 2H, NCH_2), 4.22–4.25 (m, 1H, CHS), 4.62 (s, 2H, CH_2 benzyl), 7.21–7.75 (m, 9H, CH Ar); δ_C 13.8 (CH_3 xanthate), 20.5 (CH_3 tolyl), 20.7 (CH_2CO), 24.9 (CH_3 acetyl), 28.0 (CH_2), 48.4 (NCH_2), 49.2 (CHS), 50.1 (CH_2 benzyl), 70.5 (OCH_2), 126.9–130.0 (9CH Ar), 133.3 (C-*ipso* phenyl), 136.1 (C-*p* tolyl), 145.3 (C-*ipso* tolyl), 154.0 (C-5″), 170.4 (CO acetyl), 212.1 (CS); *m/z* 548 (MH^+).

3.1.3.8. *O*-Ethyl-*S*-[1-(*N*-acetyl-4-toluenesulfonylaminomethyl)-4-cyclopropyl-4-oxo-butyl]dithiocarbonate 4h. Isolated as an oil, 77%; ν_{max}/cm^{-1} 1705 (CO, CON), 1366, 1169 (NSO_2), 1224, 1050 (C═S, SC–O); δ_H 0.89–0.84 (m, 2H, CH_2), 1.04–1.0 (m, 2H, CH_2), 1.45 (t, 3H, *J*=7.1 Hz, CH_3 xanthate), 1.95–1.81 (m, 2H, CH, CHCO), 2.20–2.11 (m, 1H, CH), 2.35 (s, 3H, CH_3CO), 2.45 (s, 3H, CH_3 Ar), 2.87–2.71 (m, 2H, CH_2CO), 4.21–4.06 (m, 3H, CHS and NCH_2), 4.66 (qd, 2H, *J*=7.2 Hz, OCH_2), 7.34 (d, 2H, *J*=8 Hz, CH Ar), 7.75 (d, 2H, *J*=8 Hz, CH Ar); δ_C 10.9 ($2CH_2$), 13.8 (CH_3 xanthate), 20.6 (CHCO), 21.7 (CH_3 Ar), 25.1 (CH_3CO), 25.4 (CH_2), 40.3 (CH_2CO), 49.1 (CH_2N), 49.7 (CHS), 70.4 (OCH_2), 127.5 (CH Ar), 130.1

(CH Ar), 136.6 (C Ar), 145.2 (C Ar), 170.6 (CON), 209.5 (*C*O), 212.9 (CS); *m*/*z* 458 (MH^+), 475 ($M+NH_4^+$).

3.1.3.9. *O*-Ethyl-*S*-[1-(*N*-acetyl-4-trifluoromethoxybenzenesulfonylaminomethyl)-4-oxo-4-(2-oxooxazolidin-3-yl)butyl]dithiocarbonate 4i. Isolated as a foam, 98%; ν_{max}/cm^{-1} 1791 (OCON), 1708 (NCO), 1384, 1167 (NSO_2), 1215 (C═S), 1048 (COS); δ_H 8.0 (d, 2H, *J*=8 Hz, CH Ar), 7.36 (d, 2H, *J*=8 Hz, CH Ar), 4.64 (q, 2H, *J*=7.2 Hz, OCH_2), 4.42 (t, 2H, *J*=8 Hz, CH_2), 4.22 (m, 1H, CHS), 4.16 (br s+br d, 2H, CH_2), 4.03 (t, 2H, *J*=8 Hz, CH_2), 3.15 (m, 2H, CH_2N), 2.38 (s, 3H, CH_3CO), 2.33–2.22 (m, 1H, CH), 2.01–1.94 (m, 1H, CH), 1.44 (t, 3H, *J*=7.2 Hz, CH_3 xanthate); δ_C 13.8 (CH_3 xanthate), 25.1 (CH_3CO), 26.0 (CH_2), 32.3 (CH_2CO), 42.6 (CH_2N), 49.3 (CH_2N), 49.4 (CHS), 62.3 (CH_2OCO), 70.7 (OCH_2), 120.9 (Ar), 130.3 (Ar), 137.5 (Ar), 153.0 (Ar), 153.6 (CO), 170.4 (CO), 172.2 (CO), 212.7 (CS); *m*/*z* 590 ($M+NH_4^+$).

3.1.3.10. Ethyl 5-(*N*-acetyl-4-methoxybenzenesulfonylamino)-4-ethoxythiocarbonylsulfanyl pentanoate 4j. Purified by flash column chromatography (petrol/CH_2Cl_2/Et_2O 8:1:1), yellow oil, 87%; ν_{max}/cm^{-1} 2981, 2941, 2839, 1736 (OC═O), 1705 (NC═O), 1597, 1498, 1367 (SO_2), 1229 (OC–S), 1163, 1049 (C═S); δ_H 1.26 (t, *J*=7.6 Hz, 3H, CH_3 ester), 1.44 (t, *J*=6.8 Hz, 3H, CH_3 xanthate), 1.87–1.94 (m, 1H, CH), 2.15–2.20 (m, 1H, CHS), 2.35 (s, 3H, CH_3 acetyl), 2.44–2.57 (m, 2H, CH_2CO), 3.88 (s, 3H, OCH_3), 4.13 (q, *J*=7.6 Hz, 2H, OCH_2 ester), 4.16–4.19 (m, 2H, NCH_2), 4.20–4.22 (m, 1H, CHS), 4.65 (q, *J*=6.8 Hz, 2H, OCH_2 xanthate), 6.99 (d, *J*=8.8 Hz, 2H, CH Ar), 7.81 (d, *J*=8.8 Hz, 2H, CH Ar); δ_C 13.8 (CH_3 xanthate), 14.2 (CH_3 ester), 25.1 (CH_3 acetyl), 26.6 (CH_2), 31.6 (CH_2CO), 49.0 (CHS), 49.5 (NCH_2), 55.9 (OCH_3), 60.8 (OCH_2 ester), 70.5 (OCH_2 xanthate), 114.6 (2CH Ar), 129.9 (2CH Ar), 130.9 (C Ar), 163.9 (C Ar), 170.6 (CO amide), 172.7 (CO ester), 212.8 (C═S); *m*/*z* 462 (MH^+), 479 ($M+NH_4^+$).

3.1.3.11. *N*-Acetyl-*N*-[2-ethoxythiocarbonylsulfanyl-4-phenoxycarbonylbutyl]-4-fluorobenzenesulfonamide 4k. Purified by flash column chromatography (petrol/EtOAc 3:1), yellow oil, 84%; ν_{max}/cm^{-1} 1761 (CO ester), 1710 (CO amide); δ_H 1.43 (t, *J*=7.1 Hz, 3H, CH_3), 1.95–2.07 (m, 1H, CH), 2.20–2.35 (m, 1H, CH), 2.35 (s, 3H, CH_3 acetyl), 2.70–2.90 (m, 2H, CH_2CO), 4.16 (d, *J*=7.3 Hz, NCH_2), 4.25–4.35 (m, 1H, CHS), 4.65 (q, *J*=7.1 Hz, 2H, OCH_2), 7.09 (d, *J*=7.6 Hz, 2H, H-*o* phenyl), 7.15–7.30 (m, 3H, H-*m* fluorophenyl and H-*p* phenyl), 7.37 (t, *J*=7.8 Hz, 2H, H-*m* phenyl), 7.93 (dd, *J*=4.8, 8.8 Hz, 2H, H-*o* fluorophenyl); δ_C 13.7 (CH_3 xanthate), 25.0 (CH_3 acetyl), 26.5 (CH_2), 31.4 (CH_2CO), 49.2 (NCH_2), 49.5 (CHS), 70.5 (OCH_2), 116.6 (d, *J*=22.7 Hz, C-*m* fluorophenyl), 121.5 (C-*o* phenyl), 125.8 (C-*p* phenyl), 129.3 (C-*m* phenyl), 130.6 (d, *J*=9.5 Hz, C-*o* fluorophenyl), 135.3 (d, *J*=3.1 Hz, C-*ipso* fluorophenyl), 150.6 (C-*ipso* phenyl), 165.6 (d, *J*=128 Hz, C-*p* fluorophenyl), 170.2 (CO), 171.0 (CO), 212.3 (CS); *m*/*z* 514 (MH^+), 531 ($M+NH_4^+$).

3.1.3.12. Ethyl 7-(*N*-acetyl-4-chlorobenzenesulfonylamino)-6-ethoxythiocarbonylsulfanyl-3-oxoheptanoate 4l. Purified by flash column chromatography (petrol/EtOAc gradient from 10:0 to 8:2), yellow oil, 75%; ν_{max}/cm^{-1} 2983, 1711 (CO), 1368 (SO_2), 1228 (OC–S), 1171, 1052 (C═S); δ_H 1.32 (t, *J*=7.2 Hz, 3H, CH_3 ester), 1.43 (t, *J*=7.2 Hz, 3H, CH_3 xanthate), 1.88–1.94 (m, 1H, CH), 2.13–2.21 (m, 1H, CH), 2.36 (s, 3H, CH_3 acetyl), 2.36 (s, 2H, $COCH_2CO$), 2.87–2.97 (m, 2H, CH_2CO), 4.11–4.12 (m, 2H, NCH_2), 4.12–4.13 (m, 1H, CHS), 4.27 (q, *J*=7.2 Hz, 2H, OCH_2 ester), 4.63 (q, *J*=7.2 Hz, 2H, OCH_2 xanthate), 7.52 (d, *J*=8 Hz, 2H, CH Ar), 7.85 (d, *J*=8 Hz, 2H, CH Ar); δ_C 13.7 (CH_3 xanthate), 14.2 (CH_3 ester), 25.0 (CH_2), 26.7 (CH_3 acetyl), 35.4 (CH_2CO), 49.3 ($COCH_2CO$), 49.6 (NCH_2), 54.9 (CHS), 61.6 (OCH_2 ester), 70.5 (OCH_2 xanthate), 129.2 (2CH Ar), 129.6 (2CH Ar), 139.5 (C Ar), 145.3 (C Ar), 170.2 (CO amide), 174.8 (CO ester), 201.9 (CO ketone), 211.8 (C═S); *m*/*z* 524 (MH^+), 541 ($M+NH_4^+$).

3.1.3.13. *N*-Acetyl-*N*-[2-ethoxythiocarbonylsulfanyl-3-(oxol-2-one-3-yl)propyl]-2-chlorobenzenesulfonamide 4m. (Two diastereomers, D1 and D2) purified by flash column chromatography (petrol/EtOAc 1:1), yellow oil, 89%; ν_{max}/cm^{-1} 1780 (CO ester), 1709 (CO amide), 1368, 1168 (SO_2), 1227 (COS), 1045 (CS); δ_H 1.42 (t, *J*=3.6 Hz, 3H, CH_3), 1.45 (t, *J*=3.6 Hz, 3H, CH_3), 1.80–1.92 (m, 2H, CH D1 and CH D2), 1.94–2.17 (m, 2H, H-4″ ring D1 and H-4″ ring D2), 2.19–2.39 (m, 2H, CH D1 and CH D2), 2.25 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.48 (dddd, *J*=2, 6.4, 8.6, 14.8 Hz, 1H, H-4″ ring D1), 2.56 (dddd, *J*=2, 6.4, 8.4, 14.8 Hz, 1H, H-4″ ring D2), 2.75–2.91 (m, 2H, H-3″ ring D1 and H-3″ ring D2), 4.14–4.27 (m, 6H, NCH_2 D1, NCH_2 D2, H-5″ ring D1 and H-5″ ring D2), 4.32–4.46 (m, 4H, CHS D1, CHS D2, H-5″ ring D1 and H-5″ ring D2), 4.59–4.73 (m, 4H, OCH_2 D1 and D2), 7.44–7.62 (m, 6H, CH Ar), 8.19 (d, *J*=8 Hz, 2H, CH Ar); δ_C 13.7 (CH_3), 24.7 (CH_3 Ac D2), 24.8 (CH_3 Ac D1), 29.1 (C-4″ ring D1), 29.4 (C-4″ ring D2), 31.9 (CH_2 D1), 32.8 (CH_2 D2), 37.2 (C-3″ ring D2), 37.4 (C-3″ ring D1), 48.1 (CHS D2), 48.6 (CHS D1), 49.4 (NCH_2 D2), 50.4 (NCH_2 D1), 66.4 (C-5″ ring D1), 66.5 (C-5″ ring D2), 70.4 (OCH_2 D2), 70.7 (OCH_2 D1), 127.3 (CH Ar), 131.8 (C Ar D2), 131.9 (C Ar D1), 132.1 (CH Ar D2), 132.2 (CH Ar D1), 132.36 (CH Ar D1), 132.41 (CH Ar D2), 134.8 (CH Ar D2), 134.9 (CH Ar D1), 136.7 (C Ar D1), 136.9 (C Ar D2), 169.8 (CO acetyl D1), 169.9 (CO acetyl D2), 178.38 (CO), 178.41 (CO), 212.4 (CS D2), 212.6 (CS D1), *m*/*z* 480 (MH^+), 497 ($M+NH_4^+$).

3.1.3.14. *N*-Acetyl-*N*-[2-ethoxythiocarbonylsulfanyl-5-oxo-5-(piperidine-1-yl)pentenyl]-4-bromobenzenesulfonamide 4n. Purified by flash column chromatography (petrol/EtOAc 1:1), yellow oil, 91%; ν_{max}/cm^{-1} 1710 (CO), 1645 (CO), 1367, 1170 (SO_2), 1224 (COS), 1054 (CS); δ_H 1.42 (t, *J*=7 Hz, 3H, CH_3), 1.45–1.65 (m, 6H), 1.80–1.95 (m, 1H, CH), 2.15–2.25 (m, 1H, CH), 2.33 (s, 3H, CH_3 acetyl), 2.42–2.58 (m, 2H, CH_2CO), 3.36 (br s, 2H, H-2″ or H-6″ piperidine), 3.52 (ddd, *J*=5.2, 13.2, 24 Hz, 2H, H-2″ or H-6″ piperidine), 4.05–4.25 (m, 3H, CHS and NCH_2), 4.62 (q, *J*=7 Hz, 2H, OCH_2), 7.66 (d, *J*=8.4 Hz, 2H, ArH), 7.78 (d, *J*=8.4 Hz, 2H, ArH); δ_C 13.7 (CH_3), 24.5 (CH_2 piperidine), 25.0 (CH_3 acetyl), 25.5, 26.4 (CH_2 piperidine), 27.0 (CH_2), 30.2 (CH_2CO), 42.8 (C-2″ or C-6″ piperidine), 46.5 (C-2″ or C-6″), 49.3 (NCH_2), 50.1 (CHS), 70.4 (OCH_2), 129.0 (C-*p*), 129.3 (CH Ar), 132.5 (CH Ar), 138.5 (C-*ipso*), 169.6 (CO), 170.3 (CO acetyl), 212.8 (CS); *m*/*z* 566 (MH^+).

3.1.3.15. *O*-Ethyl *S*-[1-(*N*-acetyl-4-iodobenzenesulfonylaminomethyl)-5,5-dimethoxy-4-oxopentyl]dithiocarbonate 4o. Purified by flash column chromatography (petrol/EtOAc 7:3), yellow oil, 91%; ν_{max}/cm^{-1} 1739 (CO), 1711 (NCO), 1367, 1170 (SO_2), 1226 (CS), 1055 (COS); δ_H 1.43 (td, 3H, J=7.2 Hz, OCH_3), 1.81–1.88 and 2.02–2.17 (2m, 2H, CH_2), 2.34 and 2.35 (2s, 3H, CH_3), 2.92 (m, 0.5H, CH), 3.07 (m, 0.5H, CH), 3.32, 3.36, 3.37 (s, br s, s, 6H, 2OCH_3), 3.71 and 3.73 (2s, 3H, CO_2CH_3), 4.15–4.03 (m, 2.5H, CHS, CH_2N), 4.18–4.25 (m, 0.5H, CHS), 4.52 (t, 1H, J=7 Hz, $CHOCH_3$), 4.63 (dq, 2H, J=7.2 Hz, OCH_2), 7.60 and 7.61 (2d, 2H, J=8.4 Hz, ArH), 7.89 and 7.90 (2d, 2H, J=8.4 Hz, ArH); δ_C 13.8 (CH_3 xanthate), 25.1 (CH_3 acetyl), 28.5 and 30.3 (CH_2), 46.6, 47.1, 48.1, 48.6 (CH), 48.9, 49.8 (CH_2N), 52.3, 53.4, 54.2, 54.9 (OCH_3), 70.5, 70.6 (OCH_2), 101.8 (CI), 104.3, 105.0 ($CHOCH_3$), 129.1, 138.6 (CH Ar), 170.4, 172.3, 172.5 (CO), 212.4 (CS).

3.1.3.16. *O*-Ethyl-*S*-[1-(*N*-acetyl-4-trifluoromethylbenzenesulfonylaminomethyl)-4-oxo-4-thiophen-2-ylbutyl]dithiocarbonate 4p. Purified by flash column chromatography (petrol/EtOAc 7:3), yellow oil, 86%; ν_{max}/cm^{-1} 1712 (CO), 1669 (CO), 1368, 1173 (SO_2), 1226 (COS), 1063 (CS); δ_H 1.40 (t, J=7 Hz, 3H, CH_3), 1.92–2.05 (m, 1H, CH), 2.30–2.42 (m, 1H, CH), 2.38 (s, 3H, CH_3 acetyl), 3.16 (t, J=7 Hz, 2H, CH_2CO), 4.18 (d, J=6.8 Hz, 2H, NCH), 4.22–4.31 (m, 1H, CHS), 4.52–4.66 (m, 2H, OCH_2), 7.13 (t, J=4.0 Hz, 1H, H-4 thiophene), 7.64 (d, J=4.8 Hz, 1H, CH thiophene), 7.73 (d, J=3.2 Hz, 1H, CH thiophene), 7.81 (d, J=8.4 Hz, 2H, H-*m*), 8.07 (d, J=8.4 Hz, 2H, H-*o*); δ_C 13.7 (CH_3 xanthate), 25.0 (CH_3 acetyl), 25.8 (CH_2), 36.0 (CH_2CO), 49.5 (NCH_2), 49.7 (CHS), 70.6 (OCH_2), 122.9 (q, J=271.4 Hz, CF_3), 126.4 (q, J=3.6 Hz, C-*m*), 128.1 (C-4 thiophene), 128.4 (C-*o*), 132.0 (CH thiophene), 133.8 (CH thiophene), 135.4 (q, J=33.2 Hz, C-*p*), 142.8 (C-*ipso*), 143.8 (C-*ipso*), 170.3 (CO acetyl), 191.6 (CO), 212.4 (CS); *m*/*z* 554 (MH^+), 571 ($M+NH_4^+$).

3.1.3.17. *O*-Ethyl-*S*-[1-(*N*-acetyl-4-cyanobenzenesulfonylaminomethyl)-5,5-dimethyl-4-oxohexyl]dithiocarbonate 4q. Purified by flash column chromatography (petrol/EtOAc 3:1), yellow oil, 93%; ν_{max}/cm^{-1} 1709 (CO); δ_H 1.12 (s, 9H, CH_3), 1.42 (t, J=7.2 Hz, 3H, CH_3 xanthate), 1.70–1.82 (m, 1H, CH), 2.07–2.20 (m, 1H, CH), 2.35 (s, 3H, CH_3 acetyl), 2.60–2.80 (m, 2H, CH_2CO), 4.05–4.20 (m, 3H, CH_2N and CHS), 4.61 (q, J=7.2 Hz, 2H, OCH_2), 7.83 (d, J=8.8 Hz, 2H, ArH), 8.07 (d, J=8.4 Hz, 2H, ArH); δ_C 13.7 (CH_3 xanthate), 24.9 (CH_3 acetyl), 25.1 (CH_2), 26.5 (CH_3 ^{t}Bu), 33.3 (CH_2CO), 44.1 (C ^{t}Bu), 49.7 (CHS), 49.8 (CH_2N), 70.6 (OCH_2), 116.9 and 117.4 (C Ar and CN), 128.7 (CH Ar), 132.8 (CH Ar), 143.4 (C Ar), 170.3 (CO acetyl), 212.6 and 214.5 (CO and CS); *m*/*z* 485 (MH^+), 502 (MNH_4^+).

3.1.3.18. *O*-Ethyl-*S*-[1-(*N*-acetyl-4-*tert*-butylbenzenesulfonylaminomethyl)-4-cyclohexyl-4-oxobutyl]dithiocarbonate 4r. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 93%; ν_{max}/cm^{-1} 1709 (CO), 1366, 1172 (SO_2), 1227, 1113 (COS), 1049 (CS); δ_H 1.10–1.40 (m, 5H, CH ring), 1.34 (s, 9H, CH_3 ^{t}Bu), 1.43 (t, J=6.8 Hz, 3H, CH_3 xanthate), 1.65 (d, J=13.2 Hz, 1H, CH cyclohexyl), 1.70–1.85 (m, 5H, CH and 4CH cyclohexyl), 2.05–2.15 (m, 1H, CH), 2.25–2.40 (m, 1H, H-1 cyclohexyl), 2.35 (s, 3H, CH_3 acetyl), 2.55–2.75 (m, 2H, CH_2CO), 4.02–4.20 (m, 3H, CH_2N and CHS), 4.58–4.70 (m, 2H, OCH_2 xanthate), 7.54 (d, J=8.4 Hz, 2H, ArH), 7.78 (d, J=8.4 Hz, 2H, ArH); δ_C 13.7 (CH_3 xanthate), 25.0 (CH_2), 25.1 (CH_3 acetyl), 25.62, 25.64, 25.8, 28.46, 28.52 (CH_2 cyclohexyl), 31.0 (CH_3 ^{t}Bu), 35.3 (C ^{t}Bu), 37.5 (CH_2CO), 49.0 (CH_2N), 49.6 (CHS), 50.9 (C-1 cyclohexyl), 70.3 (OCH_2 xanthate), 126.4 (CH Ar), 127.3 (CH Ar), 136.5 (C Ar), 158.0 (C Ar), 170.3 (CO acetyl), 212.5 and 212.8 (CO and CS); *m*/*z* 542 (MH^+), 559 (MNH_4^+).

3.1.3.19. Methyl 4-ethoxythiocarbonylsulfanyl-5-(*N*-methoxycarbonyl-4-toluenesulfonylamino)pentanoate 4c2. Purified by flash column chromatography (petrol/CH_2Cl_2/Et_2O 6:2:2), pale yellow oil, 93%; ν_{max}/cm^{-1} 2982, 2933, 1742 (CO), 1367, 1173 (SO_2), 1223 (OCS), 1051 (C=S); δ_H 1.43 (t, J=6.8 Hz, 3H, CH_3 xanthate), 1.84–1.98 (m, 1H, CH), 2.16–2.28 (m, 1H, CH), 2.44 (s, 3H, CH_3 Ar), 2.47–2.67 (m, 2H, CH_2CO), 3.69 (OCH_3), 3.72 (s, 3H, OCH_3), 4.06–4.15 (m, 2H, NCH_2), 4.19–4.25 (m, 1H, CHS), 4.64 (q, J=6.8 Hz, 2H, OCH_2), 7.30 (d, J=7.2 Hz, 2H, CH Ar), 7.86 (d, J=7.2 Hz, 2H, CH Ar); δ_C 13.9 (CH_3 xanthate), 21.8 (CH_3 Ar), 26.7 (CH_2), 31.3 (CH_2CO), 49.5 (NCH_2), 49.8 (OCH_3), 51.9 (CHS), 54.1 (OCH_3), 70.5 (OCH_2), 128.8 (CH Ar), 129.5 (CH Ar), 136.1 (C Ar), 144.9 (C Ar), 153.0 (CO), 173.1 (CO), 212.7 (CS); *m*/*z* 464 (MH^+), 481 ($M+NH_4^+$).

3.1.3.20. Methyl 4-ethoxythiocarbonylsulfanyl-5-(*N*-*tert*-butoxycarbonyl-4-toluenesulfonylamino)pentanoate 4c3. Purified by flash column chromatography (petrol/EtOAc gradient from 10:0 to 8:2), pale yellow oil, 93%; ν_{max}/cm^{-1} 2982, 2933, 1738 (CO), 1369, 1171 (SO_2), 1222 (OCS), 1048 (C=S); δ_H 1.35 (s, 9H, $3CH_3$), 1.44 (t, J=6.8 Hz, 3H, CH_3 xanthate), 1.84–1.98 (m, 1H, CH), 2.16–2.28 (m, 1H, CH), 2.43 (s, 3H, CH_3 Ar), 2.47–2.67 (m, 2H, CH_2CO), 3.68 (s, 3H, OCH_3), 4.06–4.15 (m, 2H, NCH_2), 4.19–4.25 (m, 1H, CHS), 4.64 (q, J=6.8 Hz, 2H, OCH_2), 7.30 (d, J=7.2 Hz, 2H, CH Ar), 7.70 (d, J=7.2 Hz, 2H, CH Ar); δ_C 13.8 (CH_3 xanthate), 21.7 (CH_3 Ar), 26.9 (CH_2), 27.9 ($3CH_3$), 31.3 (CH_2CO), 49.1 (NCH_2), 50.1 (OCH_3), 51.8 (CHS), 70.4 (OCH_2), 85.0 (C), 128.2 (CH Ar), 129.3 (CH Ar), 137.1 (C Ar), 144.4 (C Ar), 151.0 (CO), 173.2 (CO), 212.8 (CS); *m*/*z* 506 (MH^+), 523 ($M+NH_4^+$).

3.1.3.21. Ethyl 4-ethoxythiocarbonylsulfanyl 5-(*N*-trifluoroacetyl-4-methoxybenzenesulfonylamino)pentanoate 4j2. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 66%; δ_H 1.26 (t, J=7 Hz, 3H, CH_3 ester), 1.43 (t, J=7.2 Hz, 3H, CH_3 xanthate), 1.80–1.92 (m, 1H, CH), 2.08–2.20 (m, 1H, CH), 2.40–2.60 (m, 2H, CH_2CO), 3.89 (s, 3H, OCH_3), 4.10–4.35 (m, 5H, OCH_2 ester, CHS and NCH_2), 4.64 (q, J=7.2 Hz, 2H, OCH_2 xanthate), 6.99 (d, J=8.8 Hz, 2H, ArH), 7.97 (d, J=8.8 Hz, 2H, ArH); *m*/*z* 436 ($M-COCF_3$), 454 ($M-COCF_3+NH_4^+$).

3.1.3.22. *N*-Acetyl-*N*-[5′-acetoxy-2′-ethoxythiocarbonylsulfanyl-6,6,6-trifluorohex-4-en-1-yl]-4-chlorobenzenesulfonamide 4s. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 49%; ν_{max}/cm^{-1} 1784

(CO), 1710 (CO), 1368, 1171 (SO_2), 1228 (COS), 1052 (CS); δ_H 1.44 (t, J=7 Hz, 3H, CH_3), 2.27 (s, 3H, CH_3 AcO), 2.35 (s, 3H, CH_3 NAc), 2.39–2.49 (m, 1H, CH), 2.53–2.62 (m, 1H, CH), 4.07 (d, J=3.2 Hz, 1H, NCH), 4.09 (d, J=2 Hz, 1H, NCH), 4.15–4.25 (m, 1H, CHS), 4.65 (q, J=7.2 Hz, 2H, OCH_2), 6.22 (t, J=7.4 Hz, 1H, CH═), 7.52 (d, J=8.8 Hz, 2H, CH Ar), 7.82 (d, J=8.8 Hz, 2H, CH Ar); δ_C 13.4 (CH_3 xanthate), 19.8 (CH_3 AcO), 24.6 (CH_3 AcN), 27.6 (CH_2), 47.9 (CHS), 70.4 (OCH_2), 119.3 (q, J=271.1 Hz, CF_3), 121.6 (q, J=13.2 Hz, CH═), 128.8, 128.9, 129.4 and 129.5 (CH Ar), 136.4 (q, J=36.3 Hz, C═), 137.2 (C Ar), 140.4 (C Ar), 166.9 (CO), 169.9 (CO), 211.5 (CS); m/z 547 (MH^+), 564 ($M+NH_4^+$).

3.1.3.23. *O*-Ethyl-*S*-[1-(*N*-acetyl-4-chlorobenzenesulfonylaminomethyl)-5,5,5-trifluoro-4-methoxyiminopentyl]dithiocarbonate 4t (two diastereomers). Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 94%; ν_{max}/cm^{-1} 1710 (CO), 1369 (SO_2), 1226 (O–CS), 1171 (SO_2), 1053 (C═S); δ_H 1.435 and 1.442 (2t, J=7.2 Hz each, 3H, CH_3 xanthate), 1.78–2.15 (m, 2H, CH_2), 2.345–2.350 (2s, 3H, CH_3 acetyl), 2.48–2.72 (m, 2H, CH_2C═N), 3.96–3.99 (2s, 3H, OCH_3), 4.07–4.15 (m, 2H, NCH_2), 4.18–4.26 (m, 1H, CHS), 4.60–4.68 (m, 2H, OCH_2), 7.49–7.55 (m, 2H, CH Ar), 7.80–7.86 (m, 2H, CH Ar); δ_C 13.7 (CH_3 xanthate), 22.3 (CH_2), 25.1 (CH_3 acetyl), 27.1 (CH_2C═N), 48.9 and 49.0 (NCH_2), 49.0 and 49.8 (CHS), 63.3 (OCH_3), 70.5 (OCH_2), 120.7 (q, J=272.5 Hz, CF_3), 129.0 and 129.1 (2CH Ar), 129.65 and 129.70 (2CH Ar), 137.7 and 137.8 (C Ar), 140.70 and 140.74 (C Ar), 145.0 (q, J=29.2 Hz, C═N), 147.8 (q, J=31.7 Hz, C═N), 170.2 (CO), 212.3 and 212.4 (CS); m/z 535 (MH^+), 552 ($M+NH_4^+$).

3.1.4. General procedure for the synthesis of the transfer products 5. *Method A*: to a solution of acetylsulfonamide **4** (1 equiv) in isopropanol (4 mL/mmol) at reflux temperature was added DLP (15% molar) every 1.5 h, until the disappearance of starting material. The reaction mixture was then evaporated, and the residue was purified by flash column chromatography.

Method B: to a solution of acetylsulfonamide **4** (1 equiv) in a mixture of 1,2-dichloroethane/isopropanol 1:1 (0.02 M) at reflux temperature was added DLP (0.5 equiv) every hour, until 2 equiv have been added. The reaction mixture was then evaporated, and the residue was purified by column chromatography.

3.1.4.1. *N*-(5-Oxo-2-*p*-tolylhexyl)acetamide 5a. Purified by flash column chromatography (petrol/EtOAc gradient from 7:3 to 1:9), yellow oil, 66% (method A, 1.5 equiv DLP); ν_{max}/cm^{-1} 3453 (NH), 2925, 1718 (C═O), 1683 (NC═O), 1512 (NH), 1363, 1261, 1160; δ_H 1.75–1.82 (m, 1H, CH), 1.75–2.05 (m, 1H, CH), 1.88 (s, 3H, CH_3), 2.05 (s, 3H, CH_3 acetyl), 2.28–2.31 (m, 2H, CH_2CO), 2.34 (s, 3H, CH_3 Ar), 2.65–2.75 (m, 1H, NCH), 3.17–3.23 (m, 1H, NCH), 3.64–3.68 (m, 1H, CHAr), 5.46 (br s, 1H, NH), 7.04 (d, J=8 Hz, 2H, CH Ar), 7.14 (d, J=8 Hz, 2H, CH Ar); δ_C 21.1 (CH_3), 23.3 (CH_3 acetyl), 27.2 (CH_2), 30.0 (CH_3 Ar), 41.2 (CH_2CO), 44.4 (CHAr), 45.0 (NCH_2), 127.6 (2CH Ar), 129.6 (2CH Ar), 136.7 (C Ar), 143.5 (C Ar), 170.1 (CO amide), 208.7 (CO ketone); m/z 248 (MH^+).

3.1.4.2. *N*-(5-Oxo-5-phenyl-2-*p*-tolylpentyl)acetamide 5b. Purified by flash column chromatography (petrol/EtOAc 1:9), yellow oil, 53% (method A, 2 equiv DLP); ν_{max}/cm^{-1} 3453, 1549 (NH), 1706 (CO), 1691 (NCO); δ_H 1.90 (s, 3H, CH_3 acetyl), 1.92–2.00 (m, 1H, CH), 2.10–2.18 (m, 1H, CH), 2.34 (s, 3H, CH_3 tolyl), 2.81–2.88 (m, 2H, CH_2CO), 2.90–2.98 (m, 1H, NCH), 3.24–3.30 (m, 1H, NCH), 3.68–3.76 (m, 1H, CHAr), 5.51 (br s, 1H, NH), 7.09 (d, J=8 Hz, 2H, ArH), 7.15 (d, J=8 Hz, 2H, ArH), 7.40–7.55 (m, 5H, ArH); δ_C 23.3 (CH_3 acetyl), 27.9 (CH_2), 30.0 (CH_3 tolyl), 36.2 (CH_2CO), 44.6 (CHAr), 45.2 (NCH_2), 127.7–133.1 (CH Ar), 136.7 (C Ar), 136.8 (C Ar), 138.8 (C Ar), 170.2 (NCO), 200.2 (CO); m/z 310 (MH^+).

3.1.4.3. Methyl 5-acetylamino-4-*p*-tolylpentanoate 5c. Purified by flash column chromatography (petrol/EtOAc 3:7), yellow oil, 71% (method A, 1.35 equiv DLP); ν_{max}/cm^{-1} 3451, 3350, 1436 (NH), 1739 (CO ester), 1685 (CO amide), 1513 (OMe); δ_H 1.88 (s, 3H, CH_3 acetyl), 2.02–2.04 (m, 1H, CH), 2.16–2.20 (m, 1H, CH), 2.33 (s, 3H, CH_3 tolyl), 2.69–2.77 (m, 1H, CHN), 3.16–3.24 (m, 1H, CHN), 3.61 (s, 3H, OCH_3), 3.66–3.71 (m, 1H, CHAr), 5.44 (br s, 1H, NH), 7.05 (d, J=8.4 Hz, 2H, ArH), 7.14 (d, J=7.6 Hz, 2H, ArH); δ_C 23.3 (CH_3 acetyl), 28.8 (CH_2), 30.0 (CH_3 tolyl), 36.2 (CH_2CO), 44.6 (CHAr), 45.2 (CH_2N), 52.0 (OCH_3), 127.7, 129.7, 129.9 (4CH Ar), 136.8 and 138.3 (C-*ipso* and C-*p*), 170.2 (CO amide), 174.0 (CO ester), m/z 264 (MH^+), 281 ($M+NH_4^+$).

3.1.4.4. *N*-[4-Cyano-2-(4-methoxyphenyl)butyl]acetamide 5d. Purified by flash column chromatography (petrol/EtOAc gradient from 9:1 to 3:7), yellow oil, 77% (method A, 1.2 equiv DLP); ν_{max}/cm^{-1} 3453 (NH), 2932, 2836, 2249 (CN), 1686, 1512 (NC═O), 1463 (NH), 1251, 1178, 1040; δ_H 1.77–1.80 (m, 1H, CH), 1.90 (s, 3H, CH_3 acetyl), 2.06–2.10 (m, 1H, CH), 2.11–2.15 (m, 1H, CHCN), 2.23–2.29 (m, 1H, CHCN), 2.83–2.87 (m, 1H, CHN), 3.19–3.26 (m, 1H, CHN), 3.65–3.72 (m, 1H, CHAr), 3.90 (s, 3H, OCH_3), 5.52 (br s, 1H, NH), 6.90 (d, J=8 Hz, 2H, CH Ar), 7.10 (d, J=8 Hz, 2H, CH Ar); δ_C 15.2 (CH_2), 23.3 (CH_3 acetyl), 29.3 (CH_2CN), 44.1 (NCH_2), 44.6 (CHAr), 55.4 (OCH_3), 114.7 (2CH Ar), 119.0 (CN), 128.7 (2CH Ar), 131.8 (C Ar), 159.1 (C Ar), 170.6 (CO); m/z 247 (MH^+), 264 ($M+NH_4^+$).

3.1.4.5. Ethyl 3-acetoxy-2-(3-acetylamino-2-phenylpropyl)-3-phenyl acrylate 5e. Purified by flash column chromatography (petrol/CH_2Cl_2/Et_2O 55:22:22), yellow oil, 29% (method A, 1.65 equiv DLP); ν_{max}/cm^{-1} 3069, 2982, 1769 (OAc), 1712 (NC═O); δ_H 1.34 (t, J=7.2 Hz, CH_3 ester), 1.85 (s, 3H, $NCOCH_3$), 2.38 (s, 3H, $OCOCH_3$), 2.41 (s, 3H, CH_3 Ar), 2.85–3.05 (m, 2H, NCH_2), 3.42–3.49 (m, 1H, CHAr), 3.86–4.10 (m, 2H, CH_2), 4.21–4.32 (m, 2H, OCH_2 ester), 7.28–7.78 (m, 9H, CH Ar); δ_C 14.4 (CH_3 ester), 21.0 ($OCOCH_3$), 21.7 (CH_3 Ar), 24.1 ($NCOCH_3$), 26.4 (CH_2), 37.5 (CHAr), 50.1 (NCH_2), 61.0 (OCH_2 ester), 114.6 (═C–CO), 123.7–130.9 (9CH Ar), 136.7 (C Ar), 137.9 (C Ar), 144.9 (C Ar), 150.3 (O–C═), 165.4 (CO), 168.8 (CO), 170.1 (CO); m/z 424 (MH^+), 441 ($M+NH_4^+$).

3.1.4.6. *N*-(5-Oxo-6-phenyl-2-*p*-tolylhexyl)acetamide 5f. Purified by flash column chromatography (petrol/EtOAc 3:7), yellow oil, 60% (method B); ν_{max}/cm^{-1} 3451 (NH),

1714 (CO ketone), 1684 (CO amide); δ_H 1.70–1.80 (m, 1H, CH), 1.87 (s, 3H, CH_3 acetyl), 1.95–2.05 (m, 1H, CH), 2.35 (s, 3H, CH_3 tolyl), 2.25–2.45 (m, 2H, CH_2CO), 2.65–2.75 (m, 1H, CHAr), 3.18 (ddd, J=4.7, 8.5, 13.3 Hz, 1H, CH_2N), 3.59 (s, 2H, CH_2Ph), 3.55–3.66 (m, 1H, CH_2N), 5.64 (br s, 1H, NH), 6.97 (d, J=7.9 Hz, 2H, ArH), 7.05–7.20 (m, 4H, ArH), 7.20–7.40 (m, 3H, ArH); δ_C 20.9 (CH_3 tolyl), 23.0 (CH_3 acetyl), 27.1 (CH_2), 39.3 (CH_2CO), 44.2 (CHAr), 44.8 (CH_2N), 49.9 (CH_2Ph), 126.8, 127.5, 128.5, 129.2, 129.4 (CH Ar), 133.9 (C Ar), 136.4 (C Ar), 138.4 (C Ar), 170.0 (CO amide), 207.9 (CO); m/z 324 (MH^+), 341 ($M+NH_4^+$); Elem. Anal. Calcd for $C_{21}H_{25}NO_2 \cdot 1/2H_2O$: C, 75.87; H, 7.88; N, 4.21; found: C, 75.39; H, 7.84; N, 4.07.

3.1.4.7. *N*-[4-(1-Benzyl-1*H*-tetrazol-5-yl)-2-*p*-tolylbutyl]acetamide 5g. Purified by flash column chromatography (petrol/EtOAc gradient from 9:1 to 3:7), yellow oil, 64% (method A, 1.5 equiv DLP), ν_{max}/cm^{-1} 3049, 2926, 1680 (C=O), 1442, 1422 (NH), 1267; δ_H 1.85–1.93 and 2.24–2.30 (m, 2H, CH_2), 1.90 (s, 3H, CH_3 acetyl), 2.35 (s, 3H, CH_3 Ar), 2.53–2.58 (m, 2H, CCH_2), 2.78–2.82 and 3.47–3.62 (m, 2H, NCH_2), 3.20–3.26 (m, 1H, CHAr), 5.32 (s, 2H, NCH_2Ph), 5.78 (br s, 1H, NH), 6.97–7.32 (m, 9H, CH Ar); δ_C 20.9 (CH_3 Ar), 21.0 (CCH_2), 23.1 (CH_3 acetyl), 30.2 (CH_2), 44.2 (NCH_2), 44.6 (CHAr), 50.5 (NCH_2Ph), 127.3–129.6 (9CH Ar), 133.0 (C Ar), 136.8 (C Ar), 137.7 (C Ar), 154.6 (C=N), 170.2 (NC=O); m/z 363 (MH^+).

3.1.4.8. *N*-(5-Cyclopropyl-5-oxo-2-*p*-tolylpentyl)acetamide 5h. Isolated as a white solid, 54% (method A); mp (petrol/Et_2O): 101–102 °C; ν_{max}/cm^{-1} 3255 (NH), 1698, 1632 (CO); δ_H 0.84–0.76 (m, 2H, CH_2), 0.98–0.90 (m, 2H, CH_2), 1.84–1.75 (m, 2H, CH, CHCO), 1.88 (s, 3H, CH_3 acetyl), 2.06–1.97 (m, 1H, CH), 2.34 (s, 3H, CH_3 Ar), 2.44 (m, 2H, CH_2CO), 2.73 (m, 1H, CHAr), 3.21 (ddd, 1H, J=4.8, 10.4, 13.2 Hz, CHN), 3.64 (m, 1H, CHN), 5.58 (m, 1H, NH), 7.05 (d, J=8 Hz, 2H, ArH), 7.14 (d, J=8 Hz, 2H, ArH); δ_C 10.7 ($2CH_2$), 20.5 and 21.0 (CH_3CO, CHCO), 23.2 (CH_3Ar), 27.5 (CH_2), 40.9 (CH_2CO), 44.5 (CHAr), 45.1 (CH_2N), 127.7 (CH Ar), 129.6 (CH Ar), 138.6 (C Ar), 138.8 (C Ar), 170.1 (NH*C*O), 210.6 (CO); Elem. Anal. Calcd for $C_{17}H_{23}NO_2 \cdot 0.25H_2O$: C, 73.53; H, 8.53; found: C, 73.52; H, 8.45.

3.1.4.9. *N*-[5-Oxo-5-(2-oxooxazolidin-3-yl)-2-(4-trifluoromethoxyphenyl)pentyl]acetamide 5i. Isolated as white crystals, 60% (method A); mp (petrol/Et_2O): 135–136 °C; ν_{max}/cm^{-1} 1791 (OCON), 1708 (NCO), 1384, 1167 (NSO_2), 1215 (C=S), 1048 (COS); δ_H 1.91 (s, 3H, CH_3CO), 2.0–1.93 (m, 1H, CH), 2.14–2.05 (m, 1H, CH), 2.82 (m, 2H, CH_2CO), 2.92 (m, 1H, CH), 3.29 (ddd, 1H, J= 5.2, 8.3, 13.5 Hz, CHN), 3.65 (td, 1H, J=6.6, 13.4 Hz, CHN), 3.95 (m, 2H, CH_2), 4.39 (t, J=8 Hz, 2H, CH_2), 5.67 (m, 1H, NH), 7.19 (d, J=8.4 Hz, 2H, ArH), 7.24 (d, J=8.4 Hz, 2H, ArH); δ_C 23.3 (CH_3CO), 28.1 (CH_2), 32.9 (CH_2CO), 42.5 (*C*H_2N), 44.5 (CH), 44.8 (CH_2N), 62.1 (CH_2OCO), 120.5 (q, J=256 Hz, OCF_3), 121.3 (Ar), 129.2 (Ar), 140.4 (Ar), 148.2 (Ar), 153.5 (CO), 170.2 (CO), 172.8 (CO); m/z 389 (MH^+), 405 ($M+NH_4^+$); Elem. Anal. Calcd for $C_{17}H_{19}F_3N_2O_5$: C, 52.58; H, 4.93; found: C, 52.91; H, 5.02.

3.1.4.10. Ethyl 5-acetylamino-4-(4-methoxyphenyl)-pentanoate 5j. Purified by flash column chromatography (petrol/EtOAc gradient from 9:1 to 3:7), yellow oil, 69% (method A, 1.6 equiv DLP); ν_{max}/cm^{-1} 3451 (NH), 2933, 1735 (C=O), 1685 (NC=O), 1513, 1251 (OMe); δ_H 1.21 (t, J=7.6 Hz, 3H, CH_3 ester), 1.79–1.85 and 1.99–2.06 (2m, 2H, CH_2), 1.88 (s, 3H, CH_3 acetyl), 2.14–2.17 (m, 2H, CH_2CO), 2.71–2.74 and 3.64–3.71 (m, 2H, NCH_2), 3.15–3.22 (m, 1H, CHAr), 3.80 (s, 3H, OCH_3), 4.06 (q, J=7.6 Hz, 2H, OCH_2 ester), 6.87 (d, J=8.8 Hz, 2H, CH Ar), 7.08 (d, J=8.8 Hz, 2H, CH Ar); δ_C 14.2 (CH_3 ester), 23.3 (CH_3 acetyl), 28.9 (CH_2), 32.0 ($COCH_2$), 44.0 (NCH_2), 44.2 (CHAr), 55.3 (OCH_3), 60.4 (OCH_2), 114.3 (2CH Ar), 128.8 (2CH Ar), 133.3 (C Ar), 158.6 (C Ar), 170.1 (NC=O), 173.5 (OC=O); m/z 294 (MH^+).

3.1.4.11. *N*-[2-(4-Fluorophenyl)-4-phenoxycarbonylbutyl]acetamide 5k. Purified by flash column chromatography (petrol/EtOAc 3:7), yellow oil, 47% (method B); ν_{max}/cm^{-1} 3456 (NH), 1761 (CO ester), 1686 (CO); δ_H 1.87 (s, 3H, CH_3 acetyl), 1.80–2.00 (m, 1H, CH), 2.05–2.15 (m, 1H, CH), 2.42 (t, J=7.6 Hz, 2H, CH_2CO), 2.82–2.95 (m, 1H, CHAr), 3.25 (ddd, J=5.1, 8.6, 13.5 Hz, 1H, CHN), 3.66 (td, J=6.5, 13.2 Hz, 1H, CHN), 6.97–7.08 (m, 4H, H-*m* fluorophenyl and H-*o* phenyl), 7.12–7.24 (m, 3H, H-*p* phenyl and H-*o* fluorophenyl), 7.35 (t, J=8 Hz, 2H, H-*m* phenyl); δ_C 23.1 (CH_3), 28.5 (CH_2), 31.9 (CH_2CO), 44.3 (CHAr), 44.9 (CH_2N), 115.8 (d, J=21.1 Hz, C-*m* fluorophenyl), 121.4 (C-*o* phenyl), 125.8 (C-*p* phenyl), 129.2 (d, J=7.8 Hz, C-*o* fluorophenyl), 129.3 (C-*m* phenyl), 137.0 (d, J=3.1 Hz, C-*ipso* fluorophenyl), 150.5 (C-*ipso* phenyl), 161.9 (d, J=243.9 Hz, C-*p* fluorophenyl), 170.1 and 171.7 (CO amide and ester); m/z 330 (MH^+), 347 ($M+NH_4^+$); Elem. Anal. Calcd for $C_{19}H_{20}FNO_3 \cdot 1/2H_2O$: C, 67.44; H, 6.26; N, 4.14; found: C, 67.66; H, 6.41; N, 4.19.

3.1.4.12. Ethyl 7-acetylamino-6-(4-chlorophenyl)-3-oxoheptanoate 5l. Purified by flash column chromatography (petrol/EtOAc gradient from 9:1 to 7:3), yellow oil, 60% (method A, 1.5 equiv DLP); ν_{max}/cm^{-1} 3455 (NH), 2981, 2929, 1743, 1709 (CO), 1687 (NC=O), 1507, 1171; δ_H 1.40 (t, J=6.8 Hz, 3H, CH_3 ester), 1.82–1.92 (m, 1H, CH), 2.05 (s, 3H, CH_3 acetyl), 2.07–2.16 (m, 1H, CH), 2.36–2.49 (m, 2H, CH_2CO), 3.20 (t, J=6.4 Hz, NCH_2), 3.80–3.84 (m, 1H, CHAr), 3.87 (s, 2H, $COCH_2CO$), 4.59 (q, J=6.8 Hz, OCH_2 ester), 5.09 (br s, 1H, NH), 6.97 (d, J=8.8 Hz, 2H, CH Ar), 7.78 (d, J=8.8 Hz, 2H, CH Ar); δ_C 14.2 (CH_3 ester), 23.3 (CH_3 acetyl), 29.6 (CH_2), 35.6 ($COCH_2$), 44.5 (NCH_2), 44.6 (CHAr), 44.8 ($COCH_2CO$), 60.9 (OCH_2 ester), 129.1 (2CH Ar), 129.2 (2CH Ar), 133.0 (C Ar), 140.3 (C Ar), 170.1 (NC=O), 195.5 (OC=O), 198.6 (C=O); m/z 339 (MH^+), 352 ($M+NH_4^+$).

3.1.4.13. *N*-[2-(2-Chlorophenyl)-3-(2-oxotetrahydrofuran-3-yl)propyl]acetamide 5m. Two diastereomers, D1 and D2, purified by flash column chromatography (petrol/EtOAc 3:7), white foam, 72% (method B); ν_{max}/cm^{-1} 1780 (CO ester), 1686 (CO amide); δ_H 1.62–1.85 (m, 3H, CH D1, CH D2, CH ring D2), 1.90–1.91 (2s, 6H, CH_3 acetyl), 1.90–2.05 (m, 1H, CH ring D1), 2.12–2.25 (m, 2H, CH ring D1, CHCO D2), 2.27–2.41 (m, 3H, CH ring D1, CH D1, CH D2), 2.52–2.62 (m, 1H, CH ring D1), 3.20–3.40 (m, 2H, CHN D1, CHN D2), 3.57–3.84 (m, 4H, CHN D1, CHN D2, CHAr D1, CHAr D2), 4.09 (ddd, J=6.4, 10.1, 19.4 Hz, 2H, CHO), 4.27 (dt, J=1.6, 8.9 Hz, 1H, CHO), 4.34 (dt, J=2,

8.8 Hz, 1H, CHO), 5.39 and 5.44 (2 br s, 2H, NH), 7.15–7.45 (m, 8H, ArH); δ_C 23.0 (CH_3), 28.8 (CH_2 ring D2), 29.3 (CH_2 ring D1), 33.3 (CH_2 D1), 33.8 (CH_2 D2), 37.1 (CH_2 ring D1), 37.7 (CH_2 ring D2), 38.7 (CHAr D1), 39.6 (CHAr D2), 43.3 (CH_2N D2), 44.8 (CH_2N D1), 66.5 (CHO D1 and D2), 127.3, 127.7, 127.8, 128.2, 128.3, 129.7, 129.8 (CH Ar), 134.4, 134.8, 138.1, 139.3 (C-*ipso* and CCl), 170.35 and 170.42 (NCO D1 and D2), 179.3 (CO D1 and D2); *m/z* 296 (MH^+), 313 ($M+NH_4^+$).

3.1.4.14. *N*-[2-(4-Bromophenyl)-5-oxo-5-piperidin-1-yl-pentyl]acetamide 5n. Purified by flash column chromatography (EtOAc/MeOH 95:5), white foam, 70% (method B); ν_{max}/cm^{-1} 3465 (NH), 1683 (CO), 1641 (CO); δ_H 1.40–1.60 (m, 6H), 1.72–1.82 (m, 1H, CH), 1.87 (s, 3H, CH_3 acetyl), 2.00–2.22 (m, 3H, CH and CH_2CO), 2.74–2.84 (m, 1H, CHAr), 3.14–3.28 (m, 3H, NCH_2 piperidine and NCH), 3.40–3.58 (m, 3H, NCH_2 piperidine and NCH), 5.99 (br s, 1H, NH), 7.03 (d, *J*=8.4 Hz, 2H, ArH), 7.41 (d, *J*=8 Hz, 2H, ArH); δ_C 23.1 (CH_3), 24.4, 25.5 and 26.3 ($3CH_2$ piperidine), 28.6 (CH_2), 30.3 (CH_2CO), 42.7 (NCH_2 piperidine), 44.4 (CHAr), 44.8 (NCH_2), 46.4 (NCH_2 piperidine), 120.6 (C Ar), 129.4 (CH Ar), 131.8 (CH Ar), 141.3 (C Ar), 170.2 (CO), 170.5 (CO amide); *m/z* 380 (MH^+); Elem. Anal. Calcd for $C_{18}H_{25}BrN_2O_2 \cdot 1/2H_2O$: C, 55.39; H, 6.71; N, 7.18; found: C, 54.99; H, 6.53; N, 6.91.

3.1.4.15. Methyl 5-acetylamino-2-dimethoxymethyl-4-(4-iodophenyl)pentanoate 5o. Purified by flash column chromatography (EtOAc), white foam, 60% (method A); ν_{max}/cm^{-1} 3453 (NH), 1739 (CO), 1687 (NCO); δ_H 1.84 (s, 1H, CH_3 acetyl), 1.85 (s, 2H, CH_3 acetyl), 1.78–2.07 (m, 2H, CH_2), 2.61–2.84 and 2.40–2.46 (2m, 2H), 3.22 and 3.14 (2s, 6H, 2 OCH_3), 3.16–3.26 (m, 1H, NCH), 3.28 and 3.29 (2s, 2H, CO_2CH_3), 3.40 (s, 1H, CO_2CH_3), 3.54–3.66 (m, 1H, CHAr), 3.68 (s, 2H, CO_2CH_3), 4.39 (d, 0.33H, *J*=7.6 Hz, $CHOCH_3$), 4.43 (d, 0.67H, *J*=7.6 Hz, $CHOCH_3$), 5.43 (m, 1H, NH), 6.90 (d, 2H, *J*=8.3 Hz, ArH), 7.64 (d, 2H, *J*=8.4 Hz, ArH); δ_C 23.3 (CH_3CO). 31.4, 31.7 (CH_2), 43.3, 43.9 (CH), 44.6, 45.1 (CH_2N), 46.6, 47.6 (CH), 52.6, 53.6, 54.5, 54.7 (OCH_3), 92.4, 92.6 (CI), 104.4, 104.9 ($CHOCH_3$), 130.0, 130.2, 137.8, 137.9, 141.4, 140.9 (CH Ar), 170.1 (CO amide), 173.0 (CO ester), *m/z* 418 (MH^+−MeOH), 450 (MH^+), 467 ($M+NH_4^+$); Elem. Anal. Calcd for $C_{17}H_{24}INO_5$: C, 45.45; H, 5.38; found: C, 45.89; H, 5.58.

3.1.4.16. *N*-[5-Oxo-5-thiophen-2-yl-2-(4-trifluoromethylphenyl)pentyl]acetamide 5p. Purified by flash column chromatography (EtOAc), yellow oil, 33% (method B); ν_{max}/cm^{-1} 3458 (NH), 1685 (CO); δ_H 1.90 (s, 3H, CH_3 acetyl), 1.92–2.03 (m, 1H, CH), 2.15–2.27 (m, 1H, CH), 2.70–2.87 (m, 1H, CH_2CO), 2.93–3.03 (m, 1H, CHAr), 3.32 (ddd, *J*=5.4, 8.2, 13.6 Hz, 1H, NCH), 3.65 (qt, *J*=6.7 Hz, 1H, NCH), 5.63 (br s, 1H, NH), 7.07 (dd, *J*=4, 4.8 Hz, 1H, H-4 thiophene), 7.31 (d, *J*=8 Hz, 2H, H-*o*), 7.54–7.64 (m, 4H, H-*m* and 2CH thiophene); δ_C 23.1 (CH_3 acetyl), 27.7 (CH_2), 36.5 (CH_2CO), 44.8 (NCH), 44.9 (CHAr), 124.1 (q, *J*=270.4 Hz, CF_3), 125.8 (q, *J*=3.65 Hz, C-*m*), 128.1 (C-4 thiophene), 128.2 (C-*o*), 129.4 (q, *J*=32.2 Hz, C-*p*), 131.9 and 133.7 (C-3 and C-5 thiophene), 143.9 (C-*ipso*), 146.1 (C-*ipso*), 170.2 (CO acetyl), 192.4 (CO); *m/z* 370 (MH^+), 387 ($M+NH_4^+$).

3.1.4.17. *N*-[2-(4-Cyanophenyl)-6,6-dimethyl-5-oxoheptyl]acetamide 5q. Purified by flash column chromatography (petrol/EtOAc 3:7), transparent oil, 81% (method B); ν_{max}/cm^{-1} 3458 (NH), 2231 (CN), 1705 (CO ketone), 1687 (CO amide); δ_H 1.07 (s, 9H, CH_3 ^tBu), 1.74–1.87 (m, 1H, CH), 1.92 (s, 3H, CH_3 acetyl), 1.98–2.10 (m, 1H, CH), 2.34 (ddd, *J*=5.5, 7.9, 18 Hz, 1H, CHCO), 2.44 (td, *J*=7.6, 17.8 Hz, 1H, CHCO), 2.92 (t, *J*=14.6 Hz, 1H, CHAr), 3.31 (ddd, *J*=5.6, 8.1, 13.6 Hz, 1H, NCH), 3.60 (td, *J*=6.5, 13.2 Hz, 1H, NCH), 5.73 (br s, 1H, NH), 7.32 (d, *J*=8.4 Hz, 2H, ArH), 7.65 (d, *J*=8 Hz, 2H, ArH); δ_C 23.1 (CH_3 acetyl), 26.3 (CH_3 ^tBu), 26.9 (CH_2), 33.6 (CH_2CO), 44.0 (C ^tBu), 44.7 (NCH), 45.1 (CHAr), 110.8 and 118.6 (C Ar and CN), 128.6 (CH Ar), 132.5 (CH Ar), 148.0 (C Ar), 170.1 (CO acetyl), 215.3 (CO); *m/z* 301 (MH^+), 318 ($M+NH_4^+$); Elem. Anal. Calcd for $C_{18}H_{24}N_2O_2 \cdot 1/2H_2O$: C, 69.87; H, 8.14; N, 9.05; found: C, 69.81; H, 8.13; N, 8.99.

3.1.4.18. *N*-[2-(4-*tert*-Butylphenyl)-5-cyclohexyl-5-oxopentyl]acetamide 5r. Purified by flash column chromatography (EtOAc), white foam, 70% (method B); ν_{max}/cm^{-1} 3453 (NH), 1708 (CO ketone), 1684 (CO amide); δ_H 1.00–1.40 (m, 5H), 1.31 (s, 9H, CH_3 ^tBu), 1.55–1.85 (m, 7H), 1.88 (s, 3H, CH_3 acetyl), 1.90–2.05 (m, 1H, CH), 2.15–2.45 (m, 3H, H-1 cyclohexyl and CH_2CO), 2.71 (t, *J*=14.6 Hz, 1H, CHAr), 3.21 (ddd, *J*=4.8, 8.2, 13.1 Hz, 1H, CHN), 3.61 (td, *J*=6.6, 13.3 Hz, 1H, CHN), 5.79 (br s, 1H, NH), 7.06 (d, *J*=8.2 Hz, 2H, ArH), 7.32 (d, *J*=8.3 Hz, 2H, ArH); δ_C 23.1 (CH_3 acetyl), 25.4, 25.5, 25.6 (CH_2 cyclohexyl), 26.9 (CH_2), 28.2, 28.4 (CH_2 cyclohexyl), 31.2 (CH_3 ^tBu), 34.3 (C ^tBu), 38.0 (CH_2CO), 44.3 (CHAr), 44.9 (CH_2N), 50.6 (C-1 cyclohexyl), 125.4 (CH Ar), 127.2 (CH Ar), 138.6 (C Ar), 149.5 (C Ar), 170.0 (CO acetyl), 213.7 (CO); *m/z* 358 (MH^+).

3.1.4.19. Methyl 5-methoxycarbonylamino-4-*p*-tolylpentanoate 5c2. Purified by flash column chromatography (petrol/CH_2Cl_2/Et_2O gradient from 10:0:0 to 60:20:20), yellow oil, 34% (method A, 1.65 equiv DLP); ν_{max}/cm^{-1} 3456 (NH), 3021, 2951, 2927, 1741 (CO), 1467, 1369; δ_H 1.81–1.98 (m, 1H, CH), 2.02–2.07 (m, 1H, CH), 2.17–2.77 (CH_2CO), 2.33 (s, 3H, CH_3 Ar), 2.71–2.77 (m, 1H, CHN), 3.19–3.25 (m, 1H, CHAr), 3.52–3.58 (m, 1H, CHN), 3.62 (s, 3H, OCH_3), 3.62 (s, 3H, OCH_3), 4.60 (br s, 1H, NH), 7.02 (d, *J*=7.2 Hz, 2H, CH Ar), 7.14 (d, *J*=7.2 Hz, 2H, CH Ar); δ_C 21.1 (CH_3 Ar), 28.4 (CH_2), 31.7 (CH_2CO), 45.1 (OCH_3), 46.4 (NCH_2), 51.6 (OCH_3), 52.2 (CHAr), 127.5 (CH Ar), 129.4 (CH Ar), 136.6 (C Ar), 138.0 (C Ar), 156.8 (CO), 173.6 (CO); *m/z* 280 (MH^+), 297 ($M+NH_4^+$).

3.1.4.20. Methyl 5-*tert*-butoxycarbonylamino-4-*p*-tolylpentanoate 5c3. Purified by flash column chromatography (petrol/CH_2Cl_2/Et_2O gradient from 10:0:0 to 50:30:20), yellow oil, 37% (method A, 1.50 equiv DLP); ν_{max}/cm^{-1} 3456 (NH), 2980, 2928, 1739 (CO), 1718 (NCO); δ_H 1.40 (s, 9H, $3CH_3$), 1.78–1.88 (m, 1H, CH), 1.97–2.07 (m, 1H, CH), 2.16–2.20 (m, 2H, CH_2CO), 2.33 (s, 3H, CH_3 Ar), 2.68–2.76 (m, 1H, NCH), 3.14–3.20 (m, 1H, CHAr), 3.43–3.51 (m, 1H, NCH), 3.61 (s, 3H, OCH_3), 4.44 (br s, 1H, NH), 7.05 (d, *J*=7.2 Hz, 2H, ArH), 7.14 (d, *J*=7.2 Hz, 2H, ArH); δ_C 21.1 (CH_3 Ar), 28.5 ($3CH_3$), 28.6 (CH_2), 31.9 (CH_2CO), 45.1 (CHAr), 46.2 (NCH_2), 51.6 (OCH_3), 76.8 (C), 127.8 (CH Ar), 129.6 (CH Ar), 136.6 (C Ar), 138.4

(C Ar), 150.4 (NCO), 173.9 (CO); *m/z* 322 (MH^+), 339 ($M+NH_4^+$).

3.1.4.21. Ethyl 4-(4-methoxyphenyl)-5-trifluoroacetylaminopentanoate 5j2. Purified by flash column chromatography (petrol/EtOAc 7:3), yellow oil, 40% (method A); δ_H 1.21 (t, *J*=7.2 Hz, 3H, CH_3), 1.78–1.82 (m, 1H, CH), 1.95–2.08 (m, 1H, CH), 2.18 (t, *J*=7.6 Hz, 2H, CH_2CO), 2.75–2.85 (m, 1H, NCH), 3.32 (ddd, *J*=4.8, 8.4, 13.2 Hz, 1H, CHAr), 3.70 (qt, *J*=6.8 Hz, 1H, NCH), 3.79 (s, 3H, OCH_3), 4.07 (q, *J*=7.2 Hz, 2H, OCH_2), 6.38 (br s, 1H, NH), 6.87 (d, *J*=8.4 Hz, 2H, ArH), 7.07 (d, *J*=8.4 Hz, 2H, ArH); *m/z* 348 (MH^+), 365 ($M+NH_4^+$).

3.1.4.22. 5-Acetylamino-4-(4-chlorophenyl)-1-trifluoromethylpent-1-enyl acetate 5s. Purified by flash column chromatography (EtOAc), yellow oil, 19% (method B); ν_{max}/cm^{-1} 3451 (NH), 1786 (CO), 1686 (CO); δ_H 1.89 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.20–2.32 (m, 1H, CH), 2.38 (dddd, *J*=1.5, 6.8, 8.3, 15.1 Hz, 1H, CH), 2.97 (qt, *J*=7.4 Hz, 1H, CHAr), 3.32 (ddd, *J*=5.6, 7.7, 13.5 Hz, 1H, NCH), 3.50 (td, *J*=6.8, 13.7 Hz, 1H, NCH), 5.67 (br s, 1H, NH), 5.92 (dd, *J*=6.8, 7.9 Hz, 1H, CH═), 7.11 (d, *J*=8.4 Hz, 2H, ArH), 7.31 (d, *J*=8.4 Hz, 2H, ArH); δ_C 20.2 (CH_3), 23.1 (CH_3), 29.8 (CH_2), 43.6 (CHAr), 44.7 (NCH_2), 119.5 (q, *J*=271 Hz, CF_3), 128.8 (CH Ar), 129.1 (CH Ar), 133.1 (C Ar), 123.5 (q, *J*=3.4 Hz, CH═), 135.5 (q, *J*=36.5 Hz, C═), 139.5 (C Ar), 167.6 (CO), 170.1 (CO); *m/z* 363 (MH^+), 380 ($M+NH_4^+$).

3.1.4.23. *N*-[2-(4-Chlorophenyl)-6,6,6-trifluoro-5-methoxyiminohexyl]acetamide 5t. Purified by flash column chromatography (petrol/EtOAc 1:1), transparent oil, 42% (method B); ν_{max}/cm^{-1} 3456 (NH), 1689 (CO, C═N); δ_H 1.69–2.08 (m, 2H, CH_2), 1.88 (s, 3H, CH_3), 2.15 (ddd, *J*=5, 11.4, 13.2 Hz, 1H, CHC═N), 2.32 (ddd, *J*=5, 11.2, 13.2 Hz, 1H, CHC═N), 2.72–2.84 (m, 1H, CHAr), 3.11 (ddd, *J*=5.2, 9.2, 13.6 Hz, 1H, NCH), 3.70 (ddd, *J*=5.6, 7.2, 13.6 Hz, 1H, NCH), 3.95 (s, 3H, OCH_3), 5.27 (br s, 1H, NH), 7.11 (d, *J*=8.4 Hz, 2H, CH Ar), 7.33 (d, *J*=8.4 Hz, 2H, CH Ar); δ_C 22.6 (CH_2), 23.2 (CH_3 acetyl), 28.8 (CH_2C═N), 44.9 (NCH_2), 45.2 (CHAr), 63.1 (OCH_3), 120.7 (q, *J*=272.3 Hz, CF_3), 129.0 (CH Ar), 129.3 (CH Ar), 133.0 (C Ar), 139.7 (C Ar), 148.5 (q, *J*=31.4 Hz, C═N), 170.0 (CO); *m/z* 351 (MH^+), 367 ($M+NH_4^+$); HRMS calcd for $C_{15}H_{18}F_3ClN_2O_2$, 350.1009; found, 350.1013.

3.1.4.24. *N*-[4-Ethoxycarbonyl-2-(3-methoxyphenyl)-butyl]propionamide 5u. Purified by flash column chromatography (petrol/EtOAc 1:1), yellow oil, 38% (method B); ν_{max}/cm^{-1} 3451 (NH), 1735 (CO ester), 1684 (CO amide); δ_H 1.07 (t, *J*=7.6 Hz, 3H, CH_3), 1.22 (t, *J*=7.2 Hz, 3H, CH_3 ester), 1.80–2.30 (m, 6H), 2.72–2.81 (m, 1H, CHAr), 3.21 (ddd, *J*=4.4, 8.8, 13.2 Hz, 1H, NCH), 3.71 (qt, *J*=6.6 Hz, 1H, NCH), 3.80 (s, 3H, OCH_3), 4.07 (q, *J*=7.2 Hz, 2H, OCH_2), 5.31 (br s, 1H, NH), 6.70 (t, *J*=2 Hz, 1H, CH Ar), 6.75 (d, *J*=8 Hz, 1H, CH Ar), 6.79 (dd, *J*=2, 8 Hz, 1H, CH Ar), 7.25 (t, *J*=8 Hz, 1H, CH Ar); δ_C 9.8 (CH_3), 14.1 (CH_3 ester), 28.5 (CH_2), 29.6 (CH_2), 31.9 (CH_2), 44.6 (NCH_2), 45.0 (CH Ar), 55.1 (OCH_3), 60.2 (OCH_2), 112.0 (CH Ar), 113.6 (CH Ar), 120.0 (CH Ar), 129.7 (CH Ar), 143.1 (C Ar), 159.8 (C Ar), 173.3 (CO), 173.9 (CO); *m/z* 308 (MH^+), 325 ($M+NH_4^+$); HRMS calcd for $C_{17}H_{25}NO_4$, 307.1784; found, 307.1784.

3.1.5. General procedure for the synthesis of addition products 6. To a solution of xanthate **3** (1.5 equiv) in 1,2-dichloroethane (1 mL/mmol) was added sulfonamide **1** (1 equiv), and the mixture was heated at reflux temperature. DLP (5% molar) was then added every 1.5 h until almost complete consumption of the starting material. Then the reaction mixture was evaporated, and the residue was purified by flash column chromatography.

3.1.5.1. Methyl 4-ethoxythiocarbonylsulfanyl-5-(4-toluenesulfonylamino)pentanoate 6c. Purified by flash chromatography (petrol/AcOEt 6:4), yellow oil, 85%; ν_{max}/cm^{-1} 1741 (CO), 1598 (NH), 1495, 1437, 1337, 1163 (SO_2), 1222 (COS), 1052 (CS); δ_H 1.41 (t, *J*=8 Hz, 3H, CH_3), 1.85–1.95 (m, 1H, CH), 2.13–2.19 (m, 1H, CH), 2.44 (s, 3H, CH_3 tolyl), 2.46–2.50 (m, 2H, CH_2CO), 3.21–3.24 (m, 2H, CH_2N), 3.68 (s, 3H, OCH_3), 3.81–3.85 (m, 1H, CHS), 4.60 (q, *J*=7.2 Hz, 2H, OCH_2), 7.30 (d, *J*=8 Hz, 2H, CH Ar), 7.71 (d, *J*=8 Hz, 2H, CH Ar); δ_C 13.8 (CH_3), 21.7 (CH_3 tolyl), 26.2 (CH_2), 31.1 (CH_2CO), 44.6 (OCH_3), 46.3 (CH_2N), 50.1 (CHS), 70.6 (OCH_2), 127.2, 127.5, 129.9, 131.2 (CH Ar), 136.7 (C-*p*), 143.7 (C-*ipso*), 176.0 (CO), 212.6 (CS); *m/z* 406 (MH^+), 423 (MNH_4^+).

3.1.5.2. Ethyl 2-benzoyl-4-ethoxythiocarbonylsulfanyl-5-(4-toluenesulfonylamino)pentanoate 6e. Purified by flash column chromatography (petrol/EtOAc gradient from 10:0 to 7:3), 97%, yellow oil; ν_{max}/cm^{-1} 3284 (NH), 3065, 2983, 2938, 1741 (OC═O), 1689 (C═O), 1598, 1342 (SO_2), 1237 (OC–S), 1164, 1052 (C═S); δ_H (2 diastereomers) 1.11–1.18 (m, 3H, CH_3 ester), 1.27–1.30 and 1.37–1.41 (2m, 3H, CH_3 xanthate), 2.05–2.19 (m, 1H, CH), 2.40 and 2.41 (2s, 3H, CH_3 Ar), 2.42–2.58 (m, 1H, CH), 3.20–3.27 (m, 2H, CH_2N), 3.73–3.81 and 3.89–3.97 (2m, 1H, CHS), 4.12–4.17 (m, 2H, OCH_2 ester), 4.38–4.51 (m, 1H, CHCO), 4.56–4.61 (m, 2H, OCH_2 xanthate), 4.89–4.93 (m, 1H, NH), 7.27–7.28 (m, 2H, CH Ar), 7.44–7.50 (m, 2H, CH Ar), 7.57–7.62 (m, 1H, CH Ar), 7.72 (t, *J*=8 Hz, 2H, CH Ar), 7.96 (t, *J*=8 Hz, 2H, CH Ar); δ_C 13.6 (CH_3 xanthate), 14.3 (CH_3 ester), 21.6 (CH_3 Ar), 30.3 (CH_2), 46.7 (CH_2N), 49.2 (CHS), 51.2 (CHCO), 61.9 (OCH_2 ester), 70.7 (OCH_2 xanthate), 127.3–133.9 (9CH Ar), 136.1 (C Ar), 136.4 (C Ar), 143.7 (C Ar), 169.3 (CO), 194.7 (CO ketone), 212.7 (CS); *m/z* 524 (MH^+), 541 ($M+NH_4^+$).

3.1.5.3. *O*-Ethyl-*S*-[4-oxo-5-phenyl-1-(4-toluenesulfonylaminomethyl)pentyl]dithiocarbonate 6f. Purified by flash chromatography (petrol/EtOAc 8:2), yellow oil, 70%; ν_{max}/cm^{-1} 3250 (NH), 1715 (CO), 1343, 1165 (SO_2), 1222 (COS), 1052 (CS); δ_H 1.39 (t, *J*=7.2 Hz, 3H, CH_3), 1.78 (ddd, *J*=6.8, 8.8, 21.6 Hz, 1H, CH), 2.06 (ddd, *J*=7.2, 12.2, 14.4 Hz, 1H, CH), 2.42 (s, 3H, CH_3 tolyl), 2.61 (t, *J*=7 Hz, 2H, CH_2CO), 3.15 (t, *J*=6.2 Hz, 2H, CH_2N), 3.67 (s, 2H, CH_2Ph), 3.66–3.78 (m, 1H, CHS), 4.52–4.66 (m, 2H, OCH_2), 5.14 (t, *J*=6.4 Hz, 1H, NH), 7.17 (d, *J*=6.8 Hz, 2H, ArH), 7.23–7.34 (m, 5H, ArH), 7.73 (d, *J*=8.4 Hz, 2H, ArH); δ_C 13.6 (CH_3), 21.5 (CH_3 tolyl), 24.6 (CH_2), 38.6 (CH_2CO), 46.2 (CH_2N), 49.8 (CHS), 50.0 (CH_2Ph), 70.3 (OCH_2), 127.0, 128.7, 129.3, 129.7 (CH

Ar), 133.8 (C Ar), 136.8 (C Ar), 143.5 (C Ar), 207.1 (CO), 212.5 (CS); *m/z* 466 (MH^+), 483 (MNH_4^+).

3.1.5.4. *O*-Ethyl-*S*-[3-(1-benzyl-1*H*-tetrazol-5-yl)-1-(4-toluenesulfonylaminomethyl)propyl]dithiocarbonate 6g. Purified by flash column chromatography (petrol/EtOAc 9:1 to 6:4), 83%, yellow oil; ν_{max}/cm^{-1} 3279 (NH), 2926, 1597, 1366, 1168 (SO_2), 1228 (OCS), 1051 (C═S); δ_H 1.37 (t, *J*=6.8 Hz, CH_3 xanthate), 1.95–2.02 and 2.24–2.30 (m, 2H, CH_2), 2.42 (s, 3H, CH_3 Ar), 2.85–2.90 (m, 2H, CCH_2), 3.14–3.21 (m, 2H, NCH_2), 3.83–3.87 (m, 1H, CHS), 4.54–4.60 (m, 2H, OCH_2 xanthate), 5.07–5.10 (m, 1H, NH), 5.51 (d, *J*=4 Hz, 2H, CH_2Ph), 7.19–7.72 (m, 9H, CH Ar); δ_C 13.8 (CH_3 xanthate), 20.8 (CH_3 Ar), 28.0 (CH_2), 46.1 (NCH_2), 49.7 (CHS), 51.0 (CH_2Ph), 70.8 (OCH_2 xanthate), 120.6 (C Ar), 127.1 (2CH Ar), 127.8 (2CH Ar), 129.1 (CH Ar), 129.4 (2CH Ar), 130.0 (2CH Ar), 133.3 (C Ar), 143.9 (C Ar), 153.6 (C═N), 212.1 (C═S); *m/z* 247 (100), 383 (82).

3.1.5.5. *O*-Ethyl-*S*-[4-cyclopropyl-4-oxo-1-(4-toluenesulfonylaminomethyl)butyl]dithiocarbonate 6h. Isolated as an oil, 93%; ν_{max}/cm^{-1} 1702 (CO), 1343, 1164 (NSO_2), 1221, 1052 (C═S, SC–O); δ_H 0.84–0.89 (m, 2H, CH_2), 0.97–1.01 (m, 2H, CH_2), 1.43 (t, 3H, CH_3CH_2O), 1.80–1.90 (m, 2H, CH, CHCO), 2.02–2.10 (m, 1H, CH), 2.45 (s, 3H, CH_3Ph), 2.73 (m, 2H, CH_2CO), 3.18 (m, 2H, CH_2N), 3.78 (m, 1H, CHS), 4.63 (q, *J*=7.2 Hz, 2H, OCH_2), 5.06 (t, *J*=6 Hz, 1H, NH), 7.33 (d, *J*=8 Hz, 2H, CH Ar), 7.74 (d, *J*=8 Hz, 2H, CH Ar); δ_C 11.1 ($2CH_2$), 13.7 (CH_3 xanthate), 20.6 and 21.6 (CH_3 and CHCO), 24.7 (CH_2), 40.0 (CH_2), 46.2 (CH_2), 50.0 (CHS), 70.4 (OCH_2), 127.1 (CH Ar), 129.8 (CH Ar), 136.9 (C Ar), 143.5 (C Ar), 209.9 (CO), 212.7 (CS), *m/z* 416 (MH^+), 433 ($M+NH_4^+$).

3.1.5.6. *O*-Ethyl-*S*-[4-oxo-4-(2-oxooxazolidin-3-yl)-1-(4-trifluoromethoxybenzene-sulfonylaminomethyl)butyl]-dithiocarbonate 6i. Isolated as an oil, 94%; ν_{max}/cm^{-1} 1792 (OCON), 1707 (NCO), 1386, 1164 (NSO_2), 1216 (C═S), 1051 (COS); δ_H 1.39 (t, 3H, *J*=7.2 Hz, CH_3 xanthate), 1.92 (m, 1H, CH), 2.18 (m, 1H, CH), 3.04 (m, 2H, CH_2), 3.29 (t, 2H, *J*=6.4 Hz, CH_2), 3.83 (m, 1H, CHS), 4.01 (t, 2H, *J*=8 Hz, CH_2), 4.43 (t, 2H, *J*=8 Hz, CH_2), 4.60 (qd, 2H, *J*=7.2 Hz, OCH_2), 5.41 (t, 1H, *J*=6 Hz, NH), 7.34 (d, *J*=8 Hz, 2H, ArH), 7.93 (d, *J*=8 Hz, 2H, ArH); δ_C 13.8 (CH_3 xanthate), 25.6 (CH_2), 32.3 (CH_2CO), 42.6 (NCH_2), 46.2 (NCH_2), 49.8 (CHS), 62.4 (OCH_2), 70.7 (OCH_2 xanthate), 121.1 (Ar), 129.4 (Ar), 138.4 (Ar), 152.2 (Ar), 153.5 (CO), 172.3, 212.7 (CS); *m/z* 531 (MH^+), 548 ($M+NH_4^+$).

3.1.5.7. Ethyl 4-ethoxythiocarbonylsulfanyl-5-(4-methoxybenzenesulfonylamino)pentanoate 6j. Purification by flash column chromatography (petrol/EtOAc 10:0 to 8:2), 93%, yellow oil; ν_{max}/cm^{-1} 3275 (NH), 2983, 2939, 2839, 1736 (OC═O), 1652, 1598, 1477, 1348 (SO_2), 1223 (OC–S), 1160, 1052 (C═S); δ_H 1.26 (t, *J*=7.6 Hz, 3H, CH_3 ester), 1.40 (t, *J*=6.8 Hz, 3H, CH_3 xanthate), 1.81–1.89 (m, 1H, CH), 2.05–2.14 (m, 1H, CH), 2.38–2.46 (m, 2H, CH_2CO), 3.21 (t, *J*=6 Hz, 2H, NCH_2), 3.79–3.83 (m, 1H, CHS), 3.87 (s, 3H, OCH_3), 4.13 (q, *J*=7.6 Hz, 2H, OCH_2 ester), 4.60 (q, *J*=6.8 Hz, 2H, OCH_2 xanthate), 5.08 (t, *J*=7.2 Hz, 1H, NH), 6.98 (d, *J*=8.8 Hz, 2H, CH Ar), 7.79 (d, *J*=8.8 Hz, 2H, CH Ar); δ_C 13.8 (CH_3 xanthate), 14.2 (CH_3 ester), 26.1 (CH_2), 31.3 (CH_2CO), 46.2 (NCH_2), 50.0 (CHS), 55.7 (OCH_3), 60.8 (OCH_2 ester), 70.5 (OCH_2 xanthate), 114.4 (2CH Ar), 129.3 (2CH Ar), 131.3 (C Ar), 163 (C Ar), 172.8 (CO), 212.6 (CS); *m/z* 436 (MH^+), 453 ($M+NH_4^+$).

3.1.5.8. *N*-(2-Ethoxythiocarbonylsulfanyl-4-phenoxycarbonylbutyl)-4-fluorobenzenesulfonamide 6k. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 42%; ν_{max}/cm^{-1} 3284 (NH), 1761 (CO), 1342, 1168 (SO_2), 1225 (CSO), 1052 (CS); δ_H 1.41 (t, *J*=7 Hz, 3H, CH_3), 1.90–2.05 (m, 1H, CH), 2.18–2.30 (m, 1H, CH), 2.69 (dd, *J*=7.2, 16.8 Hz, 1H, CHCO), 2.76 (dd, *J*=6.6, 17 Hz, 1H, CHCO), 3.29 (br s, 2H, NCH_2), 3.85–3.95 (m, 1H, CHS), 4.63 (q, *J*=7 Hz, 2H, OCH_2), 5.10 (br s, 1H, NH), 7.07 (d, *J*=8.4 Hz, 2H, H-*o* phenoxy), 7.17 (t, *J*=8.4 Hz, 2H, H-*m* fluorophenyl), 7.24 (t, *J*=7 Hz, 1H, H-*p* phenoxy), 7.38 (t, *J*=7.8 Hz, 2H, H-*m* phenoxy), 7.87 (d, *J*=5.2 Hz, 1H, H-*o* fluorophenyl), 7.89 (d, *J*=5.2 Hz, 1H, H-*o* fluorophenyl); δ_C 13.7 (CH_3), 26.1 (CH_2), 31.3 (CH_2CO), 46.4 (NCH_2), 50.1 (CHS), 70.6 (OCH_2), 116.4 (d, *J*=22.6 Hz, C-*m* fluorophenyl), 121.4 (C-*o* phenoxy), 125.9 (C-*p* phenoxy), 129.4 (C-*m* phenoxy), 129.8 (d, *J*=9.3 Hz, C-*o* fluorophenyl), 136.0 (d, *J*=3.1 Hz, C-*ipso* fluorophenyl), 150.5 (C-*ipso* phenoxy), 165.1 (d, *J*=253.3 Hz, C-*p* fluorophenyl), 171.2 (CO), 212.5 (CS); *m/z* 472 (MH^+), 489 ($M+NH_4^+$).

3.1.5.9. Ethyl 7-(4-chlorobenzenesulfonylamino)-6-ethoxythiocarbonylsulfanyl-3-oxoheptanoate 6l. Purification by flash column chromatography (petrol/EtOAc gradient from 10:0 to 8:2), 76%, yellow crystals; ν_{max}/cm^{-1} 3294 (NH), 2983, 2929, 1740 (OC═O), 1720 (C═O), 1652, 1588, 1477, 1410, 1347 (SO_2), 1224 (OC–S), 1167, 1052 (C═S); δ_H 1.26 (t, *J*=7.2 Hz, 3H, CH_3 ester), 1.40 (t, *J*=7.2 Hz, 3H, CH_3 xanthate), 1.78–1.88 (m, 1H, CH), 2.07–2.17 (m, 1H, CH), 2.72 (q, *J*=7.2 Hz, 2H, CH_2CO), 3.23 (t, *J*=6 Hz, 2H, CH_2N), 3.44 (s, 2H, $COCH_2CO$), 3.75–3.83 (m, 1H, CHS), 4.20 (q, *J*=7.2 Hz, 2H, OCH_2 ester), 4.60 (q, *J*=7.2 Hz, 2H, OCH_2 xanthate), 5.28 (t, *J*=6 Hz, 1H, NH), 7.49 (d, *J*=8 Hz, 2H, CH Ar), 7.80 (d, *J*=8 Hz, 2H, CH Ar); δ_C 13.8 (CH_3 xanthate), 14.2 (CH_3 ester), 24.4 (CH_2), 39.8 (CH_2CO), 46.4 ($COCH_2CO$), 49.3 (CH_2N), 49.9 (CHS), 61.6 (OCH_2 ester), 70.7 (OCH_2 xanthate), 128.6 (2CH Ar), 129.5 (2CH Ar), 138.4 (C Ar), 139.3 (C Ar), 167.1 (CO ester), 201.9 (CO ketone), 212.6 (CS), *m/z* 482 (MH^+), 499 ($M+NH_4^+$).

3.1.5.10. *O*-Ethyl-*S*-[2-(2-chlorobenzenesulfonylamino)-1-(2-oxotetrahydrofuran-3-ylmethyl)ethyl]dithiocarbonate 6m. Two diastereomers, D1 and D2, purified by flash chromatography (petrol/EtOAc 8:2), yellow oil, 92%; ν_{max}/cm^{-1} 3392, 1572 (NH), 1352, 1172 (SO_2); δ_H 1.39 and 1.41 (2t, *J*=6.4 Hz, 6H, CH_3), 1.78 (ddd, *J*=7, 8.4, 15 Hz, 1H, CH D2), 1.87–2.07 (m, 3H, CH D1, CH ring D1 and CH ring D2), 2.16 (ddd, *J*=4.3, 10.5, 14.7 Hz, 1H, CH D1), 2.27 (dt, *J*=6.9, 14.8 Hz, 1H, CH D2), 2.36–2.50 (m, 2H, CH ring D1 and CH ring D2), 2.70 (ddd, *J*=7, 10.8, 14.8 Hz, 1H, CHCO D2), 2.78 (ddd, *J*=4.4, 9.8, 19.4 Hz, 1H, CHCO D1), 3.16–3.36 (m, 4H, CH_2N), 3.92 (td, *J*=5.6, 10.8 Hz, 1H, CHS D1), 4.08 (dt, *J*=5.8, 15.2 Hz, 1H, CHS D2), 4.18 (dd, *J*=9.2, 16.4 Hz, 2H,

CHO ring D1 and CHO ring D2), 4.36 (dd, J=7.8, 15.8 Hz, 1H, CHO ring D1 and CHO ring D2), 4.57–4.65 (m, 4H, OCH_2), 5.52 (t, J=7.2 Hz, 1H, NH), 5.56 (t, J=6.8 Hz, 1H, NH), 7.40–7.45 (m, 2H, ArH), 7.50–7.55 (m, 4H, ArH), 8.08 (t, J=7.6 Hz, 2H, ArH); δ_C 13.7 (CH_3), 29.2 (CH_2 ring D1), 29.4 (CH_2 ring D2), 31.5 (CH_2 D1), 32.2 (CH_2 D2), 36.96 (CHCO D1), 37.00 (CHCO D2), 46.4 (CH_2N D2), 46.7 (CH_2N D1), 48.8 (CHS D2), 49.0 (CHS D1), 66.45 (CH_2O ring D2), 66.51 (CH_2O ring D1), 70.5 (OCH_2 D2), 70.7 (OCH_2 D1), 127.3 (CH Ar), 131.1 (CH Ar D2), 131.3 (CH Ar D1), 131.39 (CCl D1), 131.42 (CCl D2), 131.6 (CH Ar D1), 131.7 (CH Ar D2), 133.8 (CH Ar D2), 133.9 (CH Ar D1), 136.9 (C-*ipso* D1), 137.0 (C-*ipso* D2), 178.4 (CO D2), 178.5 (CO D1), 211.9 (CS D2), 212.2 (CS D1); m/z 438 (MH^+), 455 (MNH_4^+).

3.1.5.11. *O*-Ethyl-*S*-[1-(4-bromobenzenesulfonylaminomethyl)-4-oxo-4-piperidin-1-ylbutyl]dithiocarbonate 6n. Purified by flash column chromatography (petrol/EtOAc 1.1), yellow oil, 66%; ν_{max}/cm^{-1} 3197, 1576 (NH), 1632 (CO), 1347, 1168 (SO_2), 1221 (COS), 1054 (CS); δ_H 1.40 (t, J=7.2 Hz, 3H, CH_3), 1.45–1.65 (m, 6H, CH_2 piperidine), 1.80–1.96 (m, 1H, CH), 2.07–2.19 (m, 1H, CH), 2.32–2.48 (m, 2H, CH_2CO), 3.13 (dt, J=6.7, 13.4 Hz, 1H, CHN), 3.26 (ddd, J=5.6, 6.4, 13.2 Hz, 1H, CHN), 3.34 (t, J=5.4 Hz, 2H, 2CH piperidine), 3.50 (t, J=5.6 Hz, 2H, 2CH piperidine), 3.74–3.83 (m, 1H, CHS), 4.53–4.66 (m, 2H, OCH_2), 6.13 (t, J=6.2 Hz, 1H, NH), 7.62 (d, J=8.8 Hz, 2H, ArH), 7.74 (d, J=8.4 Hz, 2H, ArH); δ_C 13.7 (CH_3), 24.4 (CH_2 piperidine), 25.5 (CH_2 piperidine), 25.7 (CH_2), 26.3 (CH_2 piperidine), 29.6 (CH_2CO), 43.0 (NCH_2 piperidine), 46.0 (NCH_2), 46.5 (NCH_2 piperidine), 49.9 (CHS), 70.4 (OCH_2), 127.3 (C Ar), 128.7 (CH Ar), 132.2 (CH Ar), 139.3 (C Ar), 169.9 (CO), 212.7 (CS); m/z 525 (MH^+).

3.1.5.12. Dithiocarbonic acid *O*-ethyl ester *S*-[1-(4-iodobenzenesulfonylaminomethyl)-5,5-dimethoxy-4-oxopentyl]ester 6o (two diastereomers). Purification by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 95%; ν_{max}/cm^{-1} 3279 (NH), 1740 (CO), 1316, 1166 (SO_2), 1221 (COS), 1054 (CS); δ_H 1.40 (t, 3H, J=7.1 Hz, OCH_3), 1.75–1.86 (m, 1H, CH), 2.00–2.13 (m, 1H, CH), 2.83–2.88 (m, 0.5H, CHCO), 2.93–2.98 (m, 0.5H, CHCO), 3.23–3.37 (m+s, 8H, CH_2N, $2OCH_3$), 3.64–3.88 (m+s, 4H, CH, CO_2CH_3), 4.49–4.52 (m, 1H, CHS), 4.58–4.65 (m, 2H, OCH_2), 5.09 (m, 1H, NH), 7.57 (d, 2H, J=7.7 Hz, ArH), 7.87 (d, 2H, J=8.3 Hz, ArH); δ_C 13.8 (CH_3) 28.4 and 28.9 (CH_2), 45.8 (CH_2N), 46.5, 46.7 (CH), 47.2 (CH_2N), 48.9 and 49.1 (CHCO), 52.3, 53.9, 54.1, 54.9 and 55.0 (OCH_3), 70.6 and 70.7 (OCH_2), 100.2 (CI), 104.5 and 104.8 ($CHOCH_3$), 128.6 and 138.5 (CH Ar), 172.5 and 172.6 (CO), 212.8 (CS); m/z 609 ($M+NH_4^+$).

3.1.5.13. Dithiocarbonic acid *O*-ethyl ester *S*-[4-oxo-4-thiophen-2-yl-1-(4-trifluoromethylbenzenesulfonylaminomethyl)butyl]ester 6p. Purified by flash column chromatography (petrol/EtOAc 7:3), yellow oil, 49%; ν_{max}/cm^{-1} 3283, 1517 (NH), 1668 (CO), 1322, 1173 (SO_2), 1226 (COS), 1063 (CS); δ_H 1.37 (t, J=7.2 Hz, 3H, CH_3), 1.94–2.04 (m, 1H, CH), 2.22–2.32 (m, 1H, CH), 3.07 (t, J=6.8 Hz, 2H, CH_2CO), 3.31 (td, J=2.1, 6.4 Hz, 2H, CH_2N), 3.82–3.90 (m, 1H, CHS), 4.50–4.63 (m, 2H, OCH_2), 5.47 (t, J=6.4 Hz, 1H, NH), 7.12 (dd, J=4, 4.8 Hz, 1H, H-4 thiophene), 7.64 (dd, J=1, 5 Hz, 1H, CH thiophene), 7.70 (dd, J=1, 5 Hz, 1H, CH thiophene), 7.77 (d, J=8.4 Hz, 2H, ArH), 8.00 (d, J=8 Hz, 2H, ArH); δ_C 13.6 (CH_3), 25.1 (CH_2), 35.9 (CH_2CO), 46.4 (CH_2N), 50.0 (CHS), 70.5 (OCH_2), 123.2 (q, J=271.1 Hz, CF_3), 126.3 (q, J=3.7 Hz, C-*m*), 127.6 (C-*o*), 128.2 (C-4 thiophene), 132.2 (CH thiophene), 134.0 (CH thiophene), 134.4 (q, J=32.9 Hz, C-*p*), 143.56 (C-*ipso*), 143.61 (C-*ipso*), 191.8 (CO), 212.4 (CS); m/z 512 (MH^+), 529 ($M+NH_4^+$).

3.1.5.14. Dithiocarbonic acid *O*-ethyl ester *S*-[1-(4-cyanobenzenesulfonylaminomethyl)-5,5-dimethyl-4-oxohexyl]ester 6q. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 81%; ν_{max}/cm^{-1} 3225 (NH), 2234 (CN), 1705 (CO), 1352, 1166 (SO_2), 1225 (COS), 1052 (CS); δ_H 1.10 (s, 9H, CH_3 ^tBu), 1.40 (t, J=7 Hz, 3H, CH_3), 1.69–1.81 (m, 1H, CH), 2.00–2.10 (m, 1H, CH), 2.55–2.72 (m, 2H, CH_2CO), 3.23 (dd, J=6.4, 13.2 Hz, 1H, CHN), 3.29 (dd, J=6, 13.2 Hz, 1H, CHN), 3.63–3.76 (m, 1H, CHS), 4.53–4.66 (m, 2H, OCH_2), 5.46 (t, J=6 Hz, 1H, NH), 7.81 (d, J=8 Hz, 2H, H-*m*), 7.99 (d, J=8 Hz, 2H, H-*o*); δ_C 13.7 (CH_3), 24.5 (CH_2), 26.4 (CH_3 ^tBu), 33.3 (CH_2CO), 44.1 (C ^tBu), 46.6 (CH_2N), 50.1 (CHS), 70.6 (OCH_2), 116.4 (C-*p*), 117.3 (CN), 127.7 (C-*o*), 132.9 (C-*m*), 144.4 (C-*ipso*), 212.8 and 215.2 (CO and CS); m/z 443 (MH^+), 460 ($M+NH_4^+$).

3.1.5.15. *O*-Ethyl-*S*-[1-(4-*tert*-butylbenzenesulfonylaminomethyl)-4-cyclohexyl-4-oxobutyl]dithiocarbonate 6r. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 80%; ν_{max}/cm^{-1} 3274, 1596 (NH), 1710 (CO), 1342, 1167 (SO_2), 1221, 1113 (COS), 1053 (CS); δ_H 1.10–1.30 (m, 5H, CH cyclohexyl), 1.32 (s, 9H, CH_3 ^tBu), 1.37 (t, J=7 Hz, 3H, CH_3), 1.63 (d, J=10.4 Hz, 1H, CH cyclohexyl), 1.67–1.75 (m, 5H, 4CH cyclohexyl and CH), 1.98–2.12 (m, 1H, CH), 2.22–2.35 (m, 1H, H-1 cyclohexyl), 2.56 (t, J=6.8 Hz, 2H, CH_2CO), 3.15 (dd, J=6.8, 13.6 Hz, 1H, CHN), 3.71 (dd, J=6.2, 13.4 Hz, 1H, CHN), 3.70–3.80 (m, 1H, CHS), 4.58 (q, J=6.3 Hz, 2H, OCH_2), 5.29 (t, J=6.2 Hz, 1H, NH), 7.49 (d, J=8 Hz, 2H, ArH), 7.76 (d, J=8 Hz, 2H, ArH); δ_C 13.6 (CH_3), 24.5 (CH_2 cyclohexyl), 25.5 (CH_2), 25.7 (CH_2 cyclohexyl), 28.4 (CH_2 cyclohexyl), 31.0 (CH_3 ^tBu), 35.0 (C ^tBu), 37.1 (CH_2CO), 46.3 (CH_2N), 50.0 (CHS), 50.7 (C-1 cyclohexyl), 70.2 (OCH_2), 126.0 (CH Ar), 126.8 (CH Ar), 136.8 (C Ar), 156.4 (C Ar), 212.6 and 212.9 (CO and CS); m/z 500 (MH^+), 517 (MNH_4^+).

3.1.5.16. *O*-Ethyl-*S*-[1-(4-chlorobenzenesulfonylaminomethyl)-4-oxo-5,5,5-trifluoropentyl]dithiocarbonate 6s. Purified by flash column chromatography (petrol/EtOAc 7:3), yellow oil, 78%; ν_{max}/cm^{-1} 3432 (NH), 1766 (CO), 1313 (SO_2), 1225 (O–C), 1167 (SO_2), 1052 (CS); δ_H 1.39 (t, J=7 Hz, 3H, CH_3 xanthate), 1.82–1.94 (m, 1H, CH), 2.22 (dtd, J=4.8, 7.2, 14.8 Hz, 1H, CH), 2.88 (td, J=3.2, 7.2 Hz, 2H, CH_2CO), 3.25 (t, J=6.4 Hz, 2H, NCH_2), 3.80 (td, J=6, 10.4 Hz, 1H, CHS), 4.54–4.63 (m, 2H, OCH_2), 5.41 (t, J=6.6 Hz, 1H, NH), 7.48 (d, J=8.4 Hz, 2H, ArH), 7.79 (d, J=8.4 Hz, 2H, ArH); δ_C 13.6 (CH_3), 23.6 (CH_2), 33.5 (CH_2CO), 46.4 (NCH_2), 49.6 (CHS), 70.8 (OCH_2), 115.3 (q, J=290 Hz, CF_3), 128.5 (CH Ar), 129.5 (CH Ar), 138.1 (C Ar), 139.4 (C Ar), 190.5 (q, J=35.4 Hz, CO), 212.0 (CS); m/z 447 (MH^+).

3.1.5.17. *O*-Ethyl-*S*-[1-(4-chlorobenzenesulfonylaminomethyl)-4-methoxyimino-5,5,5-trifluoropentyl]dithiocarbonate 6t. Two isomers, purified by flash column chromatography (petrol/EtOAc 9:1), yellow oil, 74%; ν_{max}/cm^{-1} 3276 (NH), 1719 (C=N), 1343 and 1166 (SO_2), 1222 (O–CS), 1052 (C=S); δ_H 1.38 (t, J=7 Hz, 3H, CH_3), 1.70–1.85 (m, 1H, CH), 1.93–2.08 (m, 1H, CH), 2.38–2.60 (m, 2H, CH_2CO), 3.19–3.30 (m, 2H, NCH_2), 3.67–3.82 (m, 1H, CHS), 3.93–3.96 (2s, 3H, OCH_3), 4.53–4.63 (m, 2H, OCH_2), 7.47 (d, J=8.4 Hz, 2H, CH Ar), 7.78 (d, J=8.4 Hz, 2H, CH Ar); δ_C 13.7 (CH_3 xanthate), 22.1 (CH_2), 26.8 and 27.2 (CH_2C=N), 46.1 and 46.4 (NCH_2), 49.8 and 50.4 (CHS), 63.4 (OCH_3), 70.6 (OCH_2), 120.6 (q, J=272.4 Hz, CF_3), 117.9 (q, J=270 Hz, CF_3), 128.5 (CH Ar), 129.5 (CH Ar), 138.3 (C Ar), 139.3 (C Ar), 144.9 (q, J=29.3 Hz, C=N), 147.6 (q, J=32.0 Hz, C=N), 212.3 (CS); m/z 493 (MH^+), 510 ($M+NH_4^+$).

3.1.5.18. Ethyl 4-ethoxythiocarbonylsulfanyl-5-(3-methoxybenzenesulfonylamino)pentanoate 6u. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow oil, 80%; ν_{max}/cm^{-1} 3282 (NH), 1736 (CO), 1345 (SO_2), 1222 (O–CS), 1161 (SO_2), 1051 (C=S); δ_H 1.22 (t, J=7.2 Hz, 3H, CH_3 ester), 1.37 (t, J=7.2 Hz, 3H, CH_3 xanthate), 1.79–1.91 (m, 1H, CH), 2.05–2.15 (m, 1H, CH), 2.32–2.49 (m, 2H, CH_2CO), 3.22 (t, J=6.4 Hz, 2H, NCH_2), 3.75–3.85 (m, 1H, CHS), 3.83 (s, 3H, OCH_3), 4.088 and 4.094 (2q, J=7.2 Hz each, 2H, OCH_2 ester), 4.52–4.62 (m, 2H, OCH_2 xanthate), 5.27 (t, J=6.4 Hz, 1H, NH), 7.07 (ddd, J=1.6, 2.8, 7.4 Hz, 1H, ArH), 7.34–7.43 (m, 3H, ArH); δ_C 13.6 (CH_3 xanthate), 14.1 (CH_3 ester), 26.0 (CH_2), 31.1 (CH_2CO), 46.2 (NCH_2), 49.9 (CHS), 55.6 (OCH_3), 60.6 (OCH_2 ester), 70.4 (OCH_2 xanthate), 111.5 (CH Ar), 119.07 (CH Ar), 119.14 (CH Ar), 130.1 (CH Ar), 140.8 (C Ar), 159.9 (C Ar), 172.6 (CO ester), 212.4 (CS); m/z 436 (MH^+), 454 ($M+NH_4^+$).

3.1.6. General procedure for the synthesis of imines 7. *Method A*: To a solution of acetamide **5** (1 equiv) in dioxane (0.4 mL/mmol) was added concentrated HCl (4 mL/mmol), and the mixture was heated at reflux temperature for 1.5 days. The reaction mixture was then evaporated, the residue dissolved in CH_2Cl_2, and washed with saturated aqueous $NaHCO_3$ solution. The organic phase was dried and concentrated, and the imine was obtained without further purification.

Method B: To a solution of acetamide **5** (1 equiv) in dioxane (0.4 mL/mmol) was added concentrated HCl (4 mL/mmol), and the mixture was heated at reflux temperature for 1.5 days. The reaction mixture was then evaporated, and the imine was obtained as the hydrochloride, which was used in the next reaction without further purification.

3.1.7. General procedure for the synthesis of piperidines 8. To a solution of imine **7** (1 equiv) in methanol (8 mL/mmol) at 0 °C were added $NaBH_3CN$ (2.5 equiv) and a few drops of glacial AcOH, and the resulting mixture was stirred at room temperature for 3 h. After that time, the reaction mixture was concentrated, CH_2Cl_2 was added, and the organic phase washed with saturated aqueous $NaHCO_3$ solution. The organic phase was dried and concentrated, and the residue was purified by flash column chromatography.

3.1.7.1. (2*SR*,5*SR*)-2-Phenyl-5-*p*-tolylpiperidine 8b. Purified by flash column chromatography (EtOAc), white solid, 89%; mp 119–121 °C; ν_{max}/cm^{-1} 3050 (NH); δ_H 1.68–1.87 (m, 2H, H-4_{ax} and H-3_{ax}), 1.96–2.15 (m, 2H, H-4_{eq} and H-3_{eq}), 2.38 (s, 3H, CH_3), 2.85 (tt, J=3.2, 11.2 Hz, 1H, H-5_{ax}), 2.91 (t, J=11.2 Hz, 1H, H-6_{ax}), 3.35 (d, J=9.6 Hz, 1H, H-2_{ax}), 3.73 (dd, J=2.4, 10.8 Hz, 1H, H-6_{eq}), 7.18 (d, J=8 Hz, 2H), 7.22 (d, J=8 Hz, 2H), 7.31 (d, J=7.2 Hz, 1H), 7.38 (t, J=7.6 Hz, 2H), 7.45 (d, J=7.2 Hz, 2H); δ_C 21.0 (CH_3), 32.5 and 35.0 (C-3 and C-4), 42.7 (C-5), 54.7 (C-6), 61.8 (C-2), 126.6, 127.0, 127.1, 128.4, 129.1 (CH Ar), 135.8, 141.5, 145.0 (C Ar); m/z 252 (MH^+).

3.1.7.2. (2*SR*,5*SR*)-2-Benzyl-5-*p*-tolylpiperidine 8f. Purified by flash column chromatography (petrol/EtOAc 1:1), off-white solid, 85%; mp 118–119 °C; ν_{max}/cm^{-1} 3100 (NH); δ_H 1.60 (ddd, J=2.6, 12.4, 24.6 Hz, 1H, H-4_{ax}), 1.75 (dt, J=2.7, 13.9 Hz, 1H, H-3_{ax}), 1.92–2.06 (m, 2H, H-4_{eq} and H-3_{ax}), 2.29 (s, 3H, CH_3), 2.88 (dd, J=10.7, 15.0 Hz, 1H, CHPh), 2.92 (t, J=12.6 Hz, 1H, H-6_{ax}), 3.09 (tt, J=3.3, 12.3 Hz, 1H, H-5_{ax}), 3.17–3.26 (m, 2H, CHAr and H-2), 3.45 (dd, J=1.8, 12.4 Hz, 1H, H-6_{eq}), 7.05 (d, J=8.3 Hz, 2H, ArH), 7.09 (d, J=8.2 Hz, 2H, ArH), 7.20–7.33 (m, 5H, ArH); δ_C 21.0 (CH_3), 28.2 (C-3), 30.0 (C-4), 39.1 (C-5), 39.7 (CH_2Ph), 50.6 (C-6), 58.7 (C-2), 126.8, 127.4, 129.0, 129.4, 129.6 (CH Ar), 134.9, 137.0, 137.3 (C Ar); m/z 266 (MH^+).

3.1.7.3. (2*SR*,5*SR*)-2-(Thiophen-2-yl)-5-(4-trifluorophenyl)piperidine 8p. Purified by flash column chromatography (petrol/EtOAc 3:7), yellow solid, 64%; mp 103–105 °C; ν_{max}/cm^{-1} 3073 (NH); δ_H 1.78 (m, 2H, H-4_{ax} and H-3_{ax}), 1.92 (br s, 1H, NH), 2.07–2.18 (m, 2H, H-4_{eq} and H-3_{eq}), 2.89 (dd, J=10.6, 17 Hz, 2H, H-2_{ax} and H-6_{ax}), 3.31 (dd, J=11, 17.4 Hz, 1H, H-5_{ax}), 4.04 (dd, J=2.4, 10 Hz, 1H, H-6_{eq}), 6.96–7.02 (dd, J=0.9, 5.2 Hz, 1H, ArH), 7.36 (d, J=8.1 Hz, 2H, ArH), 7.57 (d, J=8.1 Hz, 2H, ArH); δ_C 31.9 and 35.7 (C-3 and C-4), 43.1 (C-5), 54.0 (C-6), 56.8 (C-2), 123.0, 123.8, 125.4, 126.4, 127.5 (CH Ar), 148.3 (C Ar), 148.6 (C Ar); m/z 311 (MH^+); Elem. Anal. Calcd for $C_{16}H_{16}F_3NS$: C, 61.72; H, 5.18; found: C, 61.41; H, 5.11.

3.1.7.4. (2*SR*,5*SR*)-2-(*tert*-Butyl)-5-(4-hydroxymethylphenyl)piperidine 8q. Purified by flash column chromatography (CH_2Cl_2/MeOH 95:5), white solid, 66%; mp 107–109 °C; ν_{max}/cm^{-1} 3617 (NH, OH); δ_H 0.93 (s, 9H, 3 CH_3), 1.29 (ddd, J=3.6, 12.8, 24.4 Hz, 1H, H-3_{ax}), 1.56 (ddd, J=3.6, 12.6, 24.2 Hz, 1H, H-4_{ax}), 1.82 (ddd, J=3, 5.8, 12.6 Hz, 1H, H-3_{eq}), 1.99 (dt, J=2.4, 13.6 Hz, 1H, H-4_{eq}), 2.22 (dd, J=2.4, 11.2 Hz, 1H, H-2_{ax}), 2.55–2.65 (m, 2H, H-6_{ax} and H-5_{ax}), 3.12 (dd, J=2, 8 Hz, 1H, H-6_{eq}), 4.62 (s, 2H, OCH_2), 7.16 (d, J=8 Hz, 2H, ArH), 7.28 (d, J=8 Hz, 2H, ArH); δ_C 26.6 ($3CH_3$), 26.9 (C-3), 32.4 (C-4), 33.2 (C), 43.3 (C-5), 54.6 (C-6), 64.8 (OCH_2), 66.1 (C-2), 127.1 (CH Ar), 127.2 (CH Ar), 139.1 (C Ar), 144.0 (C Ar); m/z 248 (MH^+); HRMS calcd for $C_{16}H_{25}NO$, 247.1936; found, 247.1941.

3.1.7.5. (2*SR*,5*SR*)-5-(4-*tert*-Butylphenyl)-2-cyclohexylpiperidine 8r. Purified by flash column chromatography (petrol/EtOAc 3:7), white solid, 77%; mp 201–204 °C; ν_{max}/cm^{-1} 3100 (NH); δ_H 1.00–1.40 (m, 5H), 1.29 (s, 9H,

CH_3), 1.55–1.75 (m, 6H, H-4_{ax}, H-3_{ax}, H-1 cyclohexyl and 3CH cyclohexyl), 1.78–1.85 (m, 2H, CH_2 cyclohexyl), 2.00–2.15 (m, 2H, H-4_{eq} and H-3_{eq}), 2.82–2.91 (m, 1H, H-2_{ax}), 2.97 (t, J=12.5 Hz, 1H, H-6_{ax}), 3.07–3.21 (m, 1H, H-5_{ax}), 3.54 (dd, J=1.2, 10.8 Hz, 1H, H-6_{eq}), 7.15 (d, J=8.3 Hz, 2H, ArH), 7.33 (d, J=8.3 Hz, 2H, ArH); δ_C 25.65, 25.7, 25.8, 26.0, 28.2 (CH_2), 29.1 and 30.1 (C-3 and C-4), 31.3 (CH_3 ^{t}Bu), 34.4 (C ^{t}Bu), 39.0 (C-5), 40.1 (C-1 cyclohexyl), 51.0 (C-6), 62.4 (C-2), 125.7 (CH Ar), 126.7 (CH Ar), 137.1 (C Ar), 150.4 (C Ar); m/z 299 (MH^+); HRMS calcd for $C_{21}H_{23}N$, 299.2613; found, 299.2613.

3.1.7.6. (2*SR*,5*SR*)-5-(4-Chlorophenyl)-2-trifluoromethylpiperidine 8t. Purified by flash column chromatography (petrol/EtOAc 95:5), white solid, 68%; mp 71–74 °C; ν_{max}/cm^{-1} 3351 (NH); δ_H 1.54–1.70 (m, 2H, H-3 and H-4), 1.94 (br s, 1H, NH), 1.99–2.12 (m, 2H, H-3 and H-4), 2.64–2.76 (m, 2H, H-5 and H-6), 3.13–3.31 (m, 2H, H-2 and H-6), 7.13 (d, J=8.4 Hz, 2H, ArH), 7.28 (d, J=8.8 Hz, 2H, ArH); δ_C 25.1 (CH_2), 30.3 (CH_2), 42.3 (C-5), 52.8 (C-6), 57.8 (q, J=28.7 Hz, C-2), 125.7 (q, J=277.4 Hz, CF_3), 128.3 (CH Ar), 128.7 (CH Ar), 132.4 (C Ar), 141.8 (C Ar); m/z 264 (MH^+), 281 ($M+NH_4^+$); HRMS calcd for $C_{12}H_{13}F_3ClN$, 263.0689; found, 263.0694.

3.1.8. General procedure for the synthesis of piperidones 9. A solution of acetamide **5** (1 equiv) in concentrated HCl (5 mL/mmol) was heated at reflux temperature for 4 h. The reaction mixture was then concentrated, and the residue was purified by flash column chromatography.

3.1.8.1. 5-*p*-Tolylpiperidin-2-one 9c. Purified by flash column chromatography (EtOAc), white solid, 88%; mp 95–97 °C; ν_{max}/cm^{-1} 3451, 3305, 1496 (NH), 1685 (CO); δ_H 2.02–2.08 (m, 2H, H-4), 2.34 (s, 3H, CH_3), 2.49–2.56 (m, 2H, H-3), 2.99–3.05 (m, 1H, H-5), 3.32–3.38 (m, 1H, H-6_{ax}), 3.46–3.50 (m, 1H, H-6_{eq}), 6.33 (br s, 1H, H-1), 7.13–7.14 (m, 4H, ArH); δ_C 21.1 (CH_3), 27.9 (C-3), 31.4 (C-4), 39.2 (C-5), 48.8 (C-6), 126.9 (CH Ar), 129.5 (CH Ar), 136.8 (C Ar), 138.8 (C Ar), 172.2 (C-2); m/z 190 (MH^+), 207 (MNH_4^+).

3.1.8.2. 5-*p*-Bromophenylpiperidin-2-one 9n. Purified by flash column chromatography (CH_2Cl_2/MeOH 95:5), white solid, 37%; mp 189–190 °C; ν_{max}/cm^{-1} 3400 (NH), 1675 (CO); δ_H 1.95–2.15 (m, 2H, H-4), 2.42–2.58 (m, 2H, H-3), 2.97–3.07 (m, 1H, H-5), 3.33 (t, J=11.4 Hz, 1H, H-6_{ax}), 3.44–3.52 (m, 1H, H-6_{eq}), 6.50 (br s, 1H, NH), 7.13 (d, J=8 Hz, 2H, ArH), 7.46 (d, J=8 Hz, 2H, ArH); δ_C 27.5 (C-4), 30.9 (C-3), 38.8 (C-5), 48.1 (C-6), 120.7 (C Ar), 128.6 (CH Ar), 131.7 (CH Ar), 140.6 (C Ar), 172.1 (C-2); m/z 254 (MH^+), 271 ($M+NH_4^+$); HRMS calcd for $C_{11}H_{12}BrNO$, 253.0102; found, 253.0103.

3.1.9. General procedure for the synthesis of pyridines 10. To a solution of imine **7** (1 equiv) in xylenes (25 mL/mmol) was added 10% Pd/C (1 equiv in weight) and heated at reflux temperature for 2.5 h. The reaction mixture was then filtered over Celite™ and concentrated. The residue was purified by the appropriate method.

3.1.9.1. 2-Phenyl-5-*p*-tolylpyridine 10. Purified by recrystallisation (EtOH), yellow solid, 83%; mp 141–143 °C; ν_{max}/cm^{-1} 2925, 2855, 1594, 1472, 1446; δ_H 2.43 (s, 3H, CH_3), 7.30–7.55 (m, 7H, CH Ar), 7.80 (d, J=8.4 Hz, 1H, H-3), 7.94 (dd, J=1.4, 8.4 Hz, 1H, H-4), 8.03 (dd, J=2.2, 8.2 Hz, 2H, CH Ar), 8.92 (d, J=1.4 Hz, 1H, H-6); δ_C 21.2 (CH_3), 120.3 (C-3), 126.77 (CH Ar), 126.80 (CH Ar), 128.8 (CH Ar), 128.9 (CH Ar), 129.8 (CH Ar), 134.7 (C-5), 134.81 (C Ar), 134.84 (C-4), 138.0 (C Ar), 139.0 (C Ar), 147.9 (C-6), 155.8 (C-2); m/z 246 (MH^+).

3.1.10. Ethyl 1-acetyl-5-(4-iodophenyl)-1,4,5,6-tetrahydropyridine-3-carboxylate 11. To a solution of acetamide **5o** (96 mg, 0.21 mmol) in CH_2Cl_2 (2 mL) was added *p*-TsOH·H_2O (45 mg, 0.24 mmol) and heated at reflux temperature for 4.5 h. After that time, the reaction mixture was cooled and washed with saturated aqueous $NaHCO_3$ solution and brine. The organic phase was dried and concentrated, and the residue was purified by flash column chromatography (petroleum ether/AcOEt 1:1). The desired piperidine was obtained as a white solid (72 mg, 89%); mp 111–113 °C; ν_{max}/cm^{-1} 1694 (CO), 1627 (CO); δ_H 2.32 (s, 3H, CH_3 acetyl), 2.38 (ddd, J=1.6, 14.8, 17.2 Hz, 1H, H-4_{ax}), 2.74 (dd, J=3.6, 17.2 Hz, 1H, H-4_{eq}), 2.87 (tt, J=4, 10.8 Hz, 1H, H-5), 3.10 (t, J=12 Hz, 1H, H-6_{ax}), 3.75 (s, 3H, OCH_3), 4.39 (d, J=12.4 Hz, 1H, H-6_{eq}), 6.96 (d, J=8.4 Hz, 2H, ArH), 7.64 (d, J=8.4 Hz, 2H, ArH), 7.88 (br s, 1H, H-2); δ_C 21.6 (CH_3 acetyl), 28.5 (C-4), 36.7 (C-5), 45.3 (C-6), 51.7 (OCH_3), 92.4 (C), 109.1 (C), 129.0 (CH Ar), 135.4 (C-2), 137.7 (CH Ar), 141.1 (C-*ipso*), 167.2 (CO), 169.1 (CO); HRMS calcd for $C_{15}H_{16}INO_3$, 385.0175; found, 385.0175.

3.1.11. Ethyl 3-(7-methoxy-1,1-dioxo-2-propionyl-1,2,3,4-tetrahydro-1λ^6-benzo[*e*][1,2]thiazin-4-yl)-propionate 12. Purified by flash column chromatography (petrol/EtOAc 9:1), yellow oil, 8%; ν_{max}/cm^{-1} 1736 (CO ester), 1708 (CO amide), 1348 (SO_2), 1162 (SO_2), 898 (S–N); δ_H 1.21 (t, J=7.4 Hz, 3H, CH_3), 1.26 (t, J=7.2 Hz, 3H, CH_3 ester), 1.65–1.75 (m, 1H, CH), 1.90–2.00 (m, 1H, CH), 2.30–2.48 (m, 1H, CHCO ester), 2.53–2.68 (m, 1H, CHCO ester), 2.91 (dq, J=7.4, 17.8 Hz, 1H, CHCO amide), 3.05 (dq, J=7.2, 17.6 Hz, 1H, CHCO amide), 3.18–3.25 (m, 1H, CHAr), 3.79 (dd, J=3.4, 15.2 Hz, 1H, NCH), 3.87 (s, 3H, OCH_3), 4.08–4.18 (m, 2H, OCH_2), 4.94 (dd, J=2.8, 14.8 Hz, 1H, NCH), 7.03 (d, J=8.4 Hz, 1H, CH Ar), 7.42 (t, J=8.4 Hz, 1H, CH Ar), 7.48 (d, J=8.4 Hz, 1H, CH Ar); δ_C 9.0 (CH_3), 14.2 (CH_3 ester), 26.2 (CH_2), 31.2 (CH_2CO amide), 31.9 (CH_2CO ester), 32.5 (CHAr), 44.1 (NCH_2), 55.9 (OCH_3), 60.3 (OCH_2), 113.9 (CH Ar), 115.7 (CH Ar), 128.5 (C Ar), 128.9 (CH Ar), 138.1 (C Ar), 156.1 (C Ar), 173.0 (CO), 173.1 (CO); m/z 370 (MH^+), 387 ($M+NH_4^+$).

3.1.12. General procedure for the synthesis of α,β-unsaturated esters 13. To a solution of ethyl methanesulfonylacetate (1 equiv) and the corresponding substituted benzenecarbaldehyde (1 equiv) in toluene (0.66 mL/mmol) was added some drops of AcOH and piperidine and the mixture was heated to reflux in a Dean–Stark apparatus. After the total consumption of the starting materials, the reaction mixture was concentrated, and the residue was purified by flash column chromatography.

3.1.12.1. Ethyl 3-(2,6-dichlorophenyl)-2-methanesulfonyl acrylate 13c. Purified by flash column

chromatography (petrol/EtOAc 9:1), two diastereomers *major* and *minor* 9:1, orange semi-solid, 60%; ν_{max}/cm^{-1} 1729 (CO), 1331 (SO_2), 1152 (SO_2); diastereomer *major* δ_H 0.99 (t, J=7.2 Hz, 3H, CH_3), 3.34 (s, 3H, CH_3), 4.14 (q, J=7.2 Hz, 2H, OCH_2), 7.20–7.40 (m, 3H, ArH), 8.05 (s, 1H, CH═); δ_C 13.3 (CH_3), 43.5 (SCH_3), 62.3 (OCH_2), 127.9 (CH Ar), 130.6 (CH Ar), 131.1 (C), 133.2 (C), 139.0 (C), 143.6 (CH═), 161.1 (CO); diastereomer *minor* δ_H 1.42 (t, J=7 Hz, 3H, CH_3), 3.25 (s, 3H, CH_3), 4.41 (q, J=7.2 Hz, 2H, OCH_2), 7.20–7.40 (m, 3H, ArH), 8.08 (s, 1H, CH═); δ_C 14.0 (CH_3), 42.5 (SCH_3), 62.9 (OCH_2), 127.4 (CH Ar), 130.1 (CH Ar), 131.1 (C), 132.2 (C), 137.1 (C), 145.3 (C═), 161.5 (CO); *m/z* 323 (MH^+), 340 ($M+NH_4^+$).

3.1.13. General procedure for the synthesis of γ,δ-unsaturated esters 14. To a solution of vinylmagnesium chloride (or bromide, 2.4 equiv) in THF (2 mL/mmol) at −78 °C was added CuI (1.2 equiv), and the temperature was raised to −40 °C for 10 min. After that time, the reaction mixture was cooled down to −78 °C and a solution of sulfone **13** (1 equiv) in THF (2 mL/mmol) was added dropwise. After 1 h, the reaction mixture was quenched by addition of aqueous saturated NH_4Cl solution, and it was extracted with EtOAc. The organic extracts were dried and concentrated, and the residue was purified by flash column chromatography.

3.1.13.1. Ethyl 3-(2-chloropyrid-5-yl)-2-methanesulfonylpent-4-enoate 14b. Purified by flash column chromatography (petrol/EtOAc 7:3), two diastereomers A and B 1:1, pale yellow oil, 76%; ν_{max}/cm^{-1} 1737 (CO); δ_H 0.96 (t, J=7.2 Hz, 1.5H, CH_3 diast. A), 1.23 (t, J=7.2 Hz, 1.5H, CH_3 diast. B), 2.98 (s, 1.5H, CH_3 diast. B), 3.15 (s, 1.5H, CH_3 diast. A), 3.98 (dq, J=1.6, 7.2 Hz, 1H, OCH_2 diast. A), 4.21 (q, J=7.2 Hz, 1H, OCH_2 diast. B), 4.40 (d, J=8.8 Hz, 0.5H, CHS diast. B), 4.47 (d, J=11.2 Hz, 0.5H, CHS diast. A), 4.62 (t, J=8.8 Hz, 0.5H, CHAr diast. B), 4.64 (t, J=11.2 Hz, 0.5H, CHAr diast. A), 5.24 (d, J=10 Hz, 0.5H, CH═diast. A), 5.27 (d, J=5.2 Hz, 0.5H, CH═diast. A), 5.29 (d, J=11.2 Hz, 0.5H, CH═diast. B), 5.33 (d, J=10.8 Hz, 0.5H, CH═diast. B), 6.00–6.20 (m, 1H, CH═), 7.15–7.25 (m, 1H, ArH), 7.61 (dd, J=2, 7.6 Hz, 0.5H, ArH diast. A), 7.68 (dd, J=2, 7.6 Hz, 0.5H, ArH diast. B), 8.27 (dd, J=1.6, 4.8 Hz, 0.5H, ArH diast. A), 8.29 (dd, J=1.6, 4.8 Hz, 0.5H, ArH diast. B); δ_C 13.5 (CH_3 diast. A), 13.8 (CH_3 diast. B), 40.2 (CH_3SO_2 diast. B), 40.4 (CH_3SO_2 diast. A), 45.1 (CHAr), 62.5 (OCH_2 diast. A), 62.6 (OCH_2 diast. B), 70.9 (CHS diast. B), 72.3 (CHS diast. A), 119.7 (CH_2═diast. A), 120.5 (CH_2═diast. B), 122.7 (CH Ar), 132.6 (C Ar diast. B), 133.0 (CH═diast. B), 133.2 (C Ar diast. A), 134.1 (CH═diast. A), 137.9 (CH Ar diast. A), 138.8 (CH Ar diast. B), 148.5 (CH Ar), 150.0 (C Ar diast. B), 150.3 (C Ar diast. A), 164.5 (CO diast. A), 165.0 (CO diast. B); *m/z* 318 (MH^+); HRMS calcd for $C_{13}H_{16}ClNO_4S$, 317.0489; found, 317.0492.

3.1.13.2. Ethyl 3-(2,6-dichlorophenyl)-2-methanesulfonylpent-4-enoate 14c. Purified by flash column chromatography (petrol/EtOAc 8:2), two diastereomers A and B 1:1, yellow oil, 94%; ν_{max}/cm^{-1} 1736 (CO), 1328 (SO_2); diastereomer A: δ_H 1.28 (t, J=7 Hz, 3H, CH_3), 2.89 (s, 3H, CH_3), 4.25 (q, J=7.2 Hz, 2H, OCH_2), 5.00–5.25 (m, 4H, CH_2═, CHS, CHAr), 6.14 (ddd, J=8.4, 9.6, 17.2 Hz, 1H, CH═), 7.12 (t, J=8 Hz, 1H, CH Ar), 7.25 (d, J=8 Hz, 1H, CH Ar), 7.33 (d, J=8 Hz, 1H, CH Ar); δ_C 13.8 (CH_3), 39.1 (SCH_3), 44.9 (CHAr), 62.4 (OCH_2), 69.2 (CHS), 120.1 (CH_2═), 129.0 (CH Ar), 129.2 (CH Ar), 129.9 (CH Ar), 132.6 (CH═), 134.7 (C Ar), 135.4 (C Ar), 165.5 (CO); diastereomer B: δ_H 0.91 (t, J=7.2 Hz, 3H, CH_3), 3.08 (s, 3H, SCH_3), 3.88 (dq, J=7.2, 10.8 Hz, 1H, OCH), 3.90 (dq, J=7.2, 10.8 Hz, 1H, OCH), 5.02 (d, J=11.6 Hz, CHS), 5.18 (dd, J=8, 10.8 Hz, 1H, CHAr), 5.21 (d, J=10.4 Hz, 1H, CH═), 5.30 (d, J=16.8 Hz, 1H, CH═), 6.50 (ddd, J=8, 10, 17.2 Hz, 1H, CH═), 7.10 (t, J=8 Hz, 1H, CH Ar), 7.22 (d, J=8 Hz, 1H, CH Ar), 7.33 (dd, J=1.2, 8 Hz, 1H, CH Ar); δ_C 13.3 (CH_3), 39.7 (SCH_3), 44.3 (CHAr), 62.1 (OCH_2), 70.6 (CHS), 119.5 (CH_2═), 128.7 (CH Ar), 129.2 (CH Ar), 129.8 (CH Ar), 133.0 (CH═), 134.3 (C Ar), 135.9 (C Ar), 164.5 (CO); *m/z* 351 (MH^+), 368 ($M+NH_4^+$).

3.1.14. General procedure for the 1,2-aryl transfer products 15/19/20. A solution of sulfone **14** (1.5 equiv) and the corresponding xanthate **3** (1 equiv) in DCE (4 mL/mmol) heated at reflux temperature was added DLP (0.15 equiv) every 1.5 h, until the disappearance of the xanthate. Then the reaction mixture was concentrated and the residue was purified by flash column chromatography.

3.1.15. General procedure for the synthesis of amines 16/17/18. To a solution of ketone **15** (1 equiv) in absolute EtOH (2.5 mL/mmol) were added 4 Å molecular sieves, the corresponding amine (as its acetate salt, 10 equiv), $NaBH_3CN$ (1.1 equiv) and the resulting mixture was heated at reflux temperature for 7 h. The reaction mixture was then concentrated, dissolved in CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ solution. The organic layer was dried and evaporated, and the residue was purified by flash column chromatography.

3.1.15.1. Ethyl (2*SR*,3*SR*,6*SR*)-[6-(4-methoxyphenyl)-3-(4-trifluoromethylphenyl)piperidin-2-yl]acetate 16a. Purified by flash column chromatography (petrol/EtOAc 8:2), yellow solid, 60%; mp 80–83 °C, ν_{max}/cm^{-1} 1731 (CO); δ_H 1.16 (t, J=7.2 Hz, 3H, CH_3), 1.55–1.75 (m, 2H, H-5_{ax} and H-4_{ax}), 1.91 (dd, J=2.2, 12.2 Hz, 1H, H-5_{eq}), 2.03 (dd, J=2.8, 12.8 Hz, 1H, H-4_{eq}), 2.23 (dd, J=3.2, 16.8 Hz, 1H, CHCO), 2.30 (dd, J=8.8, 16.8 Hz, 1H, CHCO), 2.62 (td, J=3.6, 11.6 Hz, 1H, H-3_{ax}), 3.39 (td, J=2.7, 10 Hz, 1H, H-2_{ax}), 3.59 (br s, 1H, NH), 3.80 (s, 3H, OCH_3), 3.86 (dd, J=1.6, 10.8 Hz, 1H, H-6_{ax}), 3.95–4.05 (m, 2H, OCH_2), 6.89 (d, J=8.4 Hz, 2H, ArH methoxyphenyl), 7.35 (d, J=8.4 Hz, 4H, 2ArH methoxyphenyl and 2 ArH trifluoromethylphenyl), 7.58 (d, J=8 Hz, 2H, ArH trifluoromethylphenyl); δ_C 14.0 (CH_3), 34.0 (C-4), 34.2 (C-5), 38.6 (CH_2CO), 48.3 (C-3), 55.2 (OCH_3), 58.4 (C-2), 60.4 (OCH_2), 61.0 (C-6), 113.8 (CH Ar methoxyphenyl), 124.2 (q, J=270 Hz, CF_3), 125.5 (q, J=2.7 Hz, C-*m* trifluoromethylphenyl), 127.8 (CH Ar methoxyphenyl), 128.2 (C-*o* trifluoromethylphenyl), 129.0 (q, J=32.1 Hz, C-*p* trifluoromethylphenyl), 136.6 (C Ar), 147.6 (C Ar), 158.8 (C Ar), 172.3 (CO); *m/z* 422 (MH^+); Elem. Anal. Calcd for $C_{23}H_{26}F_3NO_3$: C, 65.55; H, 6.22; found: C, 65.39; H, 6.52.

3.1.15.2. Ethyl (2*SR*,3*SR*,6*RS*)-[6-(4-methoxyphenyl)-3-(4-trifluoromethylphenyl)piperidin-2-yl]acetate 16b. Purified by flash column chromatography (petrol/EtOAc

1:1), yellow solid, 11%; mp 85–86 °C; ν_{max}/cm^{-1} 1729 (CO); δ_H 1.24 (t, J=7.2 Hz, 3H, CH_3), 1.67–1.76 (m, 1H, H-4_{ax}), 1.81 (ddd, J=4, 9, 18 Hz, 1H, H-4_{eq}), 2.00 (tt, J=4.2, 12.5 Hz, 1H, H-5_{ax}), 2.26 (dd, J=3.8, 15.8 Hz, 1H, CHCO), 2.32 (dd, J=9, 16.2 Hz, 1H, CHCO), 2.20–2.35 (m, 1H, H-5_{eq}), 2.50 (br s, 1H, NH), 2.60 (td, J=4, 9.6 Hz, 1H, H-3_{ax}), 3.47 (t, J=4, 8.8 Hz, 1H, H-2_{ax}), 4.05–4.15 (br s, 1H, H-6_{eq}), 6.95 (d, J=8.4 Hz, 2H, ArH methoxyphenyl), 7.28 (d, J=8 Hz, 2H, H-*o* trifluoromethylphenyl), 7.46 (d, J=8.4 Hz, 2H, ArH methoxyphenyl), 7.50 (d, J=8 Hz, 2H, H-*m* trifluoromethylphenyl); δ_C 14.2 (CH_3), 28.4 (C-4), 29.2 (C-5), 39.0 (CH_2CO), 48.2 (C-3), 51.9 (C-2), 53.3 (C-6), 55.3 (OCH_3), 60.5 (OCH_2), 114.0 (CH Ar methoxyphenyl), 124.2 (q, J=270 Hz, CF_3), 125.4 (q, J=3.7 Hz, C-*m* trifluorophenyl), 127.9 (CH Ar methoxyphenyl), 128.2 (C-*o* trifluoromethylphenyl), 128.8 (q, J=32.4 Hz, C-*p* trifluorophenyl), 134.5 (C Ar), 148.2 (C Ar), 158.2 (C Ar), 172.4 (CO); m/z 423 (MH^+); Elem. Anal. Calcd for $C_{23}H_{26}F_3NO_3 \cdot 3/4H_2O$: C, 63.51; H, 6.37; N, 3.22; found: C, 63.41; H, 6.18; N, 2.81.

3.1.15.3. Ethyl (2*SR*,3*SR*,6*SR*)-[1-cyclopropyl-6-(4-methoxyphenyl)-3-(4-trifluoromethylphenyl)piperidin-2-yl]acetate 17. Purified by flash column chromatography (petrol/EtOAc 9:1), yellow solid, 86%; mp 78–80 °C; ν_{max}/cm^{-1} 1737 (CO); δ_H 0.02 (q, J=3.2 Hz, 2H, CH_2 cyclopropyl), 0.13 (qt, J=3.4 Hz, 2H, CH_2 cyclopropyl), 1.11 (t, J=7.2 Hz, 3H, CH_3), 1.82 (ht, J=3.6 Hz, 1H, CH cyclopropyl), 1.87 (ddd, J=2.8, 5.6, 12.4 Hz, 1H, H-5_{ax}), 1.94–2.06 (m, 2H, H-4), 2.02 (dd, J=5.2, 14.8 Hz, 1H, CHCO), 2.07–2.18 (m, 1H, H-5_{eq}), 2.77 (dd, J=8.4, 14.8 Hz, CHCO), 3.38–3.44 (m, 1H, H-3_{ax}), 3.81 (s, 3H, OCH_3), 3.85 (q, J=6.8 Hz, 2H, OCH_2), 3.86–3.92 (m, 1H, H-2_{ax}), 3.93–3.97 (m, 1H, H-6_{ax}), 6.84 (d, J=8.4 Hz, 2H, ArH methoxyphenyl), 7.24 (d, J=8.4 Hz, 2H, ArH methoxyphenyl), 7.38 (d, J=8 Hz, 2H, ArH trifluoromethylphenyl), 7.58 (d, J=8.4 Hz, 2H, ArH trifluoromethylphenyl); δ_C 7.4 and 8.9 (CH_2 cyclopropyl), 14.0 (CH_3), 23.9 (C-4), 29.7 (CH_2CO), 29.9 (C-5), 32.7 (CH isopropyl), 42.5 (C-3), 55.2 (OCH_3), 59.4 (C-2), 60.2 (OCH_2), 62.4 (C-6), 113.1 (CH Ar methoxyphenyl), 124.2 (q, J=270 Hz, CF_3), 125.2 (q, J=3.7 Hz, C-*m* trifluoromethylphenyl), 128.0 (C-*o* trifluoromethylphenyl), 128.6 (q, J=32.2 Hz, C-*p* trifluoromethylphenyl), 129.8 (CH Ar methoxyphenyl), 134.8 (C Ar), 146.8 (C Ar), 158.6 (C Ar), 172.6 (CO); m/z 462 (MH^+); Elem. Anal. Calcd for $C_{26}H_{30}F_3NO_3$: C, 67.66; H, 6.55; N, 3.03; found: C, 67.59; H, 6.59; N, 2.88.

3.1.15.4. (1*SR*,7*SR*,10*SR*)-7-(4-Methoxyphenyl)-10-(4-trifluoromethylphenyl)octahydropyrido[1,2-*d*][1,4]diazepin-2-one 18a. Purified by flash column chromatography (EtOAc), white solid, 56%; mp 220–222 °C; ν_{max}/cm^{-1} 1679; δ_H 1.60 (ddd, J=3.3, 12.3, 24.3 Hz, 1H, H-9_{ax}), 1.72 (ddd, J=2.8, 13, 24.2 Hz, 1H, H-8_{ax}), 1.79 (tdd, J=3.2, 6.4, 13.2 Hz, 1H, H-8_{eq}), 1.87 (ddd, J=3.2, 6, 12.8 Hz, 1H, H-9_{eq}), 2.07 (dd, J=9.6, 13.6 Hz, 1H, H-5), 2.30 (d, J=14.4 Hz, 1H, H-1), 2.62 (dd, J=8.4, 14 Hz, 1H, H-1), 2.65–2.78 (m, 2H, H-10 and H-11), 2.93 (qt, J=7.1 Hz, 1H, H-4), 3.03 (dd, J=6.2, 13.4 Hz, 1H, H-5), 3.23 (dd, J=3, 11 Hz, 1H, H-7), 3.27 (dd, J=4, 9.6 Hz, 1H, H-4), 6.80 (br s, 1H, H-3), 6.87 (d, J=8.8 Hz, 2H, CH Ar methoxyphenyl), 7.26 (d, J=8.4 Hz, 2H, H-*o* trifluoromethylphenyl), 7.32 (d, J=8 Hz, 2H, CH Ar methoxyphenyl), 7.57 (d, J=8.4 Hz, 2H, H-*m* trifluoromethylphenyl); δ_C 34.0 and 35.6 (C-8 and C-9), 42.3 (C-1 and C-5), 49.5 (C-10), 55.2 (OCH_3), 56.2 (C-4), 63.4 (C-7), 68.5 (C-11), 114.0 (CH Ar methoxyphenyl), 124.1 (q, J=271 Hz, CF_3), 125.8 (C-*m* trifluoromethylphenyl), 128.1 (CH Ar methoxyphenyl and C-*o* trifluoromethylphenyl), 128.8 (q, J=32 Hz, C-*p* trifluoromethylphenyl), 136.8 (C Ar), 148.2 (C Ar), 158.6 (C Ar), 176.6 (C-2); m/z 419 (MH^+); HRMS calcd for $C_{23}H_{25}F_3N_2O_2$, 418.1868; found, 418.1871.

3.1.15.5. (1*SR*,7*RS*,10*SR*)-7-(4-Methoxyphenyl)-10-(4-trifluoromethylphenyl)octahydropyrido[1,2-*d*][1,4]diazepin-2-one 18b. Purified by flash column chromatography (EtOAc/MeOH 99:1), white foam, 16%; ν_{max}/cm^{-1} 3429 (NH), 1676 (CO); δ_H 1.64–1.77 (m, 2H, H-10), 1.78–1.87 (m, 1H, H-9_{ax}), 1.98 (dt, J=4.1, 10.6 Hz, 1H, H-9_{eq}), 2.25 (d, J=14.8 Hz, H-6), 2.72–2.84 (m, 1H, H-3), 2.84 (dd, J=9.6, 14.8 Hz, H-2), 2.97 (q, J=4.8 Hz, H-8), 3.10 (dd, J=5.6, 14.8 Hz, 1H, H-2), 3.38 (dd, J=9.8, 13 Hz, 1H, H-6), 3.59 (ddd, J=4.8, 9.6, 14.8 Hz, 1H, H-3), 3.77–3.83 (m, 1H, H-7), 3.81 (s, 3H, OCH_3), 4.08 (dd, J=4, 8 Hz, 1H, H-11_{eq}), 6.28 (br s, 1H, NH), 6.88 (d, J=8.4 Hz, 2H, ArH methoxyphenyl), 7.27 (d, J=8.4 Hz, 2H, ArH methoxyphenyl), 7.57 (dd, J=8.4 Hz, 2H, ArH trifluoromethylphenyl), 7.61 (d, J=8.4 Hz, 2H, ArH trifluoromethylphenyl); δ_C 27.4 and 28.6 (C-9 and C-10), 38.7 (C-6), 39.4 (C-2), 44.3 (C-8), 52.9 (C-3), 55.2 (OCH_3), 56.0 and 59.1 (C-11 and C-7), 114.0 (CH Ar methoxyphenyl), 125.1 (C-*m* trifluoromethylphenyl), 128.5 (CH Ar methoxyphenyl), 128.6 (C-*o* trifluoromethylphenyl), 134.6 (C Ar), 148.6 (C Ar), 158.6 (C Ar), 177.0 (C-5); m/z 419 (MH^+).

3.1.15.6. Ethyl (4*RS*,6*SR*)-(*E*)-6-acetylamino-4-(2-chloropyrid-5-yl)-7,7,7-trifluorohept-2-enoate 19a. Purified by flash column chromatography (petrol/EtOAc 1:1), white solid, 32%; mp 107–113 °C; ν_{max}/cm^{-1} 3441 (NH), 1711 (CO), 1656 (CO amide); δ_H 1.30 (t, J=7.2 Hz, 3H, CH_3), 1.89 (ddd, J=3.5, 11.3, 14.5 Hz, 1H, CH), 2.07 (s, 3H, CH_3 acetyl), 2.25 (ddd, J=2.8, 10.4, 14.4 Hz, 1H, CH), 3.96–4.04 (m, 1H, CHAr), 4.21 (q, J=7.2 Hz, 2H, OCH_2), 4.60–4.80 (m, 1H, $CHCF_3$), 5.49 (d, J=9.2 Hz, 1H, NH), 5.99 (dd, J=1.2, 15.6 Hz, 1H, =CHCO), 6.96 (dd, J=8, 15.6 Hz, 1H, =CH), 7.28 (dd, J=4.4, 7.6 Hz, 1H, ArH), 7.62 (dd, J=1.8, 7.8 Hz, 1H, ArH), 8.33 (dd, J=1.8, 4.4 Hz, 1H, ArH); δ_C 14.0 (CH_3), 22.7 (CH_3 acetyl), 32.8 (CH_2), 39.8 (CH Ar), 48.6 (q, J=30.7 Hz, $CHCF_3$), 60.7 (OCH_2), 123.1 (CH Ar), 124.6 (=CHCO), 124.8 (q, J=279.8 Hz, CF_3), 135.4 (C Ar), 137.2 (CH Ar), 144.9 (=CH), 148.2 (CH Ar), 150.4 (C Ar), 165.8 (CO amide), 170.4 (CO ester); m/z 379 (MH^+), 396 ($M+NH_4^+$); HRMS calcd for $C_{16}H_{18}F_3ClN_2O_3$, 378.0958; found, 378.0967.

3.1.15.7. Ethyl (4*RS*,6*RS*)-(*E*)-6-acetylamino-4-(2-chloropyrid-5-yl)-7,7,7-trifluorohept-2-enoate 19b. Purified by flash column chromatography (petrol/EtOAc 4:6), white solid, 25%; mp 115 °C; ν_{max}/cm^{-1} 3441 (NH), 1709 (CO); δ_H 1.28 (t, J=7.2 Hz, 3H, CH_3), 2.00 (s, 3H, CH_3 acetyl), 2.01–2.12 (m, 1H, CH), 2.39 (ddd, J=3.6, 9.2, 14.4 Hz, 1H, CH), 4.10–4.25 (m, 1H, CHAr), 4.18 (q, J=7.2 Hz, 2H, OCH_2), 4.45–4.55 (m, 1H, $CHCF_3$), 5.45 (d, J=10 Hz, 1H, NH), 5.83 (dd, J=1.2, 15.6 Hz, 1H, =CHCO), 6.98 (dd, J=7.2, 15.6 Hz, 1H, =CH), 7.30 (dd, J=4.4, 7.6 Hz, 1H, CH Ar), 7.55 (dd, J=1.6, 7.6 Hz, 1H, CH Ar), 8.35 (dd,

J=2, 4.8 Hz, 1H, CH Ar); δ_C 14.1 (CH_3), 22.6 (CH_3 acetyl), 31.3 (CH_2), 40.2 (CHAr), 48.4 (q, J=30.6 Hz, $CHCF_3$), 60.6 (OCH_2), 122.5 (=CHCO), 123.2 (CH Ar), 124.8 (q, J=279.8 Hz, CF_3), 133.7 (C Ar), 137.1 (CH Ar), 147.0 (=CH), 148.5 (CH Ar), 151.2 (C Ar), 165.9 (CO amide), 170.3 (CO ester); m/z 379 (MH^+), 396 ($M+NH_4^+$); HRMS calcd for $C_{16}H_{18}F_3ClN_2O_3$, 378.0958; found, 378.0946.

3.1.15.8. Ethyl (*E*)-6-acetylamino-4-(2,6-dichlorophenyl)-7,7,7-trifluorohept-2-enoate 20a. Purified by flash column chromatography (petrol/EtOAc 8:2), white solid, 24%; mp 120 °C; ν_{max}/cm^{-1} 3443 (NH), 1714 (CO ester), 1651 (CO amide); δ_H 1.28 (t, J=7 Hz, 3H, CH_3), 1.94 (s, 3H, CH_3 acetyl), 2.00 (ddd, J=4.8, 11.6, 14.4 Hz, 1H, CH), 2.73 (ddd, J=2.4, 8.8, 14.4 Hz, 1H, CH), 4.18 (q, J=7.2 Hz, 2H, OCH_2), 4.48–4.56 (m, 1H, CH), 4.65–4.78 (m, 1H, CH), 5.38 (br s, 1H, NH), 5.86 (dd, J=1.4, 15.8 Hz, 1H, CH=), 7.15 (t, J=8 Hz, 1H, CH Ar), 7.23 (dd, J=6.8, 16 Hz, 1H, CH=), 7.28–7.36 (m, 2H, CH Ar); δ_C 14.0 (CH_3), 22.5 (CH_3 acetyl), 31.0 (CH_2), 40.0 (CHAr), 49.2 (q, J=30.5 Hz, $CHCF_3$), 60.5 (OCH_2), 123.4 (CH=), 124.7 (q, J=279.7 Hz, CF_3), 128.6 (CH Ar), 128.9 (CH Ar), 129.9 (CH Ar), 134.9 (C Ar), 135.4 (C Ar), 136.5 (C Ar), 145.4 (CH=), 166.1 (CO), 170.4 (CO); m/z 412 (MH^+), 429 ($M+NH_4^+$); HRMS calcd for $C_{17}H_{18}F_3Cl_2NO_3$, 411.0616; found, 411.0633.

3.1.15.9. Ethyl (*E*)-6-acetylamino-4-(2,6-dichlorophenyl)-7,7,7-trifluorohept-2-enoate 20b. Purified by flash column chromatography (petrol/EtOAc 7:3), white solid, 28%; mp 184–186 °C; ν_{max}/cm^{-1} 3444 (NH), 1714 (CO ester), 1651 (CO amide); δ_H 1.26 (t, J=7.2 Hz, 3H, CH_3), 1.94 (s, 3H, CH_3 acetyl), 2.06 (ddd, J=4.5, 12.8, 14 Hz, 1H, CH), 2.93 (ddd, J=2.8, 10.8, 14 Hz, 1H, CH), 4.17 (q, J=7.2 Hz, 3H, OCH_2 and $CHCF_3$), 4.60–4.68 (m, 1H, CHAr), 5.75 (dd, J=1.6, 15.6 Hz, 1H, CH=), 6.78 (d, J=9.2 Hz, 1H, NH), 7.15 (t, J=8 Hz, 1H, CH Ar), 7.16 (dd, J=6, 16 Hz, 1H, CH=), 7.26–7.33 (m, 2H, CH Ar); δ_C 14.1 (CH_3), 22.8 (CH_3 acetyl), 29.2 (CH_2), 39.8 (CH Ar), 48.5 (q, J=30.5 Hz, $CHCF_3$), 60.6 (OCH_2), 122.1 (CH=), 124.9 (q, J=280.1 Hz, CF_3), 128.9 (CH Ar), 129.4 (CH Ar), 130.3 (CH Ar), 133.8 (C Ar), 134.9 (C Ar), 136.4 (C Ar), 146.6 (CH=), 166.3 (CO), 170.2 (CO); m/z 412 (MH^+), 429 ($M+NH_4^+$); HRMS calcd for $C_{17}H_{18}F_3Cl_2NO_3$, 411.0616; found, 411.0616.

3.1.16. General procedure for the synthesis of pyrrolidines 21/22. To a solution of amidoester **19/20** (1 equiv) in THF (4 mL/mmol) cooled at 0 °C was added *t*-BuOK (0.8 equiv) and stirred at that temperature for 1 h. After that time, the reaction mixture was concentrated, and the residue dissolved in EtOAc and washed with brine. The organic layer was dried and concentrated, and the residue was purified by flash column chromatography.

3.1.16.1. (2*SR*,3*SR*,5*RS*)-*N*-Acetyl-3-(2-chloropyrid-5-yl)-2-ethoxycarbonylmethyl-5-trifluoromethylpyrrolidine 21a. Purified by flash column chromatography (petrol/EtOAc 1:1), white foam, 17%; ν_{max}/cm^{-1} 1738 (CO ester), 1686 (CO amide); δ_H 1.08 (t, J=7.2 Hz, 3H, CH_3), 2.19 (dd, J=8.4, 16 Hz, 1H, CHCO), 2.28 (s, 3H, CH_3 acetyl), 2.43 (dd, J=6, 16 Hz, 1H, CHCO), 2.44–2.60 (m, 2H, CH_2), 3.68–3.88 (m, 3H, OCH_2 and CHAr), 4.93 (brm, 1H, $CHCF_3$), 5.07 (brm, 1H, NCH), 7.28 (dd, J=4.8, 7.6 Hz, 1H, CHAr), 7.67 (dd, J=1.8, 7.6 Hz, 1H, CH Ar), 8.33 (dd, J=1.8, 7.6 Hz, 1H, CH Ar); δ_C 13.9 (CH_3), 22.6 (CH_3 acetyl), 26.4 (CH_2), 36.1 (CH_2CO), 43.6 (CHAr), 55.7 (q, J=26.4 Hz, $CHCF_3$), 57.7 (NCH), 60.9 (OCH_2), 122.5 (CH Ar), 125.1 (q, J=279.4 Hz, CF_3), 129.9 (C Ar), 136.9 (CH Ar), 148.7 (CH Ar), 152.6 (C Ar), 169.4 (CO), 171.6 (CO); m/z 379 (MH^+), 396 ($M+NH_4^+$); HRMS calcd for $C_{16}H_{18}F_3ClN_2O_3$, 378.0958; found, 378.0950.

3.1.16.2. (2*SR*,3*SR*,5*SR*)-*N*-Acetyl-3-(2-chloropyrid-5-yl)-2-ethoxycarbonylmethyl-5-trifluoromethylpyrrolidine 21b. Purified by flash column chromatography (petrol/EtOAc 4:6), white foam, 25%; ν_{max}/cm^{-1} 1736 (CO ester), 1675 (CO amide); δ_H 1.02 (br m, 3H, CH_3), 2.20 (br m, 4H, CH_3 acetyl and CH), 2.46 (br m, 1H, CHCO), 2.62 (br m, 1H, CH), 3.13 (br m, 1H, CHCO), 3.88 (br m, 3H, OCH_2 and CHAr), 4.49 (br m, 1H, $CHCF_3$), 4.75 (br m, 1H, NCH), 7.25 (dd, J=4.8, 7.6 Hz, 1H, CH Ar), 7.66 (br m, 1H, CH Ar), 8.29 (d, J=3.2 Hz, 1H, CH Ar); δ_C 13.8 (CH_3), 22.4 (CH_3 acetyl), 33.9 (CH_2), 39.7 (CH_2CO), 45.4 (CHAr), 59.9 (q, J=31.4 Hz, $CHCF_3$), 60.58 (OCH_2), 60.62 (NCH), 123.0 (CH Ar), 125.0 (q, J=280.6 Hz, CF_3), 134.9 (C Ar), 136.9 (CH Ar), 148.3 (CH Ar), 151.0 (C Ar), 170.2 (CO), 170.6 (CO); m/z 379 (MH^+), 396 ($M+NH_4^+$); HRMS calcd for $C_{16}H_{18}F_3ClN_2O_3$, 378.0958; found, 378.0958.

3.1.16.3. (2*SR*,3*SR*,5*RS*)-*N*-Acetyl-3-(2,6-dichlorophenyl)-2-ethoxycarbonylmethyl-5-trifluoromethylpyrrolidine 22a and (2*SR*,3*SR*,5*SR*)-*N*-acetyl-3-(2,6-dichlorophenyl)-2-ethoxycarbonylmethyl-5-trifluoromethylpyrrolidine 22b. Purified by flash column chromatography (petrol/EtOAc 7:3), white solid, 48%; mp 85 °C; ν_{max}/cm^{-1} 1737 (CO ester), 1675 (CO amide); δ_H 0.98 (t, J=7 Hz, 3H, CH_3 **22a**), 1.07 (t, J=7 Hz, 3H, CH_3 **22b**), 2.22 (s, 6H, $2CH_3$ acetyl), 2.36 (dd, J=9.4, 13.4 Hz, 2H, CH **22b** and CH **22a**), 2.47 (dd, J=10, 15.6 Hz, 1H, CHCO **22b**), 2.55–2.66 (m, 1H, CH_2 **22a**), 2.75–2.92 (m, 3H, CH_2 **22b** and CH_2CO **22a**), 3.18 (dd, J=3.6, 16 Hz, 1H, CHCO **22b**), 3.75–4.05 (m, 4H, $2OCH_2$), 4.30–4.46 (m, 2H, 2CHAr), 4.56 (qt, J=8 Hz, 1H, $CHCF_3$ **22b**), 4.88 (br m, 1H, NCH **22a**), 5.17 (br m, 1H, NCH **22b**), 5.20–5.30 (m, 1H, $CHCF_3$ **22a**), 7.10–7.18 (m, 2H, ArH), 7.28–7.36 (m, 4H, ArH); δ_C 13.7 (CH_3 ester), 21.5 (CH_3 acetyl **22a**), 22.3 (CH_3 acetyl **22b**), 29.3 (C-3 **22a**), 30.3 (C-3 **22b**), 40.2 (CH_2CO **22b**), 42.3 (CH_2CO **22a**), 44.9 (C-4 **22b**), 47.2 (C-4 **22a**), 57.7 (q, J=32.1 Hz, C-2 **22a**), 58.9 (C-5 **22b**), 60.2 (q, J=31.3 Hz, C-2 **22b**), 60.3 (C-5 **22a**), 60.4 (OCH_2 **22b**), 60.9 (OCH_2 **22a**), 128.5 (CH Ar), 128.7 (CH Ar), 128.8 (CH Ar), 130.3 (CH Ar), 134.3 (C Ar), 135.8 (C Ar), 136.15 (C Ar), 136.23 (C Ar), 169.8 (CO), 169.9 (CO), 170.3 (CO), 170.6 (CO); m/z 412 (MH^+); HRMS calcd for $C_{17}H_{18}F_3Cl_2NO_3$, 411.0616; found, 411.0625.

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