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A convergent, modular access to α-chloro-trifluoromethyl derivatives and to 1,1-difluoroalkenes

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This article is dedicated with respect to the memory of Professor Alan R. Katritzky

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ABSTRACT

An efficient protocol for the preparation of *S*-(1-chloro-2,2,2-trifluoroethyl)-*O*-ethyl xanthate is reported. This reagent serves as a versatile precursor of highly functionalized *gem*-difluoroalkenes through various inter- and intramolecular radical reactions and subsequent reduction with activated magnesium metal.

1. Introduction

Over the last two decades, the proportion of useful fluorine containing molecules has substantially increased. It is presently in about a third of all compounds on the pharmaceutical and agrochemical markets.[1] Indeed, the ability of fluorine to deeply alter the chemical and physical properties of organic molecules is now well established,[2] and provides a unique and formidable tool for drug designers. Of all valuable fluorinated groups, terminal gem-difluoro alkenes exhibit broad applicability, for they can be easily used and transformed into important fluorinated derivatives.[3] In addition, they have an exclusive isosteric property to act as a carbonyl group mimic,[4] and are in some cases responsible for the biological activity of certain enzyme inhibitors and pesticides.[5]

To date, there are various methods to prepare terminal *gem*-difluoroalkenes. Several pathways, such as the Wittig,[6] the Horner-Wadsworth-Emmons,[7] the Julia type reaction[8] or the Julia-Kociensky olefinations,[9] start from ketones or aldehydes. Others rely on elimination reactions, such as metal induced eliminations,[10] base induced elimination of sulfones[11] or the thermal elimination of sulfoxides and β-hydroxy sulfoxides.[12] Finally, the use of difluorovinyl metal derivatives, such as difluorovinyllithium,[13] or cross-coupling[14] and S_N2' type reactions[15] can offer suitable and powerful alternatives. Most of these sequences exploit the presence of reactive functions, such as ketones or alkyl halides. However, there remains a dearth of methods starting from much less reactive groups, such as terminal alkenes.

2. Result and discussion

A few years ago, we reported the synthesis of *S*-(1-chloro-2,2,2-trifluoroethyl)-*O*-ethyl xanthate **1** and its use in a limited number of radical addition reactions.[16] This work also involved the preparation and study of the acetate and benzoate analogs **2** and **3**. However, it seemed to us that the synthetic potential of **1** had remained largely underexploited (Fig. 1).

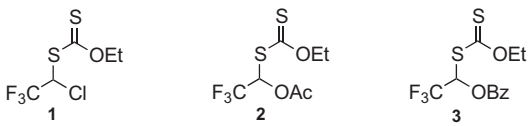

Fig. 1. A few fluorinated xanthates.

With the aim of extending this work, we considered using this xanthate as a unique precursor to highly functionalized α-chloro-trifluoromethyl derivatives, as well as to heterocycles bearing a gem-difluorovinyl motif on the side chain. The pathway envisaged

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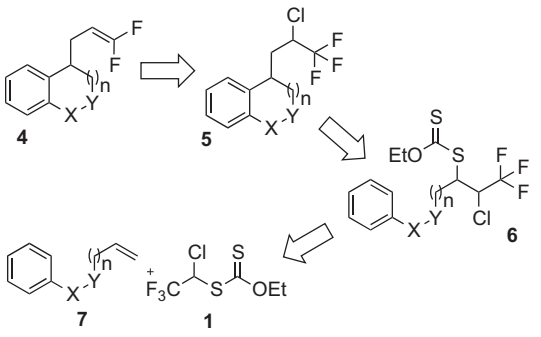
0040-4020/

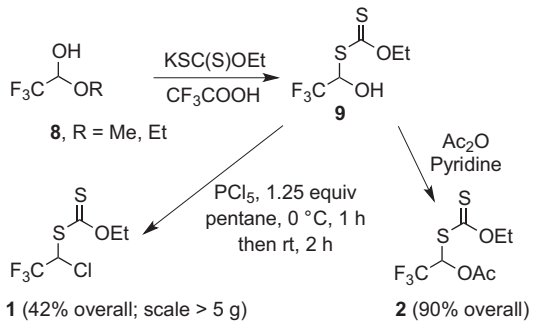
to access these heterocycles would begin with simple radical additions of xanthate **1** onto olefins bearing an aromatic ring **7**, then harness the ability of xanthates to promote radical cyclizations onto aromatic rings to form bicyclic compounds **5**.[17] The desired difluoro alkene **4** would finally be brought about by a metal induced formal elimination of 'Cl–F' (Scheme 1).



Scheme 1. A route to difluoroalkenes.

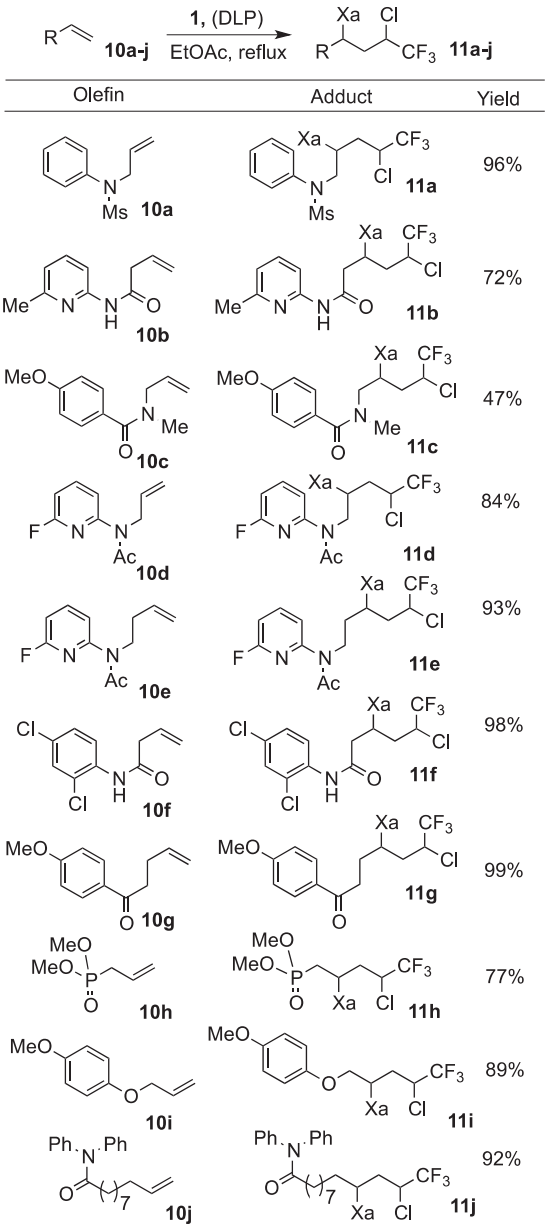
Our investigations began with an optimization of the synthesis of xanthate **1** because, unfortunately, we were unable to duplicate the earlier reported protocol. The desired substance was obtained, but in a very poor yield. Furthermore, we found that, contrary to what had been previously stated, compound **1** is totally stable to chromatographic purification. We therefore considered revising the experimental conditions for the whole sequence.

We rapidly identified trifluoroacetic acid as a much better acid/solvent than the originally used sulfuric acid in acetone (Scheme 2). Indeed, the xanthate intermediate **9** could be easily removed from the medium by simple extraction with pentane. Moreover, pentane appeared to be a suitable solvent for the next step. While we were screening conditions for the second step using PCl_5 as a chlorinating reagent, we noticed that the evaporation of the solvent from crude mixture before purification was mainly responsible for the yield loss. Finally, by conducting the first reaction in trifluoroacetic acid and the second in pentane, followed by direct purification of the crude mixture, we were able to isolate xanthate **1** in a good 42% overall yield from commercially available hemiacetal **8**. This reproducible protocol is very straightforward and was easily scaled up. Alcohol **9** may also be readily acetylated to give acetate **2**, which is also a useful xanthate for additions to alkenes (Scheme 2).[16]



Scheme 2. Synthesis of xanthates **1** and **2**.

With the desired xanthate **1** in hand, we were able to validate its good reactivity towards several olefins, using lauroyl peroxide (DLP) as a thermal radical initiator. The results are displayed in Scheme 3 [Xa=–SC(=S)OEt]. In contrast to the moderate yields reported in the previous publication where **1** was mainly used without purification, we isolated the xanthate adducts **11a**–**j** in



Scheme 3. Addition of xanthate **1** to alkenes.

excellent yields, up to 99%. A substantial increase was for instance observed with allylphosphonate, where the yield of the adduct **11h** was raised from 27% to 77%. As usual, xanthate chemistry showed a great tolerance towards several functional groups such as ketones, amides, ethers or pyridine rings. A small excess of xanthate **1** was used in these additions (typically 1.5 equiv) but it could be easily recovered at the end of the reaction.

Xanthate adducts **11a**–**g** were next transformed into their corresponding polycyclic aromatic or heteroaromatic derivatives by subsequent treatment with a stoichiometric amount of lauroyl peroxide. The reactions were performed in either refluxing ethyl acetate or refluxing chlorobenzene, following literature protocols,[18] and ultimately produced bicyclic compounds **12a**–**g** in good yields relative to their complexity. For instance, azaindoline, tetrahydronaphthyridin-2-one and tetrahydroisoquinolin-1-one derivatives were readily obtained in only two steps from easily accessible precursors (Scheme 4). The cyclization of compound **12f** represents a new feature, as it is one of the very rare examples of radical cyclizations leading to dihydronaphthyridin-2-ones not substituted on the lactam nitrogen.[19]

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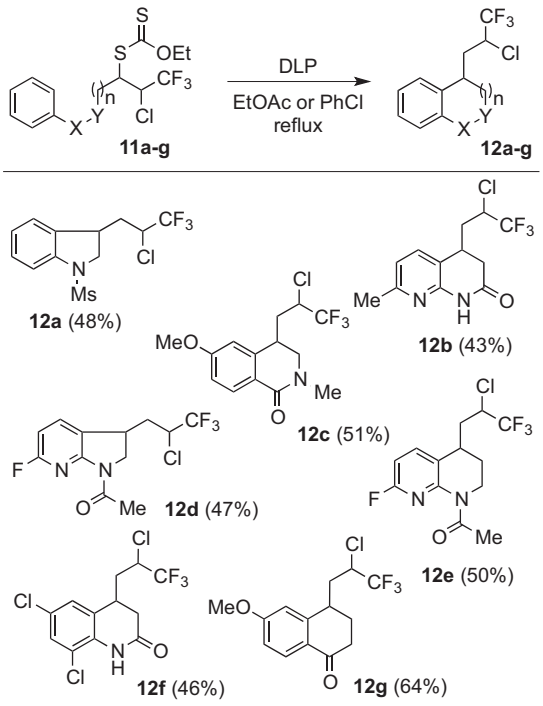
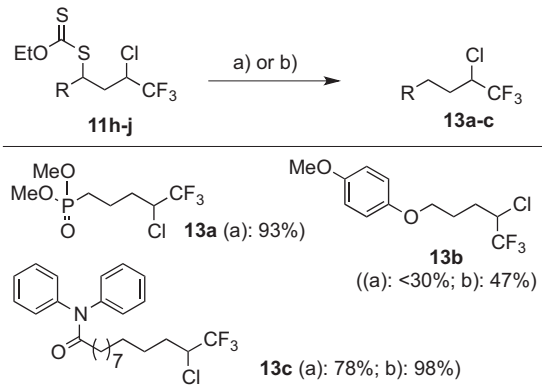


Scheme 4. Ring-closure onto aromatic and heteroaromatic rings.

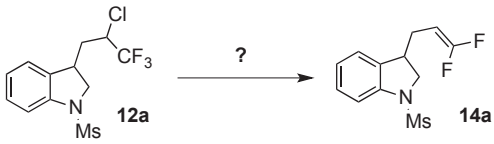
For compounds **11h**–**j**, we proceeded to the simple reductive removal of the xanthate moiety, by using either the hypophosphorous salt of triethylamine[20] or tris(trimethylsilyl)silane[21] as the hydrogen atom donor (Scheme 5).



Scheme 5. Reductive dexanthylations of adducts **11h**–**j**.

More synthetically interesting is the conversion of β-chlorotrifluoromethyl derivatives into 1,1-difluoroalkenes using dissolving metal reductions. Such transformations are already known; however, only bromides[10c] or activated chlorides[10b] have been employed in this reaction. In our case, the issue was to induce the insertion of a metal into the un-activated carbon-chloride bond to promote the elimination. Taking compound **12a** as a model substrate, we screened several experimental conditions. The first promising result was obtained by treatment with zinc flakes in refluxing ethyl acetate (Table 1, entry 3) so that we were able to isolate the desired compound in a quantitative yield. Unfortunately, this reaction proved non-reproducible and forced us to examine other more reducing metals such as lithium and magnesium. Promising results were obtained with *tert*-butyl lithium but, to our dismay, it again turned out to be unreliable. Finally, magnesium, activated in situ by a substoichiometric amount of 1,2-dibromoethane, promoted the elimination efficiently. After a few trials, we concluded that the periodic addition of 1,2-dibromoethane permitted a quantitative conversion systematically. The optimized protocol is easy to implement, and a standard work-up yields the desired 1,1-difluoroalkene essentially quantitatively.

Table 1
Optimization trials for the reductive elimination



Entry	Reagent	Solvent	*T* °C	Conversion
1	Zn,[a] CuI cat.	DMF	20–50 °C	0%
2	Zn,[b] CuI cat.	DMF	20–50 °C	0%
3	Zn[a]	AcOEt	Reflux	0–100%[c]
4	Zn[a]	$EtCO_2H$	Reflux	8%[c]
5	*i*-PrMgCl	THF	0 °C—rt	0%
6	*i*-PrMgCl, LiCl	THF	0 °C—rt	0%
7	*n*-BuLi	THF	−78 °C—rt	0%
8	*t*-BuLi	THF	−78 °C—rt	40–75%[c]
9	Mg	MeOH	Reflux, 2 h	0–30%[c]
10	Mg	MeOH	Reflux, 24 h	0–30%[c]
11	Mg, I_2	MeOH	Reflux	0%
12	Mg	THF	Reflux	0–5%
13	Mg	EtOH	Reflux	0%
14	Mg	CF_3CH_2OH	Reflux	0%
15	Mg	MeOH/PhMe	Reflux	0%
16	Mg, $Br(CH_2)_2Br$	THF	Reflux	50–85%
17	Mg, $Br(CH_2)_2Br$[d]	THF	Reflux	100%

[a] Zinc flakes.
[b] Zinc powder.
[c] Reactions not reproducible.
[d] Periodic addition of 1,2-dibromoethane during the reaction.

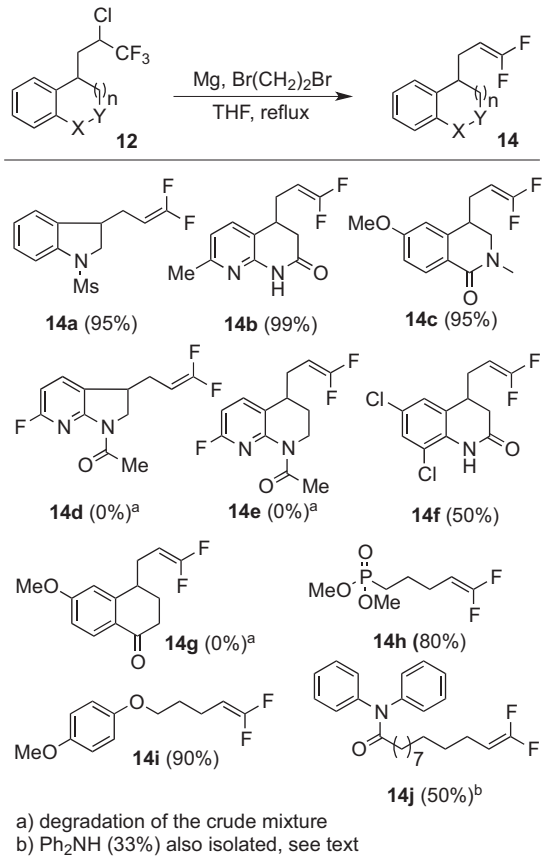
We were further pleased to find that the same conditions were equally efficient for most of the other derivatives (Scheme 6). Compound **14f** and **14j** were obtained in only 50% yield, because of the competing cleavage of the amide functions. Indeed, in the case of **14j**, besides the desired product, diphenylamine resulting from the cleavage of the amide was isolated in 33% yield.

As far as compound **14d** and **14e** are concerned, we assumed that the degradation observed came from the hydrolytic instability of the acetyl moiety. We therefore proceeded with the quantitative removal of the acetyl protecting group by treatment with potassium carbonate in methanol and subjected the naked substrates **15a** and **15b** to the elimination conditions. To our delight, the desired terminal *gem*-difluoroalkenes **16a** and **16b** were formed in very good yield (Scheme 7).

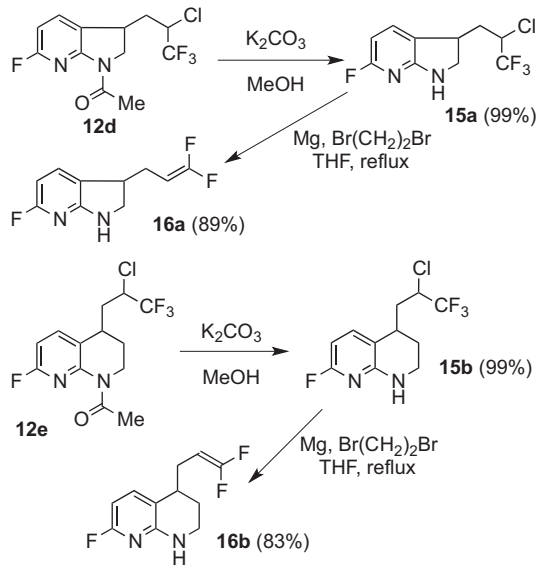
In a further variation, we found that xanthate **1** is able to undergo a radical allylation reaction we recently developed. It involves the use of 2-fluoropyridyl derivatives of allylic alcohols as the allylating agents and overcomes the activation barrier resulting from the strong and difficult to homolyze carbon–oxygen bond.[22] As depicted in Scheme 8, the reaction of xanthate **1** with substrate **17** gave the desired product in a good 75% yield. The β-chlorotrifluoromethyl derivative **18**, bearing a double bond at the δ position and a masked aldehyde, would be very tedious to make by more conventional methods. Interestingly, base induced elimination of HCl from compound **18** would lead in principle to the formation of a trifluoromethyl-substituted diene.

3. Conclusion

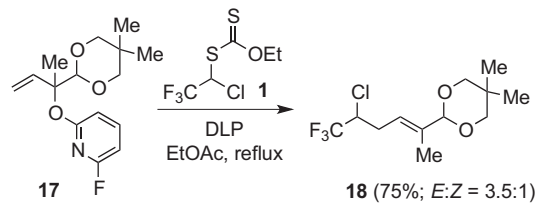
In conclusion, we now have in hand a unified, flexible, and convergent strategy for the synthesis of various acyclic and



Scheme 6. Synthesis of difluoroalkenes.



Scheme 7. Synthesis of azaindolines and tetrahydroazaquinolines.



Scheme 8. Radical allylation of xanthate **1**.

heterocyclic substances bearing a terminal difluoro alkene side chain. The methodology is based on the use of *S*-1-chloro-2,2,2-trifluoroethyl-*O*-ethyl xanthate **1** as a fluorinated precursor, the synthesis of which has been re-examined and is now easily reproducible and scalable. Reagent **1** represents in fact the synthetic equivalent of a 2,2-difluorovinyl radical ($F_2C{=}CH^{\bullet}$), which is too reactive to undergo cleanly intermolecular additions to unactivated alkenes.

4. Experimental

4.1. General experimental methods

Purification procedures were in accordance with the instructions in D. D. Perrin and W. L. F. Armarego, 'Purification of Laboratory Chemicals', Fourth Edition, The Bath Press, Bath, 2002. All reactions were carried out under dry, oxygen free nitrogen. Flash chromatography was performed on silica gel (SDS, 60 Å C. C. 40–63 mm) as the stationary phase. Thin Layer Chromatography (TLC) was performed on alumina plates pre-coated with silica gel (Merck silica gel, 60 F254), which were visualized by the quenching of UV fluorescence when applicable (λ_{max}=254 nm and/or 366 nm) and/or by staining with vanillin or anisadehyde in acidic ethanol followed by heating. Infrared spectra were recorded as solutions in CH_2Cl_2 using NaCl cells, on a Perkin–Elmer FT 2000. Absorption maxima (nmax) are reported in wavenumbers (cm^{-1}) and only selected peaks are reported. Magnetic resonance spectra were recorded at room temperature on a Bruker Avance DPX 400 instrument. Proton magnetic resonance spectra (^1H NMR) were recorded at 400 MHz and coupling constants (*J*) are reported to ±0.5 Hz. The following abbreviations were utilized to describe peak patterns when appropriate: br=broad, s=singlet, d=doublet, t=triplet, q=quartet, quint=quintuplet, hex=hexuplet, hept=heptuplet, oct=octuplet and m=multiplet. Carbon magnetic resonance spectra (^{13}C NMR) were recorded in the same instrument at 100.6 MHz. Chemical shifts (δ_H, δ_C) are quoted in parts per million (ppm) and are referenced to TMS (0 ppm). Low-resolution mass spectra (*m*/*z*) were recorded by chemical ionization (CI/NH_3) on a Hewlett–Packard HP 5989B and only report molecular species ([M+H]+, [M+NH_4]+) and other major fragments. High-resolution mass spectra were recorded by positive electron impact ionization (EI+) at 70 e.V. on a JEOL JMS-GCmate II mass spectrometer. The quoted masses are accurate to ±5 ppm. The names of the molecules that appear in the following pages were generated using either Beilstein AutoNom 2000 (CAS) or ChemBioDraw Ultra 11.0.

4.2. General procedures

4.2.1. General procedure A for the addition reaction. A solution of olefin (n mmol) and xanthate (between 1.3 n and 2 n mmol) in AcOEt (n mL) was refluxed under a flow of nitrogen for 15 min. Lauroyl peroxide (DLP) 5 mol % was then added every hour until total conversion of the starting olefin was observed. The mixture was cooled to room temperature and the solvent evaporated under reduced pressure. Flash column chromatography afforded the desired adduct as a mixture of two diastereoisomers.

4.2.2. General procedure B for the cyclization reaction. A solution of the xanthate adduct (n mmol) in either AcOEt or chlorobenzene (50 n mL) was refluxed under a flow of nitrogen for 15 min. Lauroyl peroxide (DLP) 20 mol % was then added every 15 min (chlorobenzene) or every hour (ethyl acetate) until total conversion of the starting olefin was observed. The mixture was cooled to room temperature and the solvent evaporated under reduced

pressure. Flash column chromatography afforded the desired product as a mixture of two diastereoisomers.

4.2.3. General procedure C for the elimination reaction. A magnetically round bottom flask was charged with the corresponding trifluorochloro compound (n mmol), freshly activated magnesium (20 n mmol), and dry THF (33 n mL) and the suspension was heated up to reflux. 1,2-Dibromoethane (0.5 n mmol) was then added every two hours until total conversion of the starting material was observed by NMR. The mixture was cooled to room temperature and a saturated solution of citric acid (15 n mL) was added. After total disappearance of solid magnesium, Et_2O was added, the layers were partitioned and the aqueous one was extracted twice with Et_2O. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Removal of the solvent and flash chromatography if necessary yielded to the desired difluoro olefin.

4.3. Experimental procedures and spectroscopic data

*4.3.1. [(1-Chloro-2,2,2-trifluoroethyl)sulfanyl](ethoxy)methanethione (**1**).* A magnetically stirred round bottom flask was charged with potassium ethyl xanthate salt (8 g, 50 mmol), 100 mL of trifluoroacetic acid and cooled to 0 °C. 2,2,2-Trifluoro-1-methoxyethan-1-ol (8.19 g, 63 mmol) was added slowly and the solution was stirred 30 min at 0 °C and 1 h at room temperature. Pentane (100 mL) and water (100 mL) were added, the layers were separated and the aqueous layer was extracted twice with pentane (100 mL). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The solution was concentrated to 100 mL in vacuo, was cooled to 0 °C and phosphorus pentachloride (13.10 g, 63 mmol) was added. The solution was stirred at 0 °C for 30 min and at room temperature for 2 h. The solution was then directly purified by silica gel column chromatography[23] (pentane 100%) and concentrated under reduced pressure at 20 °C to afford **1** (5.01 g, 42%) as a pale yellow liquid. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 6.26 (q, J=6.9 Hz, 1H), 4.74 (q, J=7.1 Hz, 2H), 1.47 (t, J=7.1 Hz); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 206.4, 122.7 (q, J=279 Hz), 72.0, 63.6 (q, J=37 Hz), 13.6. The spectral data were incorrectly reported in the original communication (Ref. 16).

*4.3.2. 1-(Ethoxycarbonothioylthio)-2,2,2-trifluoroethyl acetate (**2**).* A magnetically stirred round bottom flask was charged with potassium ethyl xanthate salt (0.8 g, 5 mmol), 10 mL of trifluoroacetic acid and cooled to 0 °C. 2,2,2-trifluoro-1-methoxyethan-1-ol (0.72 mL, 7.5 mmol) was added slowly and the solution was stirred 30 min at 0 °C and 1 h at room temperature. Acetic anhydride (0.47 mL, 5 mmol) and pyridine (0.4 mL, 5 mmol) were then added drop-wise and the solution was stirred 30 min. DCM (30 mL) and water (30 mL) were added, the layers were separated and the aqueous layer was extracted twice with DCM (30 mL). The combined organic layers were washed with HCl (1%), water, brine, and dried over anhydrous $MgSO_4$. The solution was concentrated in vacuo (cold bath water) and the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 98:2) to afford **2** (1.2 g, 90%) as a yellow oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.19 (q, J=6.8 Hz, 1H), 4.69 (dq, J=7.2, 1.6 Hz, 2H), 2.18 (s, 3H), 1.44 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 205.7, 167.6, 122.4 (q, J=278 Hz), 76.5 (q, J=36 Hz), 71.4, 20.3, 13.5; IR (CCl_4): ν_{max} 2987, 1780, 1443, 1371, 1345, 1231, 1131, 1112, 1030. The spectral data were incorrectly reported in the original communication (Ref. 16).

*4.3.3. N-{4-Chloro-2-[(ethoxymethanethioyl)sulfanyl]-5,5,5-trifluoropentyl}-N-phenylmethanesulfonamide (**11a**).* Following general procedure A, the reaction was carried out using *N*-phenyl-*N*-(prop-2-en-1-yl)methanesulfonamide[24] (1.27 g, 6.0 mmol), xanthate **1** (1.86 g, 7.8 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 80:20) to afford the corresponding xanthate adduct **11a** (2592 mg, 96%) as a mixture of two diastereoisomers 80:20 and as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.50–7.35 (m, 5H), 4.60–4.51 (m, 2H), 4.47–4.39 (m, 0.2H), 4.39–4.29 (m, 0.8H), 4.10–4.00 (m, 1.2H), 3.98–3.82 (m, 1.8H), 2.90 (s, 2.4H), 2.89 (s, 0.6H), 2.75 (ddd, J=15.1, 6.9, 5.3 Hz, 0.2H), 2.56 (ddd, J=14.7, 11.9, 2.6 Hz, 0.8H), 2.19 (ddd, J=15.3, 11.9, 2.1 Hz, 0.8H), 2.19–2.12 (m, 0.2H), 1.34 (t, J=7.1 Hz, 0.6H), 1.32 (t, J=7.1 Hz, 2.4H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 210.5, 137.9, 129.7 (2C), 128.9 (2C), 128.8, 123.8 (q, J=279 Hz), 70.6, 54.9 (d, J=33.7 Hz), 53.6, 44.9, 37.1, 31.4, 13.6; minor diastereoisomer: 211.0, 138.3, 129.7, 128.9, 128.7, 123.8 (q, J=279 Hz), 70.4, 54.4 (q, J=33 Hz), 52.76, 45.9, 37.0, 33.1, 13.6; IR (CCl_4): ν_{max} 2987, 1493, 1357, 1267, 1225, 1185, 1161, 1132, 1052; HRMS (EI^+): calculated (found) for $C_{12}H_{10}^{35}ClF_3NO_2$: 328.0386 (328.0390).

*4.3.4. 5-Chloro-3-[(ethoxymethanethioyl)sulfanyl]-6,6,6-trifluoro-N-(6-methylpyridin-2-yl)hexanamide (**11b**).* Following general procedure A, the reaction was carried out using *N*-(6-methylpyridin-2-yl)but-3-enamide (500 mg, 2.83 mmol), xanthate **1** (1.0 g, 4.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 85:15) to afford the xanthate adduct **11b** (850 mg, 72%) as a mixture of two diastereoisomers 60:40 and as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 9.25 (br s, 0.4H), 9.11 (br s, 0.6H), 8.04–7.88 (m, 1H), 7.56 (t, J=7.8 Hz, 1H), 6.87 (d, J=7.4 Hz, 1H), 4.66–4.52 (m, 2H), 4.48–4.29 (m, 2H), 3.04–2.80 (m, 2H), 2.71–2.52 (m, 1H), 2.39 (s, 3H), 2.35–2.20 (m, 1H), 1.41–1.33 (m, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 211.7, 168.0, 156.5, 150.3, 138.7, 123.7 (q, J=279 Hz), 119.5, 111.3, 70.4, 55.3 (q, J=33 Hz), 43.5, 41.8, 34.6, 23.7, 13.5; minor diastereoisomer: 211.6, 168.0, 156.5, 150.2, 138.7, 123.7 (q, J=279 Hz), 119.6, 111.4, 70.3, 54.8 (q, J=33 Hz), 43.1, 39.2, 34.4, 23.7, 13.5; IR (CCl_4): ν_{max} 3419, 2928, 1702, 1456, 1267, 1230, 1128, 1051; HRMS (EI^+): calculated (found) for $C_{15}H_{18}^{35}ClF_3N_2O_2S_2$: 414.0450 (414.0448).

*4.3.5. Ethyl ({4-chloro-5,5,5-trifluoro-1-[1-(4-methoxyphenyl)-N-methylformamido]pentan-2-yl}sulfanyl)carbothioate (**11c**).* Following general procedure A, the reaction was carried out with 4-methoxy-*N*-methyl-*N*-(prop-2-en-1-yl)benzamide[18b] (609 mg, 3.0 mmol), xanthate **1** (928 mg, 3.9 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diether ether 80:20 to 20:80) to afford the xanthate adduct **11c** (620 mg, 47%) as a mixture of two diastereoisomers 65:35 and as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.36 (d, J=8.6 Hz, 2H), 6.90 (d, J=8.7 Hz, 2H), 4.71–4.58 (m, 2.35H), 4.53–4.12 (m, 2H), 3.90–3.75 (m, 4H), 3.57–3.39 (m, 0.65H), 3.12 (s, 1.95H), 3.09 (s, 1.05H), 2.53–2.08 (m, 2H), 1.44–1.39 (m, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 211.6, 172.1, 160.7, 128.9 (2C), 127.8, 123.7 (q, J=279 Hz), 113.7 (2C), 70.7, 55.3, 55.7–54.2(m), 50.5, 45.3, 38.4, 32.4, 13; minor diastereoisomer: 211.8, 171.9, 160.8, 128.9 (2C), 127.6, 123.6 (q, 279 Hz), 113.7 (2C), 70.5, 55.3, 55.7–54.2 (m), 49.5, 45.9, 39.5, 34.1, 13.6; IR (CCl_4): ν_{max} 2933, 1642, 1610, 1483, 1393, 1303, 1252, 1223, 1173, 1130, 1052; HRMS (EI^+): calculated (found) for $C_{14}H_{16}^{35}ClF_3NO_2$: 322.0822 (322.0832).

*4.3.6. N-{4-Chloro-2-[(ethoxymethanethioyl)sulfanyl]-5,5,5-trifluoropentyl}-N-(6-fluoropyridin-2-yl)acetamide (**11d**).* Following general procedure A, the reaction was carried out with *N*-(6-fluoropyridin-2-yl)-*N*-(prop-2-en-1-yl)acetamide[18a] (2.00 g, 10.3 mmol), xanthate **1** (4.17 g, 17.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 75:25) to afford the xanthate adduct **11d** (3.86 mg, 84%) as a mixture of two diastereoisomers 60:40 and as a yellow oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H major diastereoisomer: 7.93 (m, 1H), 7.24–7.15 (m, 1H), 6.99–6.93 (m, 1H), 4.66–4.55 (m, 2H), 4.49 (dd, J=13.7, 8.5 Hz, 1H), 4.43–4.35 (m, 1H), 4.22–4.06 (m, 1H), 4.03 (dd, J=13.7, 6.2 Hz, 1H), 2.31 (dd, J=8.4, 5.9 Hz, 2H), 2.12 (s, 3H), 1.40 (t, J=7.1 Hz, 3H); minor diastereoisomer: 7.93 (m,

1H), 7.24–7.15 (m, 1H), 6.99–6.93 (m, 1H), 4.66–4.55 (m, 3H), 4.28 (dd, J=6.1, 4.6 Hz, 2H), 4.22–4.06 (m, 1H), 2.53 (ddd, J=14.8, 8.7, 4.1 Hz, 1H), 2.23 (ddd, J=15.1, 9.8, 5.5 Hz, 1H), 2.11 (s, 3H), 1.41 (t, J=7.1 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 211.1, 170.6, 162.5 (d, J=244 Hz), 152.8 (d, J=13 Hz), 143.0 (d, J=7 Hz), 123.8 (q, J=279 Hz), 118.8 (d, J=5 Hz), 108.2 (d, J=36 Hz), 70.5, 55.2 (q, J=33 Hz), 49.9, 45.9, 32.3, 23.0, 13.6; minor diastereoisomer: 211.3, 170.8, 162.4 (d, J=244 Hz), 152.9 (d, J=13 Hz), 143.0 (d, J=7 Hz), 123.9 (q, J=279 Hz), 118.8 (d, J=5 Hz), 108.2 (d, J=36 Hz), 70.4, 54.6 (q, J=33 Hz), 48.4, 46.3, 33.9, 23.0, 13.6; IR (CCl_4): ν_{max} 2928, 1684, 1600, 1452, 1378, 1311, 1267, 1226, 1131, 1049; HRMS (EI^+): calculated (found) for $C_{12}H_{12}^{35}ClF_4N_2O$: 311.0574 (311.0576).

*4.3.7. N-{5-Chloro-3-[(ethoxymethanethioyl)sulfanyl]-6,6,6-trifluorohexyl}-N-(6-fluoropyridin-2-yl)acetamide (**11e**).* Following general procedure A, the reaction was carried out with *N*-(but-3-en-1-yl)-*N*-(6-fluoropyridin-2-yl)acetamide[18e] (370 g, 1.78 mmol), xanthate **1** (550 g, 2.31 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 60:40) to afford the xanthate adduct **11e** (740 mg, 93%) as a mixture of two diastereoisomers 60:40 and as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.87–7.77 (m, 1H), 7.25–7.11 (m, 1H), 6.87–6.76 (m, 1H), 4.60 (q, J=6.8 Hz, 2H), 4.47–4.37 (m, 0.45H), 4.33 (dqd, J=11.0, 6.6, 2.3 Hz, 0.55H), 4.05–3.77 (m, 3H), 2.38–2.20 (m, 2H), 2.19–2.08 (m, 2H), 2.07 (s, 1.35H), 2.06 (s, 1.65H), 1.38 (t, J=7.1 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 211.7, 170.1, 162.2 (d, J=243 Hz), 153.2 (d, J=13.3 Hz), 142.7 (d, J=7.7 Hz), 123.8 (q, J=279 Hz), 117.7 (d, J=5 Hz), 107.3 (d, J=36 Hz), 70.4, 55.1 (q, J=33 Hz), 45.2, 45.1, 35.4, 33.9, 23.2, 13.5; minor diastereoisomer: 211.6, 170.2, 162.1 (d, J=243 Hz), 153.2 (d, J=13.3 Hz), 142.8 (d, J=7.7 Hz), 123.8 (q, J=279 Hz), 117.4 (d, J=5 Hz), 107.2 (d, J=36 Hz), 70.2, 54.4 (q, J=33 Hz), 45.2, 44.2, 35.4, 30.0, 23.2, 13.5; IR (CCl_4): ν_{max} 2985, 1682, 1600, 1453, 1376, 1268, 1224, 1130, 1050; HRMS (EI^+): calculated (found) for $C_{16}H_{19}^{35}ClF_4N_2O_2S_2$: 446.0513 (446.0514).

*4.3.8. 5-Chloro-N-(2,4-dichlorophenyl)-3-[(ethoxymethanethioyl)sulfanyl]-6,6,6-trifluorohexanamide (**11f**).* Following general procedure A, the reaction was carried out with *N*-(2,4-dichlorophenyl)but-3-enamide[18d] (690 mg, 3.0 mmol), xanthate **1** (928 mg, 3.9 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 60:40) to afford the xanthate adduct **11f** (1.37 g, 98%) as a mixture of two diastereoisomers 65:35 and as a yellow oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 8.33 (br s, 0.35H), 8.25 (br s, 0.65H), 7.40–7.36 (m, 2H), 7.06 (s, 1H), 4.68–4.58 (m, 2H), 4.45–4.32 (m, 2H), 3.01 (dd, J=15.7, 5.2 Hz, 0.65H), 2.89 (dd, J=15.7, 7.5 Hz, 1.35H), 2.61 (ddd, J=14.7, 8.9, 3.7 Hz, 0.35H), 2.53 (ddd, J=13.7, 11.6, 1.9 Hz, 0.65H), 2.35 (ddd, J=15.1, 10.3, 5.4 Hz, 0.35H), 2.24 (ddd, J=14.9, 11.6, 3.2 Hz, 0.65H), 1.45–1.36 (m, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 212.0, 168.4, 138.8, 135.1 (2C), 124.7, 123.7 (q, J=279 Hz), 118.5 (2C), 70.9, 55.1 (q, J=33 Hz), 43.7, 42.3, 34.8, 13.6; minor diastereoisomer: 211.8, 168.4, 138.7, 135.1 (2C), 124.7, 123.7 (q, J=279 Hz), 118.6 (2C), 70.7, 54.7 (q, J=33 Hz), 43.3, 39.9, 34.9, 13.6; IR (CCl_4): ν_{max} 3434, 2987, 1709, 1586, 1518, 1444, 1406, 1268, 1228, 1129, 1050; HRMS (EI^+): calculated (found) for $C_{15}H_{15}^{35}Cl_3F_3NO_2S_2$: 466.9562 (466.9557).

*4.3.9. 6-Chloro-4-[(ethoxymethanethioyl)sulfanyl]-7,7,7-trifluoro-1-(4-methoxyphenyl)heptan-1-one (**11g**).* Following general procedure A, the reaction was carried out using 1-(4-methoxyphenyl)pent-4-en-1-one (380 mg, 2.0 mmol), xanthate **1** (619 mg, 2.6 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10) to afford the corresponding xanthate adduct **11g** (850 mg, 99%) as a mixture of two diastereoisomers 60:40 and as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.99 (d, J=8.9 Hz, 2H), 6.99 (d, J=8.9 Hz, 2H), 4.76–4.57 (m, 2H), 4.50–4.40 (m, 1H), 4.23–4.14 (m, 0.6H), 4.14–4.06 (m, 0.4H), 3.92 (s, 3H), 3.29–3.10 (m, 2H), 2.47–2.09 (m, 3.6H), 1.96 (ddt, J=14.0, 10.4, 6.7 Hz, 0.4H), 1.49–1.41 (m, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 212.0, 197.1, 163.6, 130.3 (2C), 129.8, 124.0 (q, J=279 Hz), 113.8 (2C), 70.5, 55.5, 55.4 (q, J=33 Hz), 47.4, 36.3, 35.1, 30.0, 13.6; minor diastereoisomer: 211.9, 197.05, 163.68, 130.3 (2C), 129.7, 124.0 (q, J=279 Hz), 113.8 (2C), 70.3, 55.5, 54.7 (q, J=33 Hz), 46.6, 36.8, 35.0, 26.1, 13.6; IR (CCl_4): ν_{max} 2937, 1682, 1602, 1510, 1263, 1223, 1170, 1127, 1052; HRMS (EI^+): calculated (found) for $C_{17}H_{20}^{35}ClF_3O_3S_2$: 428.0494 (428.0504).

*4.3.10. N,N-Diphenylundec-10-enamide (**10j**).* A magnetically round bottom flask was charged with *N*-phenylaniline (13.50 g, 80 mmol), undec-10-enoyl chloride (4.04 g, 20 mmol), and 20 mL of toluene and the solution was heated up to reflux. After 3 h, 37% HCl solution (6.7 mL, 80 mmol) was added slowly, the salts filtered off and the solvent evaporated under reduced pressure. The residue was recrystallized from petroleum ether to afford the desired olefin **10j** (6.7 g, 100%) as white crystals. Mp: 51 °C. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.44–7.30 (m, 4H), 7.29–7.18 (m, 6H), 5.80 (ddt, J=16.9, 10.2, 6.7 Hz, 1H), 4.98 (dd, J=17.1, 1.7 Hz, 1H), 4.92 (d, J=10.2, 1H), 2.25 (t, J=7.5 Hz, 2H), 2.02 (m, 2H), 1.64 (m, 2H), 1.44–1.17 (m, 10H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 172.8, 142.6 (2C), 138.6, 129.7–124.8 (10C), 113.8, 37.9, 33.4, 28.9, 28.9, 28.8, 28.6, 28.5, 25.13; IR (CCl_4): ν_{max} 2928, 2856, 1679, 1493, 1370, 1274; HRMS (EI^+): calculated (found) for $C_{15}H_{18}^{35}ClF_3O_2S_2$: 335.2249 (335.2249).

*4.3.11. Dimethyl 4-chloro-2-[(ethoxymethanethioyl)sulfanyl]-5,5,5-trifluoropentane-1-phosphonate (**11h**).* Following general procedure A, the reaction was carried out using dimethyl (prop-2-en-1-yl) phosphonate (150 mg, 1 mmol), xanthate **1** (476 mg, 2 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 30:70) to afford the corresponding xanthate adduct **11h** (300 mg, 77%) as a mixture of two diastereoisomers 65:35 and as a pale yellow oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 4.72–4.61 (m, 2H), 4.48–4.18 (m, 2H), 3.83–3.74 (m, 6H), 2.69 (ddd, J=14.8, 8.7, 4.1 Hz, 0.35H), 2.59–2.46 (m, 1.3H), 2.41–2.21 (m, 2.35H), 1.44 (t, J=7.1 Hz, 1.95H), 1.43 (t, J=7.1 Hz, 1.05H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 211.0, 123.8 (q, J=279 Hz), 70.5, 55.2 (q, J=34 Hz), 52.8–52.6 (m, 2C), 42.1 (d, J=2 Hz), 34.6, 31.5 (d, J=137 Hz), 13.7; minor diastereoisomer: 211.5, 123.9 (q, J=279 Hz), 70.4, 54.8 (q, J=34 Hz), 52.8–52.6 (m, 2C), 41.4 (d, J=4 Hz), 35.3 (d, J=3 Hz), 28.9 (d, J=141 Hz), 13.7; IR (CCl_4): ν_{max} 2954, 1269, 1227, 1127, 1048; HRMS (EI^+): calculated (found) for $C_{10}H_{17}^{35}ClF_3O_4PS_2$: 387.9946 (Found: 387.9950).

*4.3.12. Ethyl {[4-chloro-5,5,5-trifluoro-1-(4-methoxyphenoxy)pentan-2-yl]sulfanyl}methanethioate (**11i**).* Following general procedure A, the reaction was carried out using 1-methoxy-4-(prop-2-en-1-yloxy)benzene (164 mg, 1.0 mmol), xanthate **1** (357 mg, 1.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 98:2) to afford the xanthate adduct **11i** (358 mg, 89%) as a mixture of two diastereoisomers 60:40 and as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 6.90–6.80 (m, 4H), 4.68 (q, J=7.1 Hz, 2H), 4.50–4.32 (m, 2H), 4.29–4.24 (m, 1H), 4.18–4.07 (m, 1H), 3.78 (s, 3H), 2.71 (ddd, J=13.5, 9.7, 3.6 Hz, 0.4H), 2.47–2.40 (m, 1H), 2.35 (ddd, J=14.6, 10.7, 5.2 Hz, 0.6H), 1.44 (t, J=7.1 Hz, 3H); ^{13}C NMR (100 MHz; CDCl3): δ_C major diastereoisomer: 211.5, 154.3, 152.1, 123.9 (q, J=278 Hz), 115.7 (2C), 114.5 (2C), 70.6, 70.4, 55.7–54.3 (m, 2C), 46.5, 32.4, 13.5; minor diastereoisomer: 211.8, 154.4, 152.0, 123.8 (q, J=278 Hz), 115.6 (2C), 114.5 (2C), 70.5, 69.9, 55.7–54.3 (m, 2C), 45.8, 32.8, 13.5; IR (CCl_4): ν_{max} 2935, 1508, 1267, 1228, 1183, 1130, 1049; HRMS (EI^+): calculated (found) for $C_{15}H_{18}^{35}ClF_3O_2S_2$: 402.0338 (402.0349).

*4.3.13. 12-Chloro-10-[(ethoxymethanethioyl)sulfanyl]-13,13,13-trifluoro-N,N-diphenyltridecanamide (**11j**).* Following general procedure A, the reaction was carried out using *N*,*N*-diphenylundec-10-enamide (1.10 g,

3.3 mmol), xanthate **1** (1.19 g, 5.0 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20) to afford the xanthate adduct **11j** (1768 mg, 92%) as a mixture of two diastereoisomers 55/45 and as a yellow oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.45–7.30 (m, 4H), 7.30–7.14 (m, 6H), 4.72–4.59 (m, 2H), 4.42–4.32 (m, 0.55H), 4.27–4.18 (m, 0.45H), 4.06–3.93 (m, 1H), 2.37–2.29 (m, 1H), 2.29–2.22 (m, 2H), 2.22–2.06 (m, 1H), 1.83–1.51 (m, 4H), 1.51–1.35 (m, 5H), 1.35–1.17 (m, 8H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 212.5, 173.2, 142.9 (2C), 130.3–125.4 (m, 10C), 123.9 (q, J=279 Hz), 70.24, 55.5 (q, J=33 Hz), 47.4, 35.7, 35.2, 31.5, 29.3–28.9 (m, 4C), 26.5, 25.4, 13.7; minor diastereoisomer: 212.5, 173.2, 142.9 (2C), 130.3–125.4 (m, 10C), 123.9 (q, J=279 Hz), 70.0, 54.6 (q, J=33 Hz), 46.7, 35.9, 35.7, 35.2, 29.3–28.9 (m, 4C), 26.3, 25.4, 13.7; IR (CCl_4): ν_{max} 2928, 2856, 1680, 1493, 1370, 1267, 1220, 1052; HRMS (EI$^+$): calculated (found) for $C_{25}H_{30}^{35}ClF_3NO$: 452.1968 (452.1968).

*4.3.14. 3-(2-Chloro-3,3,3-trifluoropropyl)-1-methanesulfonyl-2,3-dihydro-1H-indole (**12a**).* A solution of xanthate adduct **11a** (5.76 mmol) in DCE (30 mL) was refluxed under a flow of nitrogen for 15 min. Lauroyl peroxide (DLP) (756 mg, 33 mol %) was then added every hour until total conversion of the starting olefin was observed. The mixture was cooled to room temperature and the solvent evaporated under reduced pressure. Recrystallization using petroleum ether and AcOEt afforded the desired compound **12a** (950 mg, 48%) as a mixture of two diastereoisomers 65:35 and as white crystals. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.47–7.39 (m, 1H), 7.33–7.19 (m, 2H), 7.12–7.06 (m, 1H), 4.21–4.12 (m, 1H), 4.12–4.02 (m, 1H), 3.82 (dd, J=10.3, 3.4 Hz, 0.65H), 3.79–3.72 (m, 0.35H), 3.71–3.65 (m, 0.65H), 3.65–3.57 (m, 0.35H), 2.91 (s, 3H), 2.37–2.07 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 141.6, 131.9, 129.3, 123.9 (q, J=279 Hz), 124.9, 123.7, 113.7, 56.7, 55.6 (q, J=34 Hz), 36.6, 35.6, 34.3; minor diastereoisomer: 141.6, 132.7, 129.0, 123.8 (q, J=279 Hz), 124.5, 124.0, 113.6, 55.3 (q, J=34 Hz), 54.8, 36.4, 35.8, 34.6; IR (CCl_4): ν_{max} 1480, 1366, 1276, 1263, 1168, 1132; HRMS (EI$^+$): calculated (found) for $C_{12}H_{13}^{35}ClF_3NO_2$: 327.0308 (327.0318).

*4.3.15. 4-(2-Chloro-3,3,3-trifluoropropyl)-7-methyl-1,2,3,4-tetrahydro-1,8-naphthyridin-2-one (**12b**).* Following general procedure B with **11b** (830 mg, 2 mmol) in chlorobenzene. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 50:50) to afford the product **12b** (250 mg, 43%) as a mixture of two diastereoisomers 60:40 and as an amorphous white solid. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 9.97 (br s, 0.4H), 9.95 (br s, 0.6H), 7.47 (d, J=7.6 Hz, 0.6H), 7.41 (d, J=7.6 Hz, 0.4H), 6.94 (d, J=7.6 Hz, 1H), 4.26 (dqd, J=12.3, 6.2, 3.6 Hz, 0.4H), 3.74 (dqd, J=12.5, 6.3, 2.4 Hz, 0.6H), 3.38–3.28 (m, 1H), 2.90 (dd, J=16.5, 6.4 Hz, 0.6H), 2.79 (dd, J=16.5, 6.9 Hz, 0.4H), 2.61–2.54 (m, 1H), 2.53 (s, 1.8H), 2.52 (s, 1.2H), 2.25–2.12 (m, 1H), 2.05 (ddd, J=14.9, 11.3, 4.6 Hz, 0.4H), 1.94 (ddd, J=14.9, 11.3, 4.6 Hz, 0.6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 170.4, 157.7, 149.7, 136.7, 123.7 (q, J=279 Hz), 118.3, 115.3, 55.5 (q, J=33 Hz), 36.7, 34.2, 31.1, 23.5; minor diastereoisomer: 169.7, 157.7, 149.7, 136.7, 123.8 (q, J=279 Hz), 118.5, 117.4, 54.4 (q, J=33 Hz), 34.4, 34.0, 31.0, 23.4; IR (CCl_4): ν_{max} 3406, 2929, 1711, 1455, 1268, 1131; HRMS (EI$^+$): calculated (found) for $C_{12}H_{12}^{35}ClF_3N_2O$: 292.0590 (292.0603).

*4.3.16. 4-(2-Chloro-3,3,3-trifluoropropyl)-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinolin-1-one (**12c**).* Following general procedure B with **11c** (500 mg, 1.13 mmol) in chlorobenzene. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 80:20) to afford the product **12c** (190 mg, 51%) as a mixture of two diastereoisomers 85:15 and as an amorphous white solid. Mp=98–102 °C. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H major diastereoisomer: 8.09 (d, J=8.7 Hz, 1H), 6.92 (dd, J=8.7, 2.5 Hz, 1H), 6.78 (d, J=2.5 Hz, 1H), 3.99 (dd, J=12.7, 4.1 Hz, 1H), 3.92–3.80 (m, 4H), 3.24 (dd, J=12.7, 1.6 Hz, 1H), 3.20–3.15 (m, 1H), 3.15 (s, 3H), 2.39 (ddd, J=13.8, 11.3, 2.4 Hz, 1H), 2.03 (ddd, J=14.2, 12.1, 3.9 Hz, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 164.0, 162.2, 140.3, 131.3, 123.9 (q, J=279 Hz), 121.3, 113.0, 112.3, 56.1 (q, J=33 Hz), 55.5, 53.6, 35.4, 34.9, 34.2; IR (CCl_4): ν_{max} 2930, 1662, 1609, 1325, 1260, 1170, 1131; HRMS (EI$^+$): calculated (found) for $C_{14}H_{15}^{35}ClF_3NO_2$: 321.0743 (321.0750).

*4.3.17. 1-[3-(2-Chloro-3,3,3-trifluoropropyl)-6-fluoro-1H,2H,3H-pyrrolo[2,3-b]pyridin-1-yl]ethan-1-one (**12d**).* Following general procedure B with **11d** (3.45 mg, 7.7 mmol) in chlorobenzene. The residue was purified by silica gel column chromatography (DCM) and recrystallized from an EP/Et_2O mixture to afford the product **12d** (895 mg, 36%) as a mixture of two diastereoisomers 55:45 and as an amorphous white solid. Mp=120 °C. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H major diastereoisomer: 7.67–7.58 (m, 1H), 6.58 (dd, 8.0, 1.9 Hz, 1H), 4.36–4.26 (m, 1H), 4.27–4.15 (m, 1H), 4.02 (dd, J=12.4, 4.0 Hz, 1H), 3.58–3.48 (m, 1H), 2.68 (s, 3H), 3.32–2.13 (m, 2H); minor diastereoisomer: 7.67–7.58 (m, 1H), 6.58 (dd, 8.0, 1.9 Hz, 1H), 4.36–4.26 (m, 1H), 4.27–4.15 (m, 1H), 3.86 (dd, J=12.2, 5.9 Hz, 1H), 3.69–3.58 (m, 1H), 2.68 (s, 3H), 3.32–2.13 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 169.8, 163.0 (d, J=239 Hz), 154.0 (d, J=17 Hz), 137.2 (d, J=9 Hz), 123.8 (q, J=279 Hz), 123.3 (d, J=5 Hz), 101.9 (d, J=37 Hz), 55.1 (q, J=33 Hz), 53.0, 36.3, 32.5, 24.9; minor diastereoisomer: 169.8, 163.0 (d, J=239 Hz), 153.8 (d, J=17 Hz), 136.9 (d, J=9 Hz), 123.8 (q, J=279 Hz), 123.9 (d, J=5 Hz), 102.1 (d, J=37 Hz), 54.9 (q, J=33 Hz), 51.0, 36.6, 32.1, 24.8; IR (CCl_4): ν_{max} 2928, 1681, 1605, 1483, 1386, 1297, 1262, 1132; HRMS (EI$^+$): calculated (found) for $C_{12}H_{11}^{35}ClF_4N_2O$: 310.0496 (310.0497).

*4.3.18. 1-[4-(2-Chloro-3,3,3-trifluoropropyl)-7-fluoro-1,2,3,4-tetrahydro-1,8-naphthyridin-1-yl]ethan-1-one (**12e**).* Following general procedure B with **11e** (500 mg, 1.15 mmol) in chlorobenzene. The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20 to 50:50) to afford the product **12e** (187 mg, 50%) as a mixture of two diastereoisomers 60:40 and as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.69–7.53 (m, 1H), 6.70–6.62 (m, 1H), 4.20 (dqd, J=12.6, 6.3, 2.8 Hz, 0.6H), 4.06–3.71 (m, 2.4H), 3.34–3.16 (m, 1H), 2.56 (s, 1.8H), 2.55 (s, 1.2H), 2.26–1.93 (m, 3.4H), 1.77–1.67 (m, 0.6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 171.3, 160.1 (d, J=239 Hz), 149.3 (d, J=15 Hz), 141.4 (d, J=8 Hz), 123.9 (q, J=279 Hz), 122.3 (d, J=5 Hz), 104.3 (d, J=37 Hz), 55.0 (q, J=33 Hz), 40.1, 36.1, 32.0, 26.1, 26.0; minor diastereoisomer: 171.7, 160.8 (d, J=239 Hz), 149.1 (d, J=15 Hz), 141.3 (d, J=8 Hz), 123.9 (q, J=279 Hz), 121.6 (d, J=5 Hz), 103.9 (d, J=37 Hz), 55.8 (q, J=33 Hz), 40.7, 34.3, 32.7, 27.5, 26.2; IR (CCl_4): ν_{max} 2934, 1682, 1585, 1465, 1435, 1370, 1274, 1131; HRMS (EI$^+$): calculated (found) for $C_{13}H_{13}^{35}ClF_4N_2O_2$: 324.0653 (not found).

*4.3.19. 6,8-Dichloro-4-(2-chloro-3,3,3-trifluoropropyl)-1,2,3,4-tetrahydroquinolin-2-one (**12f**).* Following general procedure B with **11f** (830 mg, 1.77 mmol) in chlorobenzene. The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20 to 50:50) to afford the product **12f** (282 mg, 46%) as a mixture of two diastereoisomers 65:35 and as an amorphous white solid. Mp=192 °C. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 9.87 (br s, 0.35H), 9.81 (s, 0.65H), 7.13 (d, J=2.0 Hz, 0.65H), 7.12 (d, J=2.0 Hz, 0.35H), 6.88 (d, J=2.0 Hz, 0.65H), 6.86 (d, J=2.0 Hz, 0.35H), 4.33–4.23 (m, 0.35H), 4.16–4.04 (m, 0.65H), 3.85–3.78 (m, 0.35H), 3.78–3.72 (m, 0.65H), 2.87–2.64 (m, 2H), 2.27 (ddd, J=14.7, 8.6, 3.0 Hz, 0.7H), 2.13–1.96 (m, 1.3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major diastereoisomer: 170.9, 138.9, 134.6, 133.9, 124.3, 123.7 (q, J=279 Hz), 122.3, 115.5, 55.3 (q, J=34 Hz), 36.2, 35.8, 30.2; minor diastereoisomer: 170.2, 138.7, 134.5, 133.9, 124.3, 123.8 (q, J=279 Hz), 122.1, 115.0, 54.3 (q, J=34 Hz), 32.7, 31.9, 29.8; IR (CCl_4):

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ν_{max} 3409, 1716, 1693, 1600, 1575, 1260, 1174, 1129; HRMS (EI^+): calculated (found) for $C_{12}H_9^{35}Cl_3F_3NO$: 344.9702 (344.9711).

*4.3.20. 4-(2-Chloro-3,3,3-trifluoropropyl)-6-methoxy-1,2,3,4-tetrahydronaphthalen-1-one (**12g**).* Following general procedure B with **11g** (850 mg, 2 mmol) in ethyl acetate. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10) to afford the product **12g** (390 mg, 64%) as a mixture of two diastereoisomers 85:15 and as an amorphous white solid. ^1H NMR (400 MHz; $CDCl_3$): δ_H 8.03 (d, J=8.7 Hz, 1H), 6.87 (dd, J=8.7, 2.4 Hz, 1H), 6.78 (d, J=2.4 Hz, 1H), 4.01 (dqd, J=12.8, 6.5, 2.7 Hz, 1H), 3.86 (s, 3H), 3.31–3.22 (m, 1H), 2.73–2.56 (m, 2H), 2.46–2.25 (m, 2H), 2.13–2.00 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 195.6, 163.6, 146.9, 130.8, 125.3, 124.0 (q, J=279 Hz), 133.3, 112.9, 56.1 (q, J=33 Hz), 55.4, 35.8, 34.1, 33.6, 28.2; IR (CCl_4): ν_{max} 2929, 1685, 1599, 1269, 1256, 1129; HRMS (EI^+): calculated (found) for $C_{14}H_{14}^{35}ClF_3O_2$: 306.0634 (306.0638).

*4.3.21. Dimethyl (4-chloro-5,5,5-trifluoropentyl)phosphonate (**13a**).* A magnetically round bottom flask was charged with **11h** (300 mg, 0.77 mmol), an aqueous solution of hypophosphorous acid (50% wt) (504 mg, 3.85 mmol), triethylamine (429 mg, 4.25 mmol), 7.6 mL of dioxane. The solution was refluxed under a flow of nitrogen for 5 min then AIBN (13 mg, 0.08 mmol) was added every hour until TLC showed total conversion of the starting xanthate. The mixture was cooled to room temperature and ethyl acetate was added. The layers were partitioned and the aqueous one was extracted twice with ethyl acetate. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The residue was purified by silica gel column chromatography (DCM/methanol 95:5) to afford the product **13a** (188 mg, 93%) as an orange oil. ^1H NMR (400 MHz; $CDCl_3$): δ_H 4.06 (dqd, J=9.8, 6.6, 3.2 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.14–1.68 (m, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 124.0 (q, J=279 Hz), 56.9 (q, J=33 Hz), 52.4 (d, J=7 Hz), 52.4 (d, J=7 Hz), 31.4 (d, J=15 Hz), 23.8 (d, J=143 Hz), 19.0 (d, J=5 Hz); IR (CCl_4): ν_{max} 3685, 3453, 2953, 1267, 1180, 1126, 1062; HRMS (EI^+): calculated (found) for $C_7H_{13}^{35}ClF_3O_3P$: 268.0243 (not found).

*4.3.22. 1-[(4-Chloro-5,5,5-trifluoropentyl)oxy]-4-methoxybenzene (**13b**).* A magnetically round bottom flask was charged with **11i** (670 mg, 1.66 mmol), tris(trimethylsilyl)silane (496 mg, 2 mmol) in 16 mL of a 1:1 solution of toluene and cyclohexane. The solution was refluxed under a flow of nitrogen for 5 min then AIBN (26 mg, 0.16 mmol) was added. After 30 min, the mixture was cooled to room temperature and the solvent evaporated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 96:4) to afford the product **13b** (230 mg, 47%) as a colorless oil. ^1H NMR (400 MHz; $CDCl_3$): δ_H 6.84 (s, 4H), 4.25–4.14 (m, 1H), 4.03–3.91 (m, 2H), 3.77 (s, 3H), 2.33–2.22 (m, 1H), 2.17–2.05 (m, 1H), 2.03–1.88 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 154.0, 152.9, 124.14 (q, J=279 Hz), 115.4 (2C), 114.7 (2C), 67.3, 57.4 (q, J=33 Hz), 55.8, 28.1, 25.6; IR (CCl_4): ν_{max} 2935, 1508, 1272, 1231, 1172, 1131; HRMS (EI^+): calculated (found) for $C_{15}H_{18}^{35}ClF_3O_2S_2$: 282.0634 (282.0632).

*4.3.23. 12-Chloro-13,13,13-trifluoro-N,N-diphenyltridecanamide (**13c**).* A magnetically round bottom flask was charged with **11j** (803 mg, 1.4 mmol), an aqueous solution of hypophosphorous acid (50% wt) (924 mg, 7.0 mmol), triethylamine (777 mg, 7.7 mmol) in 14 mL of dioxane. The solution was refluxed under a flow of nitrogen for 5 min then AIBN (23 mg, 0.14 mmol) was added every hour until TLC showed total conversion of the starting xanthate. The mixture was cooled to room temperature and ethyl acetate was added. The layers were partitioned and the aqueous one was extracted twice with ethyl acetate. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20) to afford the product **13c** (625 mg, 98%) as an orange oil. ^1H NMR (400 MHz; $CDCl_3$): δ_H 7.46–7.32 (m, 4H), 7.31–7.17 (m, 6H), 4.07 (dqd, J=10.0, 6.7, 3.3 Hz, 1H), 2.27 (t, J=7.5 Hz, 2H), 2.04–1.93 (m, 1H), 1.86–1.72 (m, 1H), 1.72–1.58 (m, 3H), 1.49–1.19 (m, 13H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 173.2, 142.9 (2C), 130.4–125.3 (m, 10C), 124.1 (q, J=280 Hz), 57.6 (q, J=33 Hz), 35.2, 30.8, 29.3 (3C), 29.1 (2C), 28.6, 25.5 (2C); IR (CCl_4): ν_{max} 2928, 2856, 1680, 1493, 1371, 1269, 1178, 1129; HRMS (EI^+): calculated (found) for $C_{25}H_{31}^{35}ClF_3NO$: 453.2046 (453.2035).

*4.3.24. 3-(3,3-Difluoroprop-2-en-1-yl)-1-methanesulfonyl-2,3-dihydro-1H-indole (**14a**).* Following general procedure C with **12a** (80 mg, 0.24 mmol). **14a** (64 mg, 95%) was obtained as a white solid without purification. ^1H NMR (400 MHz; $CDCl_3$): δ_H 7.45 (d, J=8.1 Hz, 1H), 7.33–7.22 (m, 2H), 7.11 (td, J=7.5, 0.9 Hz, 1H), 4.21 (dtd, J=24.7, 8.0, 2.2 Hz, 1H), 4.10 (dd, J=10.4, 9.2 Hz, 1H), 3.69 (dd, J=10.4, 5.9 Hz, 1H), 3.50–3.41 (m, 1H), 2.93 (s, 3H), 2.50–2.40 (m, 1H), 2.36–2.26 (m, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 157.1 (t, J=288 Hz), 141.8, 133.3, 128.7, 124.6, 123.7, 113.5, 74.7 (dd, J=23, 20 Hz), 55.3, 39.7 (t, J=2 Hz), 34.5, 27.3 (d, J=4 Hz); IR (CCl_4): ν_{max} 1746, 1480, 1460, 1364, 1166; HRMS (EI^+): calculated (found) for $C_{12}H_{13}F_2NO_2$: 273.0635 (273.0640).

*4.3.25. 4-(3,3-Difluoroprop-2-en-1-yl)-7-methyl-1,2,3,4-tetrahydro-1,8-naphthyridin-2-one (**14b**).* Following general procedure C with **12b** (50.0 mg, 0.17 mmol). **14b** (40.4 mg, 100%) was obtained as a colorless oil without purification. ^1H NMR (400 MHz; $CDCl_3$): δ_H 8.51 (br s, 1H), 7.35 (d, J=7.6 Hz, 1H), 6.82 (d, J=7.6 Hz, 1H), 4.12 (dtd, J=24.5, 8.0, 2.0 Hz, 1H), 3.01–2.93 (m, 1H), 2.77 (dd, J=16.4, 6.3 Hz, 1H), 2.56 (dd, J=16.4, 4.6 Hz, 1H), 2.48 (s, 3H), 2.33–2.20 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 170.1, 158.4 (t, J=287 Hz), 156.6, 149.5, 136.12, 118.2, 117.4, 74.6 (dd, J=24, 21 Hz), 35.8, 34.9 (t, J=2 Hz), 27.0 (d, J=4 Hz), 23.6; IR (CCl_4): ν_{max} 3408, 2927, 1745, 1709, 1608, 1456, 1350, 1275, 1156; HRMS (EI^+): calculated (found) for $C_{12}H_{12}F_2N_2O$: 238.0918 (238.0925).

*4.3.26. 4-(3,3-Difluoroprop-2-en-1-yl)-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinolin-1-one (**14c**).* Following general procedure C with **12c** (95 mg, 0.29 mmol). **14c** (75.1 mg, 97%) was obtained as a pale yellow oil without purification. ^1H NMR (400 MHz; $CDCl_3$): δ_H 8.02 (d, J=8.7 Hz, 1H), 6.84 (dd, J=8.7, 2.5 Hz, 1H), 6.63 (d, J=2.5 Hz, 1H), 4.17 (dddd, J=24.8, 9.3, 7.2, 2.2 Hz, 1H), 3.82 (s, 3H), 3.73 (dd, J=12.6, 4.4 Hz, 1H), 3.28 (dd, J=12.6, 3.3 Hz, 1H), 3.10 (s, 3H), 2.84–2.76 (m, 1H), 2.42–2.31 (m, 1H), 2.30–2.19 (m, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 164.25, 162.21, 157.0 (dd, J=288, 287 Hz), 142.7, 130.5, 121.5, 112.5, 111.8, 75.4 (dd, J=23, 21 Hz), 55.3, 51.3, 37.9 (t, J=2 Hz), 35.14, 26.5 (d, J=4 Hz); IR (CCl_4): ν_{max} 2930, 1745, 1660, 1608, 1485, 1259; HRMS (EI^+): calculated (found) for $C_{14}H_{15}F_2NO_2$: 267.1071 (267.1069).

*4.3.27. 6,8-Dichloro-4-(3,3-difluoroprop-2-en-1-yl)-1,2,3,4-tetrahydroquinolin-2-one (**14f**).* Following general procedure C with **12f** (130 mg, 0.38 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 70:30) to afford **14f** (55 mg, 50%) as an amorphous white solid. Mp: 136–138 °C. ^1H NMR (400 MHz; $CDCl_3$): δ_H 9.65 (br s, 1H), 7.09 (d, J=2.0 Hz, 1H), 6.82 (d, J=2.0 Hz, 1H), 4.18 (dtd, J=24.5, 8.2, 2.1 Hz, 1H), 3.47–3.40 (m, 1H), 2.77–2.64 (m, 2H), 2.32–2.13 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 171.0, 155.8 (q, J=288 Hz), 138.7, 134.1, 133.9, 124.0, 122.5, 114.9, 74.5 (dd, J=23, 21 Hz), 34.2, 33.4, 25.7; IR (CCl_4): ν_{max} 2952, 1745, 1691, 1601, 1578, 1394, 1373, 1317; HRMS (EI^+): calculated (found) for $C_{12}H_9^{35}Cl_2F_2NO$: 291.0029 (291.0024).

*4.3.28. 3-(3,3-Difluoroprop-2-en-1-yl)-6-fluoro-1H,2H,3H-pyrrolo[2,3-b]pyridine (**16a**).* Following general procedure C with **15a**[25a]

(110 mg, 0.41 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 70:30) to afford **16a** (75 mg, 88%) as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.30–7.22 (m, 1H), 6.07 (dd, J=7.7, 1.0 Hz, 1H), 4.67 (br s, 1H), 4.17 (dtd, J=24.9, 8.0, 2.4 Hz, 1H), 3.82–3.72 (m, 1H), 3.40–3.29 (m, 2H), 2.41–2.22 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 163.9 (d, J=236 Hz), 163.1 (d, J=18 Hz), 157.0 (dd, J=288, 287 Hz), 134.6 (d, J=9 Hz), 120.1 (d, J=5 Hz), 95.3 (d, J=37 Hz), 75.0 (dd, J=23, 21 Hz), 50.3, 39.1 (t, J=2 Hz), 27.2 (d, J=4 Hz); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 163.9 (d, J=236 Hz), 163.1 (d, J=18 Hz), 157.0 (dd, J=288, 287 Hz), 134.6 (d, J=9 Hz), 120.1 (d, J=5 Hz), 95.3 (d, J=37 Hz), 75.0 (dd, J=23, 21 Hz), 50.3, 39.1 (t, J=2 Hz), 27.2 (d, J=4 Hz); IR (CCl_4): ν_{max} 3444, 2927, 1746, 1620, 1595, 1445; HRMS (EI$^+$): calculated (found) for $C_{10}H_9^{35}ClF_3N_2$: 214.0718 (214.0722).

*4.3.29. 1-[4-(3,3-Difluoroprop-2-en-1-yl)-7-fluoro-1,2,3,4-tetrahydro-1,8-naphthyridin-1-yl]ethan-1-one (**16b**).* Following general procedure C with **15b**[26(b)] (52 mg, 0.18 mmol). **16b** (35 mg, 83%) was obtained as an amorphous white solid without purification. Mp=64–66 °C. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.25 (t, J=8.0 Hz, 1H), 6.06 (dd, J=7.9, 2.4 Hz, 1H), 5.29 (br s, 1H), 4.18 (dddd, J=25.1, 8.6, 7.5, 2.4 Hz, 1H), 3.44–3.37 (m, 2H), 2.80–2.73 (m, 1H), 2.33–2.15 (m, 2H), 1.94–1.84 (m, 1H), 1.83–1.74 (m, 1H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 162.0 (d, J=235 Hz), 156.9 (dd, J=287, 288 Hz), 154.3 (d, J=17 Hz), 140.0 (d, J=9 Hz), 114.2 (d, J=4 Hz), 95.0 (d, J=37 Hz), 75.5 (dd, J=23, 21 Hz), 37.7, 34.8, 28.1 (d, J=4 Hz), 25.0; IR (CCl_4): ν_{max} 3447, 3272, 2931, 1745, 1618, 1462, 1355, 1224; HRMS (EI$^+$): calculated (found) for $C_{11}H_{11}F_3N_2$: 228.0874 (228.0881).

*4.3.30. Dimethyl (5,5-difluoropent-4-en-1-yl)phosphonate (**14h**).* Following general procedure C with **13a** (150 mg, 0.57 mmol). The residue was purified by silica gel column chromatography (DCM/methanol 95:5) to afford **14h** (98 mg, 80%) as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 4.10 (dtd, J=25.2, 7.9, 2.4 Hz, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 2.13–1.98 (m, 2H), 1.79–1.59 (m, 4H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 156.6 (t, J=287 Hz), 76.9–76.3 (m), 52.3 (d, J=6 Hz, 2C), 23.9 (d, J=142 Hz), 22.9 (dd, J=18, 4 Hz), 22.2; IR (CCl_4): ν_{max} 2953, 1747, 1248, 1064, 1036; HRMS (EI$^+$): calculated (found) for $C_7H_{13}F_2O_3P$: 214.0570 (214.0567).

*4.3.31. 1-[(5,5-Difluoropent-4-en-1-yl)oxy]-4-methoxybenzene (**14i**).* Following general procedure C with **13b** (210 mg, 0.74 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 97:3) to afford the product **14i** (153 mg, 90%) as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 6.83 (s, 4H), 4.19 (dtd, J=25.3, 7.9, 2.5 Hz, 1H), 3.92 (t, J=6.2 Hz, 2H), 3.77 (s, 3H), 2.21–2.13 (m, 2H), 1.84 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 156.4 (dd, J=287, 285 Hz), 153.9, 153.1, 115.5 (2C), 114.7 (2C), 77.5–77.0 (m), 67.6, 55.8, 29.1 (t, J=2 Hz), 19.0 (d, J=4 Hz); IR (CCl_4): ν_{max} 2951, 1746, 1509, 1231; HRMS (EI$^+$): calculated (found) for $C_{15}H_{18}^{35}ClF_3O_2S_2$: 228.0962 (228.0964).

*4.3.32. 13,13-Difluoro-N,N-diphenyltridec-12-enamide (**14j**).* Following general procedure C with **13c** (225 mg, 0.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20) to afford the product **14j** (100 mg, 50%) as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H 7.47–7.31 (m, 4H), 7.31–7.19 (m, 6H), 4.13 (dtd, J=25.6, 7.9, 2.7 Hz, 1H), 2.27 (t, J=7.5 Hz, 2H), 2.00–1.93 (m, 2H), 1.66 (q, J=7.2 Hz, 2H), 1.40–1.19 (m, 14H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 173.2, 156.1 (t, J=285 Hz), 142.9 (2C), 131.5–123.7 (10C), 78.0 (t, J=21 Hz), 35.2, 29.4, 29.3 (2C), 29.2 (2C), 28.8, 25.5, 22.1 (2C); IR (CCl_4): ν_{max} 2928, 2856, 1746, 1680, 1594, 1493, 1369, 1271; HRMS (EI$^+$): calculated (found) for $C_{25}H_{31}F_2NO$: 399.2374 (399.2371).

*4.3.33. 2-(5-Chloro-6,6,6-trifluorohex-2-en-2-yl)-5,5-dimethyl-1,3-dioxane (**18**).* A magnetically stirred round bottom flask was charged with **17** (205 mg, 0.73 mmol), xanthate **1** (260.0 mg, 1.09 mmol), ethyl acetate (1.1 mL) and the solution was heated to reflux. DLP (58 mg, 0.14 mmol) was then added by portion every hour until total consumption of the starting olefin was observed. The crude mixture was passed through a pad of basic Al_2O_3, the solvent evaporated and the residue was purified on flash column chromatography (petroleum ether/ethyl acetate 95:5) to afford compound **18** (158 mg, 75%) as two isomers in a 3.5:1 ratio. ^{1}H NMR (400 MHz; $CDCl_3$): δ_H major isomer: 5.68 (t, J=6.8 Hz, 1H), 4.74 (s, 1H), 4.14–4.04 (m, 1H), 3.66 (d, J=11.2 Hz, 2H), 3.50 (d, J=10.8 Hz, 2H) 2.79 (ddd, J=15.6, 6.8, 3.6 Hz, 1H), 2.58 (ddd, J=15.6, 9.6, 7.2 Hz, 1H), 2.10 (s, 3H), 1.76 (s, 3H), 1.22 (s, 3H), 0.74 (s, 3H); minor isomer: 5.45 (t, J=7.2 Hz, 1H), 5.05 (s, 1H), 4.16–4.05 (m, 1H), 3.69–3.62 (m, 2H), 3.50 (d, J=11.2 Hz, 2H), 2.91 (dddd, J=15.2 Hz, 7.6, 3.6, 1.2 Hz, 1H), 2.57 (dddd, J=15.2, 10.0, 7.6 1.2 Hz, 1H), 1.85 (d, J=1.2 Hz, 3H), 1.22 (s, 3H), 0.75 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ_C major isomer: 137.6, 124.0 (q, J=277 Hz), 121.7, 104.1, 77.2 (2C), 56.9 (q, J=33 Hz), 30.1, 29.5, 22.9, 21.8, 11.7; minor isomer: 137.8, 124.0 (q, J=277 Hz), 122.5, 99.4, 77.3 (2C), 57.4 (q, J=32 Hz), 30.1, 29.5, 22.9, 21.9, 18.6; IR (CCl_4): ν_{max} major isomer: 2958, 2848, 1469, 1394, 1261, 1185, 1128, 1016, 983; minor isomer: 2959, 2851, 1470, 1395, 1365, 1262, 1183, 1127, 1016, 983.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.11.021.

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