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A Convergent, Modular Access to α-Chloro-trifluoromethyl Derivatives and to 1,1-Difluoroalkenes

Pierre Salomon, Wioletta Kosnik and Samir Z. Zard *

Graphical abstract
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 Prof. Alan R. Katritzky

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.

Keywords: Radical addition; xanthates; fluorine.

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 difluorovinylithium,\(^13\) 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 \(S-(1\text{-chloro-2,2,2-trifluoroethyl})-O\text{-ethyl xanthate} \) 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 analogues 2 and 3. However, it seemed to us that the synthetic potential of 1 had remained largely underexploited.

![Figure 1. A few fluorinated xanthates](image)

To view this image, please refer to the original document.
With the aim of extending this work, we considered using this xanthate as a unique precursor to highly functionalized α-chlorotrifluoromethyl derivatives, as well as to heterocycles bearing a gem-difluorovinyl motif on the side chain. The pathway envisaged 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 cyclisations onto aromatic rings to form bicyclic compounds 5.\textsuperscript{17} The desired difluoro alkene 4 would finally be brought about by a metal induced formal elimination of “Cl-F” (Scheme 1).

\begin{equation}
\begin{array}{c}
\text{4} \quad \text{Cl} \quad \text{F} \\
\text{5} \quad \text{EtO} \quad \text{S} \quad \text{F} \quad \text{F} \\
\text{6} \quad \text{EtO} \quad \text{S} \quad \text{F} \quad \text{F} \\
\text{7} \quad \text{F}_3\text{C} \quad \text{S} \quad \text{OEt} \quad \text{X} \quad \text{Y}
\end{array}
\end{equation}

**Scheme 1.** A Route to difluoroalkenes

Our investigations began with an optimisation 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\textsubscript{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.\textsuperscript{16}

\begin{center}
\begin{tikzpicture}
  \node (a) {8, \(R = \text{Me, Et}\)}; 
  \node (b) [right=of a, below] {9}; 
  \node (c) [below=of a] {F\textsubscript{3}C\textsubscript{OAc}}; 
  \node (d) [left=of c] {F\textsubscript{3}C\textsubscript{Cl}}; 
  \node (e) [above=of b] {F\textsubscript{3}C\textsubscript{O}Et}; 
  \node (f) [right=of b] {11j}; 
  \node (g) [left=of f] {1 (42\% overall; scale > 5 g)}; 

  \draw[-latex] (a) -- node[above] {\text{KSC(S)OEt}} (b); 
  \draw[-latex] (b) -- node[above] {\text{CF\textsubscript{3}COOH}} (c); 
  \draw[-latex] (b) -- node[above] {\text{Pyridine}} (d); 
  \draw[-latex] (b) -- node[above] {Ac\textsubscript{2}O} (e); 
  \draw[-latex] (b) -- node[above] {\text{PCl\textsubscript{5}, 1.25 equiv}} (f); 
  \draw[-latex] (f) -- node[above] {pentane, 0 °C, 1 h then rt, 2 h} (g); 
\end{tikzpicture}
\end{center}

\textbf{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 4 [\(Xa = -\text{SC(=S)OEt}\)]. 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 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.
Scheme 3. Addition of xanthate 1 to alkenes

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, 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 cyclisation 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.

![Diagram of reaction](image)

**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 or tris(trimethyl)silylsilane as the hydrogen atom donor (Scheme 5).
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\textsuperscript{22} or activated chlorides\textsuperscript{23} 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 \textit{in situ} by a sub-stoichiometric 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>
<thead>
<tr>
<th>Entry</th>
<th>Reagent</th>
<th>Solvent</th>
<th>T °C</th>
<th>Conversion</th>
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<tr>
<td>1</td>
<td>Zn, Cul cat.</td>
<td>DMF</td>
<td>20-50°C</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>Zn, Cul cat.</td>
<td>DMF</td>
<td>20-50°C</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>Zn, AcOEt</td>
<td>reflux</td>
<td></td>
<td>0-100%</td>
</tr>
<tr>
<td>4</td>
<td>Zn, EtCO₂H</td>
<td>reflux</td>
<td></td>
<td>8%</td>
</tr>
<tr>
<td>5</td>
<td>i-PrMgCl</td>
<td>THF</td>
<td>0 °C-rt</td>
<td>0%</td>
</tr>
<tr>
<td>6</td>
<td>i-PrMgCl, LiCl</td>
<td>THF</td>
<td>0 °C-rt</td>
<td>0%</td>
</tr>
<tr>
<td>7</td>
<td>n-BuLi</td>
<td>THF</td>
<td>−78 °C-rt</td>
<td>0%</td>
</tr>
<tr>
<td>8</td>
<td>t-BuLi</td>
<td>THF</td>
<td>−78 °C-rt</td>
<td>40-75%</td>
</tr>
<tr>
<td>9</td>
<td>Mg</td>
<td>MeOH</td>
<td>reflux, 2h</td>
<td>0-30%</td>
</tr>
<tr>
<td>10</td>
<td>Mg</td>
<td>MeOH</td>
<td>reflux, 24h</td>
<td>0-30%</td>
</tr>
<tr>
<td>11</td>
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<td>MeOH</td>
<td>reflux</td>
<td>0%</td>
</tr>
<tr>
<td>12</td>
<td>Mg</td>
<td>THF</td>
<td>reflux</td>
<td>0-5%</td>
</tr>
<tr>
<td>13</td>
<td>Mg</td>
<td>EtOH</td>
<td>reflux</td>
<td>0%</td>
</tr>
<tr>
<td>14</td>
<td>Mg</td>
<td>CF₃CH₂OH</td>
<td>reflux</td>
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</tr>
<tr>
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<td>Mg</td>
<td>MeOH/PhMe</td>
<td>reflux</td>
<td>0%</td>
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<tr>
<td>16</td>
<td>Mg, Br(CH₂)₂Br</td>
<td>THF</td>
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<tr>
<td>17</td>
<td>Mg, Br(CH₂)₂Br</td>
<td>THF</td>
<td>reflux</td>
<td>100%</td>
</tr>
</tbody>
</table>

a) zinc flakes; b) zinc powder; c) reactions not reproducible; d) periodic addition of 1,2-dibromoethane during the reaction.

Table 1. Optimisation trials for the reductive elimination

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.
Scheme 6. Synthesis of difluoroalkenes

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. 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 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 (F₂C=CH•), which is too reactive to undergo cleanly intermolecular additions to un-activated 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 (ʎmax = 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 CH₂Cl₂ 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 (¹³C NMR) were recorded in the same instrument at 100.6 MHz. Chemical shifts (δH, δC) 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/NH₃) on a Hewlett-Packard HP 5989B and only report molecular species ([M+H]+, [M+NH₄]+) and other major fragments. High-resolution mass spectra were recorded by positive electron impact ionization (EI+) at 70 eV. 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 minutes. 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 cyclisation 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 minutes. 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
4.3 Experimental Procedures and Spectroscopic Data

4.3.1 [(1-Chloro-2,2,2-trifluoroethyl)sulfonyl](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 hour 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 MgSO₄. Removal of the solvent and flash chromatography if necessary yielded to the desired difluoro olefin.

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 hour 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 MgSO₄. 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. ¹H NMR (400 MHz; CDCl₃): δH 6.26 (q, J = 6.9 Hz, 1H), 4.74 (q, J = 7.1 Hz, 2H), 1.47 (t, J = 7.1 Hz); ¹³C NMR (100 MHz; CDCl₃): δC 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).

4.3.3 N-[4-Chloro-2-[(ethoxymethanethioyl)sulfonyl]-5,5,5-trifluoropentyl]-N-phenylmethanesulfonamide (11a)

Following general procedure A, the reaction was carried out using N-phenyl-N-(prop-2-ene-1-yl)methanesulfonamide ²⁶ (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$_3$): $\delta_{H}$ 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$_3$): $\delta_{C}$ 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$_4$): $\nu_{max}$ 2987, 1493, 1357, 1267, 1225, 1185, 1161, 1132, 1052; HRMS (El$^+$): calculated (found) for C$_{12}$H$_{10}^{35}$ClF$_3$NO$_2$: 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, 4.5mmol). 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$_3$): $\delta_{H}$ 9.25 (bs, 0.4H), 9.11 (bs, 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$_3$): $\delta_{C}$ 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$_4$): $\nu_{max}$ 3419, 2928, 1702, 1456, 1267, 1230, 1128, 1051; HRMS (El$^+$): calculated (found) for C$_{15}$H$_{18}^{35}$ClF$_3$N$_2$O$_2$: 414.0450 (414.0448)

4.3.5 Ethyl [(4-chloro-5,5,5-trifluoro-1-[1-(4-methoxyphenyl)-N-methylformamido]pentan-2-yl)sulfonyl]carbothioate (11c)

Following general procedure A, the reaction was carried out with 4-methoxy-N-methyl-N-(prop-2-en-1-yl)benzamide$^{27}$ (609 mg, 3.0 mmol), xanthate 1 (928 mg, 3.9mmol). 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$_3$): $\delta_{H}$ 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$_3$): $\delta_{C}$ 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, $J = 279$ 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$_4$): $\nu_{max}$ 2933, 1642, 1610, 1483, 1393, 1303, 1252, 1223, 1173, 1130, 1052; HRMS (El$^+$): calculated (found) for C$_{14}$H$_{16}^{35}$ClF$_3$NO$_2$: 322.0822 (322.0832).
4.3.6  \( N\{-4\text{-Chloro-2-}\{\text{ethoxymethanethioyl}\text{sulfanyl}\}-5,5,5\text{-trifluoropentyl}\}-N\{-6\text{-fluoropyridin-2-yl}\}\)acetamide (11d)

Following general procedure A, the reaction was carried out with \( N\{-6\text{-fluoropyridin-2-yl}\}-N\{-\text{prop-2-en-1-yl}\}\)acetamide\(^{28}\) (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 g, 84%) as a mixture of two diastereoisomers 60:40 and as a yellow oil. \(^1H\) NMR (400 MHz; CDCl\(_3\)): \( \delta_H \) 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 (dd, \( J = 15.1 \), 9.8, 5.5 Hz, 1H), 2.11 (s, 3H), 1.41 (t, \( J = 7.1 \) Hz, 3H); \(^{13}C\) NMR (100 MHz; CDCl\(_3\)): \( \delta_C \) 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\(_4\)): \( \nu_{\text{max}} \) 2928, 1684, 1600, 1452, 1378, 1311, 1267, 1226, 1131, 1049; HRMS (EI\(^+\)) calculated (found) for C\(_{12}\)H\(_{12}\)ClF\(_{4}\)N\(_2\)O: 311.0574 (311.0576).

4.3.7  \( N\{-5\text{-Chloro-3-}\{\text{ethoxymethanethioyl}\text{sulfanyl}\}-6,6,6\text{-trifluorohexyl}\}-N\{-6\text{-fluoropyridin-2-yl}\}\)acetamide (11e)

Following general procedure A, the reaction was carried out with \( N\{-\text{but-3-en-1-yl}\}-N\{-6\text{-fluoropyridin-2-yl}\}\)acetamide\(^{29}\) (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. \(^1H\) NMR (400 MHz; CDCl\(_3\)): \( \delta_H \) 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\(_3\)): \( \delta_C \) 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\(_4\)): \( \nu_{\text{max}} \) 2985, 1682, 1600, 1453, 1376, 1268, 1224, 1130, 1050; HRMS (EI\(^+\)) calculated (found) for C\(_{16}\)H\(_{19}\)ClF\(_4\)N\(_2\)O\(_2\): 446.0513 (446.0514).

4.3.8  \( 5\text{-Chloro-2,4-dichlorophenyl}-3-\{\text{ethoxymethanethioyl}\text{sulfanyl}\}-6,6,6\text{-trifluorohexanamide} \) (11f)

Following general procedure A, the reaction was carried out with \( N\{-2,4\text{-dichlorophenyl}\}\)but-3-enamide\(^{30}\) (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 (bs, 0.35H), 8.25 (bs, 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$_4$): $\nu_{max}$ 3434, 2987, 1709, 1586, 1518, 1444, 1406, 1268, 1228, 1129, 1050; HRMS (EI$^+$): calculated (found) for C$_{15}$H$_{15}$Cl$_3$F$_3$NO$_2$S$_2$: 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$_4$): $\nu_{max}$ 2937, 1682, 1602, 1510, 1263, 1223, 1170, 1127, 1052; HRMS (EI$^+$) calculated (found) for C$_{17}$H$_{20}$ClF$_3$O$_3$S$_2$: 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 hours, 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$_4$): $\nu_{max}$ 2928, 2856, 1679, 1493, 1370, 1274; HRMS (EI$^+$): calculated (found) for C$_{17}$H$_{20}$ClF$_3$O$_3$S$_2$: 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. \( ^1H \) 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); \( ^13C \) 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\(_4\)): \( \nu_{max} \) 2954, 1269, 1227, 1127, 1048; HRMS (El\(^+\)): 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-yl)oxy)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. \( ^1H \) 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); \( ^13C \) NMR (100 MHz; CDCl\(_3\)): 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\(_4\)): \( \nu_{max} \) 2935, 1508, 1267, 1127, 1049; HRMS (El\(^+\)): 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, 5.0mmol). 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. \( ^1H \) 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); \( ^13C \) 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\(_4\)): \( \nu_{max} \) 2928, 2856, 1680, 1493, 1370, 1267, 1220, 1052; HRMS (El\(^+\)): 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 minutes. Lauryl 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 product 12a (950 mg, 48%) as a mixture of two diastereoisomers 65:35 and as white crystals. $^1$H NMR (400 MHz; CDCl$_3$): $\delta_{H}$ 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$_3$): $\delta_c$ 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$_4$): $\nu_{max}$ 1480, 1366, 1276, 1263, 1168, 1132; HRMS (EI$^+$): calculated (found) for C$_{12}$H$_{13}$ClF$_3$NO$_2$: 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$_3$): $\delta_{H}$ 9.97 (bs, 0.4H), 9.95 (bs, 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 (dd, $J = 12.3$, 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$_3$): $\delta_c$ 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$_4$): $\nu_{max}$ 3406, 2929, 1711, 1455, 1268, 1131; HRMS (EI$^+$): calculated (found) for C$_{12}$H$_{12}$ClF$_3$N$_2$O: 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$_3$): $\delta_{H}$ 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$_3$): $\delta_c$ 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 (CCCl$_4$): $\nu_{max}$ 2930, 1662, 1609, 1325, 1260, 1170, 1131; HRMS (EI$^+$): calculated (found) for C$_{14}$H$_{15}$ClF$_3$NO$_2$: 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/EtO 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. ¹H NMR (400 MHz; CDCl₃): δₜ 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); ¹³C NMR (100 MHz; CDCl₃): δtres 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 (CCl₄): νmax 2928, 1681, 1483, 1386, 1297, 1262, 1132; HRMS (El⁺): calculated (found) for C₁₂H₁₁⁻¹⁻Cl₃F₄N₂O : 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. ¹H NMR (400 MHz; CDCl₃): δₜ 7.67-7.58 (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); ¹³C NMR (100 MHz; CDCl₃): δtres 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 (CCl₄): νmax 2934, 1682, 1585, 1465, 1435, 1370, 1274, 1131; HRMS (El⁺): calculated (found) for C₁₃H₁₃⁻¹⁻Cl₃F₄N₂O₂ : 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. ¹H NMR (400 MHz; CDCl₃): δₜ 8.97 (bs, 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); ¹³C NMR (100 MHz; CDCl₃): δtres 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 (CCl₄): υ_max 3409, 1716, 1693, 1600, 1575, 1260, 1174, 1129; HRMS (El⁺): calculated (found) for C₁₂H₉³⁵Cl₃F₃NO : 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; CDCl₃): 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); ¹³C NMR (100 MHz; CDCl₃): 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 (CCl₄): υ_max 2929, 1685, 1599, 1269, 1256, 1129; HRMS (El⁺): calculated (found) for C₁₄H₁₄³⁵ClF₃O₂ : 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 minutes 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 MgSO₄. 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; CDCl₃): 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); ¹³C NMR (100 MHz; CDCl₃): 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 (CCl₄): υ_max 3685, 3453, 2953, 1267, 1180, 1126, 1062; HRMS (El⁺): calculated (found) for C₇H₇O₃Cl₂F₃P : 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 minutes then AIBN (26mg, 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; CDCl₃): 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); ¹³C NMR (100 MHz; CDCl₃): 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 (CCl₄): υ_max 2935, 1508, 1272, 1231, 1172, 1131; HRMS (El⁺): calculated (found) for C₁₅H₁₈O₃F₃S₂ : 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 minutes 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 MgSO4. 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; CDCl3): δH 7.46-7.32 (m, 4H), 7.31-7.17 (m, 6H), 4.07 (dq, 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); 13C NMR (100 MHz; CDCl3): δC 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 (CCl4): νmax 2928, 2856, 1680, 1493, 1371, 1269, 1178, 1129; HRMS (EI): calculated (found) for C25H31+ClF3NO: 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; CDCl3): δH 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 (ddt, 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); 13C NMR (100 MHz; CDCl3): δC 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 (CCl4): νmax 1746, 1480, 1460, 1364, 1166; HRMS (EI): calculated (found) for C12H13F2NO2: 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; CDCl3): δH 8.51 (bs, 1H), 7.35 (d, J = 7.6 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 4.12 (ddt, 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); 13C NMR (100 MHz; CDCl3): δC 170.1, 158.4 (t, J = 287 Hz), 156.6, 149.5, 136.1, 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 (CCl4): νmax 3408, 2927, 1745, 1709, 1608, 1456, 1350, 1275, 1156; HRMS (EI): calculated (found) for C12H12F2N2O: 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; CDCl3): δH 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 (ddddd, 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); 13C NMR (100 MHz; CDCl3): δC 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 (CCl₄): \( \nu_{\text{max}} \) 2930, 1745, 1660, 1608, 1485, 1259; HRMS (EI⁺): calculated (found) for C₁₄H₁₅F₂NO₂: 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; CDCl₃): \( \delta \) 9.65 (bs, 1H), 7.09 (d, J = 2.0 Hz, 1H), 6.82 (d, J = 2.0 Hz, 1H), 4.18 (ddt, 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); ¹³C NMR (100 MHz; CDCl₃): \( \delta \)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 (CCl₄): \( \nu_{\text{max}} \) 2952, 1745, 1691, 1601, 1578, 1394, 1373, 1317; HRMS (EI⁺): calculated (found) for C₁₂H₉ClF₂NO: 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 ⁴³(a) (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. ¹H NMR (400 MHz; CDCl₃): \( \delta \) H 7.30-7.22 (m, 1H), 6.07 (dd, J = 7.7, 1.0 Hz, 1H), 4.67 (bs, 1H), 4.17 (ddt, 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); ¹³C NMR (100 MHz; CDCl₃): \( \delta \)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); ¹³C NMR (100 MHz; CDCl₃): \( \delta \)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 (CCl₄): \( \nu_{\text{max}} \) 3444, 2927, 1746, 1620, 1595, 1445; HRMS (EI⁺): calculated (found) for C₁₀H₉ClF₂: 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 ⁴³(b) (52 mg, 0.18 mmol). 16b (35 mg, 83%) was obtained as an amorphous white solid without purification. Mp = 64-66 °C. ¹H NMR (400 MHz; CDCl₃): \( \delta \) H 7.25 (t, J = 8.0 Hz, 1H), 6.06 (dd, J = 7.9, 2.4 Hz, 1H), 5.29 (bs, 1H), 4.18 (ddddd, 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); \( \delta \)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 (CCl₄): \( \nu_{\text{max}} \) 3447, 3272, 2931, 1745, 1618, 1462, 1355, 1224; HRMS (EI⁺): calculated (found) for C₁₁H₁₁F₃N₂: 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. ¹H NMR (400 MHz; CDCl₃): \( \delta \) H 4.10 (ddt, 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); \( \delta \)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 (CCl₄): \( \nu_{\text{max}} \) 2953, 1747, 1248, 1064, 1036; HRMS (EI⁺): calculated (found) for C₇H₁₃F₂O₃P: 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. 1H NMR (400 MHz; CDCl3): δH 6.83 (s, 4H), 4.19 (dtd, J = 25.3, 7.9, 2.5 Hz, 2H), 3.92 (t, J = 6.2 Hz, 2H), 3.77 (s, 3H), 2.21-2.13 (m, 2H), 1.84 (m, 2H); 13C NMR (100 MHz; CDCl3): δC 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 (CCl4): vmax 2951, 1746, 1509, 1231; HRMS (EI⁺): calculated (found) for C15H13ClF3O2S2: 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. 1H NMR (400 MHz; CDCl3): δH 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); 13C NMR (100 MHz; CDCl3): δC 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 (CCl4): vmax 2928, 2856, 1746, 1680, 1594, 1493, 1369, 1271; HRMS (EI⁺): calculated (found) for C25H31F2NO: 399.2374 (399.2371).

4.3.33 2-(S-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 (58mg, 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 Al2O3, 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. 1H NMR (400 MHz; CDCl3): δH 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 (ddd, J = 15.2 Hz, 7.6, 3.6, 1.2 Hz, 1H), 2.57 (ddd, 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); 13C NMR (100 MHz; CDCl3): δC 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 (CCl4): vmax 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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