S-(3-Chloro-2-oxo-propyl)-*O*-ethyl xanthate: a linchpin radical coupling agent for the synthesis of heterocyclic and polycyclic compounds

Olga Bergeot, Camilla Corsi, Myriem El Qacemi and Samir Z. Zard*

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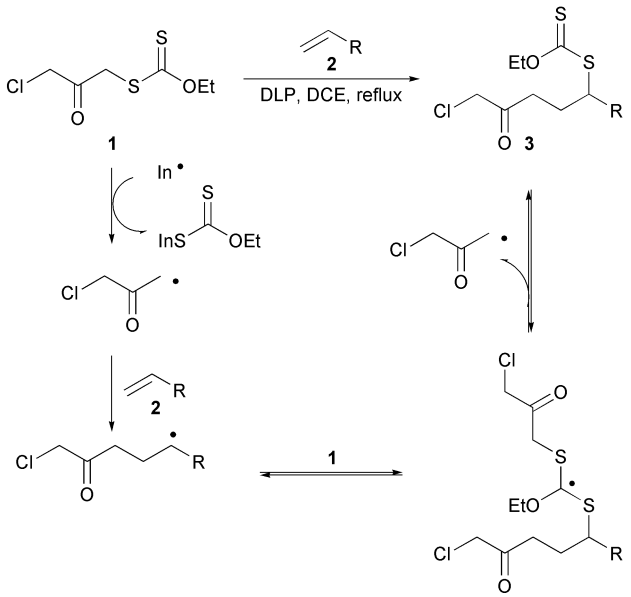
The preparation and use of *S*-(3-chloro-2-oxo-propyl)-*O*-ethyl xanthate to directly introduce an α-chloroketone motif is described, along with applications for the synthesis of heterocyclic and polycyclic structures.

Introduction

α-Haloketones, and α-chloroketones in particular, are key starting materials for numerous named classical syntheses of heteroaromatic compounds such as pyrroles, thiazoles, imidazoles, furans (Benary-Feist, Hantzsch reactions)[1] in addition to being useful and versatile general synthetic intermediates. A variety of methods exist for their regiospecific formation including the traditional direct halogenation of the parent ketone.[2] In more recent approaches, α-haloketones have been obtained from the corresponding vinyl halides by the action of NCS, NBS or NIS in aqueous acetonitrile[3] or by treatment with an aqueous sodium hypochlorite solution in an acetic acid–acetone mixture.[4] A conceptually different route involves the reaction of *N*-methoxy-*N*-methylchloroacetamide with an organometallic reagent[5] or, as in the case of the synthesis of 19- and 20-fluororetinal, by reaction of the corresponding *N*-methoxy-*N*-methylamide and chloroiodomethane in the presence of methyllithium.[6] In yet another approach, disubstituted internal olefins were efficiently converted into α-chloroketones by reaction with chromic anhydride–chlorotrimethylsilane in carbon tetrachloride.[7]

We were attracted by the synthetic importance of this functionality and its wide use in the field of medicinal chemistry for the synthesis of biologically active substances. Therefore, we explored the possibility of introducing this motif using the xanthate (dithiocarbonate) radical transfer we have developed recently.[8] In general, α-chloroketones are generated at the stage in the synthesis at which they are needed, since their high reactivity as electrophiles usually precludes carrying them over several synthetic operations. It seemed that the tin-free radical chemistry based on xanthates would be compatible with such a functional group and would allow the creation of one or more carbon–carbon bonds in its presence. The fact that the radical process takes place in a neutral medium should limit ionic side reactions of the α-chloroketone, and the absence of tin (or silicon) centred radicals should eliminate unwanted but otherwise well precedented abstraction of the chlorine atom.

Our approach, outlined in Scheme 1, involves the synthesis of a xanthate such as **1** and its addition to various olefins according to the now accepted radical chain mechanism. Several potential problems could be identified from the outset and affect the success of this enterprise. Reagent **1** had to be stable under the reaction conditions and its preparation had to be practical. The presence in the same molecule and in close proximity of a strong electrophile and a sulfur based, potentially nucleophilic, group was worrying and, as will become clear later in the discussion, we were fortunate that the decomposition of xanthate **1** was a little slower than the radical addition process. The product xanthate **3** also had to be stable to allow isolation or the implementation of another radical sequence.

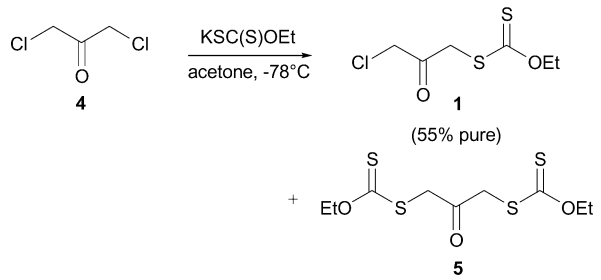


Scheme 1 Radical addition of **1** to an olefin, in the presence of lauroyl peroxide (DLP). (In• = initiating radical).

Results and discussion

The simplest approach for the synthesis of xanthate **1** was by displacing one chlorine atom from commercially available 1,3-dichloroacetone **4** with potassium *O*-ethyl xanthate salt in acetone (Scheme 2). Various experimental conditions, such as different temperatures and numbers of equivalents, were explored in order to avoid the undesired formation of the bis-xanthate **5**. In a preliminary study, it was concluded that the selective formation of **1** could be achieved by performing the reaction in excess of dichloroacetone (3 equivalents) and at very low temperature.

Laboratoire de Synthèse Organique associé au CNRS, Ecole Polytechnique, 91128, Palaiseau, France. E-mail: zard@poly.polytechnique.fr; Fax: +33 169 333851; Tel: +33 169 334872

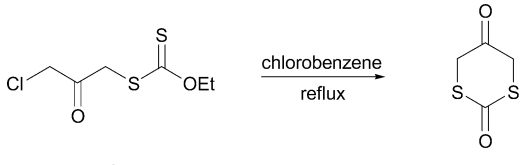


Scheme 2 Preparation of xanthate **1**.

Unfortunately, after numerous attempts, no practical purification of the crude mixture could be achieved and fractional recrystallisations revealed the lability of the product **1** which slowly decomposed upon heating. We therefore decided to use the xanthate as a crude mixture still contaminated by dichloroketone **4**. We hoped that the latter would not interfere with the radical step and that purification would be easier at the product stage. The initial radical additions were thus performed using an impure reagent. Later in the project, a simple solution was found for the synthesis of **1** and resulted in improved yields in many cases (*vide infra*).

The feasibility of the radical sequence was examined using a number of different olefins. The results of the radical additions, using an excess of the olefins, are collected in Table 1. Octene, vinyl pivalate, and allyl silane gave high yields of the expected adducts **7a,c,d** (entries 1, 3, and 4). The reaction with phenyl vinyl sulfone proceeded poorly (entry 2), presumably because both olefin and the radical are electrophilic in character resulting in lower reactivity. Finally, radical additions of the novel xanthate to various *N*-allyl anilides **6e–h** furnished the desired adducts in synthetically useful yields. These preliminary experiments, despite being imperfect in that they were carried out using an impure reagent, answered nevertheless one main concern and that is that xanthate **1** was sufficiently stable to allow the radical addition to proceed unimpeded. They also demonstrated the possibility of creating a new C–C bond in the presence of the highly reactive chloroketone.

At this stage a better procedure for the synthesis of **1** was found. It consisted of simply using water as the solvent in the displacement step. The dichloroacetone was added to a solution of potassium *O*-ethyl xanthate salt in water at near 0 °C. The desired mono-xanthate **1** is highly insoluble in water and precipitated out. This physically prevented it from reacting further to give the unwanted bis-xanthate **5**. The mono-xanthate **1** formed in this manner was simply filtered and dried; it was sufficiently pure for our purposes. We could now significantly improve the radical addition process, as will be seen shortly. Furthermore, a ready access to large amounts of good quality xanthate allowed us to better study its thermal stability. We thus found that heating the xanthate alone in chlorobenzene resulted in the formation of a cyclic derivative **8** as the main product (Scheme 3). The slow thermal generation of



Scheme 3 Thermal rearrangement of xanthate **1**.

Table 1 Radical addition of impure xanthate **1** on various olefins

Entry	Olefin	Addition product
1	**6a**	**7a** 89%
2	**6b**	**7b** 35%
3	**6c**	**7c** 85%
4	**6d**	**7d** 77%
5	X = OMe, R = SO_2Me **6e** X = Cl, R = Ac **6f** X = Br, R = Ac **6g** X = F, R = Ac **6h**	**7e** 61% (81%)[a] **7f** 55% **7g** 57% **7h** 55%

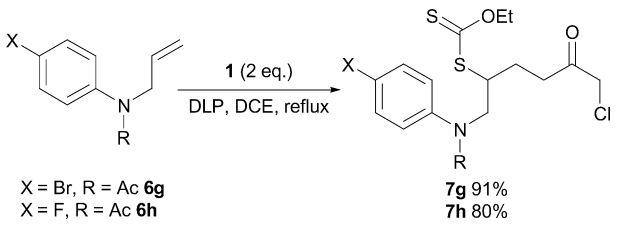
[a] In this case, pure xanthate was used for the radical addition.

this derivative consumes the xanthate in a non productive manner during the reactions and causes a lowering in the yield, even if it does not interfere with the radical addition itself. Surprisingly, compound **8**, which represents an interesting building block, has not been described in the literature as far as we can tell.

We repeated some of the experiments displayed in Table 1. We thus used the higher purity xanthate in slight excess and the olefin as the limiting reagent. In this manner, the yield of adducts **7g–h** were greatly improved (Scheme 4).

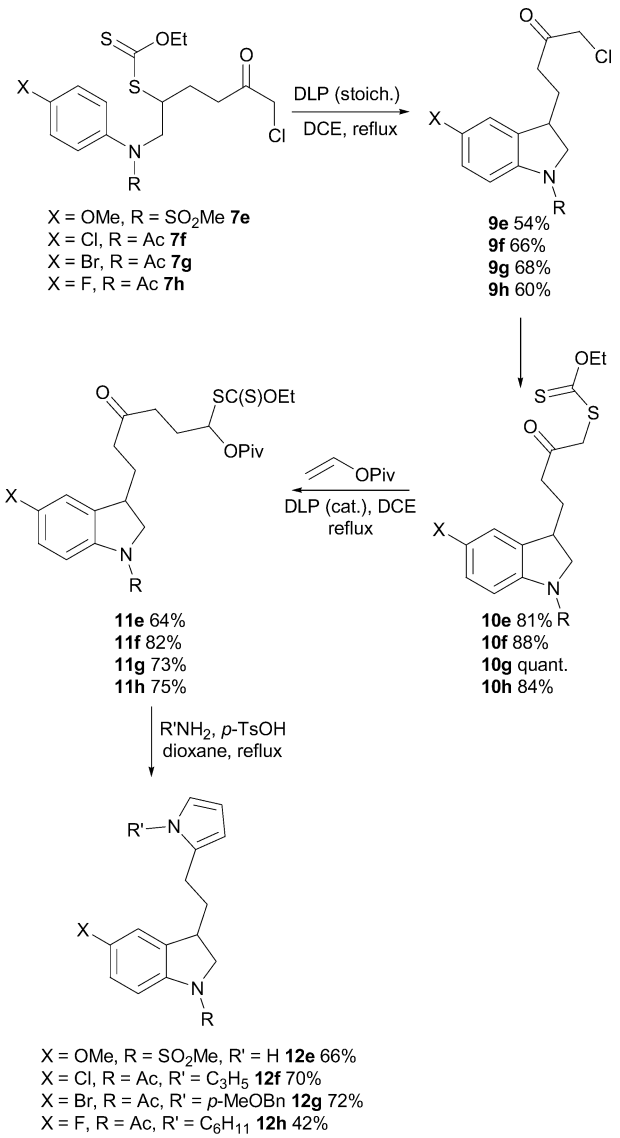
In addition to simplicity, cheapness, absence of heavy metals for the generation of radicals, ease of scale up, and the possibility of working under quite concentrated conditions, the starting xanthate can be used without further purification.

Also, this approach has numerous synthetically useful features; in fact, the addition products (**7**) could be utilised as starting points for multiple radical sequences and for the synthesis of



Scheme 4 Optimisation of radical additions.

heterocyclic structures. Thus, upon further exposure of **7e–h** to a stoichiometric amount of the peroxide, the radical formed can now cyclise onto the aromatic ring[9,10] forming indolines (**9e–h**) in good yield (Scheme 5), or azaindolines as has been described in a previous paper.[11]

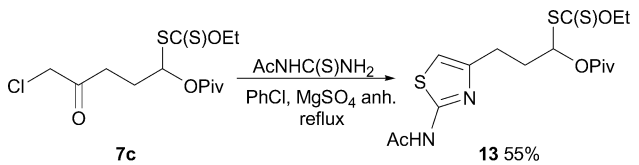


Scheme 5 Sequence of radical additions to synthesise pyrroles through Paal–Knorr condensations.

Further transformations could then be performed using indolines (**9e–h**). Displacement of the chlorine atom by the xanthate group, followed by an addition to vinyl pivalate, furnished addition products of type **11e–h**, where the carbon bearing both the pivaloxy and xanthate group is at the oxidation level of an aldehyde. In particular, in our case, the intermediates **11e–h** are 1,4-ketoaldehyde equivalents and therefore able to undergo Paal–Knorr[12,13] reactions. In fact, as previously reported,[14] reaction of vinyl pivalate adducts with different primary amines or ammonia in the presence of *para*-toluenesulfonic acid leads to the corresponding pyrroles. Intermediates **11e–h** were therefore treated with cyclopropylamine, 4-methoxybenzylamine and cyclohexylamine to afford pyrroles **12f–h** in good yield. Unsubstituted pyrrole **12e** could be prepared by using excess of ammonia and ammonium acetate, in dioxane at room temperature (Scheme 5). However, it is important to state that the pyrroles proved to be somewhat unstable when exposed to air giving rise to highly coloured side products.

The chemistry of these different chloroketones could then be further exploited by performing Hantzsch[15] reactions for the synthesis of thiazoles, by condensing α-halo carbonyl compounds with thioamides.[16,17] Thiazoles have also been prepared from amino nitrile[16c] or from amino thiols and carbonyl compounds[18] and by other procedures that are less important due to either the limited availability of starting materials and/or lack of overall generality.[16c]

In our case, it was possible to synthesise in few steps rather complicated structures that would not be easily accessible by other more classical routes. In fact, after attempting various conditions for the reactions, the condensation was optimised by refluxing the mixture in chlorobenzene with anhydrous magnesium sulfate. As depicted in Scheme 6, the Hantzsch reaction using **7c** in the presence of *N*-acetylthiourea furnished compound **13** in good yield where, as stated above, the carbon bearing the pivalate group is at the oxidation level of an aldehyde, and therefore could then undergo a variety of reactions.

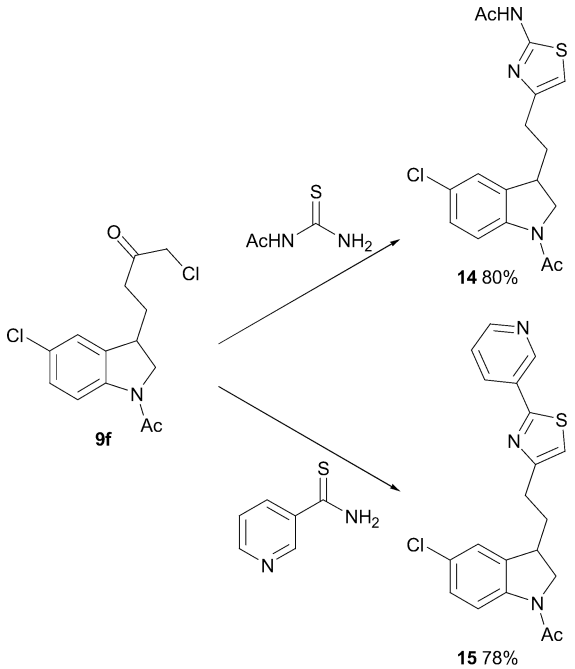


Scheme 6 Hantzsch reaction on compound **7c**.

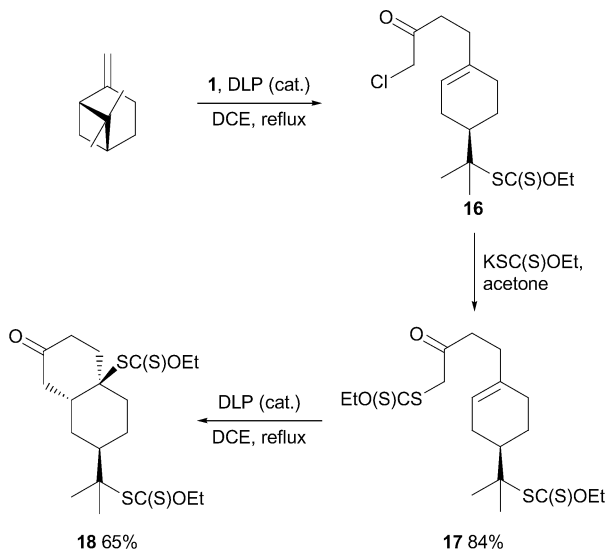
When the same methodology was extended to the chloro indoline derivative **9f** with *N*-acetylthiourea **14** or thionicotinamide **15**, new heterocycles were isolated and characterised (Scheme 7). Nevertheless, all these yields remain unoptimised, and there is certainly room for further improvement.

Model studies toward natural product syntheses

In addition to the preparation of various heterocycles, the two-dimensional nature of the starting dichloroketone allows us to construct complex polycyclic molecules using the xanthate technology. An interesting example is the preparation of an octahydronaphthalen-2-one in a three-step sequence starting from the commercially available β-(−)-pinene (Scheme 8). The first addition of xanthate **1** to the external double bond is immediately followed by the fragmentation to produce a tertiary xanthate. This sequence also generates a suitably located double bond which can be submitted to a new radical addition. This was achieved by



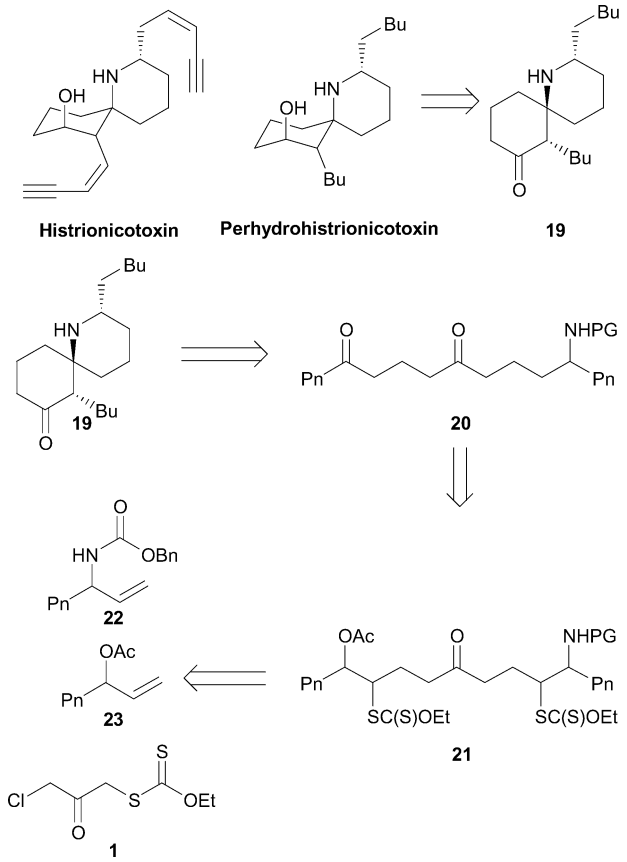
Scheme 7 Hantzsch reactions with compound **9f**.



Scheme 8 Radical cascade starting from β-(−)-pinene.

substituting the chlorine atom by a xanthate group. The second radical addition then provides compound **18** in good yield, and as only one isomer. Spectral analysis indicated it to possess the *cis*-decalin backbone, in accord with precedent in this area.[19] A nicely functionalised bicyclic compound is rapidly constructed by this short sequence; it contains two xanthate groups that can be further modified by radical or ionic reactions. This approach holds promise for the synthesis of various terpene structures.

Another way of using the title xanthate **1** is illustrated by preliminary studies toward (−)-histrionicotoxin (HTX)[20] and its hydrogenation product, the nonnatural perhydrohistrionicotoxin (Scheme 9). In combination with the parent compound's low abundance in nature, the remarkable biological activity and the challenging azaspirocyclic framework of these substances have prompted considerable synthetic interest over the last few decades.[21]

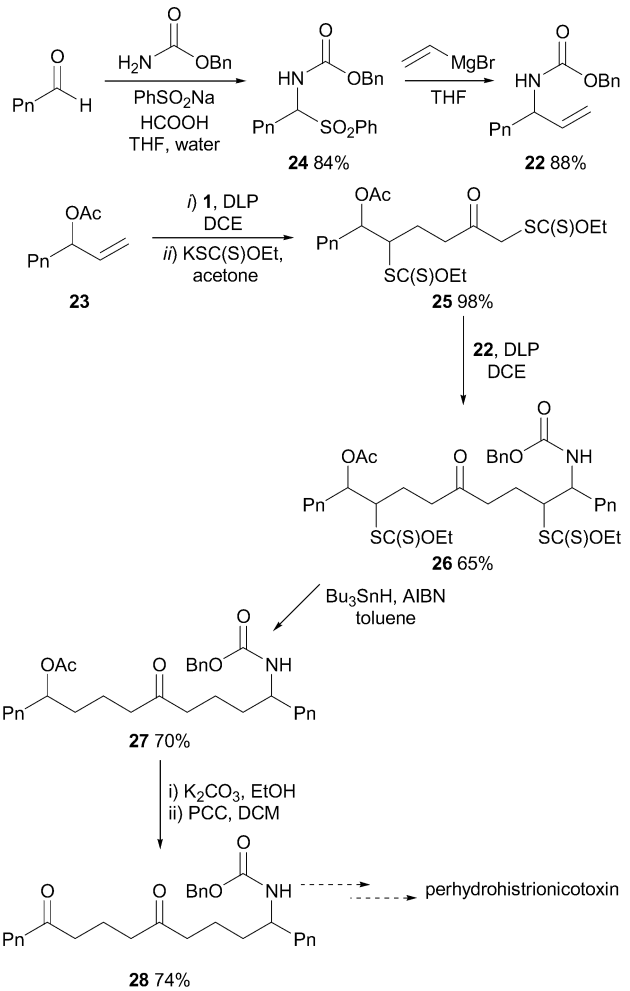


Scheme 9 Perhydrohistrionicotoxin retrosynthesis (Pn = pentyl).

Taking advantage of a two-directional approach, which offers the possibility of substantially reducing the number of chemical operations required to synthesise complex target molecules of biological and pharmaceutical interest, we explored first the formal synthesis of perhydrohistrionicotoxin.

Our retrosynthesis of a known intermediate for perhydrohistrionicotoxin[22] is shown in Scheme 9. We envisioned the azaspirocyclic core of **19** to be constructed through an intramolecular Mannich reaction of the diketo compound **20**.[23] The requisite linear compound **20** could be secured through a sequence of radical reduction and deprotection followed by oxidation of xanthate **21**, which in turn could be constructed through our key disconnection. The linear compound could then arise from xanthate **1**, following two successive intermolecular radical additions to olefins **22** and **23**.

The synthesis of allylamine **22** was performed as illustrated in Scheme 10. Amidoalkyl sulfones are known to be synthetic equivalents of *N*-acyl imines toward the addition of organometallic reagents.[24] Amidopentyl sulfone **24**, envisioned as a precursor of allylamine **22**, was easily prepared by reaction of benzylcarbamate with hexanal and sodium benzenesulfinate, in the presence of formic acid. Sulfone **24** is particularly convenient because it is a stable solid that can be recovered from the reaction mixture by simple filtration and purified by crystallisation. Vinylmagnesium bromide reacted smoothly with sulfone **24** at low temperature in THF, affording in good yield the corresponding *N*-protected allylamine **22**.



Scheme 10 Synthesis of intermediate **28**.

With all the precursors in hand, we were now set to carry out the two-directional radical additions. The first intermolecular addition of xanthate **1** to olefin **23** was carried out in refluxing DCE, using a small amount of lauroyl peroxide. Once the addition was complete, it was followed without purification by nucleophilic substitution of the chlorine atom with the xanthate salt in acetone. This sequence resulted in the isolation of compound **25**, bearing two xanthate groups, in 98% overall yield. The difference in stability of the two radicals corresponding to the two xanthates in **25** was deemed to be sufficient to conduct the second radical intermolecular addition on protected allylamine **22** in a clean manner. Indeed, when xanthate **25** was treated under the same conditions with **22**, adduct **26** was obtained in good yield.

Following this sequence, removal of the xanthate groups was achieved using a tributyltin hydride reduction, providing the linear compound **27** in 70% yield. Subsequent saponification of the acetate group under weakly basic conditions and oxidation of the resulting alcohol with PCC furnished diketo compound **28** in 74% yield for the two steps. Unfortunately, initial efforts to perform the intramolecular Mannich reaction have not been successful so far. Experiments are ongoing in the laboratory to achieve the last steps as well as to develop an asymmetric version of this formal synthesis.

Conclusions

In conclusion, the present methodology can be clearly extended to numerous examples. To summarise, the new reagent **1**, readily obtained from cheap starting materials, furnishes an alternative route to the existing methods for the synthesis of α-chloroketones and, in an simple manner, allows the selective synthesis of heterocycles in good yield as well as complex structures which can be used as templates for the synthesis of natural products belonging to various families.

Experimental

Commercial reagents were used as received, without further purification. Anhydrous magnesium sulfate was used for drying organic extracts, and all volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial aluminium backed thin layer chromatography (TLC) plates (Merck Kieselgel 60 F_{254}). The plates were observed under UV light at 254 nm and subsequently revealed using a vanillin or anisaldehyde-based stain. Flash chromatography were performed using SDS Silica Gel 60 C.C. 40–63 and a small layer of basic alumina was placed on top of the silica to remove any lauric acid present. Melting points were determined using a Reichert microscope apparatus. IR spectra were recorded on a Perkin-Elmer 1600 Fourier Transform spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX400 instrument (at 400 and 100 MHz respectively); chemical shifts are given in ppm using tetramethylsilane as a reference and coupling constants are given in hertz. Mass spectra were recorded on an HP 5989B and on a Q-TOF MS or JEOL JMS-GCmate II mass spectrometer for HRMS. Petrol refers to light petroleum ether (PE), bp 40–60 °C. The addition of dilauroyl peroxide (DLP), after degassing the solution for 20 min, was performed portionwise as 5 mol% every 90 min for the radical additions and as 20 mol% every hour for the cyclisation steps, until complete disappearance of the starting material was observed. *N*-Allyl-*N*-(4-chloro-phenyl)acetamide, *N*-allyl-*N*-(4-bromo-phenyl)acetamide, *N*-allyl-*N*-(4-fluoro-phenyl)acetamide and *N*-allyl-*N*-(4-methoxy-phenyl)methanesulfonamide were prepared by a simple two step procedure; firstly, protection of the corresponding *p*-substituted aniline using acetyl or mesyl chloride was performed, followed by reaction with allyl bromide in the presence of sodium hydroxide or potassium carbonate. All pyrrole derivatives proved to be unstable when exposed to air, and consequently their immediate characterisation was required.

N-Allyl-*N*-(4-methoxy-phenyl)methanesulfonamide 6e[9]

White crystals, mp 42 °C (from EtOH), ν_{max} (CCl_4)/cm^{-1} 3094m, 3013m, 2963s, 2931s, 2256m, 1606s, 1512s, 1344s, 1250s, 1156m, 1031m; δ_H (400 MHz; $CDCl_3$) 2.90 (3H, s, SO_2CH_3), 3.81 (3H, s, OCH_3), 4.23 (2H, d, *J* 6.1, NCH_2), 5.13 (1H, d, *J* 9.9, CH_2CH), 5.15 (1H, d, *J* 15.9, CH_2CH), 5.84 (1H, m, $CHCH_2$), 6.90 (2H, d, *J* 9.0, Ar*H*), 7.25 (2H, d, *J* 9.0, Ar*H*); δ_C (100 MHz; $CDCl_3$) 38.1 (SO_2CH_3), 54.1 (NCH_2), 55.6 (OCH_3), 114.7 (2 × Ar*C*H), 119.2 (CH_2CH), 129.3 (Ar*C*), 130.2 (2 × Ar*C*H), 133.1 ($CHCH_2$), 159.3 (Ar*C*); *m*/*z* (CI, NH_3) 259 (MNH_4^+, 100%), 242 (MH^+, 48), 164 (46).

_N_-Allyl-_N_-(4-chloro-phenyl)acetamide 6f[25]

White crystals, mp 42–43 °C (from EtOH), ν_{max} (CCl_4)/cm^{-1} 3083m, 3013m, 2985s, 2925s, 1667s (C=O), 1592w, 1549m, 1495s, 1381s, 1279s, 1230s, 1094s, 1016s; δ_H (400 MHz; $CDCl_3$) 1.82 (3H, s, C*H*$_3$), 4.23 (2H, d, *J* 6.5, NC*H*$_2$), 4.99–5.08 (2H, m, C*H*$_2$CH), 5.80 (1H, m, C*H*CH$_2$), 7.07 (2H, d, *J* 8.2, Ar*H*), 7.33 (2H, d, *J* 8.2, Ar*H*); δ_C (100 MHz; $CDCl_3$) 22.6 (*C*H$_3$), 51.9 (NCH$_2$), 118.1 (*C*H$_2$CH), 129.4 (2 × Ar*C*H), 129.8 (2 × Ar*C*H), 132.8 (*C*HCH$_2$), 133.5 (Ar*C*), 141.3 (Ar*C*), 169.6 (*C*=O); *m*/*z* (CI, NH_3) 210 (MH^+, 100%).

_N_-Allyl-_N_-(4-bromo-phenyl)acetamide 6g[25]

White crystals, mp 43–44 °C (from EtOH), ν_{max} (CCl_4)/cm^{-1} 3083m, 3013m, 2986m, 2925m, 1668s (C=O), 1586m, 1488s, 1431s, 1385s, 1278s, 1231s, 1141m, 1071s, 1013s; δ_H (400 MHz; $CDCl_3$) 1.86 (3H, s, C*H*$_3$), 4.22 (2H, d, *J* 6.5, NC*H*$_2$), 5.03–5.13 (2H, m, C*H*$_2$CH), 5.84 (1H, m, C*H*CH$_2$), 7.04 (2H, d, *J* 8.8, Ar*H*), 7.53 (2H, d, *J* 8.8, Ar*H*); δ_C (100 MHz; $CDCl_3$) 22.3 (*C*H$_3$), 51.9 (NCH$_2$), 118.2 (*C*H$_2$CH), 121.7 (Ar*C*), 129.1 (2 × Ar*C*H), 132.8 (2 × Ar*C*H and *C*HCH$_2$), 141.9 (Ar*C*), 169.7 (*C*=O); *m*/*z* (CI, NH_3) 254 (M^+, 100%).

_N_-Allyl-_N_-(4-fluoro-phenyl)acetamide 6h

White crystals, mp 77–78 °C (from EtOH), ν_{max} (CCl_4)/cm^{-1} 3082w, 3050w, 2985w, 2924w, 1668s (C=O), 1509s, 1431s, 1385s, 1296s, 1278s, 1239s, 1220s, 1152m, 1091m, 1013w; δ_H (400 MHz; $CDCl_3$) 1.86 (3H, s, C*H*$_3$), 4.27 (2H, d, *J* 6.2, NC*H*$_2$), 5.09 (2H, dd, *J* 12.0, 18.5, C*H*$_2$CH), 5.85 (1H, m, C*H*CH$_2$), 7.08–7.18 (4H, m, Ar*H*); δ_C (100 MHz; $CDCl_3$) 22.6 (*C*H$_3$), 52.0 (NCH$_2$), 116.4 (d, J_{C-F} 23, 2 × Ar*C*H), 118.1 (*C*H$_2$CH), 129.9 (d, J_{C-F} 8, 2 × Ar*C*H), 132.9 (*C*H$_2$*C*H), 158.8 (Ar*C*), 161.8 (d, J_{C-F} 246, Ar*C*), 170.0 (*C*=O); *m*/*z* (CI, NH_3) 194 (MH^+, 100%); HRMS, Found: M^+, 193.0900. $C_{11}H_{12}ONF$ requires *M*, 193.0902.

Dithiocarbonic acid (3-chloro-2-oxo-propyl) ester ethyl ester 1

To a solution of potassium *O*-ethyl xanthate (1.21 g, 7.54 mmol) in water (10 mL), under argon at 0 °C, was added portionwise 1,3-dichloro-propan-2-one (957 mg, 7.53 mmol, 0.99 eq.). The solution was stirred for 1 h at 0 °C and then filtered. The solid was then washed with water and dried to give compound **1** in 72% yield as a white solid.

Recrystallisations gave white crystals, mp 49–50 °C (from PE–AcOEt), ν_{max} (CCl_4)/cm^{-1} 2987s, 2939s, 2899m, 1738s, 1365m, 1232s, 1113s, 1058s; δ_H (400 MHz; $CDCl_3$) 1.43 (3H, t, *J* 7.1, C*H*$_3$), 4.15 (2H, s, C*H*$_2$), 4.32 (2H, s, C*H*$_2$), 4.64 (2H, q, *J* 7.1, C*H*$_2$CH$_3$); δ_C (100 MHz; $CDCl_3$) 13.7 (*C*H$_3$), 42.8 (*C*H$_2$), 47.9 (*C*H$_2$), 71.2 (OCH$_2$), 195.7 (*C*=O), 212.8 (*C*=S); *m*/*z* (CI, NH_3) 213 (MH^+, 100%); HRMS, Found: M^+, 211.9733. $C_6H_9ClO_2S_2$ requires *M*, 211.9732.

Dithiocarbonic acid [1-(4-chloro-3-oxo-butyl)-heptyl] ester ethyl ester 7a

Xanthate **1** (0.689 g, 1.79 mmol) and 1-octene (0.401 g, 3.58 mmol) were dissolved in DCE (2 ml) and the resulting solution refluxed under nitrogen for 15 min. DLP (53 mg, 0.13 mmol) was then added. Heating was continued until the complete consumption of the starting material. The crude mixture was concentrated *in vacuo* and the residue was purified by column chromatography (PE–AcOEt, 95 : 5) to give **7a** as yellow oil (0.520 g, 89%), ν_{max} (CCl_4)/cm^{-1} 2957s, 2930s, 2857m, 1722s (C=O), 1455w, 1367w, 1216s, 1119m, 1052s; δ_H (400 MHz; $CDCl_3$) 0.88 (3H, t, *J* 7.0, C*H*$_3$), 1.22–1.34 (6H, m, C*H*$_2$), 1.35–1.49 (2H, m, C*H*$_2$), 1.43 (3H, t, *J* 7.0, OCH$_2$C*H*$_3$), 1.66 (2H, q, *J* 7.04, C*H*$_2$), 1.86 (1H, m, C*H*$_2$), 2.13 (1H, m, C*H*$_2$), 2.66–2.84 (2H, m, C*H*$_2$), 3.75 (1H, m, C*H*S), 4.1 (2H, s, C*H*$_2$Cl), 4.64 (2H, q, *J* 7.0, OC*H*$_2$CH$_3$); δ_C (100 MHz; $CDCl_3$) 13.9 (*C*H$_3$), 14.2 (*C*H$_3$), 22.7 (*C*H$_2$), 26.9 (*C*H$_2$), 28.1 (*C*H$_2$), 29.1 (*C*H$_2$), 31.7 (*C*H$_2$), 34.7 (*C*H$_2$), 37.0 (*C*H$_2$), 48.3 (*C*H$_2$), 51.0 (*C*HS), 70.1 (O*C*H$_2$), 202.0 (*C*=O), 214.7 (*C*=S); *m*/*z* (CI, NH_3) 341 (MNH_3^+, 25%), 324 (M^+, 100); HRMS, Found: MH^+, 325.1180. $C_{14}H_{26}ClO_2S_2$ requires MH^+, 325.1160.

Dithiocarbonic acid (1-benzenesulfonyl-5-chloro-4-oxo-pentyl) ester ethyl ester 7b

Treatment of the xanthate **1** (0.561 g, 2.65 mmol) with phenyl vinyl sulfone (0.890 g, 5.29 mmol) in DCE (3 ml), furnished after addition of DLP (0.105 g, 0.26 mmol) a crude mixture which was concentrated *in vacuo* and purified by column chromatography (PE–AcOEt, 60 : 40). Compound **7b** was obtained as a yellow oil (0.357 g, 35%), ν_{max} (CCl_4)/cm^{-1} 3069w, 2983w, 2899w, 1724s (C=O), 1447m, 1327s, 1240s, 1153s, 1046s; δ_H (400 MHz; $CDCl_3$) 1.33 (3H, t, *J* 7.3, OCH$_2$C*H*$_3$), 2.18 (1H, m, C*H*$_2$), 2.67 (1H, m, C*H*$_2$), 2.79–3.02 (2H, m, C*H*$_2$), 4.08 (2H, s, C*H*$_2$Cl), 4.38–4.57 (2H, m, OCH$_2$C*H*$_3$), 5.30 (1H, m, C*H*S), 7.51–7.58 (2H, m, Ar*H*), 7.66 (1H, m, Ar*H*), 7.95 (2H, d, *J* 7.3, Ar*H*); δ_C (100 MHz; $CDCl_3$) 13.6 (*C*H$_3$), 21.9 (*C*H$_2$), 35.9 (*C*H$_2$), 48.0 (*C*H$_2$), 70.8 (*C*HS), 71.7 (OCH$_2$), 129.4 (2 × Ar*C*H), 129.8 (2 × Ar*C*H), 134.3 (Ar*C*H), 136.5 (Ar*C*), 200.7 (*C*=O), 209.1 (*C*=S); *m*/*z* (CI, NH_3) 397 (MNH_4^+, 100%), 239 (20); HRMS, Found: MNa^+, 402.9862, $C_{14}H_{17}ClNaO_4S_3$ requires MNa^+, 402.9875.

2,2-Dimethyl-propionic acid 5-chloro-1-ethoxythiocarbonylsulfanyl-4-oxo-pentyl ester 7c

After the addition of DLP (0.08 g, 0.192 mmol), the reaction between **1** (1 g, 2.58 mmol) and vinyl pivalate **6c** (0.662 g, 5.17 mmol) in refluxing DCE (2.5 ml) furnished a crude mixture which was concentrated *in vacuo* and purified by column chromatography (PE–AcOEt, 95 : 5). Compound **7c** was obtained as a yellow oil (0.750 g, 85%), ν_{max} (CCl_4)/cm^{-1} 2976s, 2933s, 2905m, 1731s (C=O), 1479s, 1397m, 1367m, 1279m, 1222s, 1128m, 1053s; δ_H (400 MHz; $CDCl_3$) 1.18 (9H, s, C*H*$_3$), 1.40 (3H, t, *J* 7.0, OCH$_2$C*H*$_3$), 2.15–2.36 (2H, m, C*H*$_2$), 2.70–2.78 (2H, m, C*H*$_2$), 4.09 (2H, s, C*H*$_2$Cl), 4.55–4.68 (2H, m, OC*H*$_2$CH$_3$), 6.59 (1H, t, *J* 6.75, C*H*S); δ_C (100 MHz; $CDCl_3$) 13.6 (*C*H$_3$), 26.9 (3 × *C*H$_3$), 27.9 (*C*H$_2$), 35.2 (*C*H$_2$), 39.5 (*C*), 48.0 (*C*H$_2$), 70.1 (O*C*H$_2$), 79.7 (*C*HS), 176.8 (*C*=O), 200.8 (*C*=O), 209.8 (*C*=S); *m*/*z* (CI, NH_3) 357 (MNH_3^+, 30%), 239 (100), 207 (20), 135 (50); HRMS, Found: MNa^+, 363.0495, $C_{13}H_{21}ClNaO_4S_2$ requires MNa^+, 363.0468.

Dithiocarbonic acid (5-chloro-4-oxo-1-trimethylsilanylmethyl-pentyl) ester ethyl ester 7d

Allyl trimethylsilane **6d** (0.591 g, 5.17 mmol) and **1** (1 g, 2.58 mmol) in DCE (2.5 ml) were reacted in the presence of DLP (0.08 g, 0.192 mmol). Concentration *in vacuo* of the reaction mixture

afforded an oil which was purified by column chromatography (PE–AcOEt, 95 : 5), to give **7d** as a yellow oil (0.650 g, 77%), ν_{max} (CCl_4)/cm^{-1} 2952s, 1736s (C=O), 1403m, 1366m, 1214s, 1111s, 1052s; δ_H (400 MHz; $CDCl_3$) 0.08 (9H, s, Si(CH_3)$_3$), 0.90–1.18 (2H, m, CH_2Si), 1.42 (3H, t, *J* 7.0, OCH$_2$$CH_3$), 1.85 (1H, m, CH_2), 2.17 (1H, m, CH_2), 2.62–2.86 (2H, m, CH_2), 3.88 (1H, m, CHS), 4.08 (2H, s, CH_2Cl), 4.56–4.70 (2H, m, OCH_2CH$_3$); δ_C (100 MHz; $CDCl_3$) −0.8 (Si(CH_3)$_3$), 13.7 (CH_3), 23.6 (CH_2), 30.6 (CH_2), 36.7 (CH_2), 48.0 (CHS), 48.2 (CH_2), 69.8 (OCH_2), 201.8 (C=O), 214.3 (C=S); *m*/*z* (CI, NH_3) 343 (MNH_4^+, 10%), 326 (M^+, 10), 205 (70), 92 (100).

Dithiocarbonic acid (5-chloro-1-{[methanesulfonyl-(4-methoxyphenyl)-amino]-methyl}-4-oxo-pentyl) ester ethyl ester 7e

To a refluxing solution of **6e** (300 mg, 1.25 mmol) and **1** (132 mg, 0.62 mmol) in DCE (2 ml), was added DLP (49 mg, 0.12 mmol). The crude mixture was concentrated *in vacuo* then purified by column chromatography (EP–Et_2O, 30 : 70) to give compound **7e** as a white foam (230 mg, 81%), ν_{max} (CCl_4)/cm^{-1} 2934m, 1723m (C=O), 1509s, 1353s, 1250s, 1222s, 1158s, 1052s; δ_H (400 MHz; $CDCl_3$) 1.31 (3H, t, *J* 7.3, OCH$_2$$CH_3$), 1.87 (1H, m, CH_2), 2.37 (1H, m, CH_2), 2.62–2.89 (2H, m, CH_2), 2.89 (3H, s, CH_3), 3.66 (1H, m, CHS), 3.83 (3H, s, OCH_3), 3.78–3.96 (2H, m, CH_2), 4.07 (2H, s, CH_2Cl), 4.55 (2H, q, *J* 7.3, OCH_2CH$_3$), 6.94 (2H, d, *J* 8.8, Ar*H*), 7.29 (2H, d, *J* 8.8, Ar*H*); δ_C (100 MHz; $CDCl_3$) 13.6 (CH_3), 24.0 (CH_2), 36.3 (CH_2), 37.1 (CH_3), 48.0 (CH_2), 48.2 (CH), 53.5 (CH_2), 55.5 (CH_3), 70.3 (CH_2), 114.8 (2 × ArCH), 130.1 (2 × ArCH), 130.7 (ArC), 159.5 (ArC), 201.4 (C=O), 212.4 (C=S); *m*/*z* (CI, NH_3) 472 (MNH_4^+, 100%), 455 (MH^+, 20), 374 (74), 348 (25), 253 (22); HRMS, Found: MH^+, 454.0581, $C_{17}H_{25}ClNO_5S_3$ requires MH^+, 454.0583.

Dithiocarbonic acid (1-{[acetyl-(4-chlorophenyl)-amino]-methyl}-5-chloro-4-oxo-pentyl) ester ethyl ester 7f

6f (1.02 g, 4.88 mmol) and **1** (0.684 g, 3.21 mmol) were refluxed in DCE (5 ml) before adding DLP (0.256 g, 0.64 mmol). The crude mixture was then concentrated *in vacuo* and purified by column chromatography (PE–AcOEt, 50 : 50). Compound **7f** was isolated as a yellow oil (0.740 g, 55%), ν_{max} (CCl_4)/cm^{-1} 2936w, 1720m (C=O), 1670s (C=O), 1491s, 1388m, 1286m, 1222s, 1112m, 1053s; δ_H (400 MHz; $CDCl_3$) 1.31 (3H, t, *J* 7.2, OCH$_2$$CH_3$), 1.82 (1H, m, CH_2), 1.86 (3H, s, CH_3), 2.26 (1H, m, CH_2), 2.79 (2H, t, *J* 6.4, CH_2), 3.69 (1H, dd, *J* 13.6, 6.4, CH_2), 3.78 (1H, m, CHS), 4.08 (2H, s, CH_2Cl), 4.22 (1H, dd, *J* 13.6, 8.0, CH_2), 4.54 (2H, q, *J* 7.2, OCH_2CH$_3$), 7.22 (2H, d, *J* 8.4, Ar*H*), 7.43 (2H, d, *J* 8.4, Ar*H*); δ_C (100 MHz; $CDCl_3$) 13.6 (CH_3), 22.8 (CH_3), 24.9 (CH_2), 36.4 (CH_2), 48.3 (CH_2), 48.4 (CH), 51.2 (CH_2), 70.3 (CH_2), 129.8 (2 × ArCH), 130.1 (2 × ArCH), 134.2 (ArC), 140.9 (ArC), 170.8 (C=O), 201.8 (C=O), 213.0 (C=S); *m*/*z* (CI, NH_3) 440 (MNH_4^+, 25%), 423 (MH^+, 100), 300 (23); HRMS, Found: MH^+, 422.0418, $C_{17}H_{22}Cl_2NO_3S_2$ requires MH^+, 422.0406.

Dithiocarbonic acid (1-{[acetyl-(4-bromophenyl)-amino]-methyl}-5-chloro-4-oxo-pentyl) ester ethyl ester 7g

To a refluxing solution of **6g** (303 mg, 1.19 mmol) and xanthate **1** (500 mg, 2.36 mmol) in DCE (2 ml) was added DLP (183 mg, 0.46 mmol). Concentration *in vacuo* gave a crude oil which was purified by column chromatography (PE–Et_2O, 40 : 60) affording **7g** as a yellow oil (507 mg, 91%), ν_{max} (CCl_4)/cm^{-1} 2984m, 2935m, 1721s (C=O), 1670s (C=O), 1550m, 1487s, 1435m, 1387m, 1286m, 1222s, 1112m, 1052s; δ_H (400 MHz; $CDCl_3$) 1.31 (3H, t, *J* 7.1, OCH$_2$$CH_3$), 1.79 (1H, m, CH_2), 1.86 (3H, s, CH_3), 2.26 (1H, m, CH_2), 2.79 (2H, t, *J* 6.9, CH_2), 3.69 (1H, dd, *J* 13.6, 6.6, CH_2), 3.78 (1H, m, CHS), 4.08 (2H, s, CH_2Cl), 4.22 (1H, dd, *J* 13.6, 8.4, CH_2), 4.54 (2H, q, *J* 7.1, OCH_2CH$_3$), 7.17 (2H, d, *J* 8.6, Ar*H*), 7.59 (2H, d, *J* 8.6, Ar*H*); δ_C (100 MHz; $CDCl_3$) 13.5 (CH_3), 22.6 (CH_3), 24.6 (CH_2), 36.2 (CH_2), 48.1 (CH_2), 48.2 (CH), 51.0 (CH_2), 70.2 (CH_2), 122.0 (ArC), 129.9 (2 × ArCH), 132.9 (2 × ArCH), 141.2 (ArC), 170.5 (C=O), 201.6 (C=O), 212.8 (C=S); *m*/*z* (CI, NH_3) 486 (20%), 484 (MNH_4^+, 15), 469 (100), 467 (MH^+, 75); HRMS, Found: MH^+, 465.9916. $C_{17}H_{22}BrClNO_3S_2$ requires MH^+, 465.9913.

Dithiocarbonic acid (1-{[acetyl-(4-fluorophenyl)-amino]-methyl}-5-chloro-4-oxo-pentyl) ester ethyl ester 7h

To a refluxing solution of **1** (670 mg, 3.16 mmol) and **6h** (303 mg, 1.57 mmol) in DCE (2 ml) was added DLP (170 mg, 0.43 mmol). The crude mixture was then concentrated *in vacuo* and the residue was purified by column chromatography (PE–Et_2O, 50 : 50). Compound **7h** was isolated as a yellow oil (504 mg, 80%), ν_{max} (CCl_4)/cm^{-1} 2984w, 2934w, 1721m (C=O), 1669s (C=O), 1510s, 1389m, 1289m, 1223s, 1112m, 1052s; δ_H (400 MHz; $CDCl_3$) 1.31 (3H, t, *J* 7.1, OCH$_2$$CH_3$), 1.77 (1H, m, CH_2), 1.84 (3H, s, CH_3), 2.20 (1H, m, CH_2), 2.80 (2H, t, *J* 6.9, CH_2), 3.67 (1H, dd, *J* 13.6, 6.5, CH_2), 3.75 (1H, m, CHS), 4.09 (2H, d, *J* 2.0, CH_2Cl), 4.16 (1H, dd, *J* 13.6, 8.6, CH_2), 4.47 (2H, qd, *J* 7.1, 2.1, OCH_2CH$_3$), 7.14 (2H, t, *J* 8.5, Ar*H*), 7.27 (2H, dd, *J* 8.6, 4.9, Ar*H*); δ_C (100 MHz; $CDCl_3$) 13.7 (CH_3), 22.8 (CH_3), 24.8 (CH_2), 36.4 (CH_2), 48.3 (CH), 48.4 (CH_2), 51.3 (CH_2), 70.3 (CH_2), 116.8 (d, J_{C-F} 23, 2 × ArCH), 130.1 (d, J_{C-F} 9, 2 × ArCH), 138.4 (ArC), 162.0 (d, J_{C-F} 247, ArC), 171.0 (NC=O), 201.8 (C=O), 213.1 (C=S); *m*/*z* (CI, NH_3) 426 (12%), 424 (MNH_4^+, 15), 407 (MH^+, 50), 405 (100); HRMS, Found: MH^+, 406.0708, $C_{17}H_{22}ClFNO_3S_2$ requires MH^+, 406.0714.

[1,3]Dithiane-2,5-dione 8

Compound **8** was prepared by refluxing a solution of compound **1** (538 mg, 2.53 mmol) in chlorobenzene (25 mL) for 10 hours. The solvent was then removed *in vacuo*. The crude residue was purified by flash column chromatography (PE–AcOEt, 10 : 0 to 8 : 2), to give compound **8** in 50% yield as white crystals (190 mg, 50%), mp 47–50 °C (from heptane–AcOEt), ν_{max} (CH_2Cl_2)/cm^{-1} 2924m, 1728s (C=O), 1648s (C=O), 1389 s, 1239 m; δ_H (400 MHz; $CDCl_3$), 3.87 (4H, s, CH_2); δ_C (100 MHz; $CDCl_3$) 39.8 (2 × CH_2), 190.5 (C=O), 198.1 (C=O); *m*/*z*, HRMS, Found: M^+, 147.9653, $C_{14}H_{16}BrClNO_2$ requires M^+, 147.9652.

1-Chloro-4-(1-methanesulfonyl-5-methoxy-2,3-dihydro-1*H*-indol-3-yl)-butan-2-one 9e

To a refluxing solution of **7e** (0.298 g, 0.66 mmol) in 1,2-dichloroethane (7 ml), was added DLP (0.262 g, 0.66 mmol). The crude mixture was concentrated *in vacuo* and purified by column chromatography (EP–AcOEt, 60 : 40) to give compound **9e** as a white solid (0.118 g, 54%), mp 81–83 °C (from PE–AcOEt),

ν_{max} (CCl_4)/cm^{-1} 2928m, 1723m (C=O), 1549s, 1488m, 1361m, 1249m, 1165m; δ_H (400 MHz; $CDCl_3$), 1.88 (1H, dddd, *J* 14.4, 8.4, 8.4, 6.0, CH_2), 2.14 (1H, m, CH_2), 2.60–2.78 (2H, m, CH_2), 2.83 (3H, s, CH_3), 3.40 (1H, m, C*H*), 3.62 (1H, dd, *J* 10.0, 5.9, NCH_2), 3.78 (3H, s, OCH_3), 4.01 (1H, t, *J* 10.0, NCH_2), 4.08 (2H, s, CH_2Cl), 6.74–6.77 (2H, m, Ar*H*), 7.31 (1H, dd, *J* 7.6, 2, Ar*H*); δ_C (100 MHz; $CDCl_3$) 28.0 (*C*H_2), 33.8 (*C*H), 36.2 (*C*H_2), 39.2 (*C*H_3), 48.1 (*C*H_2), 55.7 (*C*H_3), 56.1 (*C*H_2), 111.0 (Ar*C*H), 113.3 (Ar*C*H), 114.6 (Ar*C*H), 135.1 (Ar*C*), 135.5 (Ar*C*), 156.7 (Ar*C*), 201.8 (*C*=O); *m/z* (CI, NH_3) 348 (MNH_4^+, 100%), 330 (M^+, 35), 253 (60), 161 (20); HRMS, Found: MH^+, 332.0731, $C_{14}H_{19}ClNO_4S$ requires *MH*$^+$, 322.0723.

4-(1-Acetyl-5-chloro-2,3-dihydro-1*H*-indol-3-yl)-1-chloro-butan-2-one 9f

In the same manner described above, **7f** (1.08 g, 2.6 mmol) was dissolved in DCE (26 ml) and DLP (1.02 g, 2.6 mmol) was added until consumption of all starting material. After concentration *in vacuo*, the crude mixture was purified by column chromatography (PE–AcOEt, 80 : 20) to give **9f** as a white solid (0.570 g, 66%), mp 135–137 °C (from AcOEt), ν_{max} (CCl_4)/cm^{-1} 2980w, 2930w, 1724m (C=O), 1672s (C=O), 1478s, 1392s; δ_H (400 MHz; $CDCl_3$), 1.90 (1H, m, CH_2), 2.08 (1H, m, CH_2), 2.19 (3H, s, CH_3), 2.60–2.68 (2H, m, CH_2), 3.42 (1H, m, C*H*), 3.68 (1H, dd, *J* 10.5, 5.5, NCH_2), 4.06 (2H, s, CH_2Cl), 4.15 (1H, t, *J* 10.0, NCH_2), 7.11 (1H, br s, Ar*H*), 7.15 (1H, dd, *J* 8.6, 2.1, Ar*H*), 8.10 (1H, d, *J* 8.6, Ar*H*); δ_C (100 MHz; $CDCl_3$) 24.1 (*C*H_3), 28.4 (*C*H_2), 36.2 (*C*H_2), 38.9 (*C*H), 48.2 (*C*H_2), 54.8 (*C*H_2), 118.0 (Ar*C*H), 124.1 (Ar*C*H), 128.1 (Ar*C*H), 128.6 (Ar*C*), 135.7 (Ar*C*), 141.4 (Ar*C*), 168.7 (*C*=O), 201.8 (*C*=O); *m/z* (CI, NH_3) 318 (MNH_3^+, 10%), 316 (15), 301 (M^+, 75), 299 (100); HRMS, Found: MH^+, 300.0543, $C_{14}H_{16}Cl_2NO_2$ requires *MH*$^+$, 300.0558.

4-(1-Acetyl-5-bromo-2,3-dihydro-1*H*-indol-3-yl)-1-chloro-butan-2-one 9g

To a refluxing solution of **7g** (0.800 g, 1.71 mmol) in DCE (17 ml), was added DLP (0.818 g, 2.05 mmol). The crude mixture was concentrated *in vacuo* and then purified by column chromatography (PE–AcOEt, 30 : 20): compound **9g** was isolated as a white solid (0.400 g, 68%), mp 140–142 °C (from AcOEt), ν_{max} (CCl_4)/cm^{-1} 2919m, 2359m, 1724m (C=O), 1673s (C=O), 1477s, 1391s, 1335m, 1256m; δ_H (400 MHz; $CDCl_3$), 1.91 (1H, m, CH_2), 2.09 (1H, m, CH_2), 2.21 (3H, s, CH_3), 2.63–2.68 (2H, m, CH_2), 3.44 (1H, m, C*H*), 3.69 (1H, dd, *J* 10.4, 5.5, NCH_2), 4.07 (2H, s, CH_2Cl), 4.16 (1H, t, *J* 9.7, NCH_2), 7.27 (1H, br s, Ar*H*), 7.32 (1H, dd, *J* 8.6, 1.9, Ar*H*), 8.07 (1H, d, *J* 8.6, Ar*H*); δ_C (100 MHz; $CDCl_3$) 24.1 (*C*H_3), 28.3 (*C*H_2), 36.1 (*C*H_2), 38.8 (*C*H), 48.0 (*C*H_2), 54.7 (*C*H_2), 116.0 (Ar*C*), 118.3 (Ar*C*H), 126.9 (Ar*C*H), 131.1 (Ar*C*H), 136.0 (Ar*C*), 141.8 (Ar*C*), 168.7 (*C*=O), 201.7 (*C*=O); *m/z* (CI, NH_3) 362 (MNH_3^+, 25%), 360 (18), 345 (M^+, 100), 343 (75); HRMS, Found: MH^+, 344.0037, $C_{14}H_{16}BrClNO_2$ requires *MH*$^+$, 344.0053.

4-(1-Acetyl-5-fluoro-2,3-dihydro-1*H*-indol-3-yl)-1-chloro-butan-2-one 9h

To a refluxing solution of **7h** (0.712 g, 1.75 mmol) in DCE (17 ml) was added DLP (0.839 g, 2.1 mmol). The crude mixture was then concentrated *in vacuo* and purified by column chromatography to give **9h** as a white solid (0.295 g, 60%), mp 80–81 °C (from PE–AcOEt), ν_{max} (CH_2Cl_2)/cm^{-1} 2935w, 1737m, 1720m (C=O), 1659s (C=O), 1609m, 1485s, 1402s, 1282s, 1263s, 1249s; δ_H (400 MHz; $CDCl_3$), 1.89 (1H, m, CH_2), 2.07 (1H, m, CH_2), 2.18 (3H, s, CH_3), 2.60–2.66 (2H, m, CH_2), 3.42 (1H, m, C*H*), 3.68 (1H, dd, *J* 10.2, 5.5, NCH_2), 4.05 (2H, s, CH_2Cl), 4.13 (1H, t, *J* 10.0, NCH_2), 6.83–6.89 (2H, m, Ar*H*), 8.12 (1H, dd, *J* 8.8, 4.9, Ar*H*); δ_C (100 MHz; $CDCl_3$) 23.9 (*C*H_3), 28.2 (*C*H_2), 36.0 (*C*H_2), 38.9 (*C*H), 48.0 (*C*H_2), 54.8 (*C*H_2), 111.1 (d, J_{C-F} 24, Ar*C*H), 114.3 (d, J_{C-F} 22, Ar*C*H), 117.7 (d, J_{C-F} 8, Ar*C*H), 135.6 (d, J_{C-F} 8, Ar*C*H), 138.7 (Ar*C*), 159.2 (d, J_{C-F} 243, Ar*C*), 168.3 (*C*=O), 201.7 (*C*=O); *m/z* (CI, NH_3) 301 (MNH_4^+, 17%), 284 (MH^+, 100); HRMS, Found: MH^+, 284.0847, $C_{14}H_{16}ClFNO_2$ requires *MH*$^+$, 284.0854.

Dithiocarbonic acid ethyl ester [4-(1-methanesulfonyl-5-methoxy-2,3-dihydro-1*H*-indol-3-yl)-2-oxo-butyl] ester 10e

To a solution of **9e** (0.200 g, 0.6 mmol) in acetone (20 ml) was added portionwise ethylxanthic acid potassium salt (0.106 g, 0.66 mmol) and the reaction was stirred at room temperature for 2 h. The solvent was then evaporated *in vacuo* and DCM (30 ml) was added to the crude mixture and washed with water (20 ml). After separation, the organic layer was dried over $MgSO_4$; evaporation furnished a crude oil which was purified by column chromatography (PE–Et_2O, 1 : 5) to give **10e** as a colourless oil (0.202 g, 81%), ν_{max} (CCl_4)/cm^{-1} 2940w, 2837w, 1718m (C=O), 1607m (C=O), 1488s, 1348s, 1227s, 1161s, 1049s; δ_H (400 MHz; $CDCl_3$), 1.42 (3H, t, *J* 7.2, OCH$_2$CH_3), 1.86 (1H, m, CH_2), 2.16 (1H, m, CH_2), 2.64–2.79 (2H, m, CH_2), 2.83 (3H, s, CH_3), 3.38 (1H, m, C*H*), 3.61 (1H, dd, *J* 10.4, 6.0, NCH_2), 3.79 (3H, s, OCH_3), 3.99 (2H, s, CH_2S), 4.02 (1H, m, NCH_2), 4.64 (2H, q, *J* 7.2, OCH_2CH$_3$), 6.75 (1H, d, *J* 8.8, Ar*H*), 6.78 (1H, s, Ar*H*), 7.31 (1H, d, *J* 8.8, Ar*H*); δ_C (100 MHz; $CDCl_3$) 13.6 (*C*H$_3$), 28.0 (*C*H$_2$), 33.7 (*C*H$_3$), 38.4 (*C*H$_2$), 39.1 (*C*H), 45.2 (*C*H$_2$), 55.6 (*C*H$_3$), 56.1 (*C*H$_2$), 71.1 (*C*H$_2$), 111.8 (Ar*C*H), 113.2 (Ar*C*H), 114.5 (Ar*C*H), 135.0 (Ar*C*), 135.6 (Ar*C*), 156.7 (Ar*C*), 202.4 (*C*=O), 213.4 (*C*=S); *m/z* (CI, NH_3) 435 (MNH_4^+, 100%), 418 (MH^+, 88), 338 (40), 252 (35); HRMS, Found: 418.0782 MH^+, $C_{17}H_{24}NO_5S_3$ requires *MH*$^+$, 418.0817.

Dithiocarbonic acid [4-(1-acetyl-5-chloro-2,3-dihydro-1*H*-indol-3-yl)-2-oxo-butyl] ester ethyl ester 10f

To a solution of **9f** (0.427 g, 1.42 mmol) in acetone (20 ml) was added portionwise a solution of ethylxanthic acid potassium salt (0.251 g, 1.56 mmol) in acetone (6 ml). After stirring for 2 h at room temperature, the crude mixture was evaporated, diluted with DCM (40 ml) and washed with water (20 ml). The organic layer was dried over $MgSO_4$ and evaporated *in vacuo*. The residue was purified by column chromatography (Et_2O) to give compound **10f** as ivory coloured needles (0.485 g, 88%), mp 131–132 °C (from AcOEt), ν_{max} (CH_2Cl_2)/cm^{-1} 2929m, 2837m, 1728w (C=O), 1663m (C=O), 1604m, 1478m, 1396m, 1338m, 1242m, 1018s; δ_H (400 MHz; $CDCl_3$) 1.41 (3H, t, *J* 7.1, OCH$_2$CH_3), 1.90 (1H, m, CH_2), 2.10 (1H, m, CH_2), 2.20 (3H, s, CH_3), 2.65–2.69 (2H, m, CH_2), 3.43 (1H, m, C*H*), 3.69 (1H, dd, *J* 10.4, 5.6, NCH_2), 3.97 (2H, s, CH_2S), 4.15 (1H, t, *J* 10.0, NCH_2), 4.62 (2H, q, *J* 7.1, OCH_2CH$_3$), 7.12 (1H, br s, Ar*H*), 7.16 (1H, dd, *J* 8.6, 2.0, Ar*H*), 8.11 (1H, d, *J* 8.6,

ArH); δ_C (100 MHz; $CDCl_3$) 13.8 (CH_3), 24.2 (CH_3), 28.4 (CH_2), 38.4 (CH_2), 38.9 (CH), 45.4 (CH_2), 55.0 (CH_2), 71.2 (CH_2), 117.9 (ArCH), 124.2 (ArCH), 128.1 (ArCH), 128.6 (ArC), 136.0 (ArC), 141.4 (ArC), 168.7 (C=O), 202.5 (C=O), 213.6 (C=S); *m/z* (CI, NH_3) 402 (MNH_3^+, 10%), 387 (50), 385 (M^+, 100); HRMS, Found: 386.0649 MH^+, $C_{17}H_{21}ClNO_3S_2$ requires MH^+, 386.0651.

Dithiocarbonic acid [4-(1-acetyl-5-bromo-2,3-dihydro-1*H*-indol-3-yl)-2-oxo-butyl] ester ethyl ester 10g

To a solution of **9g** (0.384 g, 1.11 mmol) in acetone (20 ml) was added portionwise ethylxanthic acid potassium salt (0.197 g, 1.23 mmol). The reaction was stirred at room temperature for 4 h before evaporation of the solvent. The crude mixture was then dissolved in DCM (40 ml) and washed with water (20 ml); after separation, the organic layer was dried over $MgSO_4$. Evaporation *in vacuo* furnished a residue which was purified by column chromatography (Et_2O) to give compound **10g** as a white solid (0.473 g, quant.), mp 117–118 °C (from AcOEt), ν_{max} (CH_2Cl_2)/cm^{-1} 1727w (C=O), 1663s (C=O), 1592w, 1477s, 1394s, 1233s, 1113m, 1049s; δ_H (400 MHz; $CDCl_3$) 1.43 (3H, t, *J* 7.0, OCH_2CH_3), 1.92 (1H, m, CH_2), 2.12 (1H, m, CH_2), 2.22 (3H, s, CH_3), 2.66–2.71 (2H, m, CH_2), 3.44 (1H, m, CH), 3.70 (1H, dd, *J* 10.3, 5.5, NCH_2), 3.99 (2H, s, CH_2S), 4.16 (1H, t, *J* 10.0, NCH_2), 4.65 (2H, q, *J* 7.0, OCH_2CH_3), 7.27 (1H, br s, ArH), 7.33 (1H, d, *J* 8.6, ArH), 8.09 (1H, d, *J* 8.6, ArH); δ_C (100 MHz; $CDCl_3$) 13.8 (CH_3), 24.2 (CH_3), 28.5 (CH_2), 38.3 (CH_2), 38.9 (CH), 45.3 (CH_2), 54.9 (CH_2), 71.2 (CH_2), 116.1 (ArC), 118.4 (ArCH), 127.0 (ArCH), 131.0 (ArCH), 136.3 (ArC), 141.9 (ArC), 168.7 (C=O), 202.4 (C=O), 213.6 (C=S); *m/z* (CI, NH_3) 450 (MNH_4^+, 10%), 448 (10), 433 (MH^+), 431 (90); HRMS, Found: M^+, 429.0068. $C_{17}H_{20}O_3NS_2Br$ requires *M*, 429.0068.

Dithiocarbonic acid [4-(1-acetyl-5-fluoro-2,3-dihydro-1*H*-indol-3-yl)-2-oxo-butyl] ester ethyl ester 10h

9h (0.295 g, 1.04 mmol) was dissolved in acetone (20 ml) and ethylxanthic acid potassium salt (0.183 g, 1.14 mmol), was added portionwise. The reaction mixture was stirred at room temperature for 4 h and then concentrated *in vacuo*. The crude solid was dissolved in DCM (40 ml) and washed with water (20 ml); after separation, drying over $MgSO_4$ and evaporation, column chromatography (EP–Et_2O, 1 : 3) gave compound **10h** as a white solid (0.321 g, 84%), mp 109–110 °C (from PE–AcOEt), ν_{max} (CH_2Cl_2)/cm^{-1} 2937m, 1718m (C=O), 1659s (C=O), 1609m, 1485s, 1401s, 1359w, 1340w, 1221s, 1114s, 1049s; δ_H (400 MHz; $CDCl_3$) 1.40 (3H, t, *J* 7.1, OCH_2CH_3), 1.90 (1H, m, CH_2), 2.07 (1H, m, CH_2), 2.19 (3H, s, CH_3), 2.64–2.69 (2H, m, CH_2), 3.42 (1H, m, CH), 3.69 (1H, dd, *J* 10.4, 5.6, NCH_2), 3.97 (2H, s, CH_2S), 4.15 (1H, t, *J* 10.0, NCH_2), 4.61 (2H, q, *J* 7.1, OCH_2CH_3), 6.85–6.90 (2H, m, ArH), 8.14 (1H, dd, *J* 8.5, 4.9, ArH); δ_C (100 MHz; $CDCl_3$) 13.6 (CH_3), 23.9 (CH_3), 28.4 (CH_2), 38.2 (CH_2), 38.9 (CH), 45.2 (CH_2), 54.9 (CH_2), 71.0 (CH_2), 111.1 (d, J_{C-F} 24, ArCH), 114.2 (d, J_{C-F} 23, ArCH), 117.7 (d, J_{C-F} 8, ArCH), 135.9 (ArC), 138.8 (ArC), 159.2 (d, J_{C-F} 241, ArC), 168.2 (C=O), 202.3 (C=O), 213.5 (C=S); *m/z* (CI, NH_3) 386 (MNH_3^+, 10%), 369 (M^+, 100), 337 (25); HRMS, Found: 370.0963 MH^+, $C_{17}H_{20}FNO_3S_2$ requires MH^+, 370.0947.

2,2-Dimethyl-propionic acid 1-ethoxythiocarbonylsulfanyl-6-(1-methanesulfonyl-5-methoxy-2,3-dihydro-1*H*-indol-3-yl)-4-oxo-hexyl ester 11e

To a refluxing solution of **10e** (0.073 g, 0.175 mmol) and vinyl pivalate (0.045 g, 0.35 mmol) in DCE (1 ml) was added DLP (0.024 g, 0.06 mmol). The crude mixture was concentrated *in vacuo* and column chromatography (PE–Et_2O, 1 : 2) gave compound **11e** as a yellow oil (0.061 g, 64%), ν_{max} (CCl_4)/cm^{-1} 2957m, 2928s, 1723s (C=O), 1488m, 1360s, 1228s, 1164s, 1111w, 1051s; δ_H (400 MHz; $CDCl_3$) 1.20 (9H, s, CH_3), 1.42 (3H, t, *J* 7.0, OCH_2CH_3), 1.50–1.91 (2H, m, CH_2), 2.05–2.33 (2H, m, CH_2), 2.36–2.62 (2H, m, CH_2), 2.83 (3H, s, CH_3), 3.38 (1H, m, CH), 3.59 (1H, m, NCH_2), 3.78 (3H, s, OCH_3), 3.01 (1H, m, NCH_2), 4.56–4.70 (2H, m, OCH_2CH_3), 6.58 (1H, t, *J* 6.8, CHS), 6.73–6.76 (2H, m, ArH), 7.30 (1H, d, *J* 8.5, ArH); δ_C (100 MHz; $CDCl_3$) 13.6 (CH_3), 26.9 (3 × CH_3), 27.9 (CH_2), 28.33 (CH_2), 29.6 (CH_2), 33.7 (CH), 38.1 (CH_2), 39.2 (C), 39.3 (SCH_3), 55.7 (OCH_3), 56.2 (CH_2), 70.2 (OCH_2), 80.0 (CHS), 110.9 (ArCH), 113.2 (ArCH), 114.6 (ArCH), 135.1 (ArC), 135.8 (ArC), 156.7 (ArC), 176.8 (C=O), 207.3 (C=O), 210.0 (C=S); *m/z* (CI, NH_3) 563 (MNH_4^+, 90%), 546 (MH^+, 20), 443 (60), 338 (55), 243 (51), 152 (30); HRMS, Found: M^+, 545.1583. $C_{24}H_{35}O_7NS_3$ requires *M*, 545.1575.

2,2-Dimethyl-propionic acid 6-(1-acetyl-5-chloro-2,3-dihydro-1*H*-indol-3-yl)-1-ethoxythiocarbonylsulfanyl-4-oxo-hexyl ester 11f

To a refluxing solution of **10f** (0.150 g, 0.39 mmol) and vinyl pivalate (0.100 g, 0.78 mmol) in DCE (1 ml), DLP (0.012 g, 0.03 mmol) was added. The crude mixture was then concentrated *in vacuo* and purified by flash chromatography (PE–AcOEt, 60 : 40) to give compound **11f** as a yellow oil (0.165 g, 82%), ν_{max} (CCl_4)/cm^{-1} 2977m, 2934m, 1723s (C=O), 1674s (C=O), 1479s, 1392s, 1333w, 1230m, 1136m, 1110w, 1051m, 1031m; δ_H (400 MHz; $CDCl_3$) 1.20 (9H, s, CH_3), 1.41 (3H, t, *J* 7.2, OCH_2CH_3), 1.88 (1H, m, CH_2), 2.08 (1H, m, CH_2), 2.15–2.30 (2H, m, CH_2), 2.22 (3H, s, CH_3), 2.41–2.48 (2H, m, CH_2), 2.51–2.56 (2H, m, CH_2), 3.44 (1H, m, CH), 3.70 (1H, m, NCH_2), 4.17 (1H, m, NCH_2), 4.58–4.67 (2H, m, OCH_2CH_3), 6.58 (1H, dt, *J* 6.4, 1.6, CHS), 7.12 (1H, s, ArH), 7.18 (1H, d, *J* 8.4, ArH), 8.13 (1H, d, *J* 8.4, ArH); δ_C (100 MHz; $CDCl_3$) 13.8 (CH_3), 24.2 (CH_3) 27.1 (3 × CH_3), 28.0 (CH_2), 28.5 (CH_2), 38.3 (2 × CH_2), 39.1 (CH), 39.2 (C), 55.0 (NCH_2), 70.4 (OCH_2), 80.2 (CHS), 114.9 (ArC), 118.0 (ArCH), 124.2 (ArCH), 128.2 (ArCH), 128.6 (ArC), 136.0 (ArC), 168.7 (C=O), 177.0 (C=O), 207.4 (C=O), 210.2 (C=S); *m/z* (CI, NH_3) 577 (MNH_3^+, 20%), 575 (17), 560 (M^+, 85), 558 (80); HRMS, Found: 514.1454 MH^+, $C_{24}H_{33}ClNO_5S_2$ requires MH^+, 514.1489.

2,2-Dimethyl-propionic acid 6-(1-acetyl-5-bromo-2,3-dihydro-1*H*-indol-3-yl)-1-ethoxythiocarbonylsulfanyl-4-oxo-hexyl ester 11g

To a refluxing solution of **10g** (0.150 g, 0.35 mmol) and vinyl pivalate (0.09 g, 0.70 mmol) in DCE (1 ml) was added DLP (0.020 g, 0.051 mmol). The mixture was then concentrated *in vacuo* and purified by column chromatography (PE–Et_2O, 10 : 30); compound **11g** was isolated as a yellow oil (0.230 g, 73%), ν_{max} (CCl_4)/cm^{-1} 2957s, 2932s, 1720s (C=O), 1666s (C=O), 1592m, 1477s, 1392s, 1334s, 1232s, 1135s, 1112s, 1045s; δ_H (400 MHz; $CDCl_3$) 1.18 (9H, s, CH_3), 1.40 (3H, t, *J* 6.5, OCH_2CH_3), 1.85 (1H, m, CH_2), 2.05 (1H, m, CH_2), 2.11–2.32 (2H, m, CH_2), 2.20

(3H, s, CH_3), 2.40–2.48 (2H, m, CH_2), 2.48–2.58 (2H, m, CH_2), 3.43 (1H, m, CH), 3.68 (1H, m, CH_2), 4.15 (1H, m, CH_2), 4.58–4.64 (2H, m, OCH_2CH$_3$), 6.75 (1H, td, *J* 6.5, 2.0, CHS), 7.25 (1H, br s, ArH), 7.30 (1H, dd, *J* 8.5, *J* 1.8 ArH), 8.06 (1H, d, *J* 8.5, ArH); δ_C (100 MHz; $CDCl_3$) 13.6 (*C*H$_3$), 24.0 (*C*H$_3$), 26.9 (3 × *C*H$_3$), 28.3 (*C*H$_2$), 28.4 (*C*H$_2$), 38.1 (*C*H$_2$), 38.8 (*C*H$_2$), 38.9 (*C*H), 39.1 (*C*), 54.7 (*C*H$_2$), 70.2 (O*C*H$_2$), 80.0 (S*C*H), 115.9 (Ar*C*), 118.3 (Ar*C*H), 126.9 (Ar*C*H), 130.9 (Ar*C*H), 136.3 (Ar*C*), 141.8 (Ar*C*), 168.6 (*C*=O), 176.8 (*C*=O), 207.2 (*C*=O), 210.0 (*C*=S); *m*/*z* (CI, NH_3) 515 (MH^+, 28%), 413 (M-OCO*t*Bu, 95), 290 (50); HRMS, Found: 558.0989 MH^+, $C_{24}H_{33}BrNO_5S_2$ requires MH^+, 558.0984.

2,2-Dimethyl-propionic acid 6-(1-acetyl-5-fluoro-2,3-dihydro-1*H*-indol-3-yl)-1-ethoxythiocarbonylsulfanyl-4-oxo-hexyl ester 11h

To a refluxing solution of **10h** (0.148 g, 0.40 mmol) and vinyl pivalate (0.102 g, 0.80 mmol) in DCE (1 ml) was added DLP (0.024 g, 0.06 mmol). The crude mixture was concentrated *in vacuo* and then purified by column chromatography (EP–AcOEt, 50 : 50) to give compound **11h** as a yellow oil (0.150 g, 75%), ν_{max} (CCl_4)/cm^{-1} 2979m, 2935w, 1739s (C=O), 1670s (C=O), 1609w, 1485s, 1397s, 1370s, 1235s, 1136m, 1110w, 1050m, 1031m; δ_H (400 MHz; $CDCl_3$) 1.19 (9H, s, CH_3), 1.40 (3H, t, *J* 7.1, OCH$_2$CH_3), 1.88 (1H, m, CH_2), 2.07 (1H, m, CH_2), 2.15–2.30 (2H, m, CH_2), 2.21 (3H, s, CH_3), 2.42–2.49 (2H, m, CH_2), 2.51–2.57 (2H, m, CH_2), 3.44 (1H, m, CH), 3.69 (1H, ddd, *J* 10.0, 5.2, 2.4, NCH_2), 4.17 (1H, dt, *J* 10.0, 4.4, NCH_2), 4.55–4.68 (2H, m, OCH_2CH$_3$), 6.58 (1H, dt, *J* 6.8, 2.0, CHS), 6.84–6.92 (2H, m, ArH), 8.15 (1H, dd, *J* 8.8, 4.8, ArH); δ_C (100 MHz; $CDCl_3$) 13.7 (*C*H$_3$), 24.1 (*C*H$_3$), 27.0 (3 × *C*H$_3$), 28.0 (*C*H$_2$), 28.4 (*C*H$_2$), 38.3 (2 × *C*H$_2$), 39.1 (*C*H), 39.6 (*C*), 55.1 (*C*H$_2$), 70.4, (O*C*H$_2$), 80.2 (S*C*H), 111.2 (d, J_{C-F} 24, Ar*C*H), 114.4 (d, J_{C-F} 22, Ar*C*H), 117.9 (d, J_{C-F} 8, Ar*C*H), 136.0 (Ar*C*), 138.9 (Ar*C*), 159.4 (d, J_{C-F} 241, Ar*C*), 168.4 (*C*=O), 176.9 (*C*=O), 207.3 (*C*=O), 210.1 (*C*=S); *m*/*z* (CI, NH_3) 498 (MH^+, 20%), 395 (90); HRMS, Found: 498.1758 MH^+, $C_{24}H_{33}FNO_5S_2$ requires MH^+, 498.1784.

1-Methanesulfonyl-5-methoxy-3-[2-(1*H*-pyrrol-2-yl)-ethyl]-2,3-dihydro-1*H*-indole 12e

To a solution of **11e** (0.077 g, 0.141 mmol) in dioxane (2 ml), were added ammonium acetate (0.109 g, 1.41 mmol) followed by a 33% solution of ammonia (0.048 g, 2.82 mmol). The reaction was stirred at room temperature for 12 h and then the solvent was evaporated *in vacuo*. The residue was purified by column chromatography (PE–Et_2O, 1 : 2) to give compound **12e** as a yellow oil (0.030 g, 66%); ν_{max} (CCl_4)/cm^{-1} 3409m (NH), 2934m, 2855w, 1487s, 1360s, 1235m, 1038m, 1164s, 1038s; δ_H (400 MHz; $CDCl_3$) 1.89 (1H, m, CH_2), 2.16 (1H, m, CH_2), 2.72 (2H, m, CH_2), 2.83 (3H, s, CH_3), 3.34 (1H, m, CH), 3.61–3.68 (2H, m, NCH_2), 3.79 (3H, s, OCH_3), 4.06 (1H, t, *J* 9.1, NCH_2), 5.97 (1H, m, ArH), 6.15 (1H, m, ArH), 6.71 (1H, m, ArH), 6.74 (1H, m, ArH), 6.76 (1H, s, ArCH), 7.32 (1H, d, *J* 8.5, ArCH), 8.0 (1H, br s, NH); δ_C (100 MHz; $CDCl_3$) 25.0 (*C*H$_2$), 33.8 (*C*H$_3$), 34.4 (*C*H$_2$), 39.7 (*C*H), 55.7 (O*C*H$_3$), 56.4 (*C*H$_2$), 105.4 (Ar*C*H), 108.5 (Ar*C*H), 111.0 (Ar*C*H), 112.9 (Ar*C*H), 114.6 (Ar*C*H), 116.7 (Ar*C*H), 130.8 (Ar*C*), 135.1 (Ar*C*), 136.4 (Ar*C*), 156.7 (Ar*C*); *m*/*z* (CI, NH_3) 321 (MH^+, 100%).

1-{5-Chloro-3-[2-(1-cyclopropyl-1*H*-pyrrol-2-yl)-ethyl]-2,3-dihydro-1*H*-indol-1-yl}-ethanone 12f

A solution of **11f** (0.088 g, 0.17 mmol), *p*-toluenesulfonic acid monohydrate (0.032 g, 0.17 mmol) and cyclopropylamine (0.01 g, 0.17 mmol) in dioxane (1 ml) was refluxed for 1 h. Additional cyclopropylamine (0.01 g, 0.17 mmol) was then added and the reaction was refluxed for a further 90 min. Evaporation of the solvent *in vacuo* furnished a crude oil which was purified by column chromatography (PE–AcOEt, 50 : 50) to give compound **12f** as a colourless oil (0.039 g, 70%); ν_{max} (CCl_4)/cm^{-1} 2980w, 2923w, 1674s (C=O), 1478s, 1391s, 1332w, 1256w; δ_H (400 MHz; $CDCl_3$) 0.87–0.99 (4H, m, CH_2), 1.96 (1H, m, CH_2), 2.17 (1H, m, CH_2), 2.22 (3H, s, CH_3) 2.72–2.86 (2H, m, CH_2), 3.10 (1H, m, CH), 3.50 (1H, m, NCH_2), 3.72 (1H, m, CH), 4.19 (1H, t, *J* 9.4, NCH_2), 5.89 (1H, m, ArH), 6.02 (1H, t, *J* 3.2, ArH), 6.61 (1H, m, ArH), 7.15 (1H, s, ArH), 7.18 (1H, dd, *J* 8.2, 2.0, ArH), 8.15 (1H, d, *J* 8.2, ArH); δ_C (100 MHz; $CDCl_3$) 6.7 (2 × *C*H$_2$), 23.8 (*C*H$_2$), 24.2 (*C*H$_3$), 28.0 (*C*H), 34.0 (*C*H$_2$), 39.7 (*C*H), 55.1 (*C*H$_2$), 106.2 (Ar*C*H), 106.6 (Ar*C*H), 118.0 (Ar*C*H), 120.7 (Ar*C*H), 125.4 (Ar*C*H), 127.9 (Ar*C*H), 128.6 (Ar*C*), 133.5 (Ar*C*), 136.8 (Ar*C*), 141.4 (Ar*C*), 168.7 (*C*=O); *m*/*z* (CI, NH_3) 328 (M^+, 100%).

1-(5-Bromo-3-{2-[1-(4-methoxybenzyl)-1*H*-pyrrol-2-yl]-ethyl}-2,3-dihydro-1*H*-indol-1-yl)-ethanone 12g

To a solution of **11g** (0.081 g, 0.140 mmol) in dioxane (1 ml), were added *p*-toluenesulfonic acid monohydrate (0.028 g, 0.14 mmol) and 4-methoxybenzyl amine (0.023 g, 0.168 mmol). The reaction was refluxed under nitrogen for 30 min. Further amine was introduced (0.019 g, 0.140 mmol) and the reaction mixture was refluxed for 30 min before evaporating the solvent *in vacuo*. Column chromatography (PE–Et_2O, 1 : 10) afforded compound **12g** as a yellow oil (0.046 g, 72%); ν_{max} (CCl_4)/cm^{-1} 2933s, 2836w, 1672s (C=O), 1513s, 1477s, 1466s, 1391s, 1353w, 1333s, 1250s, 1174m, 1040m; δ_H (400 MHz; $CDCl_3$) 1.74 (1H, m, CH_2), 1.96 (1H, m, CH_2), 2.15 (3H, s, CH_3), 2.53 (2H, t, *J* 8.2, CH_2), 3.35 (1H, m, CH), 3.52 (1H, m, CH_2), 3.80 (3H, s, OCH_3), 3.99 (1H, t, *J* 9.9, CH_2), 4.97 (2H, s, NCH_2), 5.99 (1H, br m, ArH), 6.15 (1H, t, *J* 3.2, ArH), 6.69 (1H, br t, *J* 2.0, ArH), 6.81–6.98 (4H, m, ArH), 7.10 (1H, s, ArH), 7.30 (1H, dd, *J* 8.5, 2.0, ArH), 8.06 (1H, d, *J* 8.5, ArH); δ_C (100 MHz; $CDCl_3$) 23.3 (*C*H$_2$), 24.0 (*C*H$_3$), 34.1 (*C*H$_2$), 39.1 (*C*H), 50.0 (*C*H$_2$), 54.7 (N*C*H$_2$), 55.3 (O*C*H$_3$), 106.5 (Ar*C*H), 107.1 (Ar*C*H), 114.2 (2 × Ar*C*H), 115.9 (Ar*C*), 118.2 (Ar*C*H), 121.5 (Ar*C*H), 126.8 (Ar*C*H), 127.5 (2 × Ar*C*H), 130.2 (Ar*C*), 130.7 (Ar*C*H), 131.3 (Ar*C*), 136.8 (Ar*C*), 141.7 (Ar*C*), 158.8 (Ar*C*), 168.6 (*C*=O); *m*/*z* (CI, NH_3) 456 (MH^+, 100%), (453, 100).

1-{3-[2-(1-Cyclohexyl-1*H*-pyrrol-2-yl)-ethyl]-5-fluoro-2,3-dihydro-1*H*-indol-1-yl}-ethanone 12h

A solution of **11h** (0.139 g, 0.28 mmol), *p*-toluenesulfonic acid monohydrate (0.053 g, 0.28 mmol) and cyclohexylamine (0.083 g, 0.84 mmol) in dioxane (2 ml) was refluxed for 30 min. Additional cyclohexylamine (0.083 g, 0.84 mmol) was then added and the reaction was refluxed for a further 30 min. Evaporation of the solvent *in vacuo* furnished a crude oil which was purified by column chromatography (PE–AcOEt, 70 : 30) to give compound **12h** as a yellow oil (0.042 g, 42%); ν_{max} (CCl_4)/cm^{-1} 2936s, 2857w, 1670s

(C=O), 1609w, 1485s, 1451w, 1397s, 1282w, 1262w; δ_H (400 MHz; $CDCl_3$) 1.17–1.31 (2H, m, CH_2), 1.32–1.48 (2H, m, CH_2), 1.70–1.54 (2H, m, CH_2), 1.92–2.00 (5H, m, CH_2), 2.12 (1H, m, CH_2), 2.20 (3H, s, CH_3), 2.57–2.74 (2H, m, CH_2), 3.48 (1H, m, CH), 3.62–3.79 (2H, m, NCH_2 and CH), 4.17 (1H, t, J 9.9, NCH_2), 5.90 (1H, br m, ArH), 6.11 (1H, t, J 3.2, ArH), 6.72 (1H, t, J 1.86, ArH), 6.83–6.98 (2H, m, ArH), 8.18 (1H, m, ArH); δ_C (100 MHz; $CDCl_3$) 23.6 (CH_2), 24.0 (CH_3), 25.5 (CH_2), 26.1 (2 × CH_2), 34.7 (CH_2), 34.8 (2 × CH_2), 39.7 (CH), 55.0 (C), 55.1 (CH_2), 105.5 (ArCH), 107.0 (ArCH), 111.1 (d, J_{C-F} 22, ArCH), 114.2 (d, J_{C-F} 22, ArCH), 116.6 (ArCH), 117.8 (ArCH), 130.5 (ArC), 137.9 (d, J_{C-F} 209, ArC), 158.2 (ArC), 160.6 (ArC), 168.4 (C=O); m/z (CI, NH_3) 354 (M^+, 100%).

2,2-Dimethyl-propionic acid 3-(2-acetylamino-thiazol-4-yl)-1-ethoxythiocarbonylsulfanyl-propyl ester 13

A solution of **7c** (0.216 g, 0.63 mmol) and *N*-acetylthiourea (0.150 g, 1.27 mmol) in chlorobenzene (15 ml) was refluxed for 16 h in the presence of $MgSO_4$. The solvent was then evaporated *in vacuo* and the crude mixture was purified by column chromatography (PE–Et_2O, 50 : 50) to give compound **13** as a colourless oil (0.140 g, 55%); ν_{max} (neat)/cm^{-1} 3195w, 2973s, 2871m, 1737s (C=O), 1694s (C=O), 1519s, 1283s, 1223s, 1135s, 1050s; δ_H (400 MHz; $CDCl_3$) 1.19 (9H, s, CH_3), 1.39 (3H, t, J 7.0, OCH$_2$CH_3), 2.24 (3H, s, CH_3), 2.23–2.37 (2H, m, CH_2), 2.78 (2H, t, J 7.9, CH_2), 4.55–4.67 (2H, m, CH_2), 6.60 (1H, s, CH), 6.66 (1H, t, J 6.5, CHS), 9.98 (1H, br s, NH); δ_C (100 MHz; $CDCl_3$) 13.6 (CH_3), 23.2 (CH_3), 26.9 (3 × CH_3), 27.3 (CH_2), 33.3 (CH_2), 38.8 (C), 70.2 (CH_2), 80.2 (CH), 108.3 (ArCH), 149.1 (ArC), 158.0 (ArC), 167.7 (C=O), 176.9 (C=O), 210.1 (C=S); m/z (CI, NH_3) 404 (M^+, 100%), 302 (66), 283 (20); HRMS, Found: MH^+, 405.0964, $C_{16}H_{25}N_2O_4S_3$ requires MH^+, 405.0976.

N-{4-[2-(1-Acetyl-5-chloro-2,3-dihydro-1*H*-indol-3-yl)-ethyl]-thiazol-2-yl)-acetamide} 14

A mixture of **9f** (0.150 g, 0.5 mmol), *N*-acetylthiourea (0.118 g, 1 mmol) and $MgSO_4$ in chlorobenzene (10 ml) was refluxed for 24 h. The solvent was then evaporated *in vacuo* and the crude was purified by column chromatography (Et_2O) to give compound **14** as a white solid (0.146 g, 80%), mp 219–220 °C (from DCM), ν_{max} (CCl_4)/cm^{-1} 3180s (NH), 2977w, 2980w, 1703s (C=O), 1674s (C=O), 1535s, 1479s, 1392s, 1282m, 1119w; δ_H (400 MHz; $CDCl_3$) 1.90 (1H, m, CH_2), 2.11 (1H, m, CH_2), 2.19 (3H, s, CH_3), 2.25 (3H, s, CH_3), 2.72 (2H, t, J 7.6, CH_2), 3.37 (1H, m, CH), 3.67 (1H, m, CH_2), 4.12 (1H, m, CH_2), 6.58 (1H, s, ArH), 7.08 (1H, s, ArH), 7.12 (1H, dd, J 8.8, 2.0, ArH), 8.1 (1H, d, J 8.8, ArH), 10.0 (1H, br s, NH); δ_C (100 MHz; $CDCl_3$) 23.1 (CH_3), 24.0 (CH_3), 28.4 (CH_2), 34.3 (CH_2), 39.1 (CH), 54.9 (CH_2), 108.2 (ArCH), 117.8 (ArCH), 124.0 (ArCH), 127.8 (ArCH), 128.4 (ArC), 136.5 (ArC), 141.1 (ArC), 150.0 (ArC), 158.0 (ArC), 167.8 (C=O), 168.8 (C=O); m/z (CI, NH_3) 366 (M^+, 33%), 363 (100); HRMS, Found: MH^+, 364.0886, $C_{17}H_{19}ClN_3O_2S$ requires MH^+, 364.0887.

1-{5-Chloro-3-[2-(2-pyridin-3-yl-thiazol-4-yl)-ethyl]-2,3-dihydro-1*H*-indol-1-yl}-ethanone 15

A suspension of **9f** (0.250 g, 0.83 mmol) and thionicotinamide (0.230 g, 1.66 mmol) in chlorobenzene (20 ml) in the presence of $MgSO_4$, was refluxed for 3 days. The solvent was then removed *in vacuo* and the crude was purified by column chromatography (Et_2O). Compound **15** was obtained as a brown solid (0.250 g, 78%) mp 122–124 °C (from AcOEt), ν_{max} (CCl_4)/cm^{-1} 2926w, 1674s (C=O), 1479s, 1392s, 1331w, 1256w; δ_H (400 MHz; $CDCl_3$) 2.06 (1H, m, CH_2), 2.22 (3H, s, CH_3), 2.29 (1H, m, CH_2), 2.93 (2H, t, J 7.9, CH_2), 3.51 (1H, m, CH), 3.79 (1H, m, CH_2), 4.22 (1H, t, J 10.0, CH_2), 7.00 (1H, s, ArH), 7.13–7.20 (2H, m, ArH), 7.39 (1H, m, ArH), 8.14 (1H, d, J 8.2, ArH), 8.23 (1H, d, J 8.2, ArH), 8.66 (1H, d, J 4.7, ArH), 9.16 (1H, br s, ArH); δ_C (100 MHz; $CDCl_3$) 23.8 (CH_3), 28.3 (CH_2), 34.3 (CH_2), 39.0 (CH), 54.7 (CH_2), 114.0 (ArCH), 117.5 (ArCH), 123.4 (ArCH), 123.8 (ArCH), 127.6 (ArCH), 128.2 (ArC), 129.3 (ArC), 133.3 (ArCH), 136.1 (ArC), 141.0 (ArC), 147.3 (ArCH), 150.4 (ArCH), 157.2 (ArC), 164.1 (ArC), 168.3 (C=O); m/z (CI, NH_3) 385 (M^+, 33%), 383 (100); HRMS; Found: MH^+, 384.0939, $C_{20}H_{19}ClN_3OS$ requires MH^+, 384.0937.

Dithiocarbonic acid {4-[(*S*)-4-(1-ethoxythiocarbonylsulfanyl-1-methyl-ethyl)-cyclohex-1-enyl]-2-oxo-butyl} ester ethyl ester 17

A solution of β-(−)-pinene (1.5 mL, 9.53 mmol, 2.0 eq.) and xanthate **1** (1.01 g, 4.68 mmol, 1 eq.) in 1,2-dichloroethane (5 mL) under argon was refluxed for 15 min before the addition of DLP (90 mg, 0.22 mmol, 0.05 eq.). The solution was then refluxed for an additional hour and DLP (40 mg, 0.10 mmol, 0.02 eq.) was added. The solution was refluxed for a further hour before being cooled to rt. The solvent was evaporated *in vacuo* and the residue was dissolved in acetone (45 mL). The solution was stirred at rt under argon for 15 min before the addition of potassium *O*-ethyl xanthate (1.06 g, 6.62 mmol, 1.4 eq.). The solution was stirred at rt for 1 h then acetone was evaporated *in vacuo*. The residue was then washed with water, extracted with dichloromethane, dried over sodium sulfate and concentrated *in vacuo*. The residue was purified by flash column chromatography (PE–Et_2O, 10 : 0 to 9 : 1) to give compound **17** (1.718 g, 84%) yield as a yellow oil, elemental analysis, Found: C, 52.65; H, 6.98. $C_{19}H_{30}S_4O_3$ requires C, 52.50; H, 6.96%; ν_{max} (CCl_4)/cm^{-1} 2924w, 1715s (C=O), 1442s, 1366s, 1231s (C=S), 1148s, 1112s, 1038s (CS), 1002s, 914s; δ_H (400 MHz; $CDCl_3$) 1.29 (1H, m, CH), 1.43 (3H, t, J 7.1, CH_3), 1.46 (3H, t, J 7.1, CH_3), 1.48 (6H, s, CH_3), 1.93–1.85 (1H, m, CH_2), 1.89 (4H, m, CH_2), 2.16 (1H, m, CH_2), 2.28 (2H, t, J 7.4, CH_2), 2.72 (2H, t, J 7.4, CH_2), 4.01 (2H, s, CH_2), 4.64 (2H, q, J 7.1, OCH_2), 4.69 (2H, q, J 7.1, OCH_2), 5.40 (1H, d, J 4.0, C=CH); δ_C (100 MHz; $CDCl_3$) 13.7 (CH_3), 13.8 (CH_3), 24.5 (CH_2), 24.7 (CH_3), 25.1 (CH_3), 27.0 (CH_2), 29.5 (CH_2), 30.9 (CH_2), 40.1 (CH_2), 42.6 (CH), 45.4 (CH_2), 59.0 (C), 69.4 (OCH_2), 70.8 (OCH_2), 120.9 (CH), 135.8 (C), 202.8 (C=O), 213.3 (C=S), 214.2 (C=S); m/z (CI, NH_3) 313 (M^+-122, 100%).

Dithiocarbonic acid [(2*S*,4a*S*,8a*S*)-2-(1-ethoxythiocarbonyl-sulfanyl-1-methyl-ethyl)-7-oxo-octahydro-naphthalen-4a-yl] ester ethyl ester 18

A solution of xanthate **17** (521 mg, 1.20 mmol) in 1,2-dichloroethane (12 mL) under argon, was refluxed for 15 min before the addition of DLP (32 mg, 0.08 mmol, 0.07 eq.). The solution was then refluxed and portions of DLP (total 106 mg, 0.27 mmol, 0.22 eq.) were added every hour. The solvent was then

evaporated *in vacuo* and the residue was purified by flash column chromatography (PE–Et_2O, 10 : 0 to 75 : 25) to give compound **18** (341 mg, 65%) as yellow crystals, mp 101–105 °C (from heptane–ethyl acetate) as a single diastereomer, elemental analysis, Found: C, 52.53; H, 6.85. $C_{19}H_{30}S_4O_3$ requires C, 52.50; H, 6.96%; ν_{max} (CH_2Cl_2)/cm^{-1} 2942w, 2868w, 1715s (C=O), 1455s, 1387s, 1367s, 1225s, 1148s, 1113s, 1036s, 1002s, 912s; δ_H (400 MHz; $CDCl_3$) 1.42 (3H, t, *J* 7.1, CH_3), 1.44 (3H, t, *J* 7.1, CH_3), 1.45 (3H, s, CH_3), 1.48 (3H, s, CH_3), 1.54 (1H, dd, *J* 2.2, *J* 14.1, C*H*), 1.72 (1H, m, C*H*), 1.96–1.87 (2H, m, CH_2), 2.23–2.10 (3H, m, CH_2), 2.36–2.27 (2H, m, CH_2), 2.72–2.43 (5H, m, CH_2), 4.70–4.60 (4H, m, OCH_2); δ_C (100 MHz; $CDCl_3$) 13.7 (*C*H_3), 14.0 (*C*H_3), 23.4 (*C*H_2), 24.9 (2 × *C*H_3), 28.5 (*C*H_2), 28.7 (*C*H_2), 36.6 (*C*H_2), 37.7 (*C*H_2), 38.2 (*C*H), 39.7 (*C*H), 43.1 (*C*H_2), 58.4 (*C*), 58.5 (*C*), 69.3 (O*C*H_2), 69.7 (O*C*H_2), 209.8 (*C*=O), 212.0 (*C*=S), 213.5 (*C*=S); *m*/*z* (CI, NH_3) 435 (MH^+, 100%).

(1-Benzenesulfonyl-hexyl)carbamic acid benzyl ester 24

To a solution of benzylcarbamate (1.51 g, 10.0 mmol, 1 eq.) in water (10 mL) and THF (4 mL) was added sodium benzenesulfinate (1.64 g, 10.0 mmol, 1 eq.), hexanal (1.3 mL, 10.1 mmol, 1.1 eq.) and formic acid (2.4 mL, 63.6 mmol, 6.4 eq.). The solution was stirred at rt overnight. The mixture was then filtered to collect a white precipitate. The solid was washed with water and dried. It was then dissolved in dichloromethane, dried over sodium sulfate and concentrated *in vacuo* to give compound **24** as white crystals (3.158 g, 84%), mp 123–127 °C (from hexane–AcOEt), ν_{max} (CH_2Cl_2)/cm^{-1} 3414w, 2959w, 2931w, 2862w, 1732s (C=O), 1507s, 1308s, 1217s, 1145s, 1083s, 1046s; δ_H (400 MHz; $CDCl_3$) 0.90 (3H, t, *J* 6.8, CH_3), 1.52–1.31 (6H, m, CH_2), 1.75 (1H, m, CH_2), 2.25 (1H, m, CH_2), 4.92–4.82 (3H, m, NC*H* and OCH_2), 5.43 (1H, d, *J* 10.6, N*H*), 7.20–7.09 (2H, m, ArC*H*), 7.36–7.33 (3H, m, ArC*H*), 7.45–7.41 (2H, m, ArC*H*), 7.59 (1H, t, *J* 7.5, ArC*H*), 7.88 (2H, d, *J* 7.5, ArC*H*); δ_C (100 MHz; $CDCl_3$) 14.0 (*C*H_3), 22.4 (*C*H_2), 25.0 (*C*H_2), 26.4 (*C*H_2), 31.2 (*C*H_2), 67.4 (O*C*H_2), 71.5 (N*C*H), 128.2 (2 × Ar*C*H), 128.4 (Ar*C*H), 128.6 (2 × Ar*C*H), 129.0 (2 × Ar*C*H), 129.3 (2 × Ar*C*H), 134.0 (Ar*C*H), 135.7 (Ar*C*), 136.7 (Ar*C*), 155.0 (*C*=O); *m*/*z* (CI, NH_3) 376 (MH^+, 100%); HRMS, Found: M^+, 375.1507. $C_{20}H_{25}O_4NS$ requires *M*, 375.1504.

(1-Vinyl-hexyl)carbamic acid benzyl ester 22

To a solution of compound **24** (768 mg, 2.0 mmol) in dry THF (15 mL) under argon, was added at −20 °C a solution of vinyl magnesium bromide (1 mol L^{-1} in THF) (4.3 mL, 4.3 mmol, 2.1 eq.) and the solution was stirred at 0 °C for 1 h. Saturated aqueous NH_4Cl was then added to quench the reaction and the mixture was neutralised with saturated aqueous Na_2CO_3, extracted with dichloromethane, dried over sodium sulfate and concentrated *in vacuo*. The residue was purified by flash column chromatography (PE–Et_2O, 10 : 0 to 9 : 1) to give compound **22** as a colourless oil (469 mg, 88%), ν_{max} (CaF_2)/cm^{-1} 3324w, 2955w, 2931w, 2858w, 1714s (C=O), 1694s, 1538s, 1505s, 1336s, 1245s, 1112s, 1072s, 1037s, 992s, 919s; δ_H (400 MHz; $CDCl_3$) 0.89 (3H, t, *J* 6.6, CH_3), 1.53–1.30 (8H, m, CH_2), 4.18 (1H, br s, NC*H*), 4.78 (1H, br s, N*H*), 5.19–5.09 (4H, m, CH=CH_2 and OCH_2), 5.77 (1H, ddd, *J* 5.7, *J* 10.3, *J* 17.1, C*H*=CH$_2$), 7.37–7.31 (5H, m, ArC*H*); δ_C (100 MHz; $CDCl_3$) 14.1 (*C*H_3), 22.6 (*C*H_2), 25.4 (*C*H_2), 31.6 (*C*H_2), 35.1 (*C*H_2), 53.4 (N*C*H), 66.7 (O*C*H_2), 114.6 (CH=*C*H_2), 128.0 (Ar*C*H), 128.1 (2 × Ar*C*H), 128.5 (2 × Ar*C*H), 136.7 (Ar*C*), 138.9 (*C*H=CH$_2$), 155.9 (*C*=O); *m*/*z* (CI, NH_3) 262 (MH^+, 100%); HRMS, Found: M^+, 261.1721. $C_{16}H_{23}O_2N$ requires *M*, 261.1728.

Acetic acid 2,6-bis(ethoxythiocarbonylsulfanyl)-5-oxo-1-pentyl-hexyl ester 25

A solution of 3-acetoxy-oct-1-yne (1.83 g, 10.8 mmol, 1.4 eq.) and xanthate **1** (1.67 g, 7.9 mmol, 1 eq.) in 1,2-dichloroethane (8 mL) under argon was refluxed for 15 min before the addition of DLP (157 mg, 0.39 mmol, 0.05 eq.). The solution was then refluxed for an additional hour and DLP (80 mg, 0.20 mmol, 0.02 eq.) was added. The solution was refluxed for a further hour before being cooled to rt. The solvent was evaporated *in vacuo* and the residue was dissolved in acetone (70 mL). The solution was stirred at rt under argon for 15 min before the addition of potassium *O*-ethyl xanthate (1.39 g, 8.61 mmol, 1.1 eq.). The solution was stirred at rt for 1 h then acetone was evaporated *in vacuo*. The residue was then washed with water, extracted with dichloromethane, dried over sodium sulfate and concentrated *in vacuo*. The residue was purified by flash column chromatography (PE–Et_2O, 10 : 0 to 9 : 1) to give compound **25** as a yellow oil (3.140 g, 98%, mixture of diastereomers), elemental analysis, Found: C, 48.67; H, 6.99. $C_{19}H_{32}O_5S_4$ requires C, 48.69; H, 6.88%; ν_{max} (CaF_2)/cm^{-1} 2930w, 2855w, 1732s (C=O), 1454s, 1372s, 1232s (C=S), 1147s, 1111s, 1048s (CS), 856s; δ_H (400 MHz; $CDCl_3$) 0.93 (3H, m, CH_3), 1.29–1.25 (5H, m, CH_2), 1.45–1.40 (6H, m, CH_3), 1.68–1.57 (3H, m, CH_2), 1.82 (1H, m, CH_2), 2.06 and 2.04 (3H, s, CH_3), 2.12 (1H, m, CH_2), 2.88–2.72 (2H, m, CH_2), 3.98–3.96 (2H, m, SCH_2), 4.02 (1H, m, C*H*), 4.69–4.61 (4H, m, OCH_2), 5.18–5.11 (1H, m, OC*H*); δ_C (100 MHz; $CDCl_3$) 13.8 (2 × *C*H_3), 14.0 (*C*H_3), 21.1 (21.0) (*C*H_3), 23.0 (22.5) (*C*H_2), 25.3 (25.2) (*C*H_2), 25.9 (*C*H_2), 31.6 (31.5) (*C*H_2), 32.0 (*C*H_2), 39.1 (39.0) (*C*H_2), 45.5 (*C*H_2), 53.9 (53.5) (*C*HS), 70.9 (70.7) (2 × O*C*H_2), 75.4 (75.2) (O*C*H), 170.6 (170.5) (*C*=O), 202.4 (202.3) (*C*=O), 213.4 (*C*=S), 214.1 (213.9) (*C*=S); *m*/*z* (CI, NH_3) 469 (MH^+, 100%).

Acetic acid 9-benzyloxycarbonylamino-2,8-bis(ethoxythiocarbonylsulfanyl)-5-oxo-1-pentyl-tetradecyl ester 26

A solution of xanthate **25** (710 mg, 1.51 mmol) and olefine **22** (783 mg, 3.0 mmol, 2 eq.) in 1,2-dichloroethane (2 mL) under argon was refluxed for 15 min before the addition of DLP (45 mg, 0.11 mmol, 0.07 eq.). The solution was refluxed under argon and DLP (115 mg, 0.29 mmol, 0.26 eq.) was added in portions (2.5 mol% every 90 min) until the disappearance of the starting material. After evaporation of the solvent and purification by flash column chromatography (PE–Et_2O, 10 : 0 to 7 : 3), compound **26** was obtained as a yellow oil (715 mg, 65%, mixture of diasteromers); ν_{max} (CaF_2)/cm^{-1} 3336w, 2955w, 2902w, 2858w, 1731s (C=O), 1714s (C=O), 1520s, 1504s, 1454s, 1372s, 1222s (C=S), 1111s, 1048s (CS), 911s; δ_H (400 MHz; $CDCl_3$) 0.92–0.86 (6H, m, CH_3), 1.36–1.21 (16H, m, CH_2), 1.45–1.39 (6H, m, CH_3), 1.84–1.57 (5H, m, CH_2), 2.07 (2.04) (3H, s, CH_3), 2.18–1.09 (2H, m, CH_2), 2.65–2.51 (3H, m, CH_2), 4.06–3.92 (2H, m, SC*H*), 4.68–4.56 (4H, m, CH_2 and C*H*), 5.17–5.06 (3H, m, C*H* and CH_2), 7.38–7.30 (5H, m, ArC*H*); δ_C (100 MHz; $CDCl_3$) 13.8 (2 × *C*H_3), 14.0 (2 × *C*H_3), 21.1 (21.0) (*C*H_3), 22.6 (2 × *C*H_2), 25.3 (*C*H_2), 25.8 (*C*H_2), 31.3 (*C*H_2), 31.6 (*C*H_2), 31.7 (3 × *C*H_2), 31.9 (*C*H_2), 33.6

(CH_2), 40.0 (CH_2), 54.4 (54.1) (CH), 54.7 (CH), 56.2 (CH), 66.9 (66.8) (OCH_2), 70.6 (70.5) (2 × OCH_2), 75.4 (75.2) (OCH), 128.0 (2 × ArCH), 128.1 (ArCH), 128.6 (2 × ArCH), 136.5 (ArC), 156.4 (156.1) (C=O), 170.6 (170.5) (C=O), 208.6 (208.4) (C=O), 214.0 (C=S), 214.2 (C=S); HRMS, Found: M^+, 729.2875. $C_{35}H_{55}O_7NS_4$ requires M, 729.2861.

Acetic acid 9-benzyloxycarbonylamino-5-oxo-1-pentyl-tetradecyl ester 27

A solution of xanthate **26** (327 mg, 0.45 mmol) in toluene (5 mL) under argon was refluxed for 15 min before the addition of tributyltin hydride (0.34 mL, 1.26 mmol, 2.8 eq.) and AIBN (14 mg, 0.08 mmol, 0.19 eq.). The solution was heated at 100 °C under argon for 90 min then AIBN was added again (14 mg, 0.08 mmol, 0.19 eq.). After 30 min of reflux, the solution was cooled to rt and the solvent was removed *in vacuo*. The crude residue was purified by flash column chromatography (pentane–Et_2O, 10 : 0 to 6 : 4), to give compound **27** as a colourless oil (153 mg, 70%); ν_{max} (CaF_2)/cm^{-1} 3335w, 2937w, 2858w, 1739s (C=O), 1694s (C=O), 1531s, 1455s, 1375s, 1247s, 1025s; δ_H (400 MHz; $CDCl_3$) 0.92–0.86 (6H, m, CH_3), 1.64–1.26 (24H, m, CH_2), 2.03 (3H, s, CH_3), 2.46–2.30 (4H, m, CH_2), 3.59 (1H, m, NCH), 4.57 (1H, m, NH), 4.84 (1H, m, OCH), 5.11–5.05 (2H, m, OCH_2), 7.35–7.27 (5H, m, CHar); δ_C (100 MHz; $CDCl_3$) 14.1 (2 × CH_3), 19.4 (CH_2), 19.9 (CH_2), 21.3 (CH_3), 22.6 (CH_2), 22.6 (CH_2), 25.0 (CH_2), 25.5 (CH_2), 31.7 (CH_2), 31.8 (CH_2), 33.5 (CH_2), 34.0 (CH_2), 34.8 (CH_2), 35.4 (CH_2), 42.3 (CH_2), 42.4 (CH_2), 51.1 (CH), 66.6 (OCH_2), 73.9 (OCH), 128.1 (ArCH), 128.0 (2 × ArCH), 128.6 (2 × ArCH), 136.8 (ArC), 156.2 (C=O), 171.0 (C=O), 210.5 (C=O); *m/z* (CI, NH_3) 490 (MH^+, 100%); HRMS, Found: M^+, 489.3461. $C_{29}H_{47}O_5N$ requires M, 489.3454.

(5,9-Dioxo-1-pentyl-tetradecyl)carbamic acid benzyl ester 28

To a solution of compound **27** (120 mg, 0.24 mmol) in methanol (4 mL) was added potassium carbonate (80 mg, 0.58 mmol) and the solution was stirred at rt for 2 d. The solution was then filtered and the solvent was evaporated *in vacuo*. The crude residue was then dissolved in dichloromethane (5 mL) and to this solution PCC was added (90 mg, 0.42 mmol, 1.7 eq.). The solution was stirred at rt for 4 h before being filtered through celite. The solvent was evaporated *in vacuo* and the crude mixture was purified by flash column chromatography (silica gel, pentane–diethyl ether, 10 : 0 to 1 : 1), to give compound **28** as white crystals (81 mg, 74% over 2 steps), mp 83–88 °C (from heptane–AcOEt); elemental analysis, Found: C, 72.29; H, 9.59. $C_{27}H_{43}NO_4$ requires C, 72.77; H, 9.73%; ν_{max} (CH_2Cl_2)/cm^{-1} 3409w, 2957w, 2932w, 1716w (C=O), 1511s, 1454s, 1220s, 1096s; δ_H (400 MHz; $CDCl_3$) 0.90–0.85 (6H, m, CH_3), 1.67–1.21 (21H, m, CH_2), 1.85–1.78 (2H, m, CH_2), 2.36 (3H, d, *J* 7.6, CH_2), 2.41 (2H, t, *J* 7.1, CH_2), 3.60 (1H, m, NCH), 4.56 (1H, br d, *J* 9.1, NH), 5.13–5.02 (2H, m, OCH_2), 7.35–7.28 (5H, m, CHar); δ_C (100 MHz; $CDCl_3$) 14.0 (CH_3), 14.1 (CH_3), 17.8 (CH_2), 19.8 (CH_2), 22.5 (CH_2), 22.6 (CH_2), 23.6 (CH_2), 25.6 (CH_2), 31.5 (CH_2), 31.8 (CH_2), 34.7 (CH_2), 35.4 (CH_2), 41.6 (CH_2), 41.7 (CH_2), 42.3 (CH_2), 42.8 (CH_2), 51.1 (NCH), 66.6 (OCH_2), 128.1 (ArCH), 128.1 (2 × ArCH), 128.6 (2 × ArCH), 136.8 (ArC), 156.2 (C=O), 210.5 (C=O), 210.9 (C=O); *m/z* (CI, NH_3) 446 (MH^+, 100%).

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