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A divergent approach to highly substituted benzothiepinones and to 2,3-dihydrothieno[2,3-*b*]thiopyran-4-ones

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This paper is dedicated with respect and admiration to professor Henri B. Kagan on the occasion of his 80th birthday

ABSTRACT

The radical addition-transfer of *S*-(2-fluoro-phenacyl)xanthates can be used to construct rapidly benzothiepinones, including libraries of complex aza-bridged derivatives, and highly functionalized 2,3-dihydrothieno[2,3-*b*]thiopyran-4-ones.

1. Introduction

Seven-membered rings fused to aromatic nuclei represent highly privileged structures in medicinal chemistry.[1] Whereas the nitrogen-based structures, such as the medicinally significant benzazepines, have been very extensively studied, the related sulfur analogues have received much less attention, despite the fact that a few such derivatives have proved to be valuable drugs. For example, Diltiazem **1** is a benzothiazepine calcium channel blocker that has been in clinical use for at least three decades for the treatment of hypertension, angina pectoris and certain types of arrhythmia. Benzothiepines of general structure **2** have recently been reported to be potent inhibitors of the apical sodium co-dependent bile acid transporter (ASBT); they inhibit the re-absorption of bile acid and could therefore lower the serum LDL cholesterol (Fig. 1).[2]

One reason for the relatively limited studies on benzothiepinones is the shortage of general methods for constructing such compounds. In most cases, the synthetic routes have relied on intramolecular Friedel–Crafts reactions or on Dieckmann-type ring closures.[3] While very useful, these approaches are severely constrained by the limited availability of appropriately substituted precursors. In the course of our work on the degenerative radical xanthate addition-transfer reaction, a simple route to benzothiepinones soon became apparent.[4]

Our approach is portrayed in Scheme 1. Thus, radical addition of xanthate **4** to an olefin would produce an adduct **5**, which should be easily aminolysed into the corresponding thiol **6**. In the presence of base, this thiol should readily engage in a nucleophilic aromatic substitution of the *ortho*-fluorine to give benzothiepine **7**. The high nucleophilicity of the thiolate anion and the strongly activating effect of the ketone group should greatly facilitate this transformation. This indeed proved to be the case, as previously reported.[5] We now present further results in this area and especially the development of an efficient, convergent route to complex polycyclic architectures. The benzothiepine structure **7** represents in fact a very interesting scaffold, with several modification points

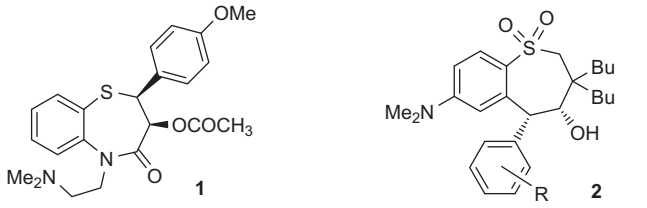
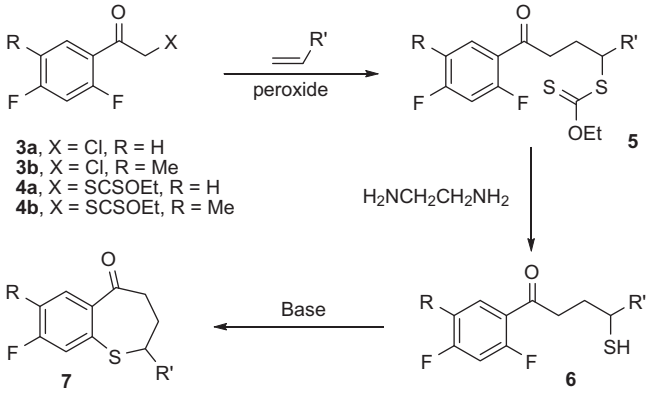


Figure 1.



Scheme 1.

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well positioned around the molecule: the aromatic ketone, the ring sulfur, the remaining activated fluorine atom and the numerous functional groups that can be introduced via the olefinic partner.

2. Results and discussion

A Friedel–Crafts reaction of 1,3-difluorobenzene with chloroacetyl chloride and aluminium trichloride afforded 2-chloro-2′,4′-difluoroacetophenone **3** in 90% yield,[6] and this was smoothly converted into nicely crystalline xanthate **4a** (94%) by treatment with potassium *O*-ethyl xanthate in acetone. Xanthate **4b** was prepared by a similar sequence from 2,4-difluorotoluene. The radical addition of these xanthates to various olefins proceeded smoothly and furnished the desired adducts **5a**–**t** in high yield (Fig. 2). Aminolysis of the xanthate group with ethylenediamine afforded the corresponding thiols **6**, which were not purified, but subjected to the action of DBU in THF to give the desired benzothiepinones **7a**–**j** mostly in good yield (Fig. 2). In the case of adduct **5b** with allyl trimethylsilane, the yield of cyclised material **7b** was low, in part because of a fluoride-induced ring opening which produced thiol **8** as the main side-product (Scheme 2).[7]

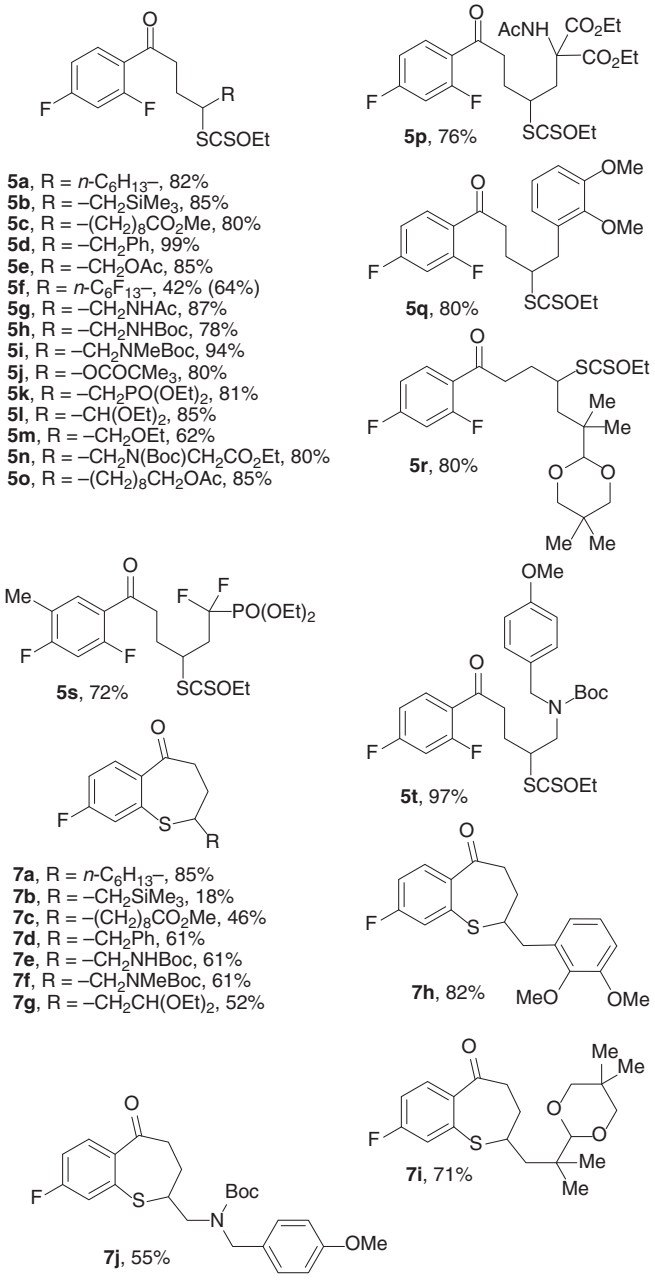
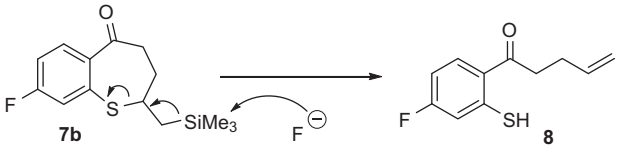
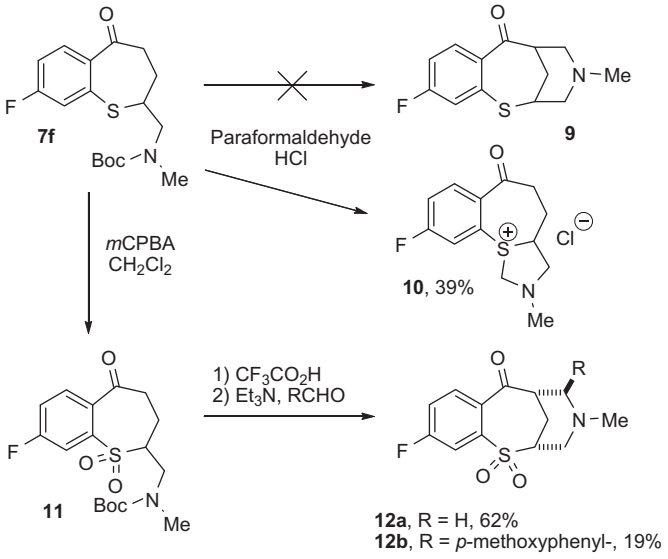


Figure 2.



Scheme 2.

A very simple access to benzothiepinones **7** with many varied substituents is now in hand and these in turn can act as versatile scaffolds for further elaborations. One illustration is with derivative **7f** containing a protected secondary amine. The presence of the neighbouring aromatic ketone should allow the construction of another ring by implementing an intramolecular Mannich reaction. However, as depicted in Scheme 3, a preliminary reaction conducted with formaldehyde furnished as the main product an interesting sulfonium derivative **10** in modest yield, instead of the expected Mannich product **9**.



Scheme 3.

In order to suppress this reaction pathway, the sulfide was oxidised to the corresponding sulfone **11** before deprotection and treatment with formaldehyde. In the absence of a nucleophilic sulfur, the Mannich reaction proceeded as expected and furnished tricyclic derivative **12a** in 62% yield. By replacing formaldehyde with *p*-anisaldehyde, the corresponding derivative **12b** was obtained in rather modest yield. This compound was obtained as only one diastereoisomer, with the stereochemistry assigned tentatively as shown on the basis of NMR spectroscopy and on steric considerations. Not unexpectedly, the methoxyphenyl substituent occupies an equatorial orientation, with respect to the newly formed piperidine ring.

Compounds **12a** and **12b** may be considered as analogues of eptazocine **13** and cytisine **14**, two important biologically active natural products (Fig. 3). Cytisine, in particular, is a potent nicotinic receptor ligand, and hundreds of analogues have been prepared as probes in the study of the central nervous system and as potential therapeutic agents.[8] Difluorobenzo derivative **15** and Varenicline

16, which has entered clinical phase studies, are two analogues recently described by chemists at Pfizer as drugs to combat addiction to smoking.[9]

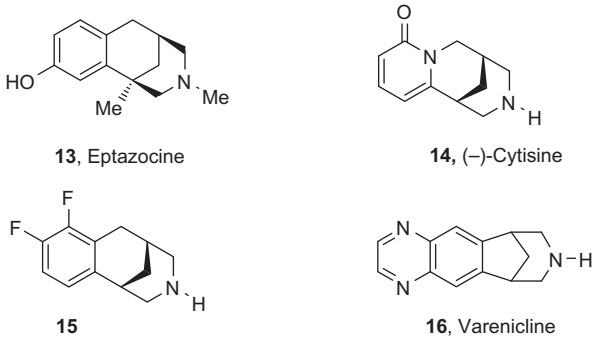
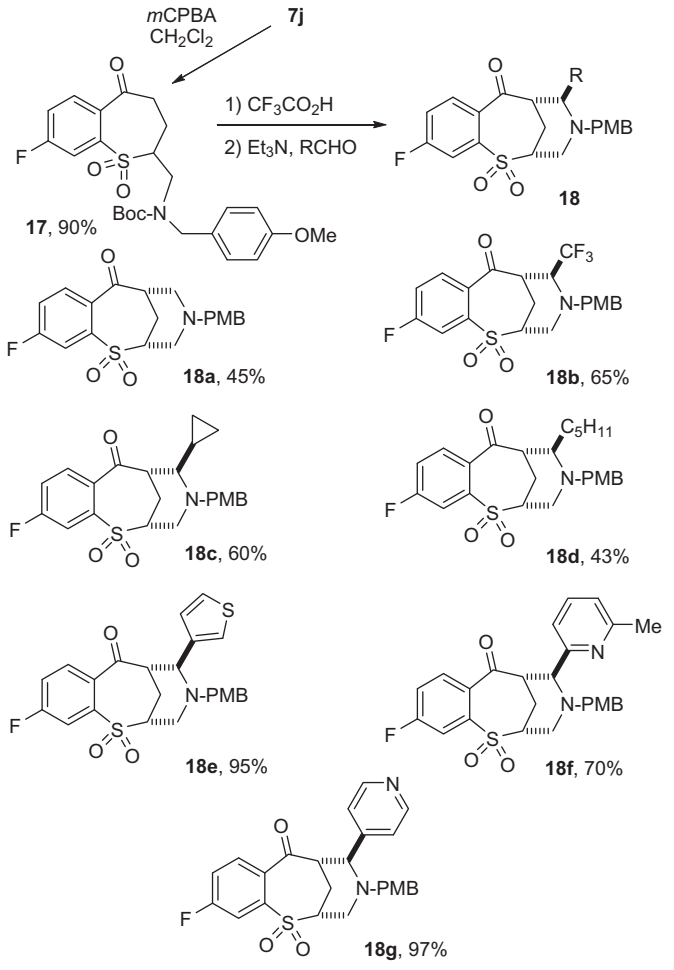


Figure 3.

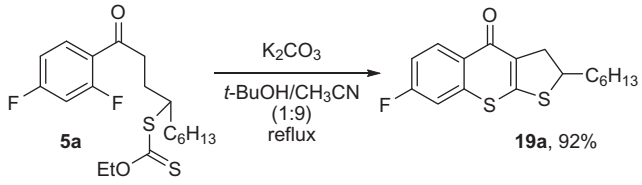
The Mannich reaction did not proceed well starting with derivative **7e**, which gives rise to a primary amine upon removal of the Boc-group. We therefore continued our study with **7j**, where the *N*-*p*-methoxybenzyl group can be removed if an unsubstituted piperidine moiety is desired in the end product. Thus, oxidation of **7j** furnished the corresponding sulfone **17**, and treatment with trifluoroacetic acid followed by triethylamine and an aldehyde gave the desired tricyclic structure. In this manner, a small library of derivatives **18a–g** could be prepared, as shown by the examples displayed in Scheme 4. The facile introduction of a trifluoromethyl



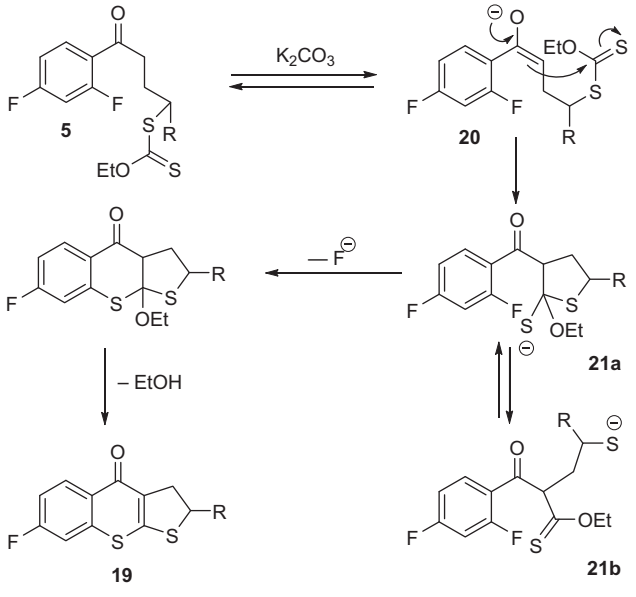
Scheme 4.

or a cyclopropyl group and various heteroaromatic side chains is noteworthy. The present expedient approach to such intricate and pharmacologically appealing structures associates flexibility and convergence. Furthermore, by choosing the appropriate initial olefin, other reactions besides the Mannich reaction could in principle be considered to augment the complexity.

In an attempt at combining the cleavage of the xanthate with the fluorine substitution into one operation, we exposed xanthate **5a** to the action of potassium carbonate in a 9:1 mixture of acetonitrile and *t*-butanol. The corresponding benzothiepinone **7a** was indeed formed but only to a very small extent. The major compound turned out to be tricyclic dihydrothieno[2,3-*b*]-benzothiopyranone **19a**, isolated in 92% yield (Scheme 5). This unexpected transformation most logically proceeds by the mechanism outlined in Scheme 6. Under the modified conditions, the formation of the enolate **20** of the ketone is faster than cleavage of the xanthate. The proximity of the enolate to the xanthate group encourages a nucleophilic attack on the thiocarbonyl group leading to thiolate **21a**, which is in equilibrium with open form **21b**. The thiolate group in the former is well positioned for a nucleophilic aromatic substitution of the fluorine giving observed product **19** following elimination of ethanol. We very recently stumbled across a transformation akin to the one described in the present study, which leads to aliphatic analogues by a Michael addition instead of the fluorine substitution.[10]



Scheme 5.



Scheme 6.

Thieno[2,3-*b*]-benzothiopyrans and their dihydro derivatives are quite rare substances, presumably because of a lack of generally applicable synthetic approaches. Two early patent applications mentioning their synthesis and use in the preparation of drugs for treating psychotic disturbances[11] were followed by a brief study by

Majumdar et al.[12] and by a report on the benzo-fused series.[13] The very few routes described in the literature all rely on a preformed benzothiopyranone ring to which the thiophene or dihydrothiophene ring is then attached. This limits severely the variety of accessible structures.

In contrast, the present serendipitous radical-based synthesis of thieno[2,3-*b*]-benzothiopyrans is extremely short, only two steps from xanthates **4a** and **4b** and lends itself very easily to structural modifications. The numerous examples collected in Figure 4 give an idea of the possibilities. In the case of derivative **5b**, the cleavage of the silyl group by the liberated fluoride anion was much less severe and a good yield (70%) of the corresponding thieno[2,3-*b*]-benzothiopyranone **19b** could be secured. Interestingly, when xanthate **5e** was subjected to the same conditions, a different product was formed in moderate yield, which was identified as episulfide **22** (Scheme 7). In this case, the equilibrium, which exists between the closed and open thiolates **23a** and **23b**, is driven towards the intermediate episulfide **24** by substitution of the acetate group. Nucleophilic aromatic substitution of the fluoride by the other sulfur then furnishes the observed product.

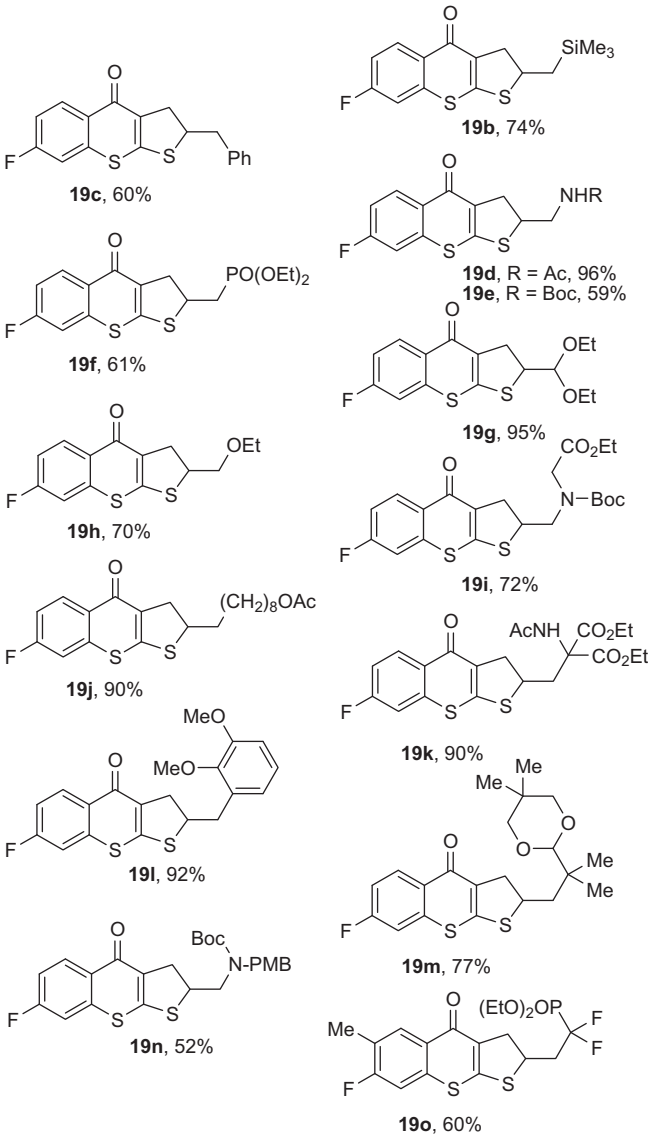
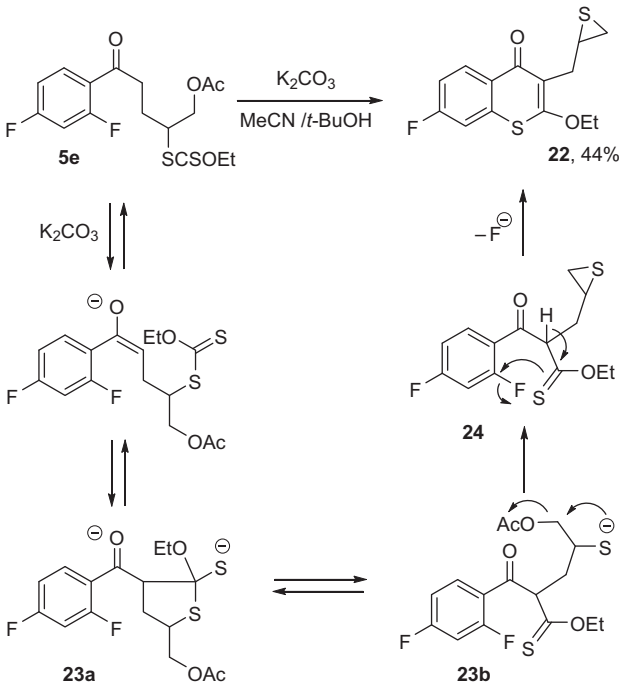


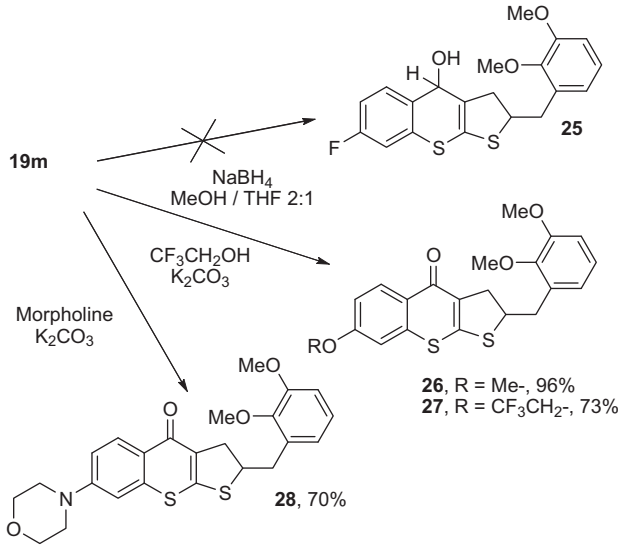
Figure 4.

We further observed the ketone group in these thieno[2,3-*b*]-benzothiopyranones to be rather unreactive towards nucleophilic



Scheme 7.

attack. Thus, no reduction with sodium borohydride occurred when compound **19m** was exposed to sodium borohydride in a mixture of methanol and THF at room temperature (Scheme 8). However, upon heating to reflux, a smooth reaction took place but instead of the expected carbinol **25** methoxy-substituted derivative **26** was isolated in excellent yield (96%). Clearly, the ketone exerted a sufficiently activating effect to allow nucleophilic substitution of the remaining fluorine. It was indeed possible to introduce a much more interesting trifluoroethoxy group by heating **19m** in trifluoroethanol in the presence of potassium carbonate. The trifluoroethoxide anion is only a very modest nucleophile, yet the substitution proved quite efficacious nevertheless and derivative **27** was obtained in 73% yield. Finally, a more classical



Scheme 8.

substitution with morpholine afforded compound **28** in equally good yield.

3. Conclusion

In summary, we have presented some unconventional approaches to a variety of highly functionalized scaffolds of potential pharmacological interest. The combination of the radical and ionic reactions of xanthates offers both flexibility and convergence and allows the introduction of tremendous diversity into the structures. We have also uncovered an unusual synthesis of thieno[2,3-*b*]-benzothiopyranones which opens an easy access to numerous new derivatives and which will hopefully facilitate the study of their chemistry.

4. Experimental

4.1. 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, Silica 60 A. C. C. 40–63 μm) or by crystallisation. Analytical TLC was carried out on Merck silica gel plates using short wave (254 nm) UV light, 1% aq $KMnO_4$ 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 thin films or as solutions 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 a Reichert microscope apparatus and are uncorrected. HRMS were performed on JEOL JMS-GcMate II, GC/MS system spectrometer. Microanalyses were carried out at the 'Service de Microanalyses' in the Institut de Chimie des Substances Naturelles in Gif-sur-Yvette.

4.1.1. Dithiocarbonic acid *S*-[2-(2,4-difluorophenyl)-2-oxo-ethyl] ester *O*-ethyl ester 4a

To a solution of 2,4-difluorophenacyl chloride **3a**[6a] (15.45 g, 81.0 mmol) in acetone (162 mL) was added portionwise and under nitrogen potassium *O*-ethylxanthogenate (15.52 g, 97.0 mmol). The reaction was monitored by tlc and, upon completion, ice water was added. The resulting precipitate was filtered off and dried to afford xanthate **4a** (20.91 g) as pale yellow crystals in 93% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (1H, ddd, J_{H-H} = 8.6 Hz, J_{H-F} = 8.6 and 6.6 Hz, C*H*Ar), 7.01 (1H, m, C*H*Ar), 6.93 (1H, m, C*H*Ar), 4.63 (2H, q, J = 7.1 Hz, OCH_2CH$_3$), 4.57 (2H, d, J_{H-F} = 3.1 Hz, CH_2S), 1.41 (3H, t, J = 7.1 Hz, OCH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.8 (*CS*), 188.8 (d, J_{C-F} = 4.7 Hz, *CO*), 166.1 (dd, J_{C-F} = 258.0 and 12.4 Hz, *CF*), 162.5 (dd, J_{C-F} = 257.1 and 12.6 Hz, *CF*), 132.9 (m, *CH*Ar), 122.1 (d, J_{C-F} = 10.1 Hz, *Cq*Ar), 112.5 (d, J_{C-F} = 20.3 Hz, *CH*Ar), 104.7 (t, J_{C-F} = 26.5 Hz, *C*HAr), 70.6 (O*C*H_2CH$_3$), 46.7 (d, J_{C-F} = 9.0 Hz, *C*H_2S), 13.6 (OCH$_2$*C*H_3). IR (nujol) 1686, 1610 cm^{-1}. MS (CI) 294 (M+NH$_4^+$), 277 (M+H$^+$).

4.2. General procedure for the preparation of addition products 5

A solution of xanthate (n mmol) and olefin (2n mmol) in cyclohexane or ethyl acetate (1 mL/mmol) was refluxed for 15 min. under nitrogen atmosphere. Lauroyl peroxide (DLP, 5 mol %) was then added to the refluxing solution followed by additional portions (2% or 2.5%) every 20 min or 1 h 30 min until there was complete consumption of the starting xanthate. The reaction mixture was then cooled to room temperature, concentrated under reduced pressure and the residue thus obtained was purified by flash chromatography on a silica gel column.

4.2.1. Dithiocarbonic acid *S*-{1-[3-(2,4-difluorophenyl)-3-oxo-propyl]-heptyl} ester *O*-ethyl ester 5a

The reaction was run in cyclohexane (3 mL) with xanthate **4a** (0.828 g, 3 mmol), octene (0.7 mL, 4.5 mmol) and DLP (11%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether: 96:4 gave the addition product **5a** (0.955 g) as a yellow oil in 82% yield. ^1H NMR (200 MHz, $CDCl_3$) δ 7.93 (1H, ddd, J_{H-H} = 8.5 Hz, J_{H-F} = 8.5 and 6.7 Hz, *CH*Ar), 6.99–6.81 (2H, m, 2*CH*Ar), 4.62 (2H, q, J = 7.1 Hz, OCH_2CH$_3$), 3.81 (1H, m, C*H*S), 3.11 (2H, m, *CH*$_2$), 2.25 (1H, m, C*H*H), 2.02 (1H, m, CH*H*), 1.77–1.65 (2H, CH_2), 1.52–1.35 (2H, CH_2), 1.40 (3H, t, J = 7.1 Hz, *O*CH$_2$CH_3), 1.28 (6H, br s), 0.88 (3H, m). ^{13}C NMR (50 MHz, $CDCl_3$) δ 214.3 (*CS*), 195.6 (d, J_{C-F} = 4.0 Hz, *CO*), 165.6 (dd, J_{C-F} = 257.0 and 12.0 Hz, *CF*), 162.7 (dd, J_{C-F} = 257.0 and 12.5 Hz, *CF*), 132.6 (dd, J_{C-F} = 10.0 and 3.5 Hz, CHAr), 122.1 (d, J_{C-F} = 13.0 Hz, *Cq*Ar), 112.0 (d, J_{C-F} = 21.5 Hz, *CH*Ar), 104.6 (t, J_{C-F} = 26.5 Hz, *CH*Ar), 69.6 (OCH_2CH$_3$), 50.9 (*CHS*), 40.5 (d, J_{C-F} = 7.0 Hz, CO*C*H_2), 34.6 (*CH*$_2$), 31.6 (*CH*$_2$), 29.0 (*CH*$_2$), 28.4 (*CH*$_2$), 26.8 (*CH*$_2$), 22.5 (*CH*$_2$), 13.9 (*CH*$_3$), 13.6 (*CH*$_3$). IR (neat) 1688, 1610 cm^{-1}. MS (CI) 406 (M+NH$_4$)$^+$, 389 (M+H)$^+$.

4.2.2. Dithiocarbonic acid *S*-[4-(2,4-difluorophenyl)-4-oxo-1-trimethylsilylmethyl-butyl] ester *O*-ethyl ester 5b

The reaction was run in cyclohexane (3 mL) with xanthate **4a** (0.828 g, 3 mmol), allyl trimethylsilane (0.9 mL, 6 mmol) and DLP (7%). Flash chromatography on a silica gel column using a gradient petroleum ether/ethyl acetate (98:2) afforded the addition product **5b** (0.995 g) as a yellow oil in 85% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (1H, ddd, J_{H-H} = 8.5 Hz, J_{H-F} = 8.5 and 7.0 Hz, C*H*Ar), 6.96 (1H, m, C*H*Ar), 6.87 (1H, m, C*H*Ar), 4.62–4.58 (2H, m, OCH_2CH$_3$), 3.95 (1H, m, C*H*S), 3.18–3.02 (2H, m, CH_2CO), 2.27 (1H, m, C*H*H), 1.95 (1H, m, CH*H*), 1.39 (3H, t, J = 7.1 Hz, OCH$_2$*C*H$_3$), 1.17 (1H, dd, J = 14.8 and 6.9 Hz, C*H*HSiMe$_3$), 1.05 (1H, dd, J = 14.8 and 8.3 Hz, CH*H*SiMe$_3$), 0.09 (9H, s, Si*Me*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.2 (*CS*), 195.7 (d, J_{C-F} = 4.3 Hz, *CO*), 165.6 (dd, J_{C-F} = 257.0 and 12.3 Hz, *CF*), 162.7 (dd, J_{C-F} = 257.0 and 12.5 Hz, *CF*), 132.6 (m, *CH*Ar), 122.0 (d, J_{C-F} = 13.0 Hz, *Cq*Ar), 112.l (d, J_{C-F} = 21.3 Hz, *CH*Ar), 104.6 (t, J_{C-F} = 24.3 Hz, *CH*Ar), 69.5 (OCH_2CH$_3$), 48.1 (*CHS*), 40.5 (d, J_{C-F} = 7.5 Hz, *CH*$_2$CO), 31.0 (*CH*$_2$), 23.5 (*CH*$_2$), 13.7 (OCH$_2$*CH*$_3$), −0.8 (Si*Me*$_3$). IR (neat) 1688, 1610 cm^{-1}.

4.2.3. Methyl 13-(2,4-difluorophenyl)-10-(ethoxycarbonothioyl-thio)-13-oxotridecanoate 5c

The reaction was run in ethyl acetate (1.8 mL) with xanthate **4a** (0.5 g, 1.8 mmol) undec-10-enoic acid methyl ester (2 equiv, 0.713 g) and DLP (10%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (95:5) afforded the addition product **5c** (0.682 g) as a yellow oil in 80% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (dt, 1H, J_{H-F} = 6.7 Hz, J_{H-H} = 8.6 Hz, C*H*Ar), 6.95 (m, 1H, C*H*Ar), 6.86 (ddd, 1H, J_{H-H} = 2.4 Hz, J_{H-F} = 8.7 Hz, J_{H-F} = 11.1 Hz, C*H*Ar), 4.61 (m, 2H, OCH_2CH$_3$), 3.79 (m, 1H, C*H*S), 3.66 (s, 3H, CO$_2$CH_3), 3.09 (tt, 2H, J = 4.6 Hz, J = 3.8 Hz, CH_2CO), 2.29 (t, 2H, J = 7.5 Hz, CH_2CO$_2$CH$_3$), 2.22 (m, 1H, C*H*HCHS), 1.97 (m, 1H, CH*H*CHS), 1.69 (dd, 2H, J = 7.3 Hz, J = 15.2 Hz, CHSCH_2), 1.59 (m, 2H, CH_2), 1.45 (m, 1H, C*H*HCH$_2$),

1.39 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 1.28 (br s, 9H, $CHCH_2$, $4CH_2$). NMR (100 MHz, $CDCl_3$) δ 214.4 (*C*S), 195.9 (d, J_{C-F} = 4.7 Hz, *C*O), 174.2 (CO_2Me), 165.7 (dd, J_{C-F} = 12.3 Hz, J_{C-F} = 256.9 Hz, *C*F), 162.7 (dd, J_{C-F} = 12.5 Hz, J_{C-F} = 257.4 Hz, *C*F), 132.6 (dd, J_{C-F} = 4.2 Hz, J = 10.5 Hz, *C*HAr), 122.10 (*C*q, dd, J_{C-F} = 3.6 Hz, J_{C-F} = 13.2 Hz), 112.2 (dd, J_{C-F} = 3.4 Hz, J_{C-F} = 21.4 Hz, *C*HAr), 104.7 (dd, J_{C-F} = 25.4 Hz, J_{C-F} = 27.8 Hz, *C*HAr), 69.8 (OCH_2CH_3), 51.4, 50.8 (*C*HS, OCH_3), 40.6 (d, J_{C-F} = 7.6 Hz, CH_2CO), 34.5 (CH_2), 34.0 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 28.3 (CH_2), 26.8 (CH_2), 24.9 (CH_2), 13.7 (OCH_2CH_3). IR ($CDCl_3$) 1740, 1690, 1609. MS (CI) 475 MH^+, 492 $MH^+NH_3^+$.

4.2.4. *S*-5-(2,4-Difluorophenyl)-5-oxo-1-phenylpentan-2-yl-*O*-ethylcarbonodithioate 5d

The reaction was run in cyclohexane (2.1 mL) with xanthate **4a** (0.60 g, 2.1 mmol), allyl benzene (4.2 mmol, 0.55 mL) and DLP (12.5%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethylether (97:3) afforded the addition product **5d** (0.82 g) as a yellow oil in 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dt, 1H, J_{H-F} = 6.7 Hz, J_{H-H} = 8.6 Hz, *CH*Ar), 7.30 (m, 4H, *CH*Ph), 7.23 (m, 1H, *CH*Ph), 6.93 (m, 1H, *CH*Ar), 6.84 (ddd, 1H, J_{H-H} = 2.4 Hz, J_{H-H} = 8.7 Hz, J_{H-F} = 11.1 Hz, *CH*Ar), 4.62 (m, 2H, OCH_2CH_3), 4.03 (m, 1H, *CH*S), 3.20 (dd, 1H, J = 6.0 Hz, J = 13.9 Hz, *CH*HPh) 3.08 (m, 2H, CH_2CO), 2.90 (dd, 1H, J = 8.5 Hz, J = 13.9 Hz, CH*H*Ph) 2.21 (m, 1H, *CH*HCHS) 1.93 (m, 1H, CH*H*CHS) 1.40 (t, 3H, J = 7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.9 (*C*S), 195.7 (*C*O), 165.8 (dd, J_{C-F} = 12.3 Hz, J_{C-F} = 257.0 Hz, *C*F), 162.7 (dd, J_{C-F} = 12.5 Hz, J_{C-F} = 257.5 Hz, *C*F), 138.3 (*C*q), 132.6 (dd, J_{C-F} = 4.3 Hz, J_{C-F} = 10.5 Hz, *C*HAr), 129.3 (*C*HPh), 128.5 (*C*HPh), 126.7 (*C*HPh), 122.0 (Cq, dd, J_{C-F} = 3.6 Hz, J = 13.2 Hz), 112.2 (dd, J_{C-F} = 3.4 Hz, J_{C-F} = 21.4 Hz, *C*HAr), 104.8 (dd, 1H, J_{C-F} = 25.4 Hz, J_{C-F} = 27.8 Hz, *C*HAr), 70.7 (OCH_2CH_3), 51.7 (*C*HS), 41.5 (CH_2Ph), 40.8 (CH_2CO), 26.8 (CH_2CHS), 14.1 (OCH_2CH_3). IR (CCl_4) 1691, 1607 cm^{-1}. MS (CI) 395 MH^+, 412 $MH^+NH_3^+$. HRMS (EI^+) [M−SCSOEt] 274.1172 (Measured mass), 274.1169 (Calculated mass).

4.2.5. Acetic acid 5-(2,4-difluorophenyl)-2-ethoxythiocarbonylsulfanyl-5-oxo-pentyl ester 5e

The reaction was run in cyclohexane (5 mL) with xanthate **4a** (1.38 g, 5 mmol), allyl acetate (1.09 mL, 10 mmol) and DLP (9%). Flash chromatography on a silica gel column using a gradient petroleum ether/ethyl acetate (9:1) afforded the addition product **5e** (1.33 g) as a yellow oil in 71% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.87 (1H, m, C*H*Ar), 6.95–6.76 (2H, m, 2C*H*Ar), 4.60–4.52 (2H, m, OCH_2CH_3), 4.32–4.16 (2H, m, CH_2OAc), 3.98 (1H, m, *CH*S), 3.09–3.04 (2H, m, CH_2CO), 2.22 (1H, m, *CH*H), 1.99 (1H, m, CH*H*), 1.36–1.29 (3H, m, OCH_2CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.7 (*CS*), 195.2 (*CO*), 170.3 ($OCOCH_3$), 165.7 (dd, J_{C-F} = 256.4 and 12.4 Hz, *CF*), 162.6 (dd, J_{C-F} = 257.5 and 12.5 Hz, *CF*), 132.6 (m, *CH*Ar), 122.0 (m, *Cq*Ar), 112.2 (d, J_{C-F} = 21.7 Hz, *CH*Ar), 104.7 (t, J_{C-F} = 26.5 Hz, *CH*Ar), 70.1 (OCH_2CH_3), 65.5 (CH_2OAc), 48.8 (*CH*S), 40.3 (d, J_{C-F} = 7.6 Hz, $COCH_2$), 24.9 (CH_2), 20.6 ($OCOCH_3$), 13.6 (OCH_2CH_3). IR (neat) 1745, 1688, 1611 cm^{-1}.

4.2.6. *S*-1-(2,4-Difluorophenyl)-5,5,6,6,7,7,8,9,10,10,10-undecafluoro-8,9-dimethyl-1-oxodecan-4-yl *O*-ethyl carbonodithioate 5f

The reaction was run in ethyl acetate (3.6 mL) with xanthate **4a** (1.0 g, 3.6 mmol), perfluoro (hexyl)ethylene (2 equiv, 1.6 mL) and DLP (12.5%). Flash chromatography on a silica gel column using a gradient petroleum ether/ethyl acetate (9:1) afforded the addition product **5f** (0.94 g) as a yellow oil in 42% (64%) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dt, 1H, J_{H-F} = 6.7 Hz, J_{H-H} = 8.6 Hz, *CH*Ar), 6.97 (m, 1H, C*H*Ar), 6.87 (ddd, 1H, J_{H-H} = 2.4 Hz, J_{H-H} = 8.6 Hz, J_{H-F} = 11.1 Hz, *CH*Ar), 4.83 (m, 1H, *CH*S), 4.64 (m, 2H, OCH_2CH_3), 3.21 (dt, 2H, J = 3.1 Hz, J = 7.1 Hz, CH_2CO), 2.62 (m, 1H, *CH*HCHS), 2.04 (m, 1H, CH*H*CHS), 1.41 (t, 3H, J = 7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.5 (*CS*), 194.8 (*CO*, d, J_{C-F} = 4.7 Hz), 166.1 (dd, J_{C-F} = 12.4 Hz, J_{C-F} = 257.7 Hz, *CF*), 162.9 (dd, J_{C-F} = 12.5 Hz, J_{C-F} = 257.5 Hz, *CF*), 132.8 (dd, J_{C-F} = 4.2 Hz, J_{C-F} = 10.6 Hz, *CH*Ar), 121.7 (*Cq*, dd, J_{C-F} = 3.6 Hz, J_{C-F} = 13.1 Hz), 119.0 (*CF*), 118.7 (*CF*), 117.0 (*CF*), 115.8 (*CF*), 113.0 (*CF*), 112.4 (dd, J_{C-F} = 3.3 Hz, J_{C-F} = 21.4 Hz, *CH*Ar), 110.4 (*CF*), 104.9 (dd, J_{C-F} = 25.5 Hz, J_{C-F} = 27.8 Hz, *CH*Ar), 71.4 (OCH_2CH_3), 51.5 (*CH*S), 39.5 (d, J_{C-F} = 8.5 Hz, CH_2CO), 22.1 (CH_2), 13.6 (OCH_2CH_3). IR ($CDCl_3$) 1687, 1611 cm^{-1}. MS (CI) 623 MH^+, 640 $MH^+NH_3^+$. HRMS (EI^+) 622.0104 (Measured mass), 622.0117 (Calculated mass).

4.2.7. *S*-1-Acetamido-5-(2,4-difluorophenyl)-5-oxopentan-2-yl *O*-ethyl carbonodithioate 5g

The reaction was run in ethyl acetate (7.2 mL) with xanthate **4a** (2.0 g, 7.2 mmol), *N*-allylacetamide (2 equiv, 0.71 g) and DLP (10%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (1:1) afforded the addition product **5g** (2.35 g) as a yellow oil in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dt, 1H, J_{H-F} = 6.6 Hz, J_{H-H} = 8.6 Hz, *CH*Ar), 6.94 (m, 1H, *CH*Ar), 6.85 (ddd, 1H, J_{H-H} = 2.4 Hz, J_{H-H} = 8.6 Hz, J_{H-F} = 11.1 Hz, *CH*Ar), 5.99 (s, 1H, N*H*), 4.62 (q, 2H, J = 7.1 Hz, OCH_2CH_3), 3.93 (m, 1H, *CH*S), 3.64 (td, 1H, J = 5.9 Hz, J = 14.0 Hz, *CH*HNHAc), 3.52 (m, 1H, CH*H*NHAc), 3.14 (dt, 2H, J = 3.1 Hz, J = 7.1 Hz, CH_2CO), 2.22 (m, 1H, *CH*HCHS), 1.97 (m, 4H, CH*H*CHS, $COCH_3$), 1.40 (t, 3H, J = 7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.5 (*CS*), 195.7 (d, J_{C-F} = 4.7 Hz, *CO*), 170.3 ($COCH_3$), 165.9 (dd, J_{C-F} = 12.3 Hz, J_{C-F} = 257.3 Hz, *CF*), 162.8 (dd, J_{C-F} = 12.5 Hz, J_{C-F} = 257.7 Hz, *CF*), 132.7 (dd, J_{C-F} = 4.2 Hz, J_{C-F} = 10.5 Hz, *CH*Ar), 122.0 (*Cq*, dd, J_{C-F} = 3.6 Hz, J_{C-F} = 13.1 Hz), 112.3 (dd, J = 3.4 Hz, J = 21.4 Hz, *CH*Ar), 104.9 (dd, J = 25.4 Hz, J = 27.8 Hz, *CH*Ar), 70.4 (OCH_2CH_3), 50.8 (*CH*S), 42.9 (CH_2NHAc), 40.4 (d, J_{C-F} = 7.8 Hz, CH_2CO), 25.6 (d, J_{C-F} = 1.8 Hz, CH_2CHS), 23.3 (CH_3CO), 13.8 (OCH_2CH_3). IR ($CDCl_3$) 1681, 1611 cm^{-1}. MS (CI) 376 MH^+, 393 $MH^+NH_3^+$. HRMS (EI^+) 375.0774 (Measured mass), 375.0774 (Calculated mass).

4.2.8. Dithiocarbonic acid *S*-[1-(*tert*-butoxycarbonylamino-methyl)-4-(2,4-difluorophenyl)-4-oxo-butyl] ester *O*-ethyl ester 5h

The reaction was run in cyclohexane (5 mL) with xanthate **4a** (1.38 g, 5 mmol), allyl amine Boc derivative (1.18 g, 7.5 mmol) and DLP (13%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (8:2) afforded the addition product **5h** (1.69 g) as a pale yellow and viscous oil in 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (1H, ddd, J_{H-H} = 8.5 Hz, J_{H-F} = 8.5 and 7.0 Hz, *CH*Ar), 6.96 (1H, ddd, J_{H-H} = 8.5 and 2.5 Hz, J_{H-F} = 8.0 Hz, C*H*Ar), 6.87 (1H, ddd, J_{H-H} = 2.5 Hz, J_{H-F} = 11.0 and 8.8 Hz, C*H*Ar), 4.90 (1H, m, NH), 4.63 (2H, q, J = 7.1 Hz, OCH_2CH_3), 3.92 (1H, m, C*H*S), 3.53 (1H, m, C*H*HN), 3.41 (1H, m, CH*H*N), 3.15 (2H, m, $COCH_2$), 2.23 (1H, m, C*H*HCHS), 1.97 (IH, m, CH*H*CHS), 1.43 (9H, s, Me_3), 1.41 (3H, t, J = 7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.4 (*CS*), 195.7 (d, J_{C-F} = 4.2 Hz, *CO*), 165.8 (dd, J_{C-F} = 257.0 and 12.2 Hz, *CF*), 162.8 (dd, J_{C-F} = 257.0 and 12.5 Hz, *CF*), 155.9 (N*CO*), 132.7 (m, *CH*Ar), 121.9 (d, J_{C-F} = 10.7 Hz, *Cq*Ar), 112.2 (d, J_{C-F} = 21.0 Hz, *CH*Ar), 104.8 (t, J_{C-F} = 26.3 Hz, *CH*Ar), 79.6 ($CqMe_3$), 70.2 (OCH_2CH_3), 51.2 (CH, *CHS*), 43.8 (CH_2N), 40.5 (d, J_{C-F} = 7.3 Hz, CH_2CO), 28.4 (Me_3), 25.4 (CH_2), 13.7 (OCH_2CH_3). IR (neat) 1714, 1690, 1610. MS (CI) 451 $(M+NH_4)^+$, 434 $(M+H)^+$.

4.2.9. Dithiocarbonic acid *S*-[1-(*tert*-butoxycarbonylamino-methyl)-4-(2,4-difluorophenyl)-4-oxo-butyl] ester *O*-ethyl ester 5i

The reaction was run in cyclohexane (6 mL) with xanthate **4a** (1.66 g, 6 mmol), allyl methylamine Boc derivative (1.54 g, 9 mmol) and DLP (11%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (8:2) afforded

the addition product **5i** (2.22 g) as a yellow oil in 83% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.92 (1H, ddd, J_{H-H} = 8.6 Hz, J_{H-F} = 8.6 and 6.8 Hz, C*H*Ar), 7.00–6.80 (2H, m, 2 C*H*Ar), 4.62 (2H, q, J = 7.1 Hz, OCH_2CH$_3$), 4.04 (1H, m, C*H*S}, 3.70 (1H, m, C*H*HN), 3.37 (1H, m, CH*H*N), 3.18–3.05 (2H, m, COCH_2), 2.95 (3H, s, NMe}, 2.28 (1H, m, C*H*HCHS), 1.88 (1H, m, CH*H*CHS), 1.50 (9H, br s, Me_3), 1.41 (3H, t, J = 7.1 Hz, OCH$_2$CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 213.7 (*C*S), 195.5 (*C*O), 165.7 (dd, J_{C-F} = 257.0 and 12.1 Hz *C*F), 162.6 (dd, J_{C-F} = 257.5 and 12.2 Hz, *C*F), 155.6 (N*C*O), 132.6 (m, *C*HAr), 122.2 (d, J_{C-F} = 12, *Cq*Ar), 112.2 (d, J_{C-F} = 21.4 Hz, *C*HAr), 104.7 (t, J_{C-F} = 26.6 Hz, *C*HAr), 79.9 (*Cq*Me$_3$), 70.1 (OCH_2CH$_3$), 52.4 (broad, CH_2N), 49.3 (*C*HS), 40.4 (d, J_{C-F} = 6.5 Hz, COCH_2), 34.8 (NCH_3), 29.6 (Me_3), 28.4 (CH_2), 13.7 (OCH$_2$CH_3). IR (neat) 1693, 1610 cm^{-1}.

4.2.10. 4-(2,4-Difluorophenyl)-1-(ethoxycarbonothioylthio)-4-oxobutyl pivalate 5j

The reaction was run in ethyl acetate (3.6 mL) with xanthate **4a** (1.0 g, 3.6 mmol), vinyl pivalate (2 equiv, 1.0 mL) and DLP (7.5%). Flash chromatography on a silica gel column using a gradient petroleum ether/ethyl acetate (9:1) afforded the addition product **5j** (1.16 g) as a yellow oil in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dt, 1H, J_{H-F} = 6.6 Hz, J_{H-H} = 8.6 Hz, C*H*Ar), 6.96 (m, 1H, C*H*Ar), 6.86 (ddd, 1H, J_{H-H} = 2.4 Hz, J_{H-H} = 8.6 Hz, J_{H-F} = 11.1 Hz, C*H*Ar), 6.68 (t, 1H, J = 6.6 Hz, C*H*S), 4.62 (m, 2H, OCH_2CH$_3$), 3.08 (dt, 2H, J = 3.1 Hz, J = 7.2 Hz, CH_2CO), 2.37 (m, 2H, J = 7.1 Hz, CH_2CHS), 1.40 (t, 3H, J = 7.2 Hz, OCH$_2$CH_3), 1.19 (s, 9H, (CH_3)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.1 (*C*S), 194.6 (d, J_{C-F} = 4.6 Hz, *C*O), 176.7 (O*C*O), 166.0 (dd, J_{C-F} = 12.4 Hz, J_{C-F} = 257.4 Hz, *C*F), 162.9 (dd, J_{C-F} = 12.5 Hz, J_{C-F} = 257.3 Hz, *C*F), 132.8 (dd, J_{C-F} = 4.2 Hz, J_{C-F} = 10.6 Hz, *C*HAr), 121.8 (*C*q, dd, J_{C-F} = 3.5 Hz, J_{C-F} = 13.1 Hz), 112.4 (dd, J_{C-F} = 3.3 Hz, J_{C-F} = 21.4 Hz, *C*HAr), 104.8 (dd, J_{C-F} = 25.5 Hz, J_{C-F} = 27.7 Hz, *C*HAr), 80.0 (*C*HOCO), 70.2 (OCH_2CH$_3$), 39.0 (d, J_{C-F} =8.3 Hz, *C*H$_2$CO), 38.9 (*C*q), 28.4 (d, J_{C-F} = 1.8 Hz, *C*H$_2$CHS), 27.0 (C(CH_3)$_3$), 13.7 (OCH$_2$CH_3). IR ($CDCl_3$) 1739, 1691, 1614 cm^{-1}. MS (CI) 422 MH$^+$NH$_3^+$. HRMS (EI$^+$) [M−SCSOEt] 284.1209 (Measured mass), 284.1224 (Calculated Mass).

4.2.11. 5-(2,4-Difluorophenyl)-2-ethoxythiocarbonylsulfanyl-5-oxo-pentyl-phosphonic acid diethyl ester 5k

The reaction was run in cyclohexane (5 mL) with xanthate **4a** (1.38 g, 5 mmol), allyl phosphonate (1.78 g, 10 mmol) and DLP (11%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (8:2) afforded the addition product **5k** (1.84 g) as a yellow oil in 81% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.90 (1H, ddd, J_{H-H} = 8.6 Hz, J_{H-F} = 8.6 and 6.6 Hz, C*H*Ar), 6.93 (1H, dddd, J_{H-H} = 8.6 and 2.5 Hz, J_{H-F} = 7.6 and 0.7 Hz, C*H*Ar), 6.84 (1H, ddd, J_{H-H} = 2.5 Hz, J_{H-F} = 11.1 and 8.7 Hz, C*H*Ar), 4.61 (2H, q, J = 7.1 Hz, OCH_2CH$_3$), 4.17–4.07 (5H, m, CHS, 2POCH_2CH$_3$), 3.16–3.06 (2H, m, COCH_2), 2.58–2.00 (4H, m, CH_2, CH_2P), 1.40 (3H, t, J = 7.1 Hz, OCH$_2$CH_3), 1.31 (6H, dt, J_{H-H} = 7.1 Hz, J_{H-P} = 2.3 Hz, 2POCH$_2$CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.6 (*C*S), 195.1 (*C*O), 165.6 (dd, J_{C-F} = 257.0 and 12.0 Hz, *C*F), 162.1 (dd, J_{C-F} = 257.0 and 12.0 Hz, *C*F), 132.5 (dd, J_{C-F} = 10.5 and 4.5 Hz, *C*HAr), 121.9 (d, J_{C-F} = 12.5 Hz, *Cq*Ar), 112.0 (d, J_{C-F} = 21.5 Hz, *C*HAr), 104.6 (t, J_{C-F} = 26.5 Hz, *C*HAr), 69.8 (OCH_2CH$_3$), 61.8, 61.7 (d, J_{C-P} = 6.0 Hz, 2POCH_2CH$_3$), 44.9 (*C*HS), 40.3 (d,. J_{C-F} = 7.4 Hz, COCH_2), 31.7 (d, J_{C-P} = 137.5 Hz, CH_2P), 27.9 (CH_2), 16.2 (d, J_{C-P} = 5.5 Hz, 2POCH$_2$CH_3)13.5 (OCH$_2$CH_3). IR (neat) 1687, 1609 cm^{-1}. MS (CI) 455 (M+H)$^+$.

4.2.12. *S*-5-(2,4-Difluorophenyl)-1,1-diethoxy-5-oxopentan-2-yl *O*-ethyl carbonodithioate 5l

The reaction was run in ethyl acetate (3.6 mL) with xanthate **4a** (1.0 g, 3.6 mmol), 4,4-diethoxy-but-1-ene (2.0 equiv, 1.03 g) and DLP (12.5%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (2:3) afforded the addition product **5l** (1.24 g) as a colourless oil in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dt, 1H, J_{H-F} = 6.8 Hz, J_{H-H} = 8.6 Hz, C*H*Ar), 6.93 (m, 1H, C*H*Ar), 6.84 (ddd, 1H, J_{H-H} = 2.4 Hz, J_{H-H} = 8.7 Hz, J_{H-F} = 11.0 Hz, C*H*Ar), 4.61 (m, 3H, C*H*(OEt)$_2$, OCH_2CH$_3$), 4.12 (m, 1H, C*H*S), 3.64 (m, 4H, 2OCH_2CH$_3$), 3.16 (m, 2H, CH_2CO), 2.41 (m, 1H, C*H*HCHS), 2.01 (m, 1H, CH*H*CHS), 1.39 (t, 1H, J = 7.1 Hz, OCH$_2$CH_3), 1.21 (dt, 6H, J = 7.1 Hz, (CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.9 (*C*S), 196.2 (*C*O, d, J_{C-F} = 4.7 Hz), 165.7 (dd, J_{C-F} = 12.2 Hz, J_{C-F} = 256.6 Hz, *C*F), 162.7 (dd, J_{C-F} = 12.6 Hz, J_{C-F} = 257.5 Hz, *C*F), 132.7 (dd, J_{C-F} = 4.3 Hz, J = 10.5 Hz, *C*HAr), 122.3 (*C*q, dd, J_{C-F} = 3.5 Hz, J_{C-F} = 13.2 Hz), 112.1 (dd, J_{C-F} = 3.4 Hz, J_{C-F} = 21.4 Hz, *C*HAr), 104.8 (dd, J_{C-F} = 25.4 Hz, J_{C-F} = 27.8 Hz, *C*HAr), 104.1 (*C*H(OEt)$_2$), 70.2 (OCH_2CH$_3$), 64.6 (OCH$_2$CH$_3$), 63.8 (OCH_2CH$_3$), 53.4 (*C*HS), 40.7 (d, J_{C-F} = 7.7 Hz, *C*H$_2$CO), 22.7 (*C*H$_2$), 15.2 (OCH$_2$CH$_3$), 15.3 (OCH$_2$CH$_3$), 13.8 (*C*H$_3$). IR ($CDCl_3$) 1685, 1609 cm^{-1}. MS (CI) 361 MH$^+$−EtOH. HRMS (EI$^+$) 406.1091 (Measured mass), 406.1084 (Calculated mass).

4.2.13. Dithiocarbonic acid *S*-[4-(2,4-difluorophenyl)-1-ethoxymethyl-4-oxo-butyl] ester *O*-ethyl ester 5m

The reaction was run in cyclohexane (8 mL) with xanthate **4a** (1.38 g, 5 mmol), allyl ethyl ether (1.7 mL, 15 mmol) and DLP (13%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (9:1) afforded the addition product **5m** (1.12 g) as a pale yellow oil in 62% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.94 (1H, ddd, J_{H-H} = 8.5 Hz, J_{H-F} = 8.5 and 7.0 Hz, C*H*Ar), 7.02–6.82 (2H, m, 2C*H*Ar), 4.62 (2H, q, J = 7.1 Hz, OCH_2CH$_3$), 4.00 (1H, m, C*H*S), 3.73 (1H, dd, J = 10.0 and 4.2 Hz, CHSC*H*HO), 3.62–3.48 (m, 3H, CHSCH*H*O, OCH_2), 3.19–3.10 (2H, m, COCH_2), 2.35 (IH, m, C*H*HCHS), 2.05 (1H, m, CH*H*CHS), 1.40 (3H, t, J = 7.1 Hz, OCH$_2$CH_3), 1.18 (3H, t, J = 7.0 Hz, CH$_2$OCH$_2$CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 213.7 (CS), 195.2 (d, J_{C-F} = 4.0 Hz, *C*O), 165.5 (Cq, dd, J_{C-F} = 257.0 and 12.5 Hz, *C*F), 162.5 (Cq, dd, J_{C-F} = 257.0 and 12.5 Hz, *C*F), 132.4 (dd, J_{C-F} = 10.0 and 4.0 Hz, *C*HAr), 121.9 (d, J_{C-F} = 13.0 Hz, *Cq*Ar), 111.8 (CH, d, J_{C-F} = 21.5 Hz, *C*HAr), 104.4 (t, J_{C-F} = 26.5 Hz, *C*HAr), 72.0 (CH_2O), 69.6 (OCH_2CH$_3$), 66.3 (OCH_2), 49.7 (*C*HS), 40.3 (d, J_{C-F} = 7.5 Hz, COCH_2), 25.2 (CH_2), 14.8, 13.4 (CH_3). IR (neat) 1687, 1610 cm^{-1}. MS (CI) 380 (M+NH$_4$)$^+$, 363 (M+H)$^+$.

4.2.14. Ethyl-2-(*tert*-butoxycarbonyl(5-(2,4-difluorophenyl)-2(ethoxycarbonothioylthio)-5-oxopentyl) amino)acetate 5n

The reaction was run in ethyl acetate (3.6 mL) with xanthate **4a** (1.0 g, 3.6 mmol), ethyl 2-(allyl (*tert*-butoxycarbonyl) amino) acetate (2 equiv, 1.75 g) and DLP (10%). Flash chromatography on a silica gel column using a gradient petroleum ether/ethyl acetate (9:1) afforded the addition product **5n** (1.49 g) as a yellow oil in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (tt, 1H, J = 6.3 Hz, J = 8.6 Hz, C*H*Ar), 6.94 (m, 1H, C*H*Ar), 6.85 (m, 1H, C*H*Ar), 4.61 (q, 2H, J = 7.1 Hz, OCH_2CH$_3$), 4.19 (m, 2H, OCH_2CH$_3$), 4.08 (d, 1H, J = 12.4 Hz, NC*H*HCO$_2$Et), 4.01 (d, 1H, J = 6.7 Hz, NC*H*HCHS), 3.88 (m, 2H, NCH*H*CO$_2$Et, C*H*S), 3.34 (m, 1H, NCH*H*CHS), 3.13 (m, 2H, CH_2CO), 2.34 (m, 1H, C*H*HCHS), 1.93 (m, 1H, CH*H*CHS), 1.43 (m, 12H, C(CH_3)$_3$, OCH$_2$CH_3), 1.27 (t, 1H, J = 7.2 Hz, OCH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.8; 214.0 (*C*S), 195.8; 195.6 (*C*O, d, J_{C-F} = 4.6 Hz; d, J_{C-F} = 4.7 Hz), 170.1; 170.0 (O*C*O), 165.8 (ddd, J_{C-F} = 8.3 Hz, J_{C-F} = 12.1 Hz, J_{C-F} = 256.9 Hz, *C*F), 162.8 (ddd, J_{C-F} = 3.5 Hz, J_{C-F} = 12.9 Hz, J_{C-F} = 257.6 Hz, *C*F), 155.5 (N*C*O), 132.7 (dd, J_{C-F} = 4.3 Hz, J_{C-F} = 10.5 Hz, *C*HAr), 122.2 (*C*q), 112.2 (ddd, J_{C-F} = 2.6 Hz, J_{C-F} = 11.7 Hz, J_{C-F} = 20.7 Hz, *C*HAr), 104.8 (m, *C*HAr), 81.1; 80.7 (*C*(CH$_3$)$_3$), 70.2; 70.3 (O*C*H$_2$CH$_3$), 61.1 (OCH$_2$CH$_3$), 52.0; 51.4 (NCH$_2$CO$_2$Et), 49.9; 49.8 (*C*HS), 49.6; 49.2 (NCH$_2$CHS), 40.83; 40.57 (d, J_{C-F} = 7.2 Hz; d, J_{C-F} = 7.1 Hz, *C*H$_2$CO), 28.4; 28.2 (*C*H$_3$)$_3$, 25.3; 24.9 (*C*H$_2$CHS), 14.4; 14.2 (OCH$_2$*C*H$_3$), 13.8 (OCH$_2$*C*H$_3$). IR ($CDCl_3$) 1746, 1690, 1611 cm^{-1}. MS (CI) 420 M$^+$−Boc, 520 MH$^+$.

HRMS (EI^+) 519.1574 (Measured mass), 519.1561(Calculated mass).

4.2.15. Acetic acid 13-(2,4-difluorophenyl)-10-ethoxythiocarbonylsulfanyl-13-oxo-tridecyl ester 5o

The reaction was run in cyclohexane (5 mL) with xanthate **4a** (1.38 g, 5 mmol), olefin (1.59 g, 7.5 mmol) and DLP (7%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (9:1) afforded the addition product **5o** (1.84 g) as a pale yellow oil in 85% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.92 (1H, ddd, J_{H-H} = 8.5 Hz, J_{H-F} = 8.5 and 7.0 Hz, C*H*Ar), 6.96 (1H, ddd, J_{H-H} = 8.5 and 2.5 Hz, J_{H-F} = 8.0, C*H*Ar), 6.87 (1H, ddd, J_{H-H} = 2.5 Hz, J_{H-F} = 11 and 9.0 Hz, C*H*Ar), 4.63 (1H, q, 7.1 Hz, OC*H*HCH$_3$), 4.60 (1H, q, 7.1 Hz, OCH*H*CH$_3$), 4.05 (2H, t, J = 6.7, CH_2OAc), 3.80 (1H, m, CHS), 3.10 (2H, m, COCH_2), 2.22 (1H, m, C*H*HCHS), 2.05 (3H, s, OCOCH_3), 1.98 (1H, m, CH*H*CHS), 1.73–1.67 (2H, m), 1.63–1.59 (2H, m), 1.46–1.38 (2H, m), 1.40 (3H, t, J = 7.1 Hz, OCH$_2$CH_3), 1.28 (10H, br s, 5CH$_2$). ^{13}C NMR (50 MHz, $CDCl_3$) δ 214.4 (*CS*), 195.8 (d, J_{C-F} = 4.0 Hz, *CO*), 171.0 (OC*O*CH$_3$), 165.7 (dd, J_{C-F} = 257.0 and 12.5 Hz, *CF*), 162.6 (dd, J_{C-F} = 257.0 and 12.5 Hz, *CF*), 132.6 (dd, J_{C-F} = 10.5 et 4.0 Hz, *CH*Ar), 122.2 (d, J_{C-F} = 13.0 Hz, *Cq*Ar), 112.1 (d, J_{C-F} = 21.5 Hz, *CH*Ar), 104.7 (t, J_{C-F} = 26.5 Hz, *CH*Ar), 69.7 (O*C*H$_2$CH$_3$), 64.5 (*C*H$_2$OAc), 50.9 (*CH*S), 40.5 (d, J_{C-F} = 7.5 Hz, CO*C*H$_2$), 34.6, 29.3, 29.2, 28.6, 28.4, 26.8, 25.9 (*C*H$_2$), 20.9 (OCO*C*H$_3$), 13.7 (OCH$_2$*C*H$_3$). IR (neat) 1738, 1687, 1610 cm^{-1}. MS (CI) 506 $(M+NH_4)^+$, 489 $(M+H)^+$.

4.2.16. 2-Acetylamino-2-[5-(2,4-difluorophenyl)-2-ethoxythiocarbonylsulfanyl-5-oxo-pentyl] -malonic acid diethyl ester 5p

The reaction was run in cyclohexane (2 mL) with xanthate **4a** (0.552 g, 2 mmol), olefin (0.771 g, 3.0 mmol) and DLP (7%). Flash chromatography on a silica gel column using a gradient petroleum ether/ethyl acetate (6:4) afforded the addition product **5p** (1.16 g) contaminated with the olefin in excess (ratio: 9:1) in 76% NMR yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (1H, ddd, J_{H-H} = 8.2 Hz, J_{H-F} = 8.2 and 7.0 Hz, C*H*Ar), 6.92 (1H, m, C*H*Ar), 6.90 (1H, s, NH), 6.83 (1H, m, C*H*Ar), 4.58 (2H, q, J = 7.1 Hz, OCH_2CH$_3$), 4.25–4.17 (4H, m, 2CO$_2$CH_2CH$_3$), 3.78 (1H, m, C*H*S), 3.12–2.95 (2H, m, COCH_2), 2.91 (1H, dd, J = 15.5 and 3.4 Hz, C*H*HCNHAc), 2.70 (1H, dd, J = 15.5 and 10.2 Hz, CH*H*CNHAc), 2.12 (1H, m, C*H*HCHS), 2.04 (3H, s, NHCOCH_3), 2.01 (IH, m, CH*H*CHS), 1.36 (3H, t, J = 7.1 Hz, OCH$_2$CH_3), 1.26–1.21 (6H, m, 2CO$_2$CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.6 (*CS*), 195.6 (d, J_{C-F} = 4.7 Hz, Ar*C*O), 169.6, 167.9, 167.5 (3*C*O), 165.7 (dd, J_{C-F} = 257.0 and 12.2 Hz, *CF*), 162.7 (dd, J_{C-F} = 257.0 and 12.5 Hz, *CF*), 132.6 (m, *CH*Ar), 122.0 (d, J_{C-F} = 12.6 Hz, *Cq*Ar), 112.2 (d, J_{C-F} = 21.2 Hz, *CH*Ar), 104.8 (t, J_{C-F} = 26.6 Hz, *CH*Ar), 70.2 (O*C*H$_2$CH$_3$), 65.4 (*Cq*NHAc), 63.1 (CO$_2$*C*H$_2$CH$_3$), 62.7 (CO$_2$*C*H$_2$CH$_3$), 46.1 (*CH*S), 40.2 (d, J_{C-F} = 7.6 Hz, CO*C*H$_2$), 36.1 (*C*H$_2$), 30.5 (*C*H$_2$), 23.0 (NHCO*C*H$_3$), 14.0 (*C*H$_3$), 13.7 (*C*H$_3$).

4.2.17. *S*-5-(2,4-Difluorophenyl)-1-(2,3-dimethoxyphenyl)-5-oxopentan-2-yl-*O*-ethyl-carbonodithi-oate 5q

The reaction was run in ethyl acetate (3.6 mL) with xanthate **4a** (1.0 g, 3.6 mmol), 1-allyl-2,3-dimethoxybenzene (2 equiv, 1.2 g) and DLP (12.5%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (4:2) afforded the addition product **5q** (1.31 g) as a yellow oil in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dt, 1H, J_{H-F} = 6.7 Hz, J_{H-H} = 8.6 Hz, C*H*Ar), 6.99 (t, 1H, J = 7.91, C*H*Ph), 6.93 (m, 1H, C*H*Ar), 6.87 (m, 1H, C*H*Ph), 6.82 (m, 2H, C*H*Ar, C*H*Ph), 4.59 (q, 2H, J = 7.1 Hz, OCH_2CH$_3$), 4.08 (m, 1H, C*H*S), 3.85 (s, 6H, 2OCH_3), 3.14 (m, 2H, CH_2Ph), 3.05 (d, 2H, J = 7.6 Hz, CH_2CO), 2.18 (m, 1H, C*H*HCHS), 1.99 (m, 1H, CH*H*CHS), 1.39 (t, 3H, J = 7.1 Hz, OCH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.4 (*CS*), 195.2 (*CO*, d, J_{C-F} = 4.6 Hz), 165.3 (dd, J_{C-F} = 12.2 Hz, J_{C-F} = 256.5 Hz, *CF*), 162.3 (dd, J_{C-F} = 12.5 Hz, J_{C-F} = 257.4 Hz, *CF*), 152.4 (*Cq*), 147.2 (*Cq*), 132.3 (dd, J_{C-F} = 4.2 Hz, J_{C-F} = 10.5 Hz, *CH*Ar), 131.7 (*Cq*), 123.4 (*CH*Ph), 122.3 (*CH*Ph), 121.8 (*Cq*, dd, J_{C-F} = 3.6 Hz, J_{C-F} = 13.2 Hz), 111.8 (dd, J_{C-F} = 3.3 Hz, J_{C-F} = 21.4 Hz, *CH*Ar), 110.8 (*CH*Ph), 104.4 (dd, J_{C-F} = 25.5 Hz, J_{C-F} = 27.8 Hz, *CH*Ar), 69.5 (O*C*H$_2$CH$_3$), 60.2 (O*C*H$_3$), 55.3 (O*C*H$_3$), 50.7 (*CH*S), 40.4 (d, J = 7.5 Hz, *C*H$_2$CO), 34.5 (*C*H$_2$), 27.3 (*C*H$_2$), 13.4 (*C*H$_3$). IR ($CDCl_3$) 1690, 1607 cm^{-1}. MS (CI) 455 MH^+, 472 $MH^+NH_3^+$. HRMS (EI^+) 454.1086 (Measured mass), 454.1084 (Calculated mass).

4.2.18. *S*-1-(2,4-Difluorophenyl)-6-(5,5-dimethyl-1,3-dioxan-2-yl)-6-methyl-1-oxoheptan-4-yl *O*-ethyl carbonodithioate 5r

The reaction was run in ethyl acetate (3.6 mL) with xanthate **4a** (1.0 g, 3.6 mmol), 5,5-dimethyl-2-(2-methylpent-4-en-2-yl)-1,3-dioxane (2.0 equiv, 1.4 g) and DLP (12.5%). Flash chromatography on a silica gel column using a gradient petroleum ether/diethyl ether (2:3) afforded the addition product **5r** (1.36 g) as a colourless oil in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dt, 1H, J_{H-F} = 6.7 Hz, J_{H-H} = 8.6 Hz, C*H*Ar), 6.95 (m, 1H, C*H*Ar), 6.85 (ddd, 1H, J_{H-H} = 2.4 Hz, J_{H-H} = 8.7 Hz, J_{H-F} = 11.1 Hz, C*H*Ar), 4.62 (m, 2H, OCH_2CH$_3$), 4.13 (s, 1H, C*H*OCH$_2$CCH$_3$), 3.94 (m, 1H, C*H*S), 3.58 (d, 2H, J = 11.0 Hz, OCH_2C(CH$_3$)$_2$), 3.38 (dd, 2H, J = 1.6 Hz, J = 11.0 Hz, OCH_2C(CH$_3$)$_2$), 3.09 (m, 2H, CH_2CO), 2.21 (m, 1H, C*H*HCHS), 2.01 (m, 1H, CH*H*CHS), 1.75 (dq, 2H, J = 5.8 Hz, J = 15.1 Hz, CHSCH_2C(CH$_3$)), 1.40 (t, 3H, J = 7.1 Hz, OCH$_2$CH_3), 1.14 (s, 3H, CH$_2$CCH_3), 1.02 (s, 3H, CCH_3), 0.99 (s, 3H, CCH_3), 0.70 (s, 3H, CH$_2$CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.5 (*CS*), 196.2 (*CO*, d, J_{C-F} = 4.7 Hz), 165.7 (dd, J_{C-F} = 12.3 Hz, J_{C-F} = 256.8 Hz, *CF*), 162.7 (dd, J_{C-F} = 12.5 Hz, J_{C-F} = 257.5 Hz, *CF*), 132.7 (dd, J_{C-F} = 4.3 Hz, J_{C-F} = 10.5 Hz, *CH*Ar), 122.3 (*Cq*, dd, J_{C-F} = 3.6 Hz, J_{C-F} = 13.2 Hz), 112.2 (dd, J_{C-F} = 3.4 Hz, J_{C-F} = 21.4 Hz, *CH*Ar), 106.5 (*CH*OCH$_2$CCH$_3$), 104.8 (dd, J_{C-F} = 25.4 Hz, J_{C-F} = 27.8 Hz, *CH*Ar), 77.33, 77.36 (2OCH_2C(CH$_3$)$_2$), 69.7 (OCH_2CH$_3$), 46.5 (*CH*S), 41.4 (*C*H$_2$C(CH$_3$)$_2$), 40.6 (d, J = 7.6 Hz, *C*H$_2$CO), 38.3 (*C*(CH$_3$)$_2$), 31.8 (d, J_{C-F} = 1.6 Hz, *C*H$_2$CHS), 30.2 (*C*(CH$_3$)$_2$), 23.0 (*C*H$_3$), 22.7 (*C*H$_3$), 22.4 (*C*H$_3$), 21.8 (*C*H$_3$), 13.8 (OCH$_2$*C*H$_3$). IR ($CDCl_3$) 1681, 1606 cm^{-1}. MS (CI) 475 MH^+, 492 $MH^+NH_3^+$. HRMS (EI^+) [M−SCSOEt] 354.2019 (Measured mass), 354.2007 (Calculated mass).

4.2.19. *tert*-Butyl-5-(2,4-difluorophenyl)-2-(ethoxycarbonothioylthio)-5-oxopentyl(4-methoxybenzyl) carbamate 5t

The reaction was run in ethyl acetate (3.6 mL) with xanthate **4a** (1.0 g, 3.6 mmol), *tert*-butyl allyl(4-methoxybenzyl)carbamate (2.0 equiv, 2.0 g) and DLP (12.5%). Flash chromatography on a silica gel column using a gradient petroleum ether/ethyl acetate (9:1) afforded the addition product **5t** (1.93 g) as a yellow oil in 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dt, 1H, J_{H-F} = 6.7 Hz, J_{H-H} = 8.6 Hz, C*H*Ar), 7.21 (m, 2H, 2C*H*Ar), 6.95 (m, 1H, C*H*Ph), 6.86 (m, 3H, CHAr, C*H*Ph), 4.61 (q, 2H, J = 7.1 Hz, OCH_2CH$_3$), 4.56 (d, 1H, J = 5.7 Hz, NC*H*HPh), 4.43 (m, 1H, NCH*H*Ph), 4.04 (m, 1H, SC*H*), 3.78 (s, 3H, OCH_3), 3.60 (m, 1H, NC*H*HCHS), 3.32 (dd, 1H, J = 7.2 Hz, J = 14.4 Hz, NCH*H*CHS), 3.09 (m, 2H, CH_2CO), 2.23 (m, 1H, C*H*HCHS), 1.88 (m, 1H, CH*H*CHS), 1.48 (m, 9H, C(CH_3)$_3$), 1.38 (t, 3H, J = 7.1 Hz, OCH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.9 (*CS*), 195.8 (*CO*), 165.7 (dd, J_{C-F} = 11.6 Hz, J_{C-F} = 256.4 Hz, *CF*), 162.7 (dd, J_{C-F} = 12.4 Hz, J_{C-F} = 257.9 Hz, *CF*), 158.9 (*Cq*), 155.8 (*NCO*), 132.6 (dd, J_{C-F} = 4.1 Hz, J_{C-F} = 10.5 Hz, *CH*Ar), 130.2 (*Cq*), 129.3; 128.8 (*CH*Ph), 122.1 (*Cq*, dd, J_{C-F} = 3.5 Hz, J_{C-F} = 6.2 Hz), 113.9 (*CH*Ph), 112.1 (d, J_{C-F} = 21.4 Hz, *CH*Ar), 104.7 (dd, J_{C-F} = 25.6 Hz, J_{C-F} = 27.6 Hz, *CH*Ar), 80.3; 80.4 (O*C*(CH$_3$)$_3$), 70.1 (OCH$_2$CH$_3$), 55.2 (O*C*H$_3$), 49.5 (*CH*S), 49.3 (NCH_2Ph), 40.5 (*C*H$_2$CO), 29.6 (NCH_2CHS), 28.4 (C(CH_3)$_3$), 25.7; 25.2 (*C*H$_2$CHS), 13.7 (OCH$_2$CH_3). IR ($CDCl_3$) 1686, 1611 cm^{-1}. MS (CI) 454 M^+−Boc, 554 MH^+. HRMS (EI^+) 553.1777 (Measured mass), 553.1768 (Calculated mass).

4.3. General procedure for the preparation of benzothiepinones 7

To a degassed solution of xanthate (n mmol) in a 1:1mixture of ethanol and diethyl ether (n mL) was added ethylenediamine (4n mmol). The reaction mixture was stirred under nitrogen at room temperature for 20–30 min and then diluted with water. After extraction with diethyl ether the combined organic layers were washed with aqueous ammonium chloride and brine, respectively, dried over magnesium sulfate and concentrated under vacuum. The residue thus obtained was taken up in THF (10n mL) and DBU (1.1 equiv) was added to the solution. The reaction mixture was heated to reflux until there was complete consumption of the starting material and then was washed with aqueous ammonium chloride and extracted with diethyl ether. The organic layers were washed with brine, dried over magnesium sulfate and evaporated under vacuum. Finally, the residue was purified by column chromatography.

4.3.1. 8-Fluoro-2-hexyl-3,4-dihydro-2*H*-benzo[*b*]thiepin-5-one 7a

The reaction was carried out with xanthate **5a** (0.388 g, 1.0 mmol) and ethylenediamine (0.270 mL, 4 mmol) in a 1:1 mixture of ethanol and diethyl ether (1 mL). After 20 min, the mixture was treated according to the general procedure (THF, 10 mL and DBU, 0.170 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether 95:5) the bicyclic product **7a** (0.224 g) as a colourless oil in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (1H, ddd, J_{H-H} = 8.7 Hz, J_{H-F} = 6.1, C*H*Ar), 7.16 (1H, dd, J_{H-H} = 2.5 Hz, J_{H-F} = 9.0, C*H*Ar), 6.94 (1H, ddd, J_{H-H} = 2.5 and 8.7 Hz, J_{H-F} = 8.0 Hz, C*H*Ar), 3.35 (1H, ddd, J = 11.5, J = 6.7 Hz, COC*H*H), 2.95 (1H, dddd, J = 5.3, J = 12.5, J = 6.8, J = 6.8 Hz, C*H*S), 2.68 (1H, ddd, J = 11.5 Hz, J = 5.3 Hz, J = 3.2 Hz, COCH*H*), 2.35 (1H, dddd, J = 12.8 Hz, J = 5.3 Hz, J = 11.5 Hz, J = 5.3 Hz, C*H*H), 1.94 (1H, dddd, J = 12.8 Hz, J = 12.5 Hz, J = 6.7 Hz, J = 3.2 Hz, CH*H*), 1.65–1.60 (2H, m, CH_2), 1.48 (1H, m), 1.38 (1H, m), 1.26 (6H, m), 0.88–0.84 (3H, m, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6 (*C*O), 163.5 (d, J_{C-F} = 255.0 Hz, *C*F), 143.9 (d, J_{C-F} = 9.Hz, *C*F), 134.9 (*Cq*Ar), 132.4 (d, J_{C-F} = 9.5 Hz, *CH*Ar), 117.1 (d, J_{C-F} = 23.0 Hz, *CH*Ar), 113.6 (d, J_{C-F} = 22.0 Hz, *CH*Ar), 51.3 (*C*HS), 40.3, 35.8, 35.3, 31.6, 29.0, 27.4, 22.5 (CH_2), 14.0 (CH_3). IR (neat) 1681, 1597 cm^{-1}. MS (CI) 298 $(M+NH_4)^+$, 281 $(M+H)^+$. Anal. Calcd for $C_{16}H_{21}FOS$: C, 68.53; H, 7.55. Found: C, 68.35; H, 7.48.

4.3.2. 8-Fluoro-2-methylsilanylmethyl-3,4-dihydro-2H-benzo[*b*]thiepin-5-one 7b and 1-(4-fluoro-2-mercaptophenyl)pent-4-en-1-one 8

The reaction was carried out with xanthate **5b** (0.25 g, 0.64 mmol) and ethylenediamine (0.17 mL, 4.0 mmol) in a 1:1 mixture of ethanol and diethyl ether (0.64 mL). After 20 min, the mixture was treated according to the general procedure (THF, 6.4 mL and DBU, 0.10 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether 97:3) the bicyclic product **7b** (0.032 g) as a colourless oil in 18% yield and the olefinic product **8** (0.012 g) as a colourless oil in 9% yield. *Compound* **7b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, 1H, J_{H-F} = 6.1 Hz, J_{H-H} = 8.8 Hz, C*H*Ar), 7.13 (dd, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 9.0 Hz, C*H*Ar) 6.93 (ddd, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 7.8 Hz, J_{H-H} = 8.8 Hz, C*H*Ar), 3.36 (dt, 1H, J = 6.8 Hz, J = 11.5 Hz, C*H*HCO), 3.08 (m, 1H, SC*H*), 2.66 (ddd, 1H, J = 2.9 Hz, J = 5.3 Hz, J = 11.5 Hz, CH*H*CO), 2.39 (m, 1H, C*H*HCHS), 1.95 (m, 1H, CH*H*CHS), 1.14 (dd, 1H, J = 6.5 Hz, J = 14.6 Hz, C*H*HSiMe$_3$), 1.00 (dd, 1H, J = 8.8 Hz, J = 14.6 Hz, CH*H*SiMe$_3$), 0.03 (s, 9H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9 (*C*O), 163.6 (d, J_{C-F} = 255.3 Hz, *C*F), 144.7 (*C*q, d, J_{C-F} = 9.1 Hz), 134.5 (*C*q, d, J_{C-F} = 2.8 Hz), 132.5 (d, J_{C-F} = 9.6 Hz, *C*HAr), 116.7 (d, J_{C-F} = 23.1 Hz, *C*HAr), 113.7 (d, J_{C-F} = 21.8 Hz, *C*HAr), 49.0 (*C*HS), 40.8 (CH_2CO), 39.1 (CH_2), 24.9 (CH_2), −0.71 (SiCH_3). IR ($CDCl_3$) 2954, 2856, 2251, 1673, 1595, 1471, 1445, 1383, 1251, 1211, 1152, 1118 1065, 1008, 937. MS (CI) 283 MH^+. HRMS (EI^+) 282.0921 (Measured mass), 282.0910 (Calculated mass). *Compound* **8**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, 1H, J_{H-F} = 5.9 Hz, J_{H-H} = 8.7 Hz, C*H*Ar), 7.21 (m, 1H, C*H*Ar), 6.93 (m, 1H, C*H*Ar), 5.87 (tdd, 1H, J = 6.6 Hz, J = 10.2 Hz, J = 16.8 Hz, C*H*=CH_2), 5.04 (m, 2H, CH=CH_2), 4.26 (s, 1H, S*H*), 3.02 (t, 2H, J = 7.4 Hz, CH_2CO), 2.47 (m, 2H, CH_2CH=CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0 (*C*O), 164.82 (d, J_{C-F} = 255.5 Hz, *C*F), 143.6 (*C*q, d, J_{C-F} = 8.6 Hz), 137.1 (*C*H=CH_2), 132.6 (d, J_{C-F} = 9.9 Hz, *C*HAr), 131.4 (Cq), 115.6 (CH=*C*H_2), 113.81 (d, J_{C-F} = 25.2 Hz, *C*HAr), 111.8 (d, J_{C-F} = 21.9 Hz, *C*HAr), 39.0 (CH_2CO), 28.2 (CH_2). IR ($CDCl_3$) 1672, 1597 cm^{-1}. HRMS (EI^+) 210.0501 (Measured mass), 210.0515 (Calculated mass).

4.3.3. 9-(8-Fluoro-5-oxo-2,3,4,5-tetrahydro-benzo[*b*]thiepin-2-yl)-nonanoic acid methyl ester 7c

The reaction was carried out with xanthate **5c** (0.2 g, 0.42 mmol) and ethylenediamine (0.1 mL, 4 mmol) in a 1:1 mixture of ethanol and diethyl ether (0.42 mL). After 20 min, the mixture was treated according to the general procedure (THF, 4.2 mL and DBU, 0.07 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether 3:2) the bicyclic product **7c** (0.070 g) as a colourless oil in 46% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, 1H, J_{H-F} = 6.1 Hz, J_{H-H} = 8.7 Hz, C*H*Ar), 7.15 (dd, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 9.0 Hz, C*H*Ar), 6.93 (dt, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 8.3 Hz, C*H*Ar), 3.65 (s, 3H, CO_2CH_3), 3.34 (dt, 1H, J = 6.7 Hz, J = 11.5 Hz, C*H*HCO), 2.94 (dt, 1H, J = 6.7 Hz, J = 12.3 Hz, C*H*S), 2.68 (ddd, 1H, J = 3.2 Hz, J = 5.2 Hz, J = 11.6 Hz, CH*H*CO), 2.34 (m, 1H, C*H*HCO$_2$CH$_3$), 2.28 (m, 2H, CH*H*CO$_2$CH$_3$, C*H*HCHS), 1.92 (m, 1H, CH*H*CHS), 1.62 (m, 4H, CH_2CH_2CH_2), 1.48 (m, 1H, C*H*HCH$_2$), 1.36 (m, 1H, CH*H*CH$_2$), 1.26 (s, 8H, 4CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9 (*C*O), 174.3 (*C*O$_2$CH$_3$), 163.6 (d, J_{C-F} = 255.3 Hz, *C*F), 143.9 (*C*q, d, J_{C-F} = 9.2 Hz), 135.0 (*C*q, d, J_{C-F} = 2.8 Hz), 132.5 (d, J_{C-F} = 9.6 Hz, *C*HAr), 117.2 (d, J_{C-F} = 23.1 Hz, *C*HAr), 113.7 (d, J_{C-F} = 21.8 Hz, *C*HAr), 51.5, 51.3 (*C*HS, O*C*H$_3$), 40.4 (CH_2CO), 35.9 ($CH_2CO_2CH_3$), 35.3 (CH_2), 34.1(CH_2), 29.28 (CH_2), 29.25 (CH_2), 29.18 (CH_2), 29.15 (CH_2), 27.4 (CH_2), 24.9 (CH_2). IR ($CDCl_3$) 1728, 1673, 1594 cm^{-1}. MS (CI) 367 MH^+. HRMS (EI^+) 366.1684 (Measured mass), 366.1665 (Calculated mass).

4.3.4. 2-Benzyl-8-fluoro-3,4-dihydro-2*H*-benzo[*b*]thiepin-5-one 7d

The reaction was carried out with xanthate **5d** (0.5 g, 1.26 mmol) and ethylenediamine (0.34 mL, 4 mmol) in a 1:1 mixture of ethanol and diethyl ether (1.26 mL). After 20 min, the mixture was treated according to the general procedure (THF, 12 mL and DBU, 0.2 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether (95:5) the bicyclic product **7d** (0.220 g) as a colourless oil in 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, 1H, J_{H-F} = 6.1 Hz, J_{H-H} = 8.8 Hz, C*H*Ar) 7.29 (m, 2H, C*H*Ph) 7.23 (m, 1H, C*H*Ar) 7.15 (m, 3H, C*H*Ph) 6.96 (m, 1H, C*H*Ar) 3.27 (m, 2H, CH_2Ph), 3.05 (dd, 1H, C*H*HCO, J = 6.8 Hz, J = 13.9 Hz) 2.89 (dd, 1H, CH*H*CO, J = 7.7 Hz, J = 13.9 Hz), 2.69 (m, 1H, C*H*S) 2.26 (m, 1H, C*H*HCHS) 1.98 (m, 1H, CH*H*CHS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.7 (*C*O), 163.6 (d, J_{C-F} = 255.6 Hz, *C*F), 142.9 (*C*q, d, J_{C-F} = 9.2 Hz), 137.9 (*C*q), 135.1 (*C*q, d, J_{C-F} = 2.9 Hz), 132.5 (d, J_{C-F} = 9.6 Hz, *C*HAr), 129.1 (*C*HPh), 128.5 (*C*HPh), 126.9 (*C*HPh), 117.5 (d, J_{C-F} = 23.1 Hz, *C*HAr), 114.0 (d, J_{C-F} = 21.7 Hz, *C*HAr), 51.7 (*C*HS), 41.6 (CH_2Ph), 40.2 (CH_2CO), 34.9 (CH_2CHS). IR ($CDCl_3$) 1691, 1608 cm^{-1}. MS (CI) 287 MH^+, 304 $MH^+NH_3^+$. HRMS (EI^+) 286.0836 (Measured mass), 286.0828 (Calculated mass).

4.3.5. (8-Fluoro-5-oxo-2,3,4,5-tetrahydro-benzo[*b*]thiepin-2-ylmethyl)-carbamic acid *tert*-butyl ester 7e

The reaction was carried out with xanthate **5h** (0.433 g, 1.0 mmol) and ethylenediamine (0.270 mL, 4 mmol) in a 1:1 mix-

ture of ethanol/diethyl ether (1 mL). After 20 min, the mixture was treated according to the general procedure (THF, 10 mL and DBU, 0.170 mL) to furnish after purification on a silica gel column (petroleum ether/ethyl acetate 8:2) the bicyclic product **7e** (0.251 g) as a white solid in 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (1H, dd, J_{H-H} = 8.7 Hz, J_{H-F} = 6.1 Hz, C*H*Ar), 7.17 (1H, dd, J_{H-H} = 2.4 Hz, J_{H-F} = 8.8 Hz, C*H*Ar), 6.98 (1H, ddd, J_{H-H} = 2.4 and 8.7 Hz, J_{H-F} = 8.8 Hz, C*H*Ar), 5.01 (1H, m, *NH*), 3.47 (1H, m, COC*H*H), 3.28–3.10 (3H, m, C*H*S, CH_2NHBoc), 2.75 (1H, m, COCH*H*), 2.34 (1H, m, C*H*H), 1.88 (1H, m, CH*H*), 1.40 (9H, s, C*Me*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6 (*CO*), 163.7 (d, J_{C-F} = 256.0 Hz, *CF*), 155.7 (NCO), 140.5 (*Cq*S, d, J_{C-F} = 9.6 Hz), 135.8 (*Cq*Ar), 132.6 (d, J_{C-F} = 8.9 Hz, *CH*Ar), 118.4 (d, J_{C-F} = 23.1 Hz, *C*HAr), 114.6 (d, J_{C-F} = 21.9 Hz, *C*HAr), 79.9 (*Cq*Me$_3$), 51.4 (*C*HS), 44.2 (*CH*$_2$NHBoc), 40.0 (COCH$_2$), 31.8 (*CH*$_2$), 28.4 (C*Me*$_3$).

4.3.6. (8-Fluoro-5-oxo-2,3,4,5-tetrahydro-benzo[b]thiepin-2-ylmethyl)-methyl-carbamic acid *tert*-butyl ester 7f

The reaction was carried out with xanthate **5i** (1.34 g, 3.0 mmol) and ethylenediamine (0.8 mL, 12 mmol) in a 1:1 mixture of ethanol/diethyl ether (3 mL). After 30 min, the mixture was treated according to the general procedure (THF, 30 mL and DBU, 0.490 mL) to furnish after purification on a silica gel column (petroleum ether/ethyl acetate 8:2) the bicyclic product **7f** (0.661 g) as a yellow oil in 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (1H, dd, J_{H-H} = 8.6 Hz, J_{H-F} = 6.2 Hz, C*H*Ar), 7.18 (1H, dd, J_{H-H} = 2.4 Hz, J_{H-F} = 8.8 Hz, C*H*Ar), 7.00 (1H, ddd, J_{H-H} = 2.4 and 8.6 Hz, J_{H-F} = 8.1 Hz, C*H*Ar), 3.46–3.40 (2H, m), 3.33–3.25 (2H, m), 2.87 (3H, s, N*CH*$_3$), 2.77 (1H, td, *J* = 4.7 and 12.6 Hz, COC*H*H), 2.29 (1H, m, C*H*H), 1.91 (1H, m, CH*H*), 1.44 (9H, s, 3*Me*). ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.4 (*C*O), 163.7 (d, J_{C-F} = 255.7 Hz, *CF*), 155.7 (N*C*O), 141.3 (*Cq*S), 135.8 (*Cq*Ar), 132.5 (d, J_{C-F} = 9.3 Hz, *CH*Ar), 118.2 (d, J_{C-F} = 23.0 Hz, *C*HAr), 114.4 (CH, d, J_{C-F} = 21.8 Hz, *C*HAr), 80.0 (*Cq*Me$_3$), 52.5 (*C*H$_2$NMeBoc), 49.3 (*CHS*), 40.0 (COCH$_2$), 35.3 (NCH$_3$), 32.0 (*C*H$_2$), 28.4 (3*Me*). MS (CI) 357 (M+NH$_4$)$^+$, 340 (M+H)$^+$.

4.3.7. 2-Diethoxymethyl-8-fluoro-3,4-dihydro-2*H*-benzo[*b*]thiepin-5-one 7g

The reaction was carried out with xanthate **5l** (0.1 g, 0.25 mmol) and ethylenediamine (0.06 mL, 4 mmol) in a 1:1 mixture of ethanol and diethyl ether (0.24 mL). After 20 min, the mixture was treated according to the general procedure (THF, 2.5 mL and DBU, 0.03 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether (2:3) the bicyclic product **7g** (0.038 g) as a colourless oil in 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, 1H, J_{H-F} = 6.1 Hz, J_{H-H} = 8.8 Hz, C*H*Ar), 7.19 (dd, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 8.9 Hz, C*H*Ar), 6.96 (ddd, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 7.9 Hz, J_{H-H} = 8.7 Hz, C*H*Ar), 4.59 (d, 1H, *J* = 4.1 Hz, C*H*(OEt)$_2$), 3.70 (m, 2H, OC*H*$_2$CH$_3$), 3.52 (m, 2H, OC*H*$_2$CH$_3$), 3.33 (m, 1H, C*H*S), 3.18 (m, 1H, C*H*HCO), 2.73 (m, 1H, CH*H*CO), 2.35 (m, 1H, C*H*HCHS), 2.24 (m, 1H, CH*H*CHS), 1.21 (m, 6H, 2OCH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9 (*C*O), 163.7 (d, J_{C-F} = 255.6 Hz, *C*F), 142.8 (*C*q, d, J_{C-F} = 9.1 Hz), 135.5 (*C*q, d, J_{C-F} = 2.8 Hz), 132.6 (d, J_{C-F} = 9.6 Hz, *C*HAr), 117.8 (d, J_{C-F} = 23.1 Hz, *C*HAr), 114.1 (d, J_{C-F} = 21.7 Hz, *C*HAr), 103.4 (*C*H (EtO)$_2$), 64.3 (OCH$_2$CH$_3$), 63.9 (OCH$_2$CH$_3$), 53.8 (*C*HS), 39.8 (*C*H$_2$), 28.6 (*C*H$_2$), 15.3 (*C*H$_3$), 15.2 (*C*H$_3$). IR ($CDCl_3$) 1676, 1597 cm^{-1}. MS (CI) 253 MH$^+$−CH$_3$CH$_2$OH. HRMS (EI$^+$) 298.1049 (Measured mass), 298.1039 (Calculated mass).

4.3.8. 2-(2,3-Dimethoxy-benzyl)-8-fluoro-3,4-dihydro-2*H*-benzo[*b*]thiepin-5-one 7h

The reaction was carried out with xanthate **5q** (2.8 g, 6.0 mmol) and ethylenediamine (1.62 mL, 4 mmol) in a 1:1 mixture of ethanol and diethyl ether (6.0 mL). After 20 min, the mixture was treated according to the general procedure (THF, 60 mL and DBU, 0.9 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether (3:2) the bicyclic product **7h** (1.70 g) as a colourless oil in 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, 1H, J_{H-F} = 6.1 Hz, J_{H-H} = 8.8 Hz, C*H*Ar), 7.14 (dd, 1H, J_{H-F} = 2.5 Hz, J_{H-F} = 9.0 Hz, C*H*Ar), 6.94 (m, 2H, C*H*Ar, C*H*Ph), 6.81 (dd, 1H, *J* = 1.4 Hz, *J* = 8.2 Hz, C*H*Ph), 6.71 (dd, 1H, *J* = 1.4 Hz, *J* = 7.7 Hz, C*H*Ph), 3.84 (s, 3H, OC*H*$_3$), 3.79 (s, 3H, OC*H*$_3$), 3.30 (m, 2H,C*H*$_2$CO), 3.02 (dd, 1H, *J* = 7.1 Hz, *J* = 13.6 Hz, C*H*HPh), 2.91 (dd, 1H, *J* = 7.7 Hz, *J* = 13.6 Hz, CH*H*Ph), 2.68 (m, 1H, C*H*S), 2.25 (m, 1H, C*H*HCHS), 1.98 (m, 1H, CH*H*CHS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5 (*C*O), 163.3 (d, J_{C-F} = 255.2 Hz, *C*F), 152.5 (*C*q), 147.1 (*C*q), 142.7 (*C*q, d, J_{C-F} = 9.1 Hz), 135.1(Cq, d, J_{C-F} = 2.8 Hz), 132.2 (d, J_{C-F} = 9.6 Hz, *C*HAr), 131.6 (*C*q), 123.6 (*C*HPh), 122.3 (*C*HPh), 117.3 (d, J_{C-F} = 23.1 Hz, *C*HAr), 113.6 (d, J_{C-F} = 21.7 Hz, *C*HAr), 111.1 (*C*HPh), 60.3 (OCH$_3$), 55.4 (OCH$_3$), 50.8 (*C*HS), 40.1 (CH$_2$CO), 35.6 (*C*H$_2$Ph), 34.7 (*C*H$_2$). IR ($CDCl_3$) 1676, 1595 cm^{-1}. MS (CI) 347 MH$^+$, 364 MH$^+$NH$_3^+$. HRMS (EI$^+$) 346.0699 (Measured mass), 346.1039 (Calculated mass).

4.3.9. 2-(2-(5,5-Dimethyl-1,3-dioxan-2-yl)-2-methylpropyl)-8-fluoro-3,4-dihydrobenzo[*b*]thiepin-5(2*H*)-one 7i

The reaction was carried out with xanthate **5r** (0.55 g, 1.16 mmol) and ethylenediamine (0.31 mL, 4 mmol) in a 1:1 mixture of ethanol and diethyl ether (1.16 mL). After 20 min, the mixture was treated according to the general procedure (THF, 11.6 mL and DBU, 0.2 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether (95:5) the bicyclic product **7i** (0.301 g) as a colourless oil in 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, 1H, J_{H-F} = 6.1 Hz, J_{H-H} = 8.8 Hz, C*H*Ar), 7.11 (dd, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 9.0 Hz, C*H*Ar), 6.91 (ddd, 1H, J_{H-H} = 2.5 Hz, J_{H-F} = 8.0 Hz, J_{H-H} = 8.6 Hz, C*H*Ar), 4.02 (s, 1H, C*H*(OEt)$_2$), 3.52 (m, 2H, OC*H*$_2$CCH$_3$), 3.30 (m, 3H, OC*H*$_2$CCH$_3$, C*H*HCO), 3.07 (m, 1H, C*H*S) 2.61 (m, 1H, CH*H*CO), 2.34 (tdd, 1H, *J* = 5.3 Hz, *J* = 10.9 Hz, *J* = 13.1 Hz, C*H*HCHS), 1.94 (ddt, 1H, *J* = 3.1 Hz, *J* = 6.7 Hz, *J* = 13.0 Hz, CH*H*CHS), 1.74 (dd, 1H, *J* = 7.3 Hz, *J* = 15.0 Hz, C*H*HC(CH$_3$)$_2$), 1.63 (dd, 1H, *J* = 3.9 Hz, *J* = 15.1 Hz, CH*H*C(CH$_3$)$_2$), 1.07 (s, 3H, C*H*$_3$), 0.91 (s, 3H, C*H*$_3$), 0.89 (s, 3H, C*H*$_3$), 0.65 (s, 3H, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6 (*C*O), 163.4 (d, J_{C-F} = 253.5 Hz, *C*F), 144.1 (*C*q, d, J_{C-F} = 9.1 Hz), 134.8 (*C*q, d, J_{C-F} = 2.7 Hz), 132.3 (d, J_{C-F} = 9.6 Hz, *C*HAr), 116.9 (d, J_{C-F} = 23.0 Hz, *C*HAr), 113.6 (d, J_{C-F} = 21.8 Hz, *C*HAr), 106.7 (*C*H(OEt)$_2$), 77.2 (2OCH$_2$CCH$_3$)$_2$), 47.3 (*C*HS), 42.8 (*C*H$_2$C(CH$_3$)$_2$), 40.2 (*C*H$_2$CO), 38.4 (*C*H$_2$CHS), 37.9 (*C*(CH$_3$)$_2$CH(OEt)$_2$), 30.0 (*C*(CH$_3$)$_2$), 22.9 (*C*H$_3$), 22.8 (*C*H$_3$), 22.4 (*C*H$_3$), 21.6 (*C*H$_3$). IR ($CDCl_3$) 1680, 1591 cm^{-1}. MS (CI) 367 MH$^+$. HRMS (EI$^+$) 366.1660 (Measured mass), 366.1665 (Calculated mass).

4.3.10. 8-Fluoro-5-oxo-2,3,4,5-tetrahydro-1-benzothiepin-2-ylmethyl)-(4-methoxy-benzyl)carbamic acid *tert*-butyl ester 7j

The reaction was carried out with xanthate **5t** (03.5 g, 6.4 mmol) and ethylenediamine (1.7 mL, 4 mmol) in a 1:1 mixture of ethanol and diethyl ether (6.4 mL). After 20 min, the mixture was treated according to the general procedure (THF, 64 mL and DBU, 1.1 mL) to furnish after purification on a silica gel column (petroleum ether/diethyl ether (95:5) the bicyclic product **7j** (1.56 g) as a colourless oil in 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, 1H, J_{H-H} = 8.65, J_{H-F} = 6.1 Hz, C*H*Ar), 7.16 (m, 3H, C*H*Ar, 2C*H*Ph), 7.02 (m, 1H, C*H*Ar), 6.81 (m, 2H, C*H*Ph), 4.57 (m, 1H, NC*H*HPh), 4.33 (m, 1H, NCH*H*Ph), 3.80 (O*Me*), 3.29 (m, 4H, C*H*S, NC*H*$_2$CHS, C*H*HCO), 2.73 (m, 1H, CH*H*CO), 2.27 (m, 1H, C*H*HCHS), 1.86 (m, 1H, CH*H*CHS), 1.51 (s, 9H, (C*H*$_3$)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6 (*C*O), 163.7 (d, J_{H-F} = 255.7 Hz, *C*F), 159.0 (*C*q), 155.8 (N*C*O), 142.2; 141.5 (*C*q, m), 135.8; 135.2 (Cq, m), 132.5 (d, J_{H-F} = 9.5 Hz, *C*HAr), 129.9 (*C*q), 129.2; 128.5 (*C*HPh), 118.1 (t, J_{H-F} = 25.4 Hz, *C*HAr), 114.3 (d, J_{H-F} = 21.7 Hz, *C*HAr), 114.0 (*C*HPh), 80.5 (*C*(CH$_3$)$_3$), 55.3 (OCH$_3$), 51.1 (NCH$_2$Ph), 50.3 (*C*HS), 50.0; 49.8 (NCH$_2$CHS), 40.0 (*C*H$_2$), 32.7; 32.2 (*C*H$_2$), 28.4 (*C*H$_3$)$_3$. IR ($CDCl_3$)

1689, 1598 cm^{-1}. HRMS (EI^+) 445.1742 (Measured mass), 445.1723 (Calculated mass).

4.3.11. 9-Fluoro-2-methyl-2,3,3a,4,5,10b-hexahydro-1*H*-10bλ^4-thia-2-aza-benzo[*e*]azulen-6-one 10

To a solution of bicyclic product **7f** (0.576 g, 1.7 mmol) in ethanol (5 mL) were added a few drops of concentrated HCl. After 30 min the solution was concentrated and the residue dissolved in ethanol (5 mL). To this solution was added *p*-formaldehyde (0.510 g, 17 mmol). The reaction mixture was refluxed for 15 h. The same quantity of *p*-formaldehyde was added every 5 h until total consumption of the starting material. A solution of sodium hydroxide (1 M) was added and the resulting solution was extracted with diethyl ether four times. The organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure to give the yellowish salt **10** (0.19 g) after chromatography on a silica gel column (petroleum ether/dichloromethane/ethyl acetate/triethylamine) 9:0.5:0.5 in 39% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (1H, dd, J_{H-H} = 8.4 Hz, J_{H-F} = 5.9 Hz, C*H*Ar), 7.18 (1H, dd, J_{H-H} = 2.4 Hz, J_{H-F} = 8.9 Hz C*H*Ar), 7.00 (1H, ddd, J_{H-H} = 2.4 and 8.4 Hz, J_{H-F} = 8.4 Hz, C*H*Ar), 3.75 (1H, m, CHS), 3.52 (1H, d, *J* = 11.2 Hz, C*H*HCO), 3.47 (1H, d, *J* = 10.7 Hz, NC*H*HS), 3.40 (1H, d, *J* = 10.7 Hz, NCH*H*S), 2.84 (1H, dd, *J* = 1.5 and 12.3 Hz, MeNC*H*H), 2.40 (1H, dd, *J* = 1.8 et 15.0 Hz, C*H*H), 2.31 (1H, dd, *J* = 2.3 and 12.3 Hz, MeNCH*H*), 2.27 (3H, s, NMe), 1.89(1H, d, *J* = 11.2 Hz, CH*H*CO), 1.85 (IH, dd, *J* = 4.6 and 15.0 Hz, CH*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.4 (*C*O), 163.6 (d, J_{C-F} = 253.3 Hz, CF), 139.4 (*Cq*Ar), 135.1 (d, J_{C-F} = 8.6 Hz, Ar*Cq*S), 131.0 (d, J_{C-F} = 9.0 Hz, *CH*Ar), 118.6 (d, J_{C-F} = 23.0 Hz, *CH*Ar), 114.5 (d, J_{C-F} = 21.4 Hz, *CH*Ar), 68.8 (S*C*H_2), 60.4 (N*C*H_2CH), 59.9 (*C*H_2CO), 46.3 (N*C*H_3), 39.6 (*C*HS), 31.5(*C*H_2). MS (CI) 252 $(M+H)^+$.

4.4. General procedure for the preparation of sulfones

To a sulfide (n mol) solution in dichloromethane (10n mL/mmol) was added *m*-CPBA (2.7–3 equiv) at 0 °C and the reaction mixture was stirred at room temperature. After complete consumption of the starting sulfide, the reaction mixture was diluted with dichloromethane and washed with saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$. The combined organic layers were dried over $MgSO_4$.

4.4.1. 8-Fluoro-1,1,5-trioxo-2,3,4,5-tetrahydro-1*H*-1 λ^6-1-benzothiepin-2-lmethylmethyl-carbamic acid *tert*-butyl ester 11

The reaction was run with sulfide **7f** (0.24 g, 0.73 mmol) and *m*-CPBA (3.0 equiv, 0.378 g) in CH_2Cl_2 (7.3 mL). A white amorphous solid **11** (0.254 g) was isolated in 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (m, 2H, C*H*Ar), 7.43 (m, 1H, C*H*Ar), 3.64 (m, 3H, NC*H*$_2$CHS, C*H*S), 3.06 (m, 2H, C*H*$_2$CO), 2.94 (s, 3H, NC*H*$_3$), 2.24 (m, 1H, C*H*HCHS), 1.88 (m, 1H, CH*H*CHS), 1.44 (s, 9H, C (C*H*$_3$)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8 (*C*O), 164.1 (d, J_{C-F} = 258.8 Hz, *C*F), 156.2 (NCO), 138.0 (*C*q), 132.7 (d, J_{C-F} = 7.1 Hz, *C*HAr), 130.2 (*C*q), 121.7 (d, J_{C-F} = 21.4 Hz, *C*HAr), 115.7 (d, J_{C-F} = 22.2 Hz, *C*HAr), 80.6 (*C*(CH$_3$)$_3$), 61.9 (*C*HS), 48.0 (NCH$_2$), 38.2 (*C*H$_2$CO), 35.7 (NCH$_3$), 28.4 (C(*C*H$_3$)$_3$), 23.3 (*C*H$_2$). IR ($CDCl_3$) 1694, 1597 cm^{-1}. MS (CI) 372 MH^+. HRMS (EI^+) 371.1235 (Measured mass), 371.1203 (Calculated mass).

4.4.2. 8-Fluoro-1,1,5-trioxo-2,3,4,5-tetrahydro-1*H*-1 λ^6-1-benzothiepin-2-ylmethyl)-(4-methoxy-benzyl)-carbamic acid *tert*-butyl ester 17

The reaction was run with sulfide **7j** (1.2 g, 2.7 mmol) and *m*-CPBA (3.0 equiv, 1.39 g) in CH_2Cl_2 (27 mL). A yellow amorphous solid **17** (1.16 g) was isolated in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, 1H, J_{H-F} = 5.2 Hz, J_{H-H} = 7.8 Hz, C*H*Ar), 7.69 (dd, 1H, J_{H-H} = 2.6 Hz, J_{H-F} = 7.6 Hz, C*H*Ar), 7.42 (m, 1H, C*H*Ar), 7.17 (d, 2H, *J* = 6.9 Hz, C*H*Ph), 6.87 (d, 2H, *J* = 8.2 Hz, C*H*Ph), 4.63 (d, 1H, *J* = 15.5 Hz, NC*H*HPh), 4.32 (d, 1H, *J* = 15.3 Hz, NCH*H*Ph), 3.80 (s, 3H, OC*H*$_3$), 3.62 (m, 3H, C*H*S, NC*H*$_2$CHS), 3.00 (m, 2H, C*H*$_2$CO), 2.17 (m, 1H, C*H*HCHS), 1.82 (m, 1H, CH*H*CHS), 1.46 (s, 9H, C(C*H*$_3$)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7 (*C*O), 163.9 (d, J_{C-F} = 258.6 Hz, *C*F), 159.2 (*C*q), 155.9 (NCO), 137.9 (*C*q, d, J_{C-F} = 6.8 Hz), 133.9 (*C*q), 132.5 (d, J_{C-F} = 8.1 Hz, *C*HAr), 128.8 (*C*HPh), 121.5 (d, J_{C-F} = 21.3 Hz, *C*HAr), 115.5 (d, J_{C-F} = 25.3 Hz, *C*HAr), 114.1 (*C*HPh), 81.0 (*C*(CH$_3$)$_3$), 62.0 (*C*HS), 55.2 (OCH$_3$), 51.1 (NCH$_2$Ph), 45.5(NCH$_2$CHS), 38.0 (*C*H$_2$CO), 28.3 (C(*C*H$_3$)$_3$), 23.4 (*C*H$_2$). IR ($CDCl_3$) 1703, 1598 cm^{-1}. HRMS (EI^+) 477.1640 (Measured mass), 477.1621 (Calculated mass).

4.4.3. 5-Fluoro-12-methyl-2,2-dioxo-2 λ^6-thia-12-aza-tricyclo[8.3.1.0^{3,8}]tetradeca-3(8),4,6-trien-9-one 12a

To a solution of sulfone **11** (0.04 g, 0.1 mmol) in dry dichloromethane (0.75 mL) was added CF_3COOH (0.25 mL). The reaction mixture was stirred at room temperature until complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (0.1 mL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under nitrogen stream, were added acetic acid (1.0 mL) and *p*-formaldehyde (1.5 equiv, 0.004 g). The reaction mixture was refluxed until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford an amorphous solid **12a** (0.013 g) in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, 1H, J_{H-F} = 2.5 Hz, J_{H-H} = 8.3 Hz, C*H*Ar), 7.58 (dd, 1H, J_{H-H} = 5.2 Hz, J_{H-F} = 8.4 Hz, C*H*Ar), 7.21 (m, 1H, C*H*Ar), 3.45 (m, 2H, C*H*SO$_2$, C*H*CO), 3.00 (m, 2H, NC*H*$_2$CHSO$_2$), 2.62 (d, 1H, *J* = 12.9 Hz, NC*H*HCHCO), 2.46 (dd, 1H, *J* = 2.8 Hz, *J* = 12.8 Hz, NCH*H*CHCO), 2.26 (m, 1H, C*H*HCHSO$_2$), 2.11 (m, 1H, CH*H*CHSO$_2$), 1.90 (s, 3H, NC*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.7 (*C*O), 163.6 (d, *J* = 256.5 Hz, *C*F), 143.9 (*C*q, d, J_{C-F} = 2.0 Hz), 134.0 (*C*q, d, J_{C-F} = 3.7 Hz), 132.1 (d, J_{C-F} = 8.2 Hz, *C*HAr), 118.7 (d, J_{C-F} = 20.8 Hz, *C*HAr), 112.2 (d, *J* = 26.3 Hz, *C*HAr), 59.6 (*C*HSO$_2$), 53.9, 52.5 (NCH$_2$CHSO$_2$, NCH$_2$CHCO), 47.7 (*C*HCO), 45.0 (NCH$_3$), 26.0 (*C*H$_2$). IR ($CDCl_3$) 1684, 1598 cm^{-1}. HRMS (EI^+) 283.0671 (Measured mass), 283.0678 (Calculated mass).

4.4.4. 5-Fluoro-12-(4-methoxy-benzyl)-2,2-dioxo-2λ^6-thia-12-aza tricyclo[8.3.1.0^{3,8}]tetradeca-3(8),4,6-trien-9-one 18a

To a solution of sulfone **17** (0.26 g, 0.55 mmol) in dry dichloromethane (4.2 mL) was added CF_3COOH (1.4 mL). The reaction mixture was stirred at room temperature until complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (0.5 mL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under a nitrogen stream, were added CH_3COOH (5.0 mL), dioxane (5.0 mL) and *p*-formaldehyde (2 equiv, 0.031 g). The reaction mixture was refluxed until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford a white amorphous solid **18a** (0.096 g) in 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, 1H, J_{H-F} = 2.5 Hz, J_{H-H} = 8.3 Hz, C*H*Ar), 7.52 (dd, 1H, J_{H-H} = 5.2 Hz, J_{H-F} = 8.4 Hz, C*H*Ar), 7.27 (m, 1H, C*H*Ar), 6.64 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 6.38 (d, 2H, *J* = 8.5 Hz, C*H*Ph), 3.76 (s, 3H, OMe), 3.58 (dd, 1H, *J* = 1.4 Hz, *J* = 12.9 Hz, NC*H*HCHSO$_2$), 3.51 (m, 1H, C*H*SO$_2$), 3.28 (d, 1H, *J* = 12.8 Hz, NC*H*HPh), 3.09 (m, 1H, C*H*CO), 3.01 (m, 2H, NCH*H*Ph, NCH*H*CHCO), 2.71 (dd, 1H, *J* = 1.2 Hz, *J* = 12.7 Hz, NC*H*HCHCO), 2.52 (dd, 1H, *J* = 3.2 Hz, *J* = 12.9 Hz, NCH*H*CHSO$_2$), 2.17 (m, 2H, C*H*$_2$CHSO$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2 (*C*O), 163.8 (d, J_{C-F} = 256.8 Hz, *C*F), 159.1 (*C*q), 143.9 (*C*q, d, J_{C-F} = 9.4 Hz), 134.1

(*C*q, d, J_{C-F} = 4.0 Hz), 132.9 (d, J_{C-F} = 8.2 Hz, *C*HAr), 130.0 (*C*HPh), 128.1 (*C*q), 118.8 (d, J_{C-F} = 21.2 Hz, *C*HAr), 113.6 (*C*HPh), 112.5 (d, J_{C-F} = 26.3 Hz, *C*HAr), 61.8 (NCH$_2$Ph), 59.7 (*C*HSO$_2$), 55.3 (OMe), 51.5, 51.2 (NCH$_2$CHSO$_2$, NCH$_2$CHCO), 47.7 (*C*HCO), 26.4 (*C*H$_2$CHSO$_2$). IR ($CDCl_3$) 1684, 1612 cm^{-1}. MS (CI) 390 MH$^+$. HRMS (EI$^+$) 389.1093 (Measured mass), 389.1097 (Calculated mass).

4.4.5. 5-Fluoro-12-(4-methoxy-benzyl)-2,2-dioxo-11-trifluoro methyl-2λ^6-thia-12-azatricyclo[8.3.1.0^{3,8}]tetradeca-3(8),4,6-trien-9-one 18b

To a solution of sulfone **17** (0.1 g, 0.21 mmol) in dry dichloromethane (1.5 mL) was added CF_3COOH (0.5 mL). The reaction mixture was stirred at room temperature until complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (0.2 mL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under a nitrogen stream, were added CH_3COOH (2.0 mL), dioxane (2.0 mL) and trifluoroacetaldehyde methyl hemiacetal (4 equiv, 0.11 g). The reaction mixture was refluxed until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford a yellow oily product **18b** (0.062 g) in 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (m, 2H, C*H*Ar), 7.35 (m, 1H, C*H*Ar), 6.65 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 6.31 (d, 2H, *J* = 8.5 Hz, C*H*Ph), 3.78 (s, 3H, OCH$_3$), 3.60 (m, 1H, NC*H*HCHSO$_2$), 3.51 (m, 3H, NC*H*$_2$Ph, C*H*SO$_2$), 3.37 (m, 2H, NCH*H*CHSO$_2$, C*H*CO), 3.23 (q, 1H, J_{H-F} = 8.8 Hz, NC*H*CF$_3$), 2.89 (d, 1H, *J* = 15.9 Hz, C*H*HCHSO$_2$), 2.57 (td, 1H, *J* = 5.8 Hz, *J* = 15.9 Hz, C*H*HCHSO$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9 (*C*O), 164.2 (d, J_{C-F} = 258.3 Hz, *C*F), 159.3 (*C*q), 142.5 (*C*q, d, J_{C-F} = 6.8 Hz), 133.5 (d, J_{C-F} = 8.4 Hz, *C*HAr), 132.2 (*C*q, d, J_{C-F} = 4.0 Hz), 128.9 (m, *C*F$_3$), 130.7 (*C*HPh), 126.9 (*C*q), 119.6 (d, J_{C-F} = 21.2 Hz, *C*HAr), 113.8 (*C*HPh), 113.5 (d, J_{C-F} = 26.2 Hz, *C*HAr), 58.8 (NCH$_2$Ph), 58.5 (*C*HSO$_2$), 55.9 (d, J_{C-F} = 25.1 Hz, NCHCF$_3$), 55.3 (OCH$_3$), 46.0 (*C*HCO), 43.8 (NCH$_2$CHSO$_2$), 21.9 (*C*H$_2$CHSO$_2$). IR ($CDCl_3$) 1684, 1612 cm^{-1}. MS (CI) 458 MH$^+$. HRMS (EI$^+$) 457.0973 (Measured mass), 457.0971 (Calculated mass).

4.4.6. 11-Cyclopropyl-5-fluoro-12-(4-methoxy-benzyl)-2,2-dioxo-2λ^6-thia-12-aza tricyclo [8.3.1.0^{3,8}]tetradeca-3(8),4,6-trien-9-one 18c

To a solution of sulfone **17** (0.1 g, 0.20 mmol) in dry dichloromethane (1.35 mL) was added CF_3COOH (0.45 mL). The reaction mixture was stirred at room temperature until there was complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (0.18 mL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under a nitrogen stream, were added CH_3COOH (1.8 mL), dioxane (1.0 mL) and cyclopropanaldehyde (2 equiv, 0.01 mL). The reaction mixture was refluxed until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford an off white solid **18c** (0.051 g) in 60% yield. Recrystallisation from (AcOEt, PE). Mp 179–181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (td, 2H, J_{H-F} = 4.1 Hz, J_{H-H} = 8.3 Hz, C*H*Ar), 7.33 (m, 1H, C*H*Ar), 6.63 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 6.24 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 3.77 (s, 3H, OMe), 3.44 (d, 2H, *J* = 13.0 Hz, NC*H*$_2$Ph), 3.35 (dd, 2H, *J* = 2.8 Hz, *J* = 13.4 Hz, NC*H*HCHSO$_2$, C*H*SO$_2$), 3.27 (d, 1H, *J* = 5.8 Hz, C*H*CO), 3.07 (dd, 1H, *J* = 3.8 Hz, *J* = 13.6 Hz, NCH*H*CHSO$_2$), 2.91 (dd, 1H, *J* = 1.5 Hz, *J* = 15.5 Hz, C*H*HCHSO$_2$), 2.52 (td, 1H, *J* = 5.7 Hz, *J* = 15.5 Hz, CH*H*CHSO$_2$), 1.89 (d, 1H, *J* = 9.8 Hz, NC*H*CHCO), 1.12 (m, 1H, NCHC*H*cyclopr), 0.77 (m, 1H, C*H*Hcyclopr), 0.53 (ddd, 1H, *J* = 5.2 Hz, *J* = 9.0 Hz, *J* = 14.0 Hz, CH*H*cyclopr), 0.32 (dt, 1H, *J* = 5.0 Hz, *J* = 10.0 Hz, C*H*Hcyclopr), −0.02 (dt, 1H, *J* = 5.1 Hz, *J* = 10.7 Hz, CH*H*cyclopr). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4 (*C*O), 163.8 (d, J_{C-F} = 256.9 Hz, *C*F), 158.9 (*C*q), 143.0 (*C*q, d, J_{C-F} = 6.8 Hz), 133.7 (*C*q, d, J_{C-F} = 4.0 Hz), 133.0 (d, J_{C-F} = 8.1 Hz, *C*HAr), 130.1 (*C*HPh), 128.6 (*C*q), 118.9 (d, J_{C-F} = 21.2 Hz, *C*HAr), 113.5 (*C*HPh), 113.0 (d, J_{C-F} = 26.2 Hz, *C*HAr), 61.7 (*C*HSO$_2$), 59.1 (*C*H), 58.8 (NC*H*$_2$Ph), 55.3 (OMe), 52.9 (*C*HCO), 44.0 (NC*H*$_2$CHSO$_2$), 22.2 (*C*H$_2$), 8.0 (*C*H$_2$), 5.9 (*C*H), 0.8 (*C*H$_2$). IR ($CDCl_3$) 1677, 1612 cm^{-1}. MS (CI) 430 MH$^+$ HRMS (EI$^+$) 429.1373 (Measured mass), 429.1410 (Calculated mass).

4.4.7. 5-Fluoro-12-(4-methoxy-benzyl)-2,2-dioxo-11-pentyl-2 λ^6-thia-12-azatricyclo[8.3.1.0^{3,8}] tetradeca-3(8),4,6-trien-9-one 18d

To a solution of sulfone **17** (0.03 g, 0.06 mmol) in dry dichloromethane (0.45 mL) was added CF_3COOH (0.15 mL). The reaction mixture was stirred at room temperature until complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (60 μL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under a nitrogen stream, were added CH_3COOH (0.2 mL), dioxane (0.4 mL) and hexanal (2 equiv, 0.01 mL).The reaction mixture was heated at 60 °C until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford a light yellow oily product **18d** (0.012 g) in 43% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, 1H, J_{H-F} = 2.4 Hz, J_{H-H} = 8.3 Hz, C*H*Ar), 7.59 (dd, 1H, J_{H-H} = 5.3 Hz, J_{H-F} = 8.4 Hz, C*H*Ar), 7.30 (m, 1H, C*H*Ar), 6.62 (d, 2H, *J* = 8.4 Hz, C*H*Ph), 6.26 (d, 2H, *J* = 8.4 Hz, C*H*Ph), 3.77 (s, 3H, OMe), 3.39 (m, 1H, C*H*SO$_2$), 3.31 (d, 1H, *J* = 13.5 Hz, NC*H*HCHSO$_2$), 3.23 (br s, 2H, NC*H*$_2$Ph), 3.04 (bd, 1H, *J* = 5.7 Hz, C*H*CO), 2.94 (dd, 1H, *J* = 3.4 Hz, *J* = 13.5 Hz, NCH*H*CHSO$_2$), 2.83 (bd, 1H, *J* = 15.5 Hz, C*H*HCHSO$_2$), 2.51 (bd, 1H, *J* = 10.3 Hz, NC*H*CHCO), 2.38 (td, 1H, *J* = 5.7 Hz, *J* = 15.6 Hz, CH*H*CHSO$_2$), 1.27 (m, 8H, 4C*H*$_2$), 0.89 (t, 3H, *J* = 6.7 Hz, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3 (*C*O), 163.9 (d, J_{C-F} = 256.8 Hz, *C*F), 159.0 (*C*q), 143.5 (d, J_{C-F} = 7.0 Hz, *C*q), 133.6 (*C*q, d, *J* = 3.7 Hz), 133.2 (d, J_{C-F} = 8.1 Hz, *C*HAr), 130.3 (*C*HPh), 128.2 (*C*q), 118.8 (d, J_{C-F} = 21.2 Hz, *C*HAr), 113.6 (*C*HPh), 112.6 (d, J_{C-F} = 26.1 Hz, *C*HAr), 59.3 (*C*HSO$_2$), 58.1 (NC*H*$_2$Ph), 55.5, 55.3 (N*C*H, OMe), 49.7 (*C*HCO), 44.1 (NC*H*$_2$CHSO$_2$), 32.0 (*C*H$_2$), 26.8 (*C*H$_2$), 22.6 (*C*H$_2$), 21.4 (*C*H$_2$), 21.3 (*C*H$_2$), 14.0 (*C*H$_3$). IR ($CDCl_3$) 1678, 1598 cm^{-1} MS (CI) 460 MH$^+$. HRMS (EI$^+$) 459.1880 (Measured mass), 459.1880 (Calculated mass).

4.4.8. 5-Fluoro-12-(4-methoxy-benzyl)-2,2-dioxo-11-thiophen-3-yl-2λ^6-thia-12-aza-tricyclo[8.3.1.0^{3,8}]tetradeca-3(8),4,6-trien-9-one 18e

To a solution of sulfone **17** (0.05 g, 0.10 mmol) in dry dichloromethane (0.75 mL) was added CF_3COOH (0.25 mL). The reaction mixture was stirred at room temperature until there was complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (0.1 mL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under nitrogen stream, were added CH_3COOH (1.0 mL), dioxane (1.0 mL) and 3-thiophenaldehyde (2 equiv, 0.024 g).The reaction mixture was refluxed until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford an off white solid **18e** (0.044 g) in 95% yield. Recrystallisation from (EtOAc, PE). Mp 173–175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, 1H, J_{H-F} = 2.6 Hz, J_{H-H} = 8.3 Hz, C*H*Ar), 7.63 (dd, 1H, J_{H-H} = 5.2 Hz, J_{H-F} =8.4 Hz, C*H*Ar), 7.37 (dd, 1H, *J* = 2.9 Hz, *J* = 5.0 Hz, C*H*thp), 7.33 (m, 1H, C*H*Ar), 7.11 (dd, 1H, *J* = 1.3 Hz, *J* = 2.8 Hz, C*H*thp), 6.95 (dd, 1H, *J* = 1.3 Hz, *J* = 5.0 Hz, C*H*thp), 6.60 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 6.19 (d, 2H, *J* = 8.6 Hz, C*H*Ph),

3.87 (s, 1H, NC*H*), 3.77 (s, 3H, OMe), 3.62 (m, 1H, C*H*SO_2), 3.46 (m, 2H, NCH_2CHSO_2), 3.15 (m, 3H, C*H*CO, NCH_2Ph), 2.93 (d, 1H, *J* = 15.7 Hz, C*H*HCHSO_2), 2.63 (m, 1H, CH*H*CHSO_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6 (*C*O), 163.9 (d, J_{C-F} = 257.1 Hz, *C*F), 159.0, (*C*q), 142.9 (*C*q d, J_{C-F} = 6.9 Hz), 138.5 (*C*q), 133.3 (d,,J_{C-F} = 8.0 Hz, *C*HAr), 130.2 (*C*HPh), 128.1 (*C*q), 127.9 (*C*Hthp), 126.4 (*C*Hthp), 123.0 (*C*Hthp), 119.2 (d, J_{C-F} = 21.3 Hz, *C*HAr), 113.5 (*C*HPh), 112.8 (d, J_{C-F} = 26.2 Hz, *C*HAr), 59.3 (*C*HSO_2), 58.5 (NCH_2Ph), 55.3 (OCH_3), 54.6 (NCH), 53.0 (*C*HCO), 45.2 (NCH_2CHSO_2), 21.8 (*C*H_2CHSO_2). IR ($CDCl_3$) 1681, 1612 cm^{-1}. MS (CI) 472 MH$^+$. HRMS (EI$^+$) 471.0974 (Measured mass), 471.0974 (Calculated mass).

4.4.9. 5-Fluoro-12-(4-methoxy-benzyl)-11-(3-methyl-pyridin-2-yl)-2,2-dioxo-2λ^6-thia-12-aza-tricyclo[8.3.1.0^{3,8}]tetradeca-3(8),4,6-trien-9-one 18f

To a solution of sulfone **17** (0.05 g, 0.1 mmol) in dry dichloromethane (0.75 mL) was added CF_3COOH (0.25 mL). The reaction mixture was stirred at room temperature until there was complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (0.1 mL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under a nitrogen stream, were added CH_3COOH (1.0 mL), dioxane (1.0 mL) and 6-methyl-2-pyridincarboxaldehyde (2 equiv, 0.024 mg). The reaction mixture was refluxed until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford a yellow oil **18f** (0.033 g) in 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, 1H, J_{H-F} = 2.6 Hz, J_{H-H} = 8.3 Hz, C*H*Ar), 7.64 (dd, 1H, J_{H-H} = 5.2 Hz, J_{H-F} = 8.4 Hz, C*H*Ar), 7.50 (t, 1H, *J* = 7.7 Hz, C*H*Pyr), 7.33 (m, 1H, C*H*Ar), 7.07 (d, 1H, *J* = 7.7 Hz, C*H*Pyr), 6.67 (d, 1H, *J* = 7.6 Hz, C*H*Pyr), 6.59 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 6.17 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 4.22 (dd, 1H, *J* = 3.9 Hz, *J* = 12.9 Hz, NC*H*HCHSO_2), 3.77 (s, 3H, OMe), 3.66 (m, 1H, C*H*SO_2), 3.54 (br s, 1H, NC*H*Pyr), 3.36 (m, 2H, NCH*H*CHSO_2, C*H*HCHSO_2), 3.16 (m, 2H, NC*H*HPh, C*H*CO), 3.10 (d, 1H, *J* = 13.0 Hz, NCH*H*Ph), 2.82 (dd, 1H, *J* = 1.3 Hz, *J* = 14.9 Hz, CH*H*CHSO_2), 2.57 (s, 3H, CH_3).^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1 (*C*O), 164.0 (d, J_{C-F} = 256.6 Hz, *C*F), 159.3 (*C*q), 158.9 (*C*q), 158.0 (*C*q), 143.3 (*C*q, d, *J* = 6.6 Hz), 136.7 (*C*HPyr), 133.4 (*C*q, d, *J* = 3.9 Hz), 133.1 (d, J_{C-F} = 8.2 Hz, *C*HAr), 130.1 (*C*HPh), 128.6 (*C*q), 122.1 (*C*HPyr), 120.5 (*C*HPyr), 118.9 (d, J_{C-F} = 21.3 Hz, *C*HAr), 113.5 (*C*HPh), 112.7 (d, J_{C-F} = 26.1 Hz, *C*HAr), 60.3 (*C*HSO_2), 58.3 (NCH_2Ph), 57.8 (NCH), 55.3 (OMe), 52.4 (*C*HCO), 45.2 (NCH_2CHSO_2), 24.9 (*C*H_3), 21.3 (*C*H_2CHSO_2). IR ($CDCl_3$) 1682, 1598 cm^{-1}. MS (CI) 481MH$^+$. HRMS (EI$^+$) 480.1502 (Measured mass), 480.1519 (Calculated mass).

4.4.10. 5-Fluoro-12-(4-methoxy-benzyl)-2,2-dioxo-11-pyridin-4-yl-2λ^6-thia-12-aza-tricyclo[8.3.1.0^{3,8}]tetradeca-3(8),4,6-trien-9-one 18g

To a solution of sulfone **17** (0.05 g, 0.1 mmol) in dry dichloromethane (0.75 mL) was added CF_3COOH (0.25 mL). The reaction mixture was stirred at room temperature until there was complete consumption of the starting sulfone. After concentrating the reaction mixture under reduced pressure without heating, Et_3N (0.1 mL) was added and the reaction mixture was stirred at room temperature for 5 min. To the residue, obtained after evaporation of Et_3N under a nitrogen stream, were added CH_3COOH (1.0 mL), dioxane (1.0 mL) and 4-pyridinecarboxaldehyde (2 equiv, 0.02 mL).The reaction mixture was refluxed until there was no more intermediate product and then evaporated under reduced pressure. The residue thus obtained was purified on silica gel (petroleum ether/diethyl ether (9:1) to afford a light yellow solid product **18g** (0.045 g) in 97% yield. Recrystallisation from (EtOAc, PE). Mp 191–192 °C. ^{1}H NMR (400 MHz, DMSO) δ 8.56 (dd, 2H, *J* = 1.4 Hz, *J* = 4.6 Hz, C*H*pyr), 7.74 (m, 2H, C*H*Ar), 7.47 (dd, 1H, J_{H-H} = 2.2 Hz, J_{H-F} = 8.3 Hz, C*H*Ar), 7.39 (dd, 2H, *J* = 1.4 Hz, *J* = 4.7 Hz,C*H*pyr) 6.65 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 6.25 (d, 2H, *J* = 8.6 Hz, C*H*Ph), 3.98 (br s, 2H, CHSO_2, NC*H*Pyr), 3.72 (s, 3H, OMe), 3.56 (dd, 1H, *J* = 4.2 Hz, *J* = 14.1 Hz, NC*H*HCHSO_2), 3.19 (d, 1H, *J* = 14.1 Hz, CH*H*CHSO_2), 3.13 (d, 1H, *J* = 13.1 Hz, C*H*HPh), 3.07 (d, 1H, *J* = 13.0 Hz, CH*H*Ph), 2.98 (d, 1H, *J* = 3.8 Hz, C*H*CO), 2.61 (m, 2H, CH_2CHSO_2).^{13}C NMR (100 MHz, DMSO) δ 202.8 (*C*O), 162.6 (d, J_{C-F} = 253.2 Hz, *C*F), 158.1(*C*q), 149.5 (*C*Hpyr), 148.4 (*C*q), 140.8 (d, *J* = 7.0 Hz, *C*q), 133.5 (*C*q, d, J_{C-F} = 3.7 Hz), 132.8 (d, J_{C-F} = 8.6 Hz, *C*HAr), 129.8 (*C*HPh), 128.1(*C*q), 123.4 (*C*Hpyr), 119.6 (d, J_{C-F} = 21.7 Hz, *C*HAr), 112.9 *C*HPh), 111.57 (d, 1H, J_{C-F} = 26.3 Hz, *C*HAr), 57.8, 57.7 (NCHCHCO, CHSO_2), 57.2 (NCH_2Ph), 54.7 (OCH_3), 52.0 (*C*HCO), 42.9 (NCH_2SO_2), 20.8 (*C*H_2CHSO_2). IR (nujol) 1678, 1615, 1596 cm^{-1}. MS (CI) 467 MH$^+$. HRMS (EI$^+$) 466.1361 (Measured mass), 466.1363 (Calculated mass).

4.4.11. 7-Fluoro-2-hexyl-1,2-dihydro-4*H*-thieno[2,3-*b*][1]benzothiopyran-4-one 19a

The reaction was carried out with xanthate **5a** (0.155 g, 0.4 mmol) and potassium carbonate (0.280 g, 2 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (4 mL). After 1 h 45 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/dichloromethane 5:5) the tricyclic product **19a** (0.119 g) as white crystals in 92% yield. Mp 84–85 °C (recrystallisation from Et_2O at 0 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.51 (1H, dd, J_{H-H} = 9.6 Hz, J_{H-F} = 6.0 Hz, C*H*Ar), 7.26–7.15 (2H, m, 2C*H*Ar), 4.05 (1H, m, C*H*S), 3.52 (1H. dd, *J* = 16.0 and 8.6 Hz, C*H*HCHS), 3.17 (1H, dd, *J* = 16.0 and 6.5 Hz, CH*H*CHS), 1.85–1.71 (2H, m, CH_2), 1.45–1.21 (8H, m, 4CH_2), 0.89 (3H, m, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2 4 (*C*O), 163.6 (d, J_{C-F} = 255.0 Hz, *C*F), 152.5 (S*Cq*S), 138.3 (d, J_{C-F} = 9.5 Hz, Ar*Cq*S), 131.5 (d, J_{C-F} = 9.4 Hz, *C*HAr), 130.5, 127.3 (2*Cq*), 115.7 (d, J_{C-F} = 22.3 Hz, *C*HAr), 111.8 (d, J_{C-F} = 24.7 Hz, *C*HAr), 52.1 (*C*HS), 40.5, 36.5, 31.6, 28.9, 27.9, 22.5 (*C*H_2), 14.0 (*C*H_3). IR ($CC1_4$) 1622, 1598 cm^{-1}. MS (CI) 323 (M+H)$^+$. Anal. Calcd for $C_{17}H_{19}FOS_2$: C, 63.32; H, 5.94. Found: C, 62.91; H, 5.91.

4.4.12. 7-Fluoro-2-trimethylsilylmethyl-1,2-dihydro-4*H*-thieno[2,3-*b*)][1]benzothiopyran-4-one 19b

The reaction was carried out with xanthate **5b** (0.390 g, 1 mmol) and potassium carbonate (0.690 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (10 mL). After 5 h 30 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/dichloromethane 5:5) the tricyclic product **19b** (0.240 g) as beige crystals in 74% yield. Mp 119–120 °C (recrystallisation from *i*Pr_2O at −20 °C). ^{1}H NMR (400 MHz, $CDCl_3$) 8.40 (1H, dd, J_{H-H} = 8.8 Hz, J_{H-F} = 5.9 Hz, C*H*Ar), 7.12–7.06 (2H, m, 2C*H*Ar), 4.22 (1H, m, C*H*S), 3.49 (1H, dd, *J* = 8.0 and 15.6 Hz, C*H*HCHS), 2.97 (1H, dd, *J* = 8.6 and 15.6 Hz, CH*H*CHS), 1.23 (1H, dd, *J* = 8.5 and 14.5 Hz, C*H*HSiMe_3), 1.17 (1H, dd, *J* = 7.0 and 14.5 Hz, CH*H*SiMe_3), 0.05 (9H, s, SiMe_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9 (*C*O), 163.3 (d, J_{C-F} = 255.1 Hz, *C*F), 153.0 (S*Cq*S), 138.1 (d, J_{C-F} = 9.7 Hz, Ar*Cq*S), 131.4 (d, J_{C-F} = 9.6 Hz, *C*HAr), 130.7, 127.2 (2*Cq*), 115.7 (d, J_{C-F} = 22.1 Hz, *C*HAr), 111.7 (d, J_{C-F} = 24.7 Hz, *C*HAr), 50.2 (*C*HS), 43.0 (*C*H_2), 24.6 (*C*H_2SiMe_3), −1.0 (Si*Me*$_3$). IR ($CC1_4$) 1621, 1597. MS (CI) 325 (M+H)$^+$. Anal. Calcd for $C_{15}H_{17}FOS_2Si$: C, 55.52; H, 5.28. Found: C, 55.39; H, 5.27.

4.4.13. 2-Benzyl-7-fluoro-2,3-dihydro-thieno[2,3-*b*]thiochromen-4-one 19c

The reaction was carried out with xanthate **5d** (0.514 g, 1.30 mmol) and potassium carbonate (0.897 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (13 mL). After 3 h 30 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/diethyl ether

8:2) the tricyclic product **19c** (0.255 g) as light pink crystals in 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (dd, 1H, J_{H-F} = 5.9 Hz, J_{H-H} = 9.6 Hz, C*H*Ar), 7.33 (m, 2H, C*H*Ph), 7.22 (m, 5H, C*H*Ar, C*H*Ph), 4.29 (tt, 1H, J = 6.5 Hz, J = 8.4 Hz, C*H*S) 3.47 (dd, 1H, J = 8.4 Hz, J = 16.1 Hz, C*H*HPh) 3.32 (dd, 1H, J = 5.9 Hz, J = 16.1 Hz, CH*H*Ph), 3.12 (dd, 1H, J = 6.7 Hz, J = 14.0 Hz, C*H*HCCO), 3.04 (dd, 1H, J = 8.5 Hz, J = 13.9 Hz, CH*H*CCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5 (*C*O), 163.6 (d, J_{C-F} = 255.3 Hz, *C*F), 152.6 (*C*q), 138.4 (*C*q, d, J_{C-F} = 9.7 Hz), 138.1 (*C*q), 131.6 (d, J_{C-F} = 9.6 Hz, *C*HAr), 130.3 (*C*q), 129.1 (2 *C*HPh), 128.8 (2*C*HPh), 127.4 (*C*q, d, J_{C-F} = 2.3 Hz), 127.1 (*C*HPh), 116.0 (d, J_{C-F} = 22.2 Hz, *C*HAr), 112.0 (d, J_{C-F} = 24.9 Hz, *C*HAr), 53.0 (*C*HS), 42.4 (*C*H$_2$), 40.0 (*C*H$_2$). IR ($CDCl_3$) 1620, 1596, cm^{-1}. MS (CI) 329 MH$^+$. HRMS (EI$^+$) 328.0392 (Measured mass), 328.0392 (Calculated mass).

4.4.14. *N*-(7-Fluoro-4-oxo-2,3-dihydro-4*H*-thieno[2,3-*b*]thiochromen-2-ylmethyl)-acetamide 19d

The reaction was carried out with xanthate **5g** (.050 g, 0.13 mmol) and potassium carbonate (0.089 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (1.3 mL). After 3 h 30 min, the mixture was extracted with diethyl ether, which furnished an off white crystalline tricyclic product **19d** (0.038 g) in 96% yield. ^{1}H NMR (400 MHz, DMSO) δ 8.52 (dd, 1H, J_{H-F} = 5.9 Hz, J_{H-H} = 9.6 Hz, C*H*Ar), 7.22 (m, 2H, C*H*Ar), 5.9 (br s, 1H, N*H*Ac), 4.23 (ddt, 1H, J = 3.8 Hz, J = 6.4 Hz, J = 8.3 Hz, C*H*S), 3.54 (td, 1H, J = 6.3 Hz, J = 13.6 Hz, C*H*HCCO), 3.38 (m, 3H, CH*H*CCO, C*H*$_2$NH), 2.01 (s, 3H, Ac). ^{13}C NMR (100 MHz, DMSO) δ 173.1 (*C*O), 169.5 (*C*OCH$_3$), 162.8 (d, J_{C-F} = 252.4 Hz, *C*F), 151.3 (*C*q), 137.6 (*C*q, d, J_{C-F} = 10.4 Hz), 130.7 (d, J_{C-F} = 9.9 Hz, *C*HAr), 129.6 (*C*q), 126.7 (*C*q, d, J_{C-F} = 2.2 Hz), 116.0 (d, J_{C-F} = 22.7 Hz, *C*HAr), 112.7 (d, J_{C-F} = 25.7 Hz, *C*HAr), 49.6 (*C*HS), 42.9 (*C*H$_2$), 37.3 (*C*H$_2$), 22.3 (CO*C*H$_3$). IR (nujol) 1650, 1616, 1591 cm^{-1}. MS (CI) 310 MH$^+$. HRMS (EI$^+$) 309.0287 (Measured mass), 309.0294 (Calculated mass).

4.4.15. 2-(*tert*-Butoxycarbonylamino-methyl)-7-fluoro-1,2-dihydro-4*H*-thieno[2,3-*b*)][1] benzo thio pyran-4-one 19e

The reaction was carried out with xanthate **5h** (0.433 g, 1 mmol) and potassium carbonate (0.690 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (10 mL). After 45 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/dichloromethane 8:2, 7.5:2.5) the tricyclic product **19e** (0.216 g) as pale yellow crystals in 59% yield. Mp 155–156 °C (recrystallisation from ethyl acetate at −20 °C). ^{1}H NMR (400 MHz, $CDCl_3$) 8.43 (1H, dd, J_{H-H} = 9.6 Hz, J_{H-F} = 5.9 Hz, C*H*Ar), 7.16–7.12 (2H, m, 2C*H*Ar), 5.35 (1H, m, *NH*), 4.17 (1H, m, C*H*S), 3.39–3.27 (4H, m, NC*H*$_2$, C*H*$_2$), 1.40 (9H, s, C*Me*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4 (*CO*), 163.5 (d, J_{C-F} = 256.0 Hz, *CF*), (155.8 NH*CO*), 152.0 (S*Cq*S), 138.3 (d, J_{C-F} = 9.7 Hz, Ar*Cq*S), 131.5 (d, J_{C-F} = 9.5 Hz, *CH*Ar), 129.9, 127.1 (2*Cq*), 115.9 (d, J_{C-F} = 22.0 Hz, *CH*Ar), 111.9 (d, J_{C-F} = 24.8 Hz, *CH*Ar), 79.8 (*Cq*Me$_3$), 50.3 (*CHS*), 45.2 (N*CH*$_2$), 37.7 (*CH*$_2$), 28.3 (*Me*$_3$). IR ($CC1_4$) 1721, 1622, 1599 cm^{-1}. MS (CI) 368 (M+H)$^+$. Anal. Calcd for $C_{17}H_{18}FNO_3S_2$: C, 57.57; H, 4.94. Found: C, 57.78; H, 4.95.

4.4.16. 7-Fluoro-4-oxo-1,2-dihydro-4*H*-thieno[2,3-*b*][1] benzothiopyran-2-ylmethyl-phosphonic acid diethyl ester 19f

The reaction was carried out with xanthate **5k** (0.4543 g, 1 mmol) and potassium carbonate (0.690 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (10 mL). After 2 h 45 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (gradient dichloromethane/ethyl acetate 5:5, 3:7) the tricyclic product **19f** (0.236 g) as yellow crystals in 61% yield. Mp 99–100 °C (recrystallisation from ethyl acetate at −20 °C). ^{1}H NMR (200 MHz, $CDCl_3$) 8.45 (1H, dd, J_{H-H} = 9.7 Hz, J_{H-F} = 5.8 Hz, C*H*Ar), 7.21–7.13 (2H, m, 2 *CH*Ar), 4.32 (1H, m, C*H*S), 4.20–4.04 (4H, m, 2P(O)OC*H*$_2$CH$_3$), 3.58 (1H, dd, J = 8.4 and 16.1 Hz, C*H*HCHS), 3.16 (1H, dd, J = 6.9 and 16.1 Hz, CH*H*CHS), 2.36–2.22 (2H, m, *CH*$_2$P), 1.40–1.29 (6H, m, 2P(O)OCH$_2$*CH*$_3$). ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.7 (*CO*), 163.3 (d, J_{C-F} = 255.2 Hz, *CF*), 151.8 (S*Cq*S), 137.9 (d, J_{C-F} = 9.6 Hz, Ar*Cq*S), 131.2 (d, J_{C-F} = 9.6 Hz, *CH*Ar), 129.5, 127.0 (2*Cq*), 115.6 (d, J_{C-F} = 22.3 Hz, *CH*Ar), 111.7 (d, J_{C-F} = 24.9 Hz, *CH*Ar), 61.9 (d, J_{C-P} = 6.0 Hz, 2P(O)O*CH*$_2$CH$_3$), 45.2 (d, J_{C-P} = 2.6 Hz *CHS*), 41.4 (d, J_{C-P} = 11.5 Hz, *CH*$_2$), 32.8 (d, J_{C-P} = 139.9 Hz, *CH*$_2$P), 16.2 (d, J_{C-P} = 5.4 Hz, 2P(O)OCH$_2$*CH*$_3$). IR ($CC1_4$) 1623, 1598 cm^{-1}. MS (CI) 389 (M+H)$^+$. Anal. Calcd for $C_{16}H_{18}FNO_4PS_2$: C, 49.48; H, 4.67. Found: C, 49.09; H, 4.62.

4.4.17. 2-Diethoxymethyl-7-fluoro-2,3-dihydro-thieno[2,3-*b*]thiochromen-4-one 19g

The reaction was carried out with xanthate **5l** (0.100 g, 0.24 mmol) and potassium carbonate (0.165 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (2.4 mL). After 3 h 30 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/diethyl ether 4:1) the tricyclic product **19g** (0.077 g) as light brown crystals in 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (dd, 1H, J_{H-F} = 5.9 Hz, J_{H-H} = 9.6 Hz, C*H*Ar), 7.20 (m, 2H, C*H*Ar), 4.59 (d, 1H, J = 7.8 Hz, C*H*(OEt)$_2$), 4.22 (ddd, 1H, J = 6.8 Hz, J = 7.8 Hz, J = 9.5 Hz, C*H*S), 3.73 (m, 2H, OC*H*$_2$CH$_3$), 3.62 (m, 2H, OC*H*$_2$CH$_3$), 3.48 (dd, 1H, J = 9.5 Hz, J = 16.5 Hz, C*H*HCCO), 3.38 (dd, 1H, J = 6.7 Hz, J = 16.5 Hz, CH*H*CCO), 1.25 (m, 3H, OCH$_2$C*H*$_3$), 1.22 (m, 3H, OCH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2 (*CO*), 163.6 (d, J_{C-F} = 255.4 Hz, *CF*), 152.4 (*C*q), 138.2 (*C*q, d, J_{C-F} = 9.6 Hz), 131.5 (d, J_{C-F} = 9.6 Hz, *CH*Ar), 130.3 (*C*q), 127.2 (*C*q, d, J_{C-F} = 2.3 Hz), 115.9 (d, J_{C-F} = 22.2 Hz, *CH*Ar), 111.9 (d, J_{C-F} = 24.9 Hz, *CH*Ar), 104.1 (*CH*(OEt)$_2$), 63.7 (O*CH*$_2$CH$_3$), 62.5 (O*CH*$_2$CH$_3$), 52.7 (*CHS*), 36.2 (*CH*$_2$), 15.3 (2*CH*$_3$). IR ($CDCl_3$) 1623, 1599 cm^{-1}. MS (CI) 341 MH$^+$. HRMS (EI$^+$) 340.0612 (Measured mass), 340.0603 (Calculated mass).

4.4.18. 2-Ethoxymethyl-7-fluoro-1,2-dihydro-4*H*-thieno[2,3-*b*][1]benzothiopyran-4-one 19h

The reaction was carried out with xanthate **5m** (0.362 g, 1 mmol) and potassium carbonate (0.690 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (10 mL). After 2 h 15 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (gradient petroleum ether/ethyl acetate 8:2) the tricyclic product **19h** (0.207 g) as yellow orange needles in 70% yield. Mp 89–90 °C (recrystallisation from *i*Pr$_2$O at −20 °C). ^{1}H NMR (400 MHz, $CDCl_3$) 8.51 (1H, dd, J_{H-H} = 9.6 Hz, J_{H-F} = 6.0 Hz, C*H*Ar), 7.22–7.18 (2H, m, 2C*H*Ar), 4.21 (1H, m, C*H*S), 3.66 (1H, dd, J = 6.1 et 9.7 Hz, C*H*HOEt)), 3.55 (1H, dd, J = 8.5 and 9.7 Hz, CH*H*OEt), 3.54 (2H, q, J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.45 (1H, dd, J = 9.1 and 16.3 Hz, C*H*HCHS), 3.29 (1H, dd, J = 5.3 and 16.3 Hz, CH*H*CHS), 1.21 (3H, t, J = 7.0 Hz, OCH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4 (*CO*), 163.5 (d, J_{C-F} = 255.4 Hz, *CF*), 152.6 (S*Cq*S), 138.2 (d, J_{C-F} = 9.8 Hz, Ar*Cq*S), 131.5 (d, J_{C-F} = 9.6 Hz, *CH*Ar), 129.9, 127.2 (2Cq), 115.9 (d, J_{C-F} = 22.2 Hz, *CH*Ar), 111.9 (d, J_{C-F} = 24.8 Hz, *CH*Ar), 73.2 (*CH*$_2$OEt), 66.9 (O*CH*$_2$CH$_3$), 36.8 (*CH*$_2$), 15.1 (OCH$_2$*CH*$_3$). IR ($CC1_4$) 1622, 1598 cm^{-1}. MS (CI) 297 (M+H)$^+$. Anal. Calcd for $C_{14}H_{13}FO_2S_2$: C, 56.73; H, 4.42. Found: C, 56.72; H, 4.35.

4.4.19. [*tert*-Butoxycarbonyl-(7-fluoro-4-oxo-2,3-dihydro-4*H*-thieno[2,3-*b*][1]benzothiopyran-2-ylmethyl)-amino]-acetic acid ethyl ester 19i

The reaction was carried out using xanthate **5n** (0.200 g, 0.38 mmol) in ethanol (0.38 mL) and ethyl acetate (2%) with DBU (1.1 equiv). After stirring at room temperature until complete consumption of starting adduct, the reaction mixture was extracted with diethyl ether. A light yellow oily tricyclic product **19i** (0.124 g) was obtained in 72% yield. The pure compound was a mixture of rotamers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (br s, 1H,

CHAr), 7.19 (br s, 2H, CHAr), 4.33 (br s, 1H, CHS), 4.11 (m, 2H, OCH_2CH_3), 3.97 (m, 2H, NCH_2CO), 3.61 (t, 1H, J = 14.2 Hz, NCHHCHS), 3.39 (m, 2H, NCHHCHS, CHHCCO), 3.28 (m, 1H, CHHCCO), 1.44, 1.41 (2s, 9H, $(CH_3)_3$), 1.25 (s, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4 (CO), 169.8 (OCO), 163.6 (d, J_{C-F} = 255.2 Hz, CF), 155.4 (NCO), 152.0 (Cq), 138.3 (Cq, dd, J_{C-F} = 6.8 Hz, J_{C-F} = 8.9 Hz), 131.6 (d, J = 9.6 Hz, CHAr), 130.0; 130.1 (Cq), 127.3 (Cq), 116.0 (dd, J_{C-F} = 8.7 Hz, J_{C-F} = 22.6 Hz, CHAr), 111.9 (d, J_{C-F} = 5.9 Hz, J_{C-F} = 24.8 Hz, CHAr), 81.1; 81.3 ($C(CH_3)_3$), 61.2 (OCH_2CH_3), 54.2; 53.4 (CH_2), 51.7; 50.3 (CH_2), 49.9; 49.8 (CHS), 37.9; 37.8 (CH_2), 28.3; 28.2 ($C(CH_3)_3$), 14.3; 14.2 (OCH_2CH_3). IR ($CC1_4$) 1752, 1708, 1620, 1599 cm^{-1}. MS (CI) 454 MH$^+$. HRMS (EI$^+$) 453.1081 (Measured mass), 453.1080 (Calculated mass).

4.4.20. Acetic acid 9-(7-fluoro-4-oxo-1,2-dihydro-4*H*-thieno [2,3-*b*)][1]benzothiopyran-2-yl)-nonyl ester 19j

The reaction was carried out with xanthate **5o** (0.488 g, 1 mmol) and potassium carbonate (0.690 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (10 mL). After 2 h 45 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/dichloromethane/ethyl acetate 7:2:1) the tricyclic product **19j** (0.380 g) as yellow crystals in 90% yield. Mp 71–72 °C (recrystallisation from iPr_2O at 0 °C). ^{1}H NMR (400 MHz, $CDCl_3$) 8.50 (1H, dd, J_{H-} = 9.6 Hz, J_{H-F} = 5.9 Hz, CHAr), 7.21–7.16 (2H, m, 2CHAr), 4.04 (2H, t, J = 6.8 Hz, CH_2OAc), 4.03 (1H, m, CHS), 3.50 (1H, dd, J = 8.7 and 15.9 Hz, CHHCHS), 3.16 (IH, dd, J = 6.4 and 15.9 Hz, CHHCHS), 2.03 (3H, s, $OCOCH_3$), 1.80–1.75 (2H, m, CH_2), 1.62–1.58 (2H, m, CH_2), 1.42–1.36 (2H, m, CH_2), 1.28 (10H, br s, $5CH_2$). ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.8 (CO), 170.6 (OCO), 163.2 (d, J_{C-F} = 254.7 Hz, CF), 152.1 (SCqS), 138.0 (d, J_{C-F} = 9.7 Hz, ArCqS), 132.2 (CH, d, J_{C-F} = 9.4 Hz, CHAr), 130.3, 127.1 (2Cq), 115.5 (d, J_{C-F} = 22.0 Hz, CHAr), 111.5 (d, J_{C-F} = 24.7 Hz, CHAr), 64.3 (CH_2OAc), 51.8 (CHS), 40.3, 36.3, 29.1, 29.0, 28.4, 27.7, 25.7 (CH_2), 20.7 ($OCOCH_3$). IR ($CC1_4$) 1741, 1622, 1598 cm^{-1}. MS (CI) 423 (M+H)$^+$. Anal. Calcd for $C_{22}H_{27}FO_3S_2$: C, 62.53; H, 6.44. Found: C, 62.39; H, 6.38.

4.4.21. 2-Acetylamino-2-(7-fluoro-4-oxo-1,2-dihydro-4*H*-thieno [2,3-*b*][1]benzothiopyran-2-yl-methyl)-malonic acid diethyl ester 19k

The reaction was carried out with xanthate **5p** (0.535 g, 0.7 mmol) and potassium carbonate (0.480 g, 3.5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (10 mL). After 1 h 30 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/dichloromethane/ethyl acetate 2:3:5) the tricyclic product **19k** (0.294 g) as white crystals in 90% yield. Mp 145–146 °C (recrystallisation from ethyl acetate at −20 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (1H, dd, J_{H-F} = 8.8 Hz, J_{H-F} = 5.9 Hz, CHAr), 7.09–7.02 (2H, m, 2CHAr), 4.23–4.15 (4H, m, $2CO_2CH_2CH_3$), 3.87 (1H, m, CHS), 3.42 (1H, dd, 7 = 8.3 and 15.8 Hz, CHHCHS), 2.98 (1H, dd, J = 15.8 Hz, CHHCHS), 2.95–2.86 (2H, m, CH_2), 2.05 (3H, s, $NHCOCH_3$), 1.18 (6H, t, J = 7.1 Hz, $CO_2CH_2CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8 (CO), 169.8 (CO), 167.3 (CO), 163.3 (d, J_{C-F} = 255.4 Hz, CF), 152.2 (SCqS), 137.8 (d, J_{C-F} = 9.7 Hz, ArCqS), 131.3 (d, J_{C-F} = 9.0 Hz, CHAr), 129.9, 126.9 (2 Cq), 115.8 (d, J_{C-F} = 21.9 Hz, CHAr), 111.7 (d, J_{C-F} = 25.2 Hz, CHAr), 65.5 (Cq), 63.0 ($CO_2CH_2CH_3$), 62.8 ($CO_2CH_2CH_3$), 47.1 (CHS), 41.0 (CH_2), 37.9 (CH_2), 22.9 ($NHCOCH_3$), 13.8 ($CO_2CH_2CH_3$). IR ($CC1_4$) 1754, 1739, 1692, 1623, 1597 cm^{-1}. MS (CI) 468 (M+H)$^+$. Anal. Calcd for $C_{21}H_{22}FNO_6S_2$: C, 53.95; H, 4.74. Found: C, 53.89; H, 4.74.

4.4.22. 2-(2,3-Dimethoxy-benzyl)-7-fluoro-2,3-dihydro-thieno [2,3-*b*]thiochromen-4-one 19l

The reaction was carried out with xanthate **5q** (2.48 g, 5.46 mmol) and potassium carbonate (3.76 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (54.6 mL). After 3 h 30 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/diethyl ether 8:2) the tricyclic product **19l** (1.95 g) as white crystals in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (dd, 1H, J_{H-F} = 5.9 Hz, J_{H-H} = 9.6 Hz, CHAr), 7.20 (m, 2H, CHAr), 7.00 (m, 1H, CHPh), 6.85 (dd, 1H, J = 1.4 Hz, J = 8.2 Hz, CHPh), 6.78 (dd, 1H, J = 1.4 Hz, J = 7.6 Hz, CHPh), 4.38 (ddt, 1H, J = 5.9 Hz, J = 7.1 Hz, J = 8.3 Hz, SCH), 3.87 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.44 (dd, 1H, J = 8.4 Hz, J = 16.0 Hz, CHHPh), 3.30 (dd, 1H, J = 5.8 Hz, J = 16.1 Hz, CHHPh), 3.11 (dd, 1H, J = 7.0 Hz, J = 13.6 Hz, CHHCCO), 3.05 (dd, 1H, J = 8.4 Hz, J = 13.6 Hz, CHHCCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4 (CO), 163.5 (d, J_{C-F} = 255.3 Hz, CF), 152.9 (Cq), 152.8 (Cq), 147.4 (Cq), 138.4 (Cq, d, J_{C-F} = 9.7 Hz),131.8 (Cq), 131.6 (d, J_{C-F} = 9.6 Hz, CHAr), 130.3 (Cq), 127.4 (Cq, d, J_{C-F} = 2.4 Hz), 123.9 (CHPh), 122.5 (CHPh), 115.8 (d, J_{C-F} = 22.2 Hz, CHAr), 111.9 (d, J_{C-F} = 24.9 Hz, CHAr), 111.6 (CHPh), 60.6 (OCH_3), 55.7 (OCH_3), 51.8 (CHS), 40.0 (CH_2), 36.9 (CH_2). IR ($CDCl_3$) 1620, 1589 cm^{-1}. MS (CI) 389 MH$^+$. HRMS (EI$^+$) 388.0603 (Measured mass), 386.0603 (Calculated mass).

4.4.23. 2-[2-(5,5-Dimethyl-[1,3]dioxan-2-yl)-2-methyl-propyl]-7-fluoro-2,3-dihydro-thieno[2,3-*b*]thiochromen-4-one 19m

The reaction was carried out with xanthate **5r** (0.210 g, 0.44 mmol) and potassium carbonate (0.303 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (4.4 mL). After 3 h 30 min, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/diethyl ether 4:1) the tricyclic product **19m** (0.138 g) as white crystals in 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (dd, 1H, J_{H-F} = 5.9 Hz, J_{H-H} = 9.6 Hz, CHAr), 7.20 (m, 2H, CHAr), 4.33 (m, 1H, $CH(OCH_2)_2$, 4.08 (s, 1H, CHS), 3.61 (m, 3H, CHHCCO, OCH_2CCH_3), 3.40 (dd, 2H, J = 2.0 Hz, J = 10.7 Hz, OCH_2CCH_3), 3.05 (dd, 1H, J = 9.7 Hz, J = 15.8 Hz, CHHCCO), 2.03 (m, 2H, $SCHCH_2$), 1.16 (s, 3H, CCH_3), 0.99 (s, 6H, $C(CH_3)_2$), 0.72 (s, 3H, CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1 (CO), 163.5 (d, J_{C-F} = 255.0 Hz, CF), 153.6 (Cq), 138.3 (Cq, d, J_{C-F} = 9.7 Hz), 131.5 (d, J_{C-F} = 9.6 Hz, CHAr), 130.6 (Cq), 127.4 (Cq, d, J_{C-F} = 2.3 Hz), 115.8 (d, J_{C-F} = 22.2 Hz, CHAr), 111.9 (d, J_{C-F} = 24.9 Hz, CHAr), 106.6 ($CHOCH_2$), 77.3 (OCH_2CCH_3), 77.2 (OCH_2CCH_3), 48.9 (CHS), 44.3 (CH_2), 42.6 (CH_2), 37.9 (Cq), 30.2 (Cq), 23.0 (CH_3), 22.9 (CH_3), 22.8 (CH_3), 21.7 (CH_3). IR ($CDCl_3$) 1617, 1590 cm^{-1}. MS (CI) 409 MH$^+$. HRMS (EI$^+$) 408.1225 (Measured mass), 408.1229 (Calculated mass).

4.4.24. (7-Fluoro-4-oxo-2,3-dihydro-4*H*-thieno[2,3-*b*][1]benzothiopyran-2-ylmethyl)-(4-methoxy-benzyl)-carbamic acid tert-butyl ester 19n

The reaction was carried out with xanthate **5t** (0.240 g, 0.38 mmol) and potassium carbonate (0.262 g, 5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (3.8 mL). After 3 h 30 min, the sample was extracted with diethyl ether. A light yellow amorphous solid **19n** (0.096 g) was obtained in 52% yield. The required product was a mixture of rotamers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, 1H, J_{H-F} = 5.9 Hz, J_{H-H} = 9.6 Hz, CHAr), 7.19 (m, 2H, CHAr), 7.11 (br s, 2H, CHPh), 6.83 (d, 2H, J = 8.7 Hz, CHPh), 4.51 (m, 1H, NCHHPh), 4.41 (m, 1H, CHS), 4.23 (m, 1H, NCHHCHS), 3.77 (s, 3H, OMe), 3.47 (m, 1H, NCHHPh), 3.35 (m, 2H, NCHHCHS, CHHCCO), 3.23 (dd, 1H, J = 4.8 Hz, J = 16.2 Hz, CHHCCO), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4 (CO), 163.6 (d, J_{C-F} = 255.5 Hz, CF), 159.0 (Cq), 155.7 (NCO), 152.1 (Cq), 138.3 (Cq, d, J_{C-F} = 9.4 Hz), 131.6; 131.5 (Cq), 130.0 (d, J_{C-F} = 23.3 Hz, CHAr), 128.7 (m, CHPh), 127.37; 127.35 (Cq), 115.9 (d, J = 22.1 Hz, CHAr), 114.1 (CHPh), 111.9 (d, J = 25.0 Hz, CHAr), 80.6 ($C(CH_3)_3$), 55.2 (OCH_3), 51.5 (NCH_2Ph), 50.8 (NCH_2CHS), 49.6 (CHS), 37.8 (CH_2), 28.4 ($C(CH_3)_3$). IR ($CDCl_3$) 1698, 1622, 1599 cm^{-1}. MS (CI) 488 MH$^+$. HRMS (EI$^+$) 487.1292 (Measured mass), 487.1287 (Calculated mass).

4.4.25. 1,1-Difluoro-2-(7-fluoro-6-methyl-4-oxo-1,2-dihydro-4*H*-thieno[2,3-*b*][1]benzothiopyran-2-yl)-ethylphosphonic acid diethyl ester 19o

The reaction was carried out with xanthate **5s**[6b] (0.259 g, 0.5 mmol) and potassium carbonate (0.345 g, 2.5 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (5 mL). After 3 h, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/dichloromethane/ethyl acetate 6:4:0 to 4:4:2) the tricyclic product **19o** (0.136 g) as beige crystals in 60% yield. Mp 144–145 °C (recrystallisation from ethyl acetate at 0 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.34 (1H, d, J_{H-F} = 8.0 Hz, C*H*Ar), 7.15 (1H, d, J_{H-F} = 9.1 Hz, C*H*Ar), 4.44 (1H, m, C*H*S), 4.34–4.26 (4H, m, 2O$CH_2$$CH_3$), 3.66 (1H, dd, J = 8.6 and 16.0 Hz, C*H*HCHS), 3.22 (1H, dd, J = 7.8 and 16.0 Hz, CH*H*CHS), 2.70–2.60 (2H, m, CH_2CF_2), 2.38 (3H, s, CH_3), 1.42–1.38 (6H, m, 2OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3 (*CO*), 162.6 (d, J_{C-F} = 254.9 Hz, *CF*), 152.3 (*SCqS*), 135.1 (d, J_{C-F} = 9.6 Hz, Ar*Cq*S), 132.0 (d, J_{C-F} = 9.6 Hz, *CH*Ar), 129.6, 126.8 (2*Cq*), 126.1 (*Cq*Ar), 119.5 (dt, J_{C-P} = 215.5, J_{C-F} = 261.3 Hz, CF_2), 111.6 (d, J_{C-F} = 26.6 Hz, *CH*Ar), 64.9 (d, J_{C-P} = 6.5 Hz, P(O)CH_2CH_3), 43.3, 41.3 (*CH*S, CH_2), 40.0 (dt, J_{C-P} = 15.1 Hz, J_{C-F} = 19.9 Hz, CH_2CF_2), 16.4 (d, J_{C-P} = 5.0 Hz, P(O)CH_2CH_3), 14.7 (ArCH_3). IR ($CC1_4$) 1626, 1599 cm^{-1}. MS (CI) 4538 (M+H)$^+$. Anal. Calcd for $C_{18}H_{20}F_3O_4PS_2$: C, 47.78; H, 4.46. Found: C, 47.66; H, 4.44.

4.4.26. 2-Ethoxy-7-fluoro-3-thiiranylmethyl-thiochromen-4-one 22

The reaction was carried out with xanthate **5e** (0.752 g, 2 mmol) and potassium carbonate (1.38 g, 10 mmol) in a 9:1 mixture of CH_3CN/*t*-BuOH (20 mL). After 2 h, the mixture was treated according to the general procedure to furnish after purification on a silica gel column (petroleum ether/dichloromethane/ethyl acetate 9:1) the episulfide **22** (0.26 g) as a white solid in 44% yield. Mp 113–115 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.52 (1H, dd, J_{H-H} = 9.7 Hz, J_{H-F} = 5.9 Hz, C*H*Ar), 7.26–7.18 (2H, m, C*H*Ar), 4.36 (2H, q, J = 7.0 Hz, OCH_2CH_3), 3.33–3.11 (2H, m), 2.89 (1H, dd, J = 7.1 and 12.5 Hz), 2.46–2.36 (2H, m), 1.51 (3H, t, J = 7.0 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.7 (*CO*), 164.8 (*SCq*OEt), 163.8 (d, J_{C-F} = 255.4 Hz, *CF*), 133.8 (d, J_{C-F} = 9.7 Hz, ArCqS), 132.0 (d, J_{C-F} = 9.5 Hz, *CH*Ar), 126.7 (*Cq*Ar), 118.7 (*Cq*), 115.9 (d, J_{C-F} = 22.4 Hz, *CH*Ar), 112.1 (CH, d, J_{C-F} = 24.8 Hz, *CH*Ar), 67.7 (OCH_2CH_3), 33.7 (*CH*CH_2S), 31.2 (CH_2), 26.0 (CH_2), 15.0 (OCH_2CH_3), IR ($CC1_4$) 1610, 1585 cm^{-1}. MS (CI) 297 (M+H)$^+$. Anal. Calcd for $C_{14}H_{13}FO_2S_2$: C, 56.73; H, 4.42. Found: C, 56.69; H, 4.37.

4.4.27. 2-(2,3-Dimethoxy-benzyl)-7-methoxy-2,3-dihydro-thieno[2,3-*b*][1]benzothiopyran-4-one 26

0.1 g (0.25 mmol) of starting tricyclic compound **19l** was dissolved in MeOH/THF (2:1) solution. $NaBH_4$ (23.6 mg, 2.5 equiv) was added to this solution which was heated at 90–100 °C. After 1 h 30 min there was complete consumption of the starting material. The reaction mixture was cooled to room temperature, the solvent was evaporated and the residue diluted in dichloromethane and washed with water to afford a white solid product **26** (0.096 g) in 96% yield. Mp 120–122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, 1H, J = 8.9 Hz, C*H*Ar), 7.01 (m, 2H, C*H*Ar, C*H*Ph), 6.89 (d, 1H, J = 2.40 Hz, C*H*Ph), 6.83 (dd, 1H, J = 8.2 Hz, J = 1.2 Hz, C*H*Ar), 6.77 (dd, 1H, J = 7.6 Hz, J = 1.1 Hz, C*H*Ph), 4.35 (m, 1H, C*H*S), 3.86, 3.85, 3.84 (3s, 9H, 3 OCH_3), 3.42 (dd, 1H, J = 15.9 Hz, J = 8.3 Hz, C*H*HPh), 3.28 (dd, 1H, J = 16.0 Hz, J = 5.8 Hz, CH*H*Ph), 3.07 (m, 2H, CH_2CHS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1 (*CO*), 161.4 (*Cq*), 152.8 (*Cq*), 151.7 (*Cq*), 147.5 (*Cq*), 138.6 (*Cq*), 132.0 (*Cq*), 130.6 (*CH*Ar), 130.2 (*Cq*), 124.5 (*Cq*), 123.9 (*CH*Ph), 122.6 (*CH*Ph), 115.9 (*CH*Ar), 111.6 (*CH*Ar), 108.5 (*CH*Ph), 60.7 (OCH_3), 55.8 (OCH_3), 55.7 (OCH_3), 51.7 (*CH*S), 40.2 (CH_2Ph), 37.0 (CH_2). IR ($CDCl_3$) 1606, 1583 cm^{-1}. MS (CI) 401 MH$^+$. HRMS (EI$^+$) 400.0799 (Measured mass), 400.0803 (Calculated mass).

4.4.28. 2-(2,3-Dimethoxy-benzyl)-7-(2,2,2-trifluoro-ethoxy)-2,3-dihydro-thieno[2,3-*b*][1]benzo-thiopyran-4-one 27

Fifty milligram (0.12 mmol) of starting tricyclic compound **19l** was dissolved in trifluoroethanol. Five equivalents of K_2CO_3 (89 mg) were added and the mixture was heated at 100 °C. After 1 h there was complete consumption of the starting material. The reaction mixture was cooled to room temperature, the solvent was evaporated and the residue diluted in dichloromethane and washed with water to afford a white solid product **27** (41 mg) in 73% yield. Mp 149–151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, 1H, J = 8.9 Hz, C*H*Ar), 7.09 (dd, 2H, J = 8.9 Hz, J = 2.3 Hz, C*H*Ar, C*H*Ph), 7.00 (dd, 1H, J = 12.8 Hz, J = 5.0 Hz, C*H*Ar), 6.85 (d, 1H, J = 8.1 Hz, C*H*Ph), 6.78 (d, 1H, J = 7.4 Hz, C*H*Ph), 4.40 (m, 3H, C*H*S, OCH_2CF_3), 3.86, 3.85 (2s, 6H, 2OCH_3), 3.43 (dd, 1H, J = 16.0 Hz, J = 8.3 Hz, C*H*HPh), 3.30 (dd, 1H, J = 16.0 Hz, J = 5.7 Hz, CH*H*Ph), 3.08 (m, 2H, CH_2CHS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7 (*CO*), 158.7 (*Cq*), 152.8 (*Cq*), 152.1 (*Cq*), 147.4 (*Cq*), 138.5 (*Cq*), 131.8 (*Cq*), 131.0 (*CH*Ar), 130.3 (*Cq*), 125.9 (*Cq*), 123.9 (*CH*Ph), 122.9 (d, J = 277.9 Hz, CF_3), 122.5 (*CH*Ph), 115.5 (*CH*Ar), 111.5 (*CH*Ar), 110.0 (*CH*Ph), 65.7 (q, J = 36.7 Hz, CH_2CF_3), 60.6 (OCH_3), 55.7 (OCH_3), 51.7 (*CH*S), 40.0 (CH_2Ph), 36.9 (CH_2CHS). IR ($CDCl_3$) 1611, 1587 cm^{-1}. HRMS (EI$^+$) 468.0679 (Measured mass), 468.0677 (Calculated mass).

4.4.29. 2-(2,3-Dimethoxy-benzyl)-7-morpholin-4-yl-2,3-dihydro-thieno[2,3-*b*][1]benzothiopyran-4-one 28

Fifty milligrams (0.12 mmol) of the starting tricyclic compound **19l** were dissolved in a minimum of morpholine. Five equivalents of K_2CO_3 (89 mg) were added to this solution which was heated at 130 °C. After 1 h 30 min there was complete consumption of the starting material. The reaction mixture was cooled to room temperature, the solvent was evaporated and the residue diluted in dichloromethane and washed with water to afford a white solid product **28** (38 mg) in 70% yield. Mp 122–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, 1H, J = 9.0 Hz, C*H*Ar), 7.02 (m, 2H, C*H*Ar, C*H*Ph), 6.84 (d, 1H, J = 7.6 Hz, C*H*Ar), 6.78 (m, 2H, C*H*Ph), 4.34 (m, 1H, C*H*S), 3.86, 3.84 (2s, 10H, 2OCH_3, CH_2OCH_2), 3.42 (dd, 1H, J = 15.9 Hz, 8.3 Hz, C*H*HPh), 3.29 (m, 5H, CH_2NCH_2, CH*H*Ph), 3.07 (m, 2H, CH_2CHS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2 (*CO*), 152.8 (*Cq*), 152.2 (*Cq*), 151.1 (*Cq*), 147.5 (*Cq*), 138.7 (*Cq*), 132.1 (*Cq*), 130.1 (*Cq*), 130.0 (*CH*Ar), 123.9 (*CH*Ph), 122.7 (*Cq*), 122.6 (*CH*Ph), 115.1 (*CH*Ar), 111.5 (*CH*Ar), 108.6 (*CH*Ph), 66.6 (CH_2OCH_2), 60.7 (OCH_3), 55.7 (OCH_3), 51.5 (*CH*S), 47.7 (CH_2NCH_2), 40.2 (CH_2Ph), 37.0 (CH_2CHS). IR ($CDCl_3$) 1606, 1582 cm^{-1}. HRMS (EI$^+$) 455.1226 (Measured mass), 455.1225 (Calculated mass).

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