

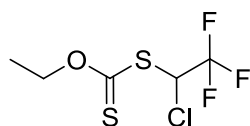
PARTIE EXPERIMENTALE

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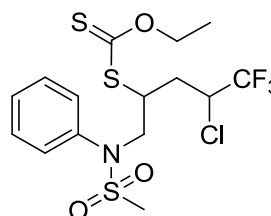
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I. Récapitulatif des molécules citées dans la partie expérimentale

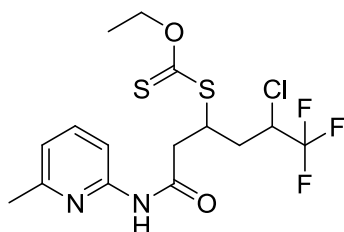
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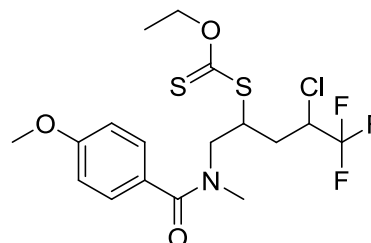
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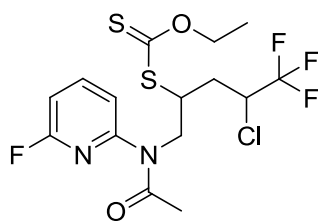
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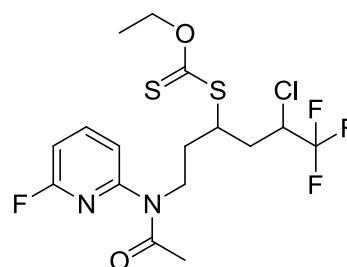
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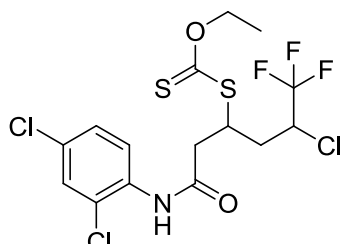
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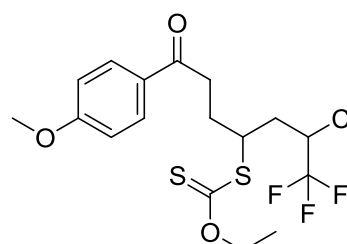
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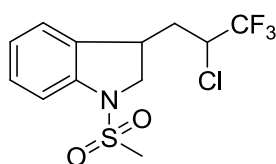
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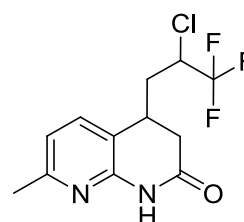
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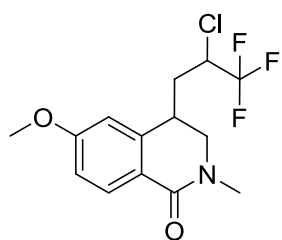


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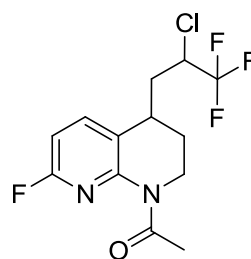


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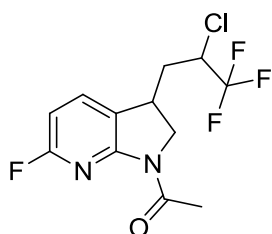
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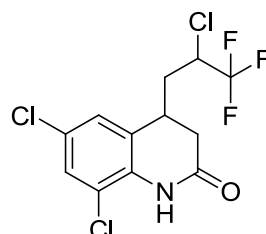
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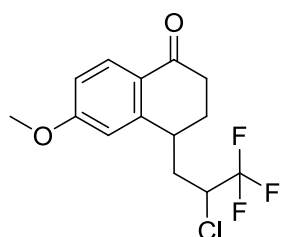
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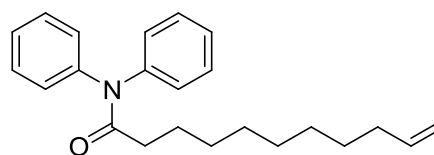
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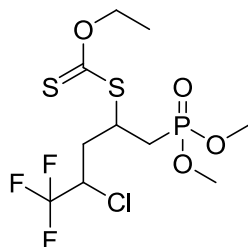
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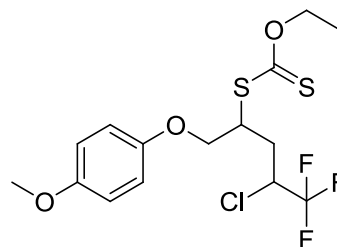
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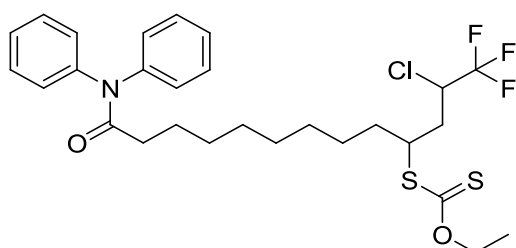
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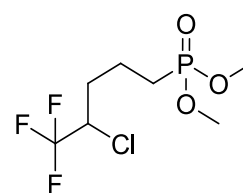
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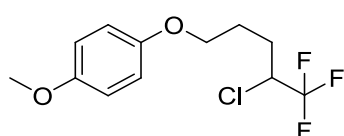
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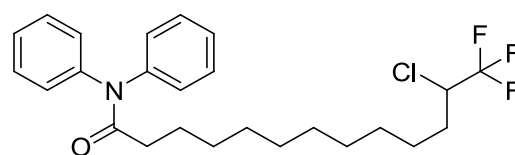
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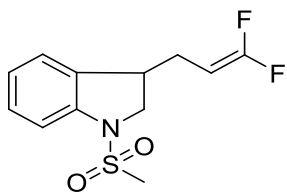
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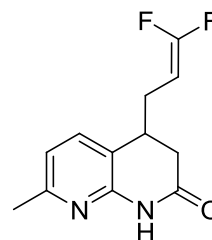
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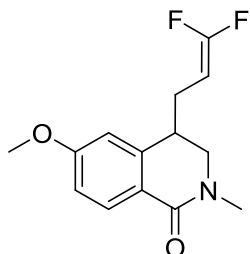
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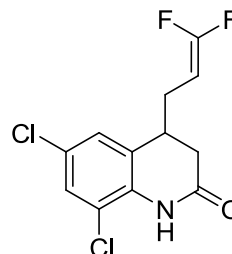
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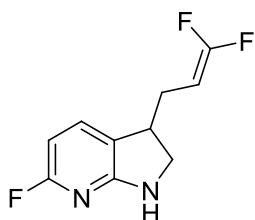
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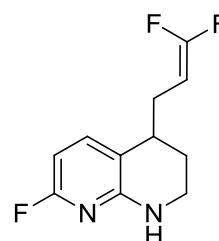
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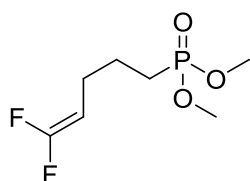
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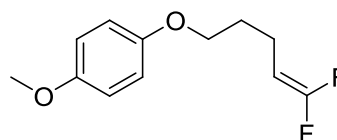
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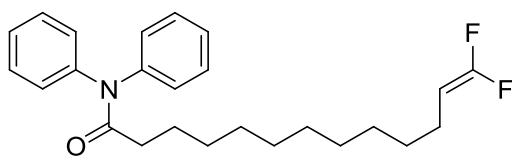
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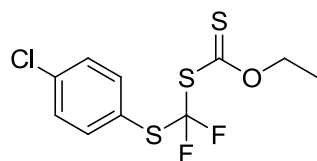


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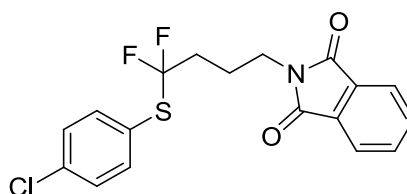


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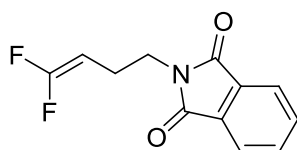
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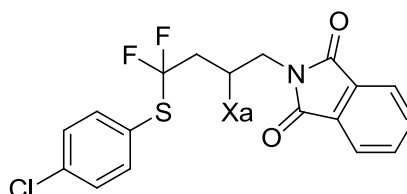
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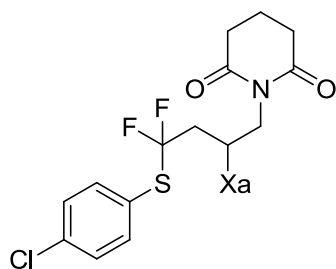
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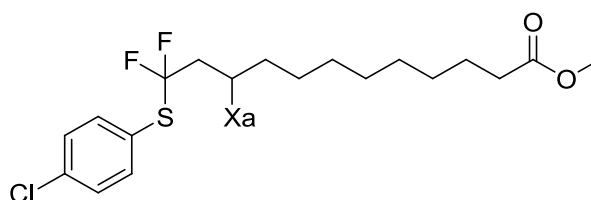
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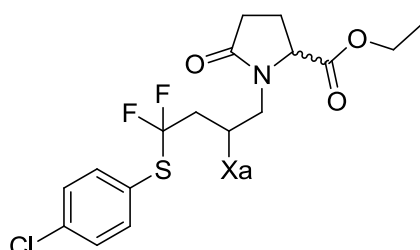
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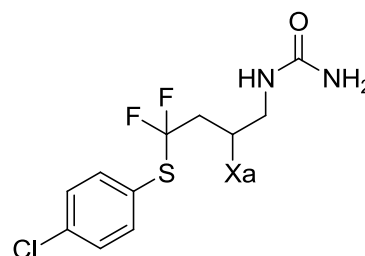
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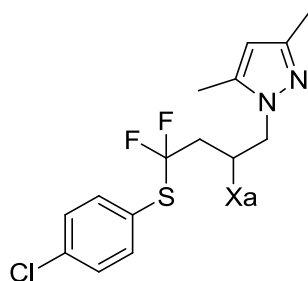
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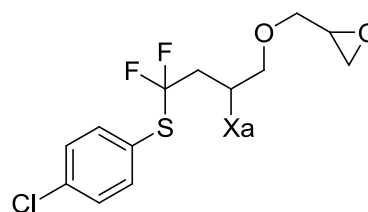
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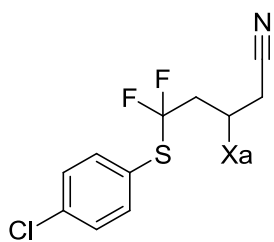


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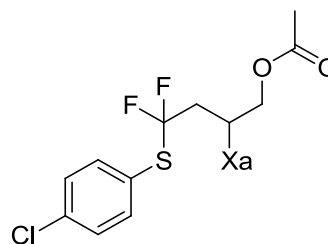


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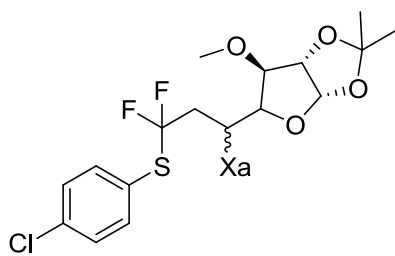
Récapitulatif des molécules citées dans la partie expérimentale



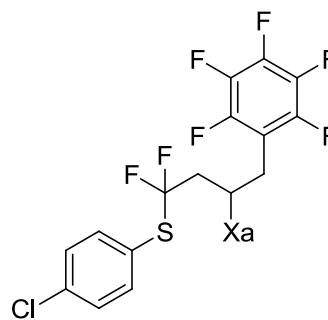
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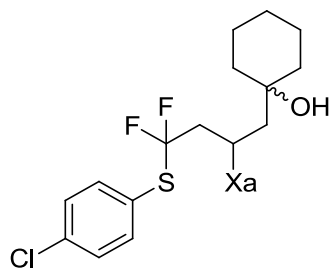
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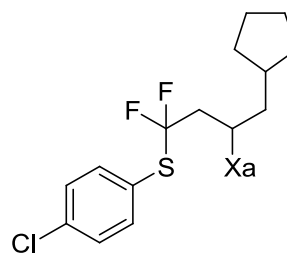
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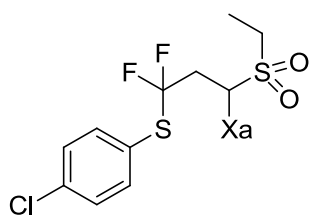
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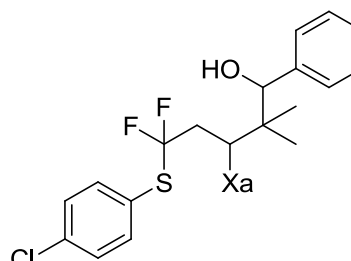
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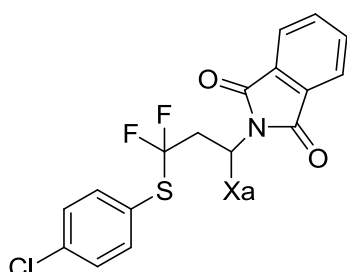
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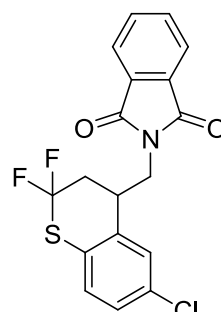
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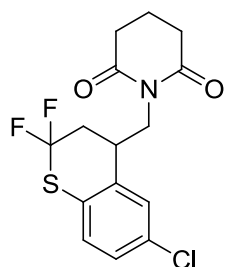


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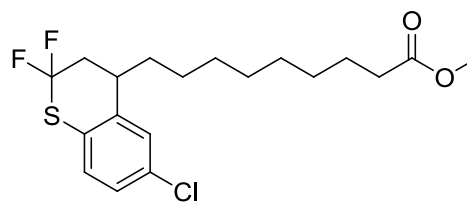


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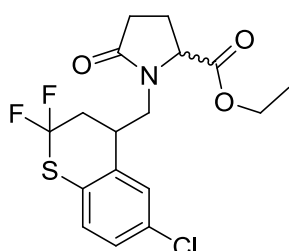
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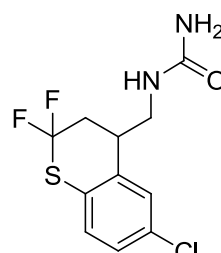
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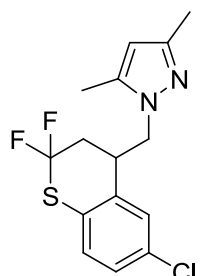
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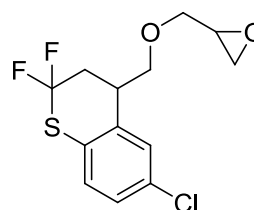
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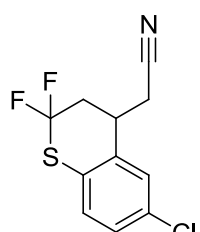
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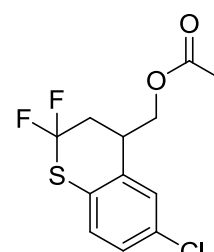
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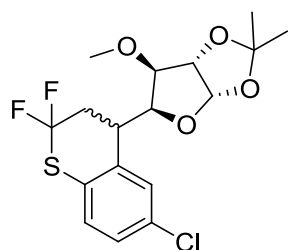
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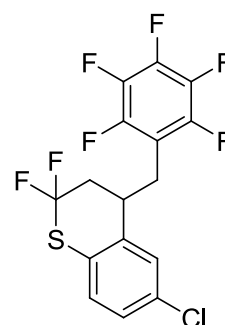
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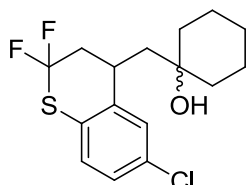
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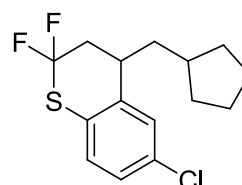
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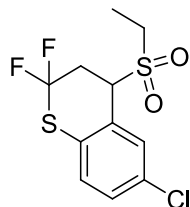
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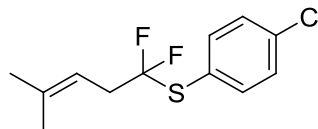
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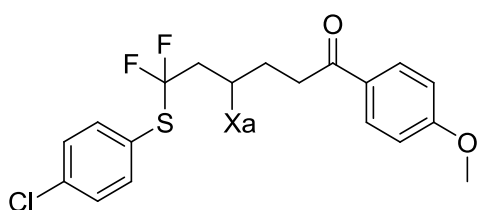
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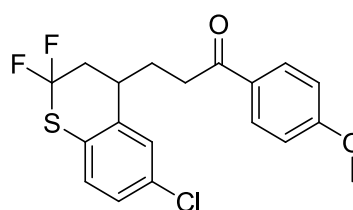
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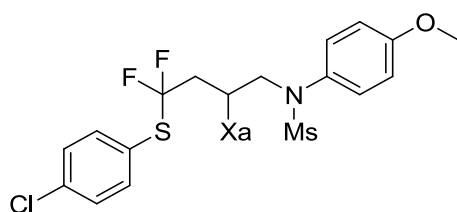
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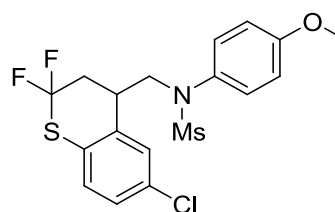
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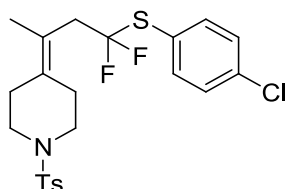
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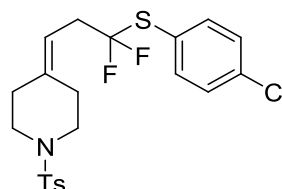
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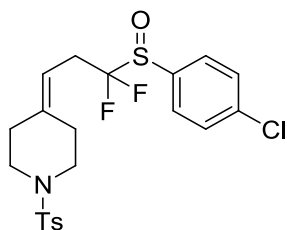
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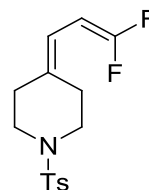
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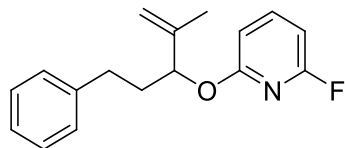


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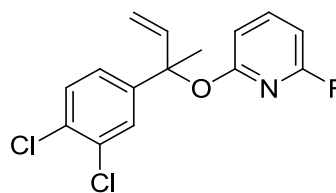


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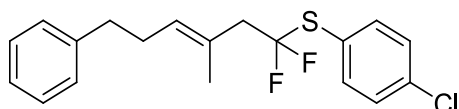
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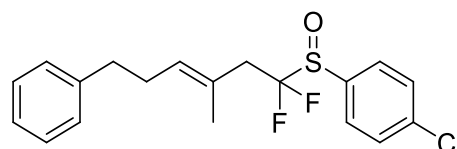
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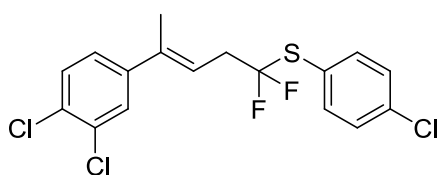
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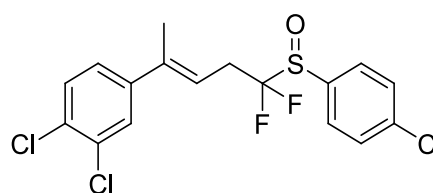
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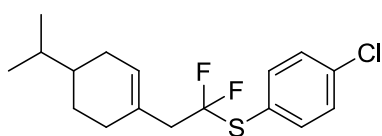
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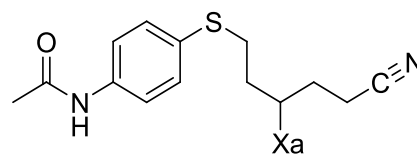
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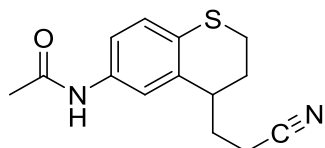
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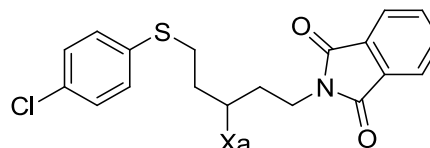
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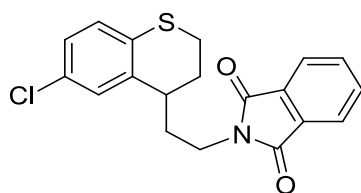
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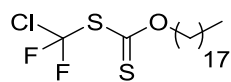


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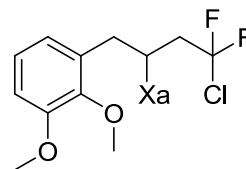


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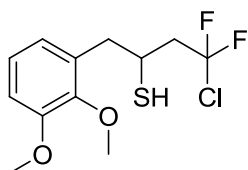
C. Chapitre IV : Synthèse et utilisation d'un nouveau précurseur du radical 1-chloro-1,1-difluorométhane



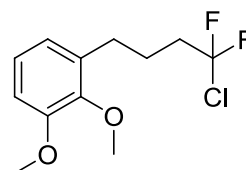
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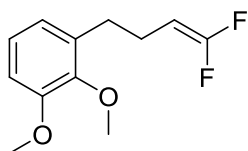
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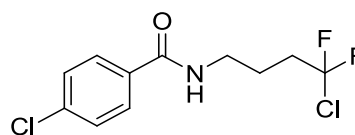
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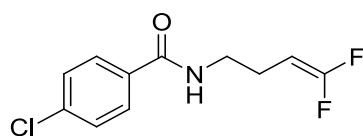
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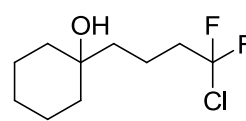
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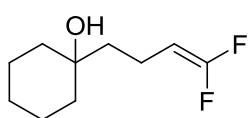
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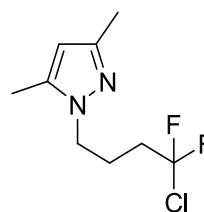
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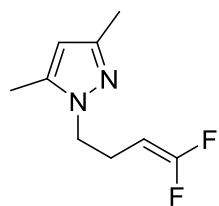


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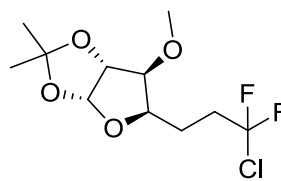


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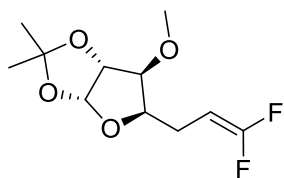
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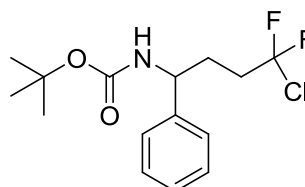
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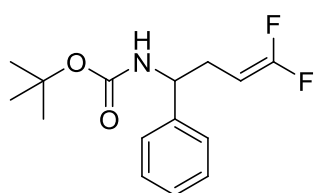
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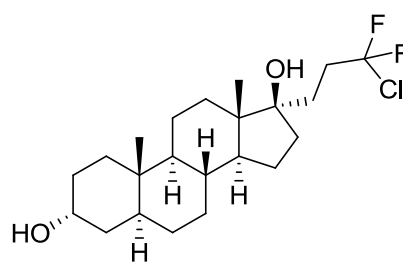
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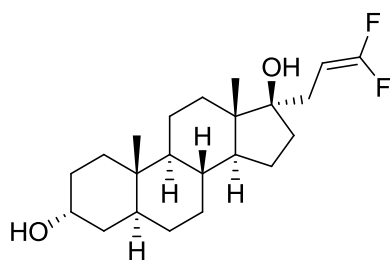
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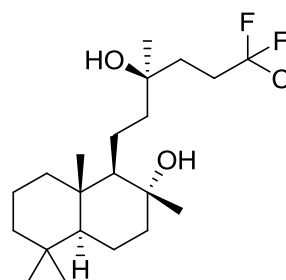
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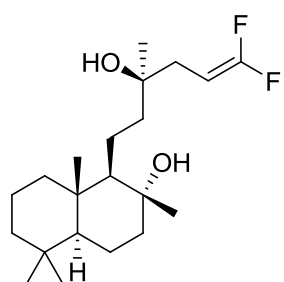
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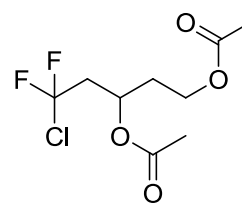
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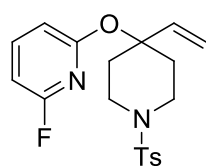
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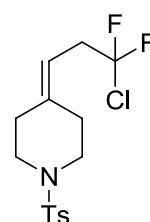
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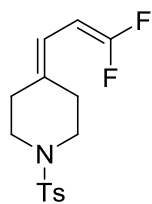
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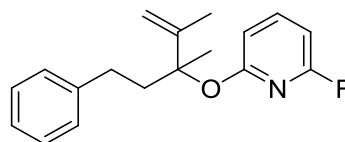
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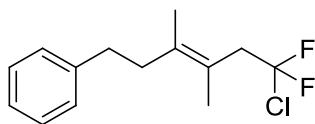
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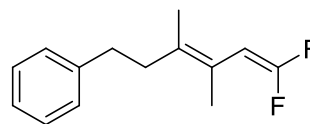
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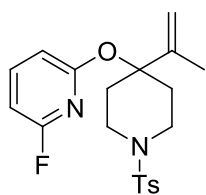
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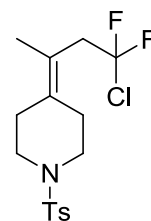
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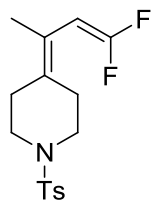
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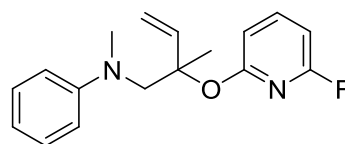
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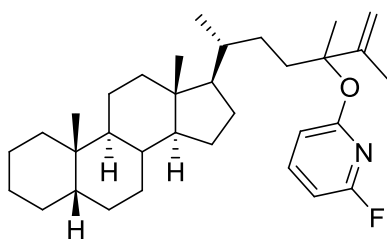
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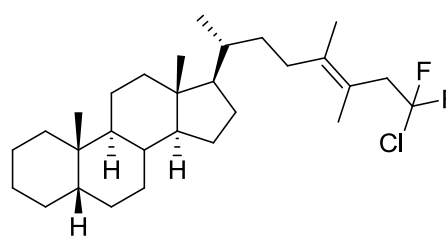
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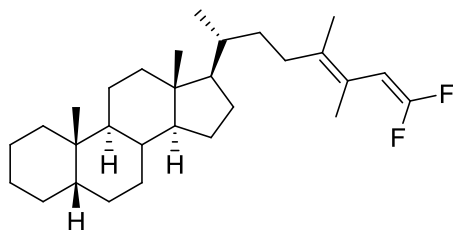
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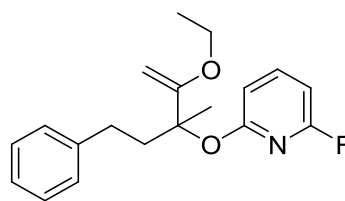
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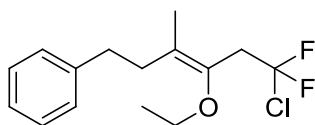
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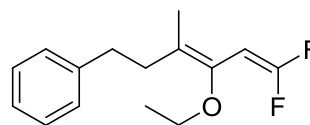
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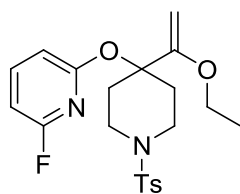


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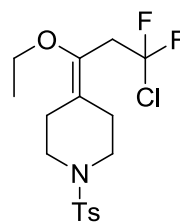


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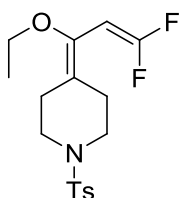
Récapitulatif des molécules citées dans la partie expérimentale



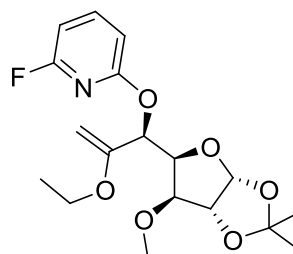
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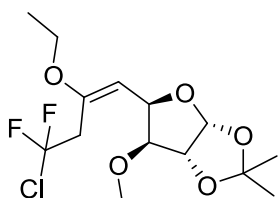
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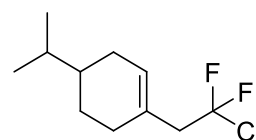
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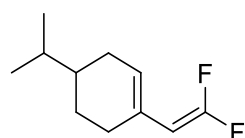
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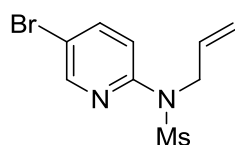
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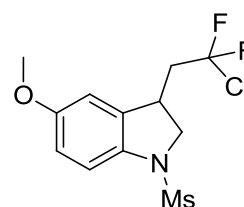
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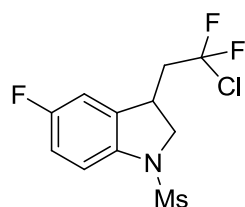
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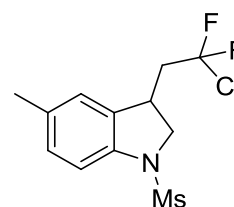
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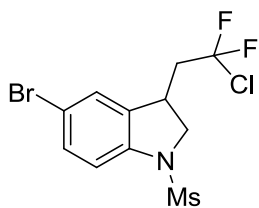
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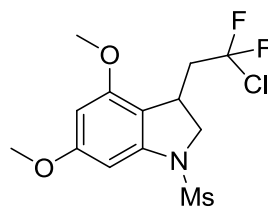
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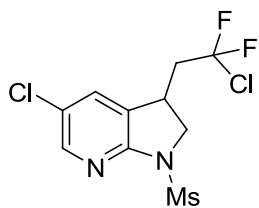
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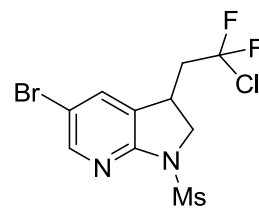
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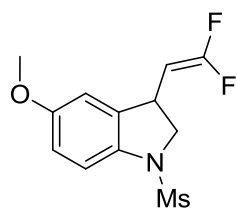
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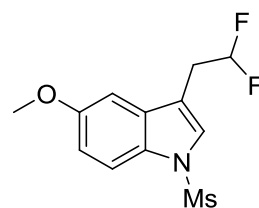
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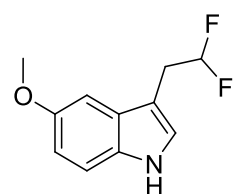
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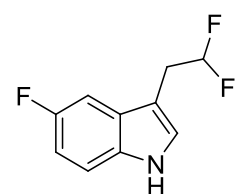
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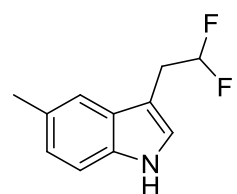
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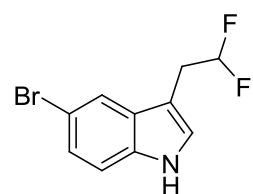
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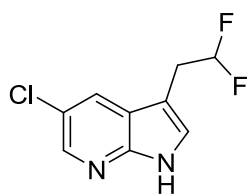
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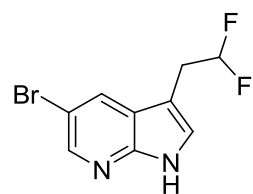
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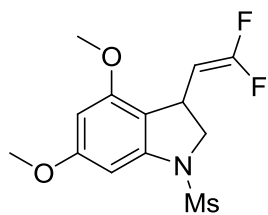


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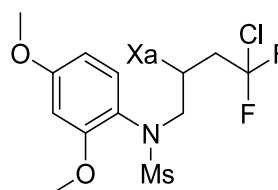


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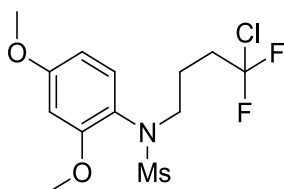
Récapitulatif des molécules citées dans la partie expérimentale



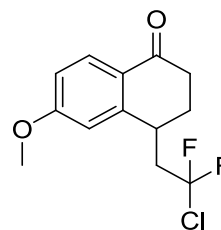
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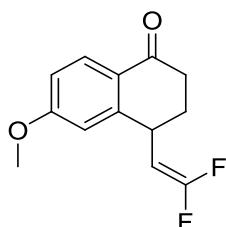
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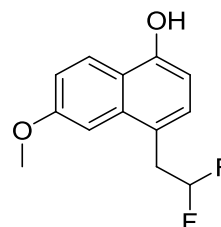
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II. Généralités

A. Abréviations

1. Unités

°C	degré Celcius
h	heure
Hz, MHz	hertz, mégahertz
g, mg	gramme, milligramme
min.	minutes
mL, μ L	millilitre, microlitre
mml	milimole
nm	nanomètre
ppm	partie par million

2. Autres

Ar	aromatique
bs	singulet large
bp	point d'ébullition
Cat.	Catalytique
TLC (CCM)	Chromatographie sur couches minces
d	doublet
IE	impact électronique
dia	diastéréoisomères
δ	déplacement chimique
equiv.	équivalent
HRMS	spectrométrie de masse haute résolution
IR	spectrométrie infra-rouge
J	constante de couplage
Mp	point de fusion
q	quadruplet
NMR	résonance magnétique nucléaire
s	singulet
t	triplet
W	watt
σ	nombre d'onde

B. Purification des solvants et réactifs

L'éther diéthylique, le dichlorométhane, le méthanol, le tétrahydrofurane et le toluène anhydre ont été obtenu grâce à un appareillage de Grubbs de purification des solvants de marque Braun. Ils ont été utilisés tels que délivrés par la machine de Grubbs.

Les réactifs ont généralement été utilisés sans purification préalable, leur pureté ayant été vérifié si nécessaire par RMN ^1H .

Toutes les réactions sensibles à l'air ou à l'eau ont été réalisées sous atmosphère inerte d'azote ou d'argon.

C. Chromatographie

Les chromatographies sur couches minces (CCM) ont été effectuées sur des plaques de silice sur aluminium 60 F₂₅₄ (Merk ou SDS).

Les CCM sont observées en lumière ultraviolette à 254 ou 366 nm. Elles sont généralement immergées dans un révélateur au permanganate de potassium, à l'anisaldéhyde ou à la vaniline puis chauffées au pistolet à décapage.

Les chromatographies flash sur gel de silice ont été réalisées avec de la silice SDS 60 A C.C. (40-63 μm).

D. Appareillage d'analyse utilisé

Les spectres de résonance magnétique nucléaire (RMN) ont été réalisés sur un appareil Bruker AMX 400 (400 MHz).

En RMN du proton (RMN ^1H), les déplacements chimiques (δ) sont exprimés en partie par million (ppm) par rapport au proton du chloroforme ($\delta = 7.26$ ppm). Les constantes de couplages (J) sont exprimées en Hertz (Hz).

En RMN du carbone (RMN ^{13}C), les déplacements chimiques (δ) sont exprimés en partie par million (ppm) en prenant la raie centrale du chloroforme deutéré ($\delta = 7.26$ ppm) comme référence externe. Les constantes de couplages (J) sont exprimées en Hertz (Hz).

Pour chaque produit, un spectre a été enregistré en « Broad Band » (découplage par bruit de protons) et un autre en séquence Jmod ou DEPT afin de déterminer et valider la parité du nombre de protons porté par chaque carbone.

Dans la plupart des cas, la détermination et l'attribution des signaux a été complétée par des expériences à deux dimensions : COSY, HSQC et nOesy.

Les spectres infra-rouge (IR) ont été réalisés sur un appareil Perkin-Elmer FT-IR 2000 à transformée de Fourier en solution dans le tétrachlorure de carbone, dans une cuve de chlorure de sodium ou de fluorure de calcium. Les spectres sont réalisés en absorptions et les nombre d'onde (σ) des bandes d'absorption sont exprimés en cm^{-1} . Les spectres ont été réalisés entre 1000 et 4000 cm^{-1} .

Les spectres à haute résolution (HRMS) ont été réalisés sur un spectromètre JEOL JMS-GCmate II, GS/MS à l'école polytechnique.

Les molécules ont été nommées grâce au logiciel ChemDraw.

III. Modes opératoires et analyses

Note : Cette partie est intégralement rédigée en langue anglaise.

A. Chapitre II : Synthèse de vinyles *gem*-di-fluorés

1. General procedures

General procedure II-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.

General procedure II-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 15min (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.

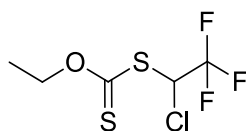
General procedure II-C for the elimination reaction

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 compound 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, Et₂O was added, the layers were partitioned and the aqueous one was extracted twice with Et₂O. 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.

2. Experimental Procedures and Spectroscopic Data

[(1-chloro-2,2,2-trifluoroethyl)sulfanyl](ethoxy)methanethione

II-4


 $C_5H_6ClF_3OS_2$
 $M = 238.7 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with potassium ethyl xanthate salt (8 g, 50 mmol), 100 mL of trifluoroacetic acid and was 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 $MgSO_4$. 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 minutes and at room temperature for 2 hours. The solution was then directly purified by silica gel column chromatography¹ (pentane 100%) and concentrated under reduced pressure at 20 °C to afford **II-4** (5.01 g, 42%) as a pale yellow liquid.

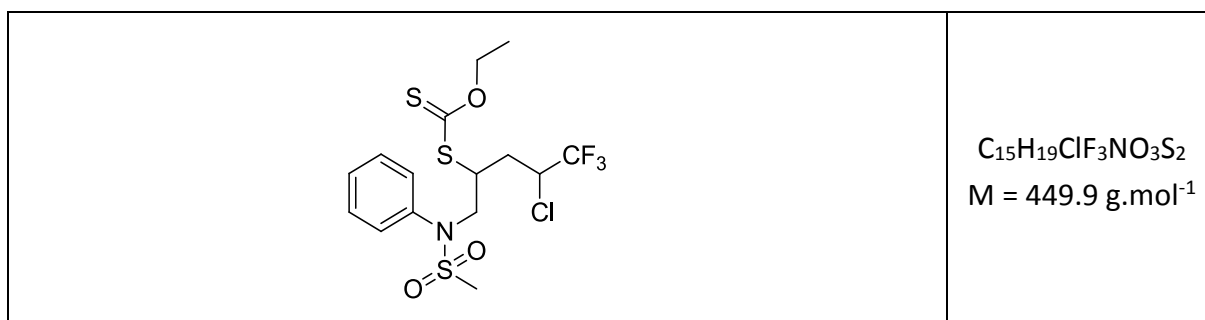
¹H NMR (δ , ppm) 6.26 (q, $J = 6.9$ Hz, 1H), 4.74 (q, $J = 7.1$ Hz, 2H), 1.47 (t, $J = 7.1$ Hz)
 (CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 206.4, 122.7 (q, $J = 279$ Hz), 72.0, 63.6 (q, $J = 37$ Hz), 13.6
 (CDCl₃, 100 MHz)

¹ Evaporation of the crude mixture leads to decomposition of the desired product

N-{4-chloro-2-[(ethoxymethanethioyl)sulfanyl]-5,5,5-trifluoropentyl}-N-phenylmethanesulfonamide

II-14a



Following general procedure II-A, the reaction was carried out using N-phenyl-N-(prop-2-en-1-yl)methanesulfonamide (1.27 g, 6.0 mmol), xanthate **II-4** (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 **II-14a** (2592 mg, 96%) as a mixture of two diastereoisomers 80:20 and as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 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, $J = 15.1, 6.9, 5.3 \text{ Hz}$, 0.2H), 2.56 (ddd, $J = 14.7, 11.9, 2.6 \text{ Hz}$, 0.8H), 2.19 (ddd, $J = 15.3, 11.9, 2.1 \text{ Hz}$, 0.8H), 2.19-2.12 (m, 0.2H), 1.34 (t, $J = 7.1 \text{ Hz}$, 0.6H), 1.32 (t, $J = 7.1 \text{ Hz}$, 2.4H).

$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 210.5, 137.9, 129.7 (2C), 128.9 (2C), 128.8, 123.8 (q, $J = 279 \text{ Hz}$), 70.6, 54.9 (d, $J = 33.7 \text{ Hz}$), 53.6, 44.9, 37.1, 31.4, 13.6.

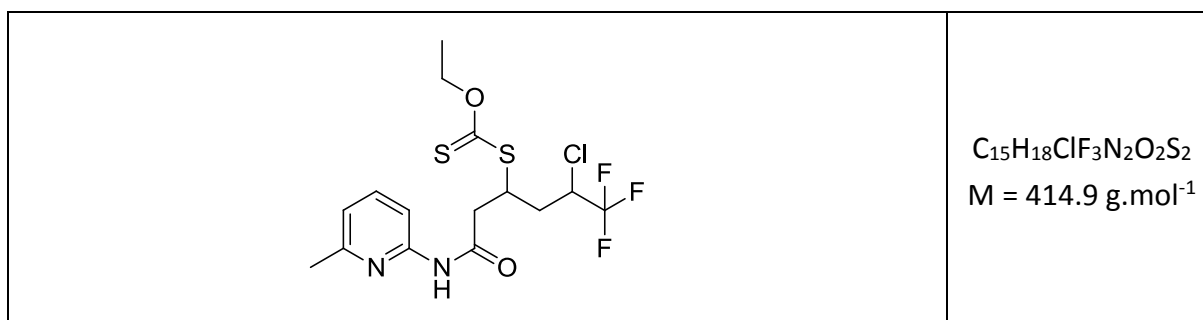
Minor Diastereoisomere : 211.0, 138.3, 129.7, 128.9, 128.7, 123.8 (q, $J = 279 \text{ Hz}$), 70.4, 54.4 (q, $J = 33 \text{ Hz}$), 52.76, 45.9, 37.0, 33.1, 13.6.

IR (σ , cm^{-1} , CCl_4) 2987, 1493, 1357, 1267, 1225, 1185, 1161, 1132, 1052.

HRMS (EI) Calcd for $C_{12}H_{10}ClF_3NO_2$: 328.0386 Found: 328.0390

5-chloro-3-[(ethoxymethanethioyl)sulfanyl]-6,6,6-trifluoro-N-(6-methylpyridin-2-yl)hexanamide

II-14b



Following general procedure II-A, the reaction was carried out using *N*-(6-methylpyridin-2-yl)but-3-enamide (500 mg, 2.83 mmol), xanthate **II-4** (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 **II-14b** (850 mg, 72%) as a mixture of two diastereoisomers 60:40 and as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 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).
 (CDCl₃, 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 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.
 (CDCl₃, 100 MHz)

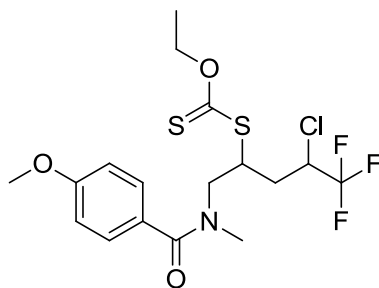
Minor Diastereoisomere : 211.6, 168.0, 156.5, 150.2, 138.7, 123.7 (q, $J = 279$ Hz), 119.6, 111.4, 70.3, 54.8 (q, $J = 33$ Hz), 43.1, 39.2, 34.4, 23.7, 13.5.

IR (σ , cm⁻¹, CCl₄) 3419, 2928, 1702, 1456, 1267, 1230, 1128, 1051

HRMS (EI) Calcd for C₁₅H₁₈ClF₃N₂O₂S₂ : 414.0450 Found: 414.0448

ethyl ({4-chloro-5,5,5-trifluoro-1-[1-(4-methoxyphenyl)-N-methylformamido]pentan-2-yl}sulfanyl)carbothioate

II-14c



$C_{17}H_{21}ClF_3NO_3S_2$
 $M = 443.9 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure II-A, the reaction was carried out with 4-methoxy-N-methyl-N-(prop-2-en-1-yl)benzamide (609 mg, 3.0 mmol), xanthate **II-4** (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 **II-14c** (620 mg, 47%) as a mixture of two diastereoisomers 65:35 and as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 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).
 (CDCl₃, 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 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, 13.6.
 (CDCl₃, 100 MHz)

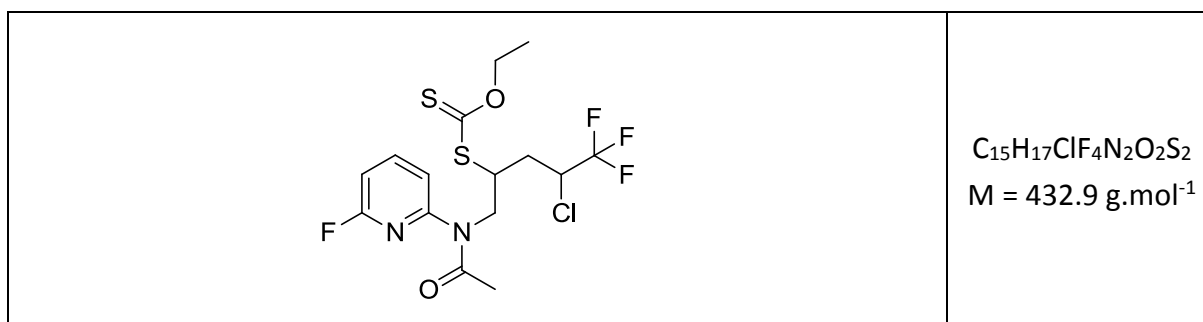
Minor Diastereoisomere : 211.8, 171.9, 160.8, 128.9 (2C), 127.6, 123.6 (q, 279 Hz), 113.7 (2C), 70.5, 55.3, 55.7-54.2 (m), 49.5, 45.9, 39.5, 34.1, 13.6.

IR (σ , cm⁻¹, CCl₄) 2933, 1642, 1610, 1483, 1393, 1303, 1252, 1223, 1173, 1130, 1052.

HRMS (EI) Calcd for C₁₄H₁₆ClF₃NO₂ : 322.0822 Found: 322.0832

N-{4-chloro-2-[(ethoxymethanethioyl)sulfanyl]-5,5,5-trifluoropentyl}-N-(6-fluoropyridin-2-yl)acetamide

II-14d



Following general procedure II-A, the reaction was carried out with *N*-(6-fluoropyridin-2-yl)-*N*-(prop-2-en-1-yl)acetamide (2.00 g, 10.3 mmol), xanthate **II-4** (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 **II-14d** (3.86 mg, 84%) as a mixture of two diastereoisomers 60:40 and as a yellow oil.

$^1\text{H NMR}$ (δ , ppm) Major Diastereoisomere : 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).
 (CDCl₃, 400 MHz)

Minor Diastereoisomere : 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).

$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 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.
 (CDCl₃, 100 MHz)

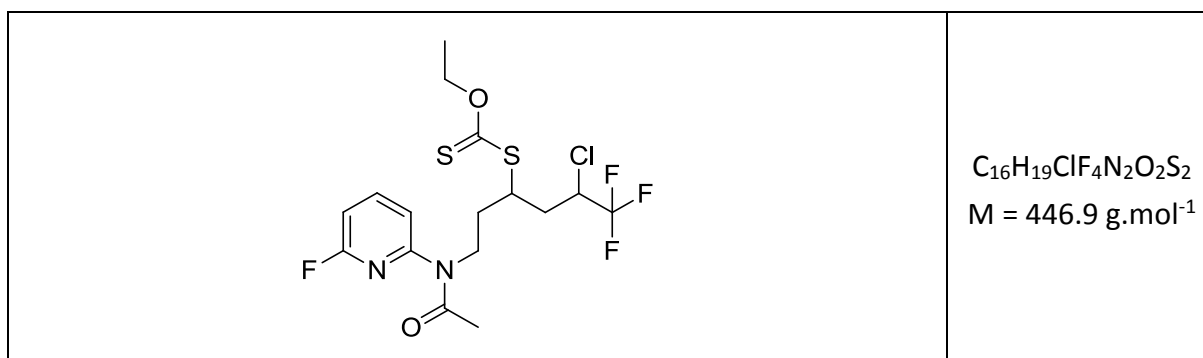
Minor Diastereoisomere : 211.3, 170.8, 162.4 (d, $J = 244$ Hz), 152.9 (d, $J = 13$ Hz), 143.0 (d, $J = 7$ Hz), 123.9 (q, $J = 279$ Hz), 118.8 (d, $J = 5$ Hz), 108.2 (d, $J = 36$ Hz), 70.4, 54.6 (q, $J = 33$ Hz), 48.4, 46.3, 33.9, 23.0, 13.6.

IR (σ , cm⁻¹, CCl₄) 2928, 1684, 1600, 1452, 1378, 1311, 1267, 1226, 1131, 1049.

HRMS (EI) Calcd for C₁₂H₁₂ClF₄N₂O : 311.0574 Found: 311.0576

N-{5-chloro-3-[(ethoxymethanethioyl)sulfanyl]-6,6,6-trifluorohexyl}-N-(6-fluoropyridin-2-yl)acetamide

II-14e



Following general procedure II-A, the reaction was carried out with *N*-(but-3-en-1-yl)-*N*-(6-fluoropyridin-2-yl)acetamide (370 g, 1.78mmol), xanthate **II-4** (550 g, 2.31mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 60:40) to afford the xanthate adduct **II-14e** (740 mg, 93%) as a mixture of two diastereoisomers 60:40 and as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 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 (dq, $J = 11.0, 6.6, 2.3$ 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).

$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) Major Diastereoisomere : 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.

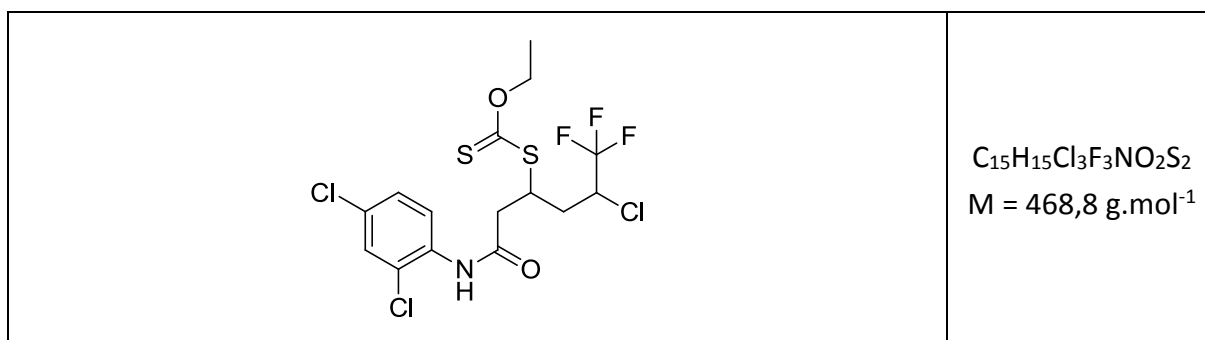
Minor Diastereoisomere : 211.6, 170.2, 162.1 (d, $J = 243$ Hz), 153.2 (d, $J = 13.3$ Hz), 142.8 (d, $J = 7.7$ Hz), 123.8 (q, $J = 279$ Hz), 117.4 (d, $J = 5$ Hz), 107.2 (d, $J = 36$ Hz), 70.2, 54.4 (q, $J = 33$ Hz), 45.2, 44.2, 35.4, 30.0, 23.2, 13.5.

IR (σ , cm⁻¹, CCl₄) 2985, 1682, 1600, 1453, 1376, 1268, 1224, 1130, 1050.

HRMS (EI) Calcd for C₁₆H₁₉ClF₄N₂O₂S₂ : 446.0513 Found: 446.0514

5-chloro-N-(2,4-dichlorophenyl)-3-[(ethoxymethanethioyl)sulfanyl]-6,6,6-trifluorohexanamide

II-14f



Following general procedure II-A, the reaction was carried out with *N*-(2,4-dichlorophenyl)but-3-enamide (690 mg, 3.0 mmol), xanthate **II-4** (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 **II-14f** (1.37 g, 98%) as a mixture of two diastereoisomers 65:35 and as a yellow oil.

1H NMR (δ , ppm) 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).
(CDCl₃, 400 MHz)

^{13}C NMR (δ , ppm) Major Diastereoisomere : 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.
(CDCl₃, 100 MHz)

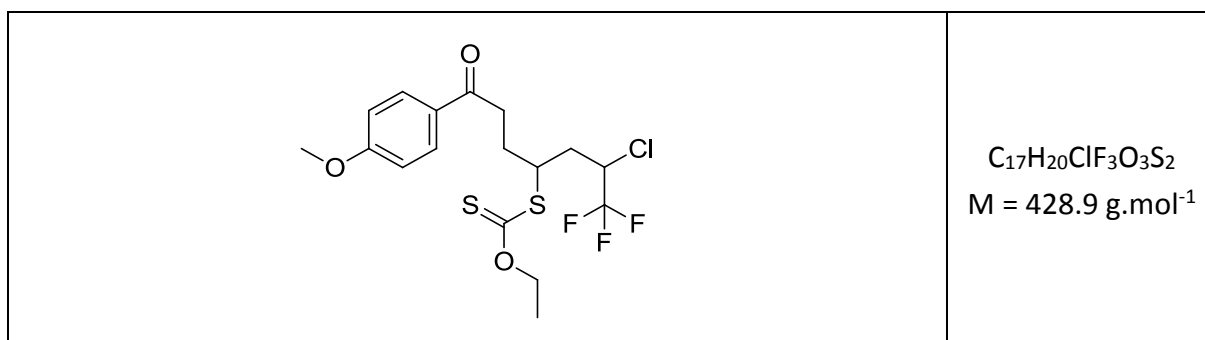
Minor Diastereoisomere : 211.8, 168.4, 138.7, 135.1 (2C), 124.7, 123.7 (q, $J = 279$ Hz), 118.6 (2C), 70.7, 54.7 (q, $J = 33$ Hz), 43.3, 39.9, 34.9, 13.6.

IR (σ , cm⁻¹, CCl₄) 3434, 2987, 1709, 1586, 1518, 1444, 1406, 1268, 1228, 1129, 1050.

HRMS (EI) Calcd for C₁₅H₁₅Cl₃F₃NO₂S₂ : 466.9562 Found: 466.9557

6-chloro-4-[(ethoxymethanethioyl)sulfanyl]-7,7,7-trifluoro-1-(4-methoxyphenyl)heptan-1-one

II-14g



Following general procedure II-A, the reaction was carried out using 1-(4-methoxyphenyl)pent-4-en-1-one (380 mg, 2.0 mmol), xanthate **II-4** (619mg, 2.6mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10) to afford the corresponding xanthate adduct **II-14g** (850 mg, 99%) as a mixture of two diastereoisomers 60:40 and as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 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).

$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) Major Diastereoisomere : 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.

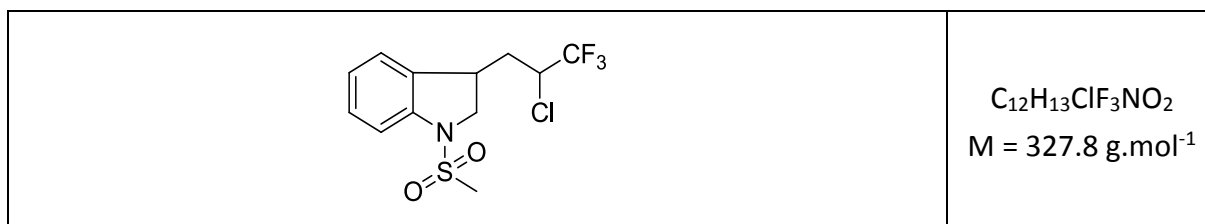
Minor Diastereoisomere : 211.9, 197.05, 163.68, 130.3 (2C), 129.7, 124.0 (q, $J = 279$ Hz), 113.8 (2C), 70.3, 55.5, 54.7 (q, $J = 33$ Hz), 46.6, 36.8, 35.0, 26.1, 13.6.

IR (σ , cm⁻¹, CCl₄) 2937, 1682, 1602, 1510, 1263, 1223, 1170, 1127, 1052.

HRMS (EI) Calcd for C₁₇H₂₀ClF₃O₃S₂ : 428.0494 Found: 428.0504

3-(2-chloro-3,3,3-trifluoropropyl)-1-methanesulfonyl-2,3-dihydro-1H-indole

II-15a



A solution of xanthate adduct **II-14a** (5.76 mmol) in DCE (30mL) was refluxed under a flow of nitrogen for 15 minutes. Lauroyl peroxide (DLP) (756mg, 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 **II-15a** (950mg, 48%) as a mixture of two diastereoisomers 65:35 and as white crystals.

$^1\text{H NMR}$ (δ , ppm) 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).

$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 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.

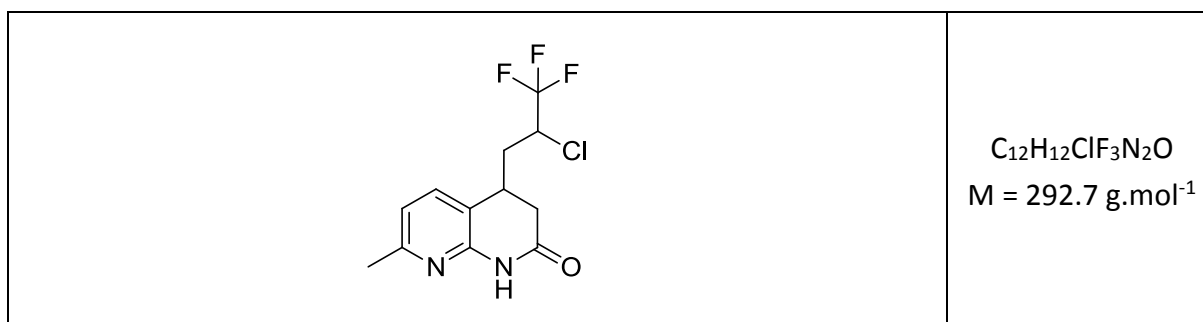
Minor Diastereoisomere : 141.6, 132.7, 129.0, 123.8 (q, $J = 279$ Hz), 124.5, 124.0, 113.6, 55.3 (q, $J = 34$ Hz), 54.8, 36.4, 35.8, 34.6.

IR (σ , cm^{-1} , CCl_4) 1480, 1366, 1276, 1263, 1168, 1132

HRMS (EI) Calcd for $C_{12}H_{13}ClF_3NO_2$: 327,0308 Found: 327.0318

4-(2-chloro-3,3,3-trifluoropropyl)-7-methyl-1,2,3,4-tetrahydro-1,8-naphthyridin-2-one

II-15b



Following general procedure II-B with **II-14b** (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 **II-15b** (250 mg, 43%) as a mixture of two diastereoisomers 60:40 and as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 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 (dq, $J = 12.3, 6.2, 3.6$ Hz, 0.4H), 3.74 (dq, $J = 12.5, 6.3, 2.4$ 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).
 (CDCl₃, 400 MHz)

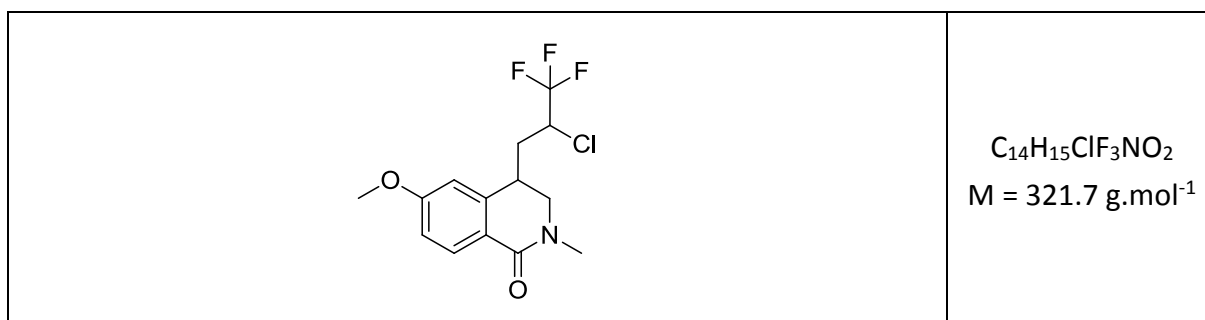
$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 170.4, 157.7, 149.7, 136.7, 123.7 (q, $J = 279$ Hz), 118.3, 115.3, 55.5 (q, $J = 33$ Hz), 36.7, 34.2, 31.1, 23.5.
 Minor Diastereoisomere : 169.7, 157.7, 149.7, 136.7, 123.8 (q, $J = 279$ Hz), 118.5, 117.4, 54.4 (q, $J = 33$ Hz), 34.4, 34.0, 31.0, 23.4.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 3406, 2929, 1711, 1455, 1268, 1131.

HRMS (EI) Calcd for C₁₂H₁₂ClF₃N₂O : 292.0590 Found: 292.0603

4-(2-chloro-3,3,3-trifluoropropyl)-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinolin-1-one

II-15c



Following general procedure II-B with **II-14c** (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 **II-15c** (190 mg, 51%) as a mixture of two diastereoisomers 85:15 and as an amorphous white solid. Mp = 98-102°C.

$^1\text{H NMR}$ (δ , ppm) Major Diastereoisomere : 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).
 (CDCl₃, 400 MHz)

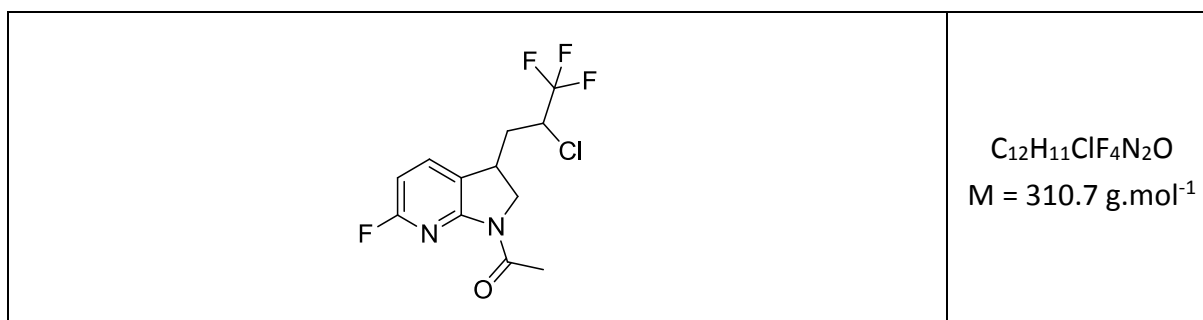
$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 164.0, 162.2, 140.3, 131.3, 123.9 (q, $J = 279$ Hz), 121.3, 113.0, 112.3, 56.1 (q, $J = 33$ Hz), 55.5, 53.6, 35.4, 34.9, 34.2.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2930, 1662, 1609, 1325, 1260, 1170, 1131.

HRMS (EI) Calcd for C₁₄H₁₅ClF₃NO₂ : 321.0743 Found: 321.0750

1-[3-(2-chloro-3,3,3-trifluoropropyl)-6-fluoro-1H,2H,3H-pyrrolo[2,3-b]pyridin-1-yl]ethan-1-one

II-15d



Following general procedure II-B with **II-14d** (3.45 mg, 7.7 mmol) in chlorobenzene. The residue was purified by silica gel column chromatography (DCM) and recrystallized from an EP/Et₂O mixture to afford the product **II-15d** (895 mg, 36%) as a mixture of two diastereoisomers 55:45 and as an amorphous white solid. Mp = 120°C.

¹H NMR (δ, ppm) Major Diastereoisomere : 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).
 (CDCl₃, 400 MHz)

Minor Diastereoisomere : 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 (δ, ppm) Major Diastereoisomere : 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.
 (CDCl₃, 100 MHz)

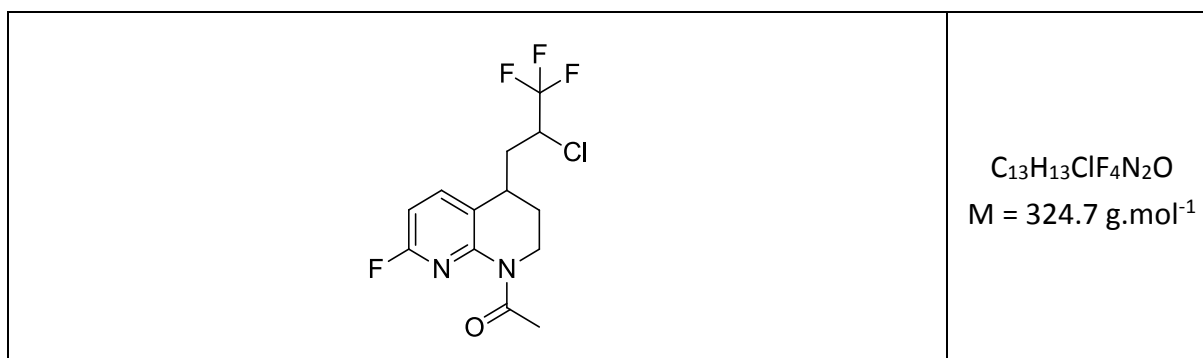
Minor Diastereoisomere : 169.8, 163.0 (d, *J* = 239 Hz), 153.8 (d, *J* = 17 Hz), 136.9 (d, *J* = 9 Hz), 123.8 (q, *J* = 279 Hz), 123.9 (d, *J* = 5 Hz), 102.1 (d, *J* = 37 Hz), 54.9 (q, *J* = 33 Hz), 51.0, 36.6, 32.1, 24.8.

IR (σ, cm⁻¹, CCl₄) 2928, 1681, 1605, 1483, 1386, 1297, 1262, 1132

HRMS (EI) Calcd for C₁₂H₁₁ClF₄N₂O : 310.0496 Found: 310.0497

1-[4-(2-chloro-3,3,3-trifluoropropyl)-7-fluoro-1,2,3,4-tetrahydro-1,8-naphthyridin-1-yl]ethan-1-one

II-15e



Following general procedure II-B with **II-14e** (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 **II-15e** (187 mg, 50%) as a mixture of two diastereoisomers 60:40 and as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 7.69-7.53 (m, 1H), 6.70-6.62 (m, 1H), 4.20 (dq, $J = 12.6, 6.3, 2.8$ 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).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) Major Diastereoisomere : 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.
(CDCl_3 , 100 MHz)

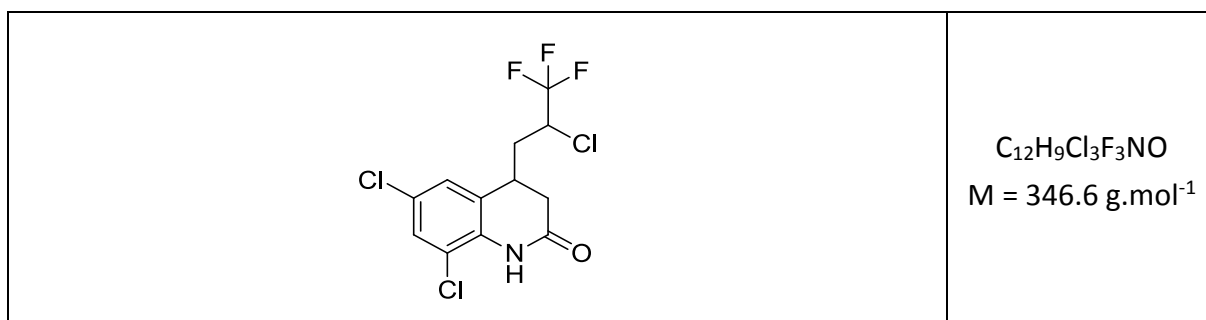
Minor Diastereoisomere : 171.7, 160.8 (d, $J = 239$ Hz), 149.1 (d, $J = 15$ Hz), 141.3 (d, $J = 8$ Hz), 123.9 (q, $J = 279$ Hz), 121.6 (d, $J = 5$ Hz), 103.9 (d, $J = 37$ Hz), 55.8 (q, $J = 33$ Hz), 40.7, 34.3, 32.7, 27.5, 26.2.

IR (σ , cm^{-1} , CCl_4) 2934, 1682, 1585, 1465, 1435, 1370, 1274, 1131.

HRMS (EI) Calcd for $C_{13}H_{13}ClF_4N_2O_2$: 324.0653 Found: NT

6,8-dichloro-4-(2-chloro-3,3,3-trifluoropropyl)-1,2,3,4-tetrahydroquinolin-2-one

II-15f



Following general procedure II-B with **II-14f** (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 **II-15f** (282 mg, 46%) as a mixture of two diastereoisomers 65:35 and as an amorphous white solid. Mp = 192°C.

1H NMR (δ , ppm) (CDCl₃, 400 MHz) 9.87 (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).

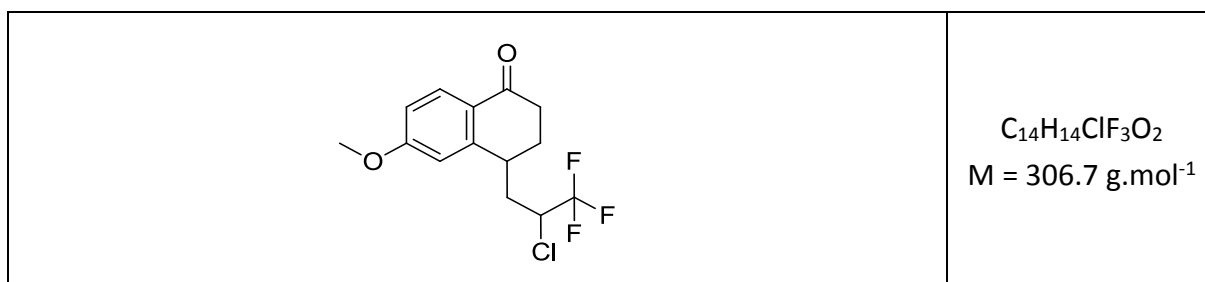
^{13}C NMR (δ , ppm) (CDCl₃, 100 MHz) Major Diastereoisomere : 170.9, 138.9, 134.6, 133.9, 124.3, 123.7 (q, $J = 279$ Hz), 122.3, 115.5, 55.3 (q, $J = 34$ Hz), 36.2, 35.8, 30.2.
 Minor Diastereoisomere : 170.2, 138.7, 134.5, 133.9, 124.3, 123.8 (q, $J = 279$ Hz), 122.1, 115.0, 54.3 (q, $J = 34$ Hz), 32.7, 31.9, 29.8.

IR (σ , cm⁻¹, CCl₄) 3409, 1716, 1693, 1600, 1575, 1260, 1174, 1129.

HRMS (EI) Calcd for C₁₂H₉Cl₃F₃NO : 344.9702 Found: 344.9711

4-(2-chloro-3,3,3-trifluoropropyl)-6-methoxy-1,2,3,4-tetrahydronaphthalen-1-one

II-15g



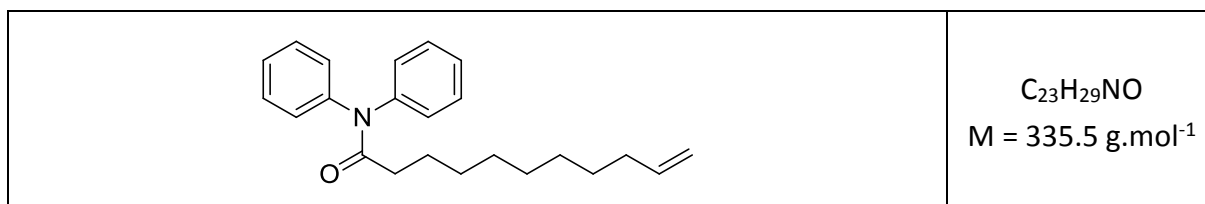
Following general procedure II-B with **II-14g** (850 mg, 2mmol) in ethyl acetate. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10) to afford the product **II-15g** (390 mg, 64%) as a mixture of two diastereoisomers 85:15 and as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 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 (dq, $J = 12.8, 6.5, 2.7$ 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).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 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.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2929, 1685, 1599, 1269, 1256, 1129.

HRMS (EI) Calcd for $C_{14}H_{14}ClF_3O_2$: 306.0634 Found: 306.0638

N,N-diphenylundec-10-enamide**II-16c**

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 **II-16c** (6.7 g, 100%) as white crystals. Mp : 51°C

¹H NMR (δ, ppm) 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)
(CDCl₃, 400 MHz)

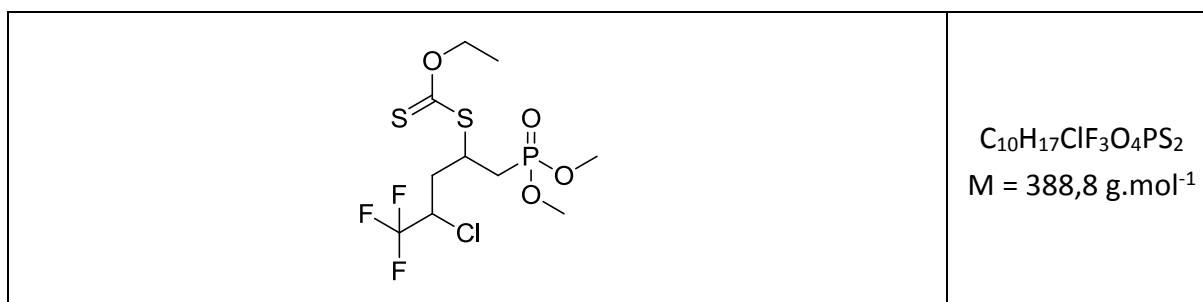
¹³C NMR (δ, ppm) 172.8, 142.6 (2C), 138.6, 129.7-124.8 (10C), 113.8, 37.9, 33.4, 28.9, 28.9, 28.8, 28.6, 28.5, 25.13
(CDCl₃, 100 MHz)

IR (σ, cm⁻¹, CCl₄) 2928, 2856, 1679, 1493, 1370, 1274

HRMS (EI) Calcd for C₁₅H₁₈ClF₃O₂S₂ : 335.2249 Found: 335.2249

dimethyl 4-chloro-2-[(ethoxymethanethiioyl)sulfanyl]-5,5,5-trifluoropentane-1-phosphonate

II-17a



Following general procedure II-A, the reaction was carried out using dimethyl (prop-2-en-1-yl)phosphonate (150 mg, 1 mmol), xanthate **II-4** (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 **II-17a** (300 mg, 77%) as a mixture of two diastereoisomers 65:35 and as a pale yellow oil.

1H NMR (δ , ppm) 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).
 (CDCl₃, 400 MHz)

^{13}C NMR (δ , ppm) Major Diastereoisomere : 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.
 (CDCl₃, 100 MHz)

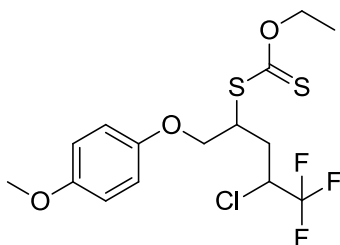
Minor Diastereoisomere : 211.5, 123.9 (q, $J = 279$ Hz), 70.4, 54.8 (q, $J = 34$ Hz), 52.8-52.6 (m, 2C), 41.4 (d, $J = 4$ Hz), 35.3 (d, $J = 3$ Hz), 28.9 (d, $J = 141$ Hz), 13.7.

IR (σ , cm⁻¹, CCl₄) 2954, 1269, 1227, 1127, 1048.

HRMS (EI) Calcd for C₁₀H₁₇ClF₃O₄PS₂ : 387.9946 Found: 387.9950

ethyl {[4-chloro-5,5,5-trifluoro-1-(4-methoxyphenoxy)pentan-2-yl]sulfanyl}methanethioate

II-17b


 $C_{15}H_{18}ClF_3O_3S_2$
 $M = 402.9 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure II-A, the reaction was carried out using 1-methoxy-4-(prop-2-en-1-yloxy)benzene (164 mg, 1.0 mmol), xanthate **II-4** (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 **II-17b** (358 mg, 89%) as a mixture of two diastereoisomers 60:40 and as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 6.86 (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).

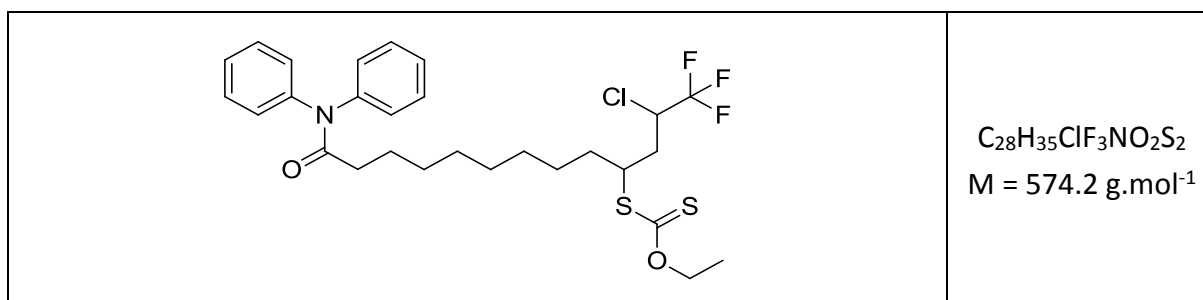
$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) Major Diastereoisomere : 211.5, 154.3, 152.1, 123.9 (q, $J = 278$ Hz), 115.7 (2C), 114.5 (2C), 70.6, 70.4, 55.7-54.3 (m, 2C), 46.5, 32.4, 13.5.
 Minor Diastereoisomere : 211.8, 154.4, 152.0, 123.8 (q, $J = 278$ Hz), 115.6 (2C), 114.5 (2C), 70.5, 69.9, 55.7-54.3 (m, 2C), 45.8, 32.8, 13.5.

IR (σ , cm⁻¹, CCl₄) 2935, 1508, 1267, 1228, 1183, 1130, 1049.

HRMS (EI) Calcd for C₁₅H₁₈ClF₃O₃S₂ : 402.0338 Found: 402.0349

12-chloro-10-[(ethoxymethanethioyl)sulfanyl]-13,13,13-trifluoro-N,N-diphenyltridecanamide

II-17c



Following general procedure II-A, the reaction was carried out using *N,N*-diphenylundec-10-enamide (1.10 g, 3.3 mmol), xanthate **II-4** (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 **II-17c** (1768 mg, 92%) as a mixture of two diastereoisomers 55/45 and as a yellow oil.

^1H NMR (δ , ppm) (CDCl₃, 400 MHz) 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 (δ , ppm) (CDCl₃, 100 MHz) Major Diastereoisomere : 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.

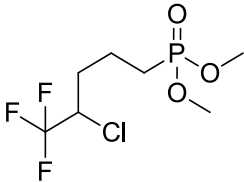
Minor Diastereoisomere : 212.5, 173.2, 142.9 (2C), 130.3-125.4 (m, 10C), 123.9 (q, $J = 279$ Hz), 70.0, 54.6 (q, $J = 33$ Hz), 46.7, 35.9, 35.7, 35.2, 29.3-28.9 (m, 4C), 26.3, 25.4, 13.7.

IR (σ , cm⁻¹, CCl₄) 2928, 2856, 1680, 1493, 1370, 1267, 1220, 1052

HRMS (EI) Calcd for C₂₅H₃₀ClF₃NO : 452,1968 Found: 452.1968

dimethyl (4-chloro-5,5,5-trifluoropentyl)phosphonate

II-18a

	$C_7H_{13}ClF_3O_3P$ $M = 268.0 \text{ g}\cdot\text{mol}^{-1}$
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A magnetically round bottom flask was charged with **II-17a** (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 $MgSO_4$. The residue was purified by silica gel column chromatography (DCM/Methanol 95:5) to afford the product **II-18a** (188 mg, 93%) as an orange oil.

1H NMR (δ , ppm) 4.06 (dq, $J = 9.8, 6.6, 3.2$ Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.14-1.68 (m, 6H)
 (CDCl₃, 400 MHz)

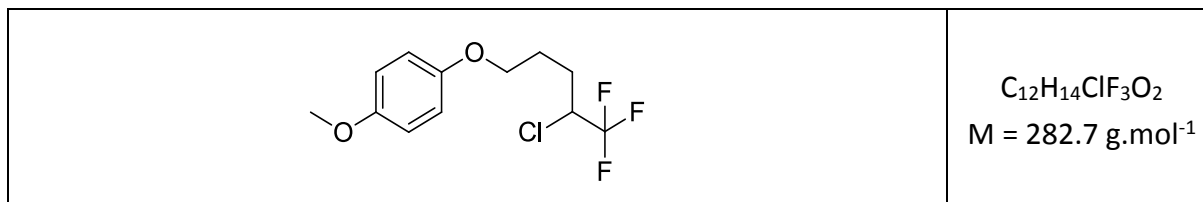
^{13}C NMR (δ , ppm) 124.0 (q, $J = 279$ Hz), 56.9 (q, $J = 33$ Hz), 52.4 (d, $J = 7$ Hz), 52.4 (d, $J = 7$ Hz), 31.4 (d, $J = 15$ Hz), 23.8 (d, $J = 143$ Hz), 19.0 (d, $J = 5$ Hz)
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 3685, 3453, 2953, 1267, 1180, 1126, 1062

HRMS (EI) Calcd for $C_7H_{13}ClF_3O_3P$: 268.0243 Found: NT

1-[(4-chloro-5,5,5-trifluoropentyl)oxy]-4-methoxybenzene

II-18b



A magnetically round bottom flask was charged with **II-17b** (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 **II-18b** (230 mg, 47%) as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 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).
(CDCl_3 , 400 MHz)

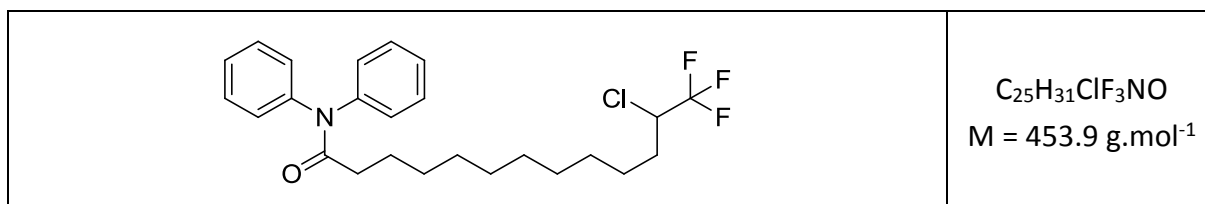
$^{13}\text{C NMR}$ (δ , ppm) 154.0, 152.9, 124.14 (q, $J = 279 \text{ Hz}$), 115.4 (2C), 114.7 (2C), 67.3, 57.4 (q, $J = 33 \text{ Hz}$), 55.8, 28.1, 25.6.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2935, 1508, 1272, 1231, 1172, 1131.

HRMS (EI) Calcd for $C_{15}H_{18}ClF_3O_2S_2$: 282.0634 Found: 282.0632

12-chloro-13,13,13-trifluoro-N,N-diphenyltridecanamide

II-18c



A magnetically round bottom flask was charged with **II-17c** (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 hours 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 **II-18c** (625 mg, 98%) as an orange oil.

1H NMR (δ , ppm) (CDCl₃, 400 MHz) 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).

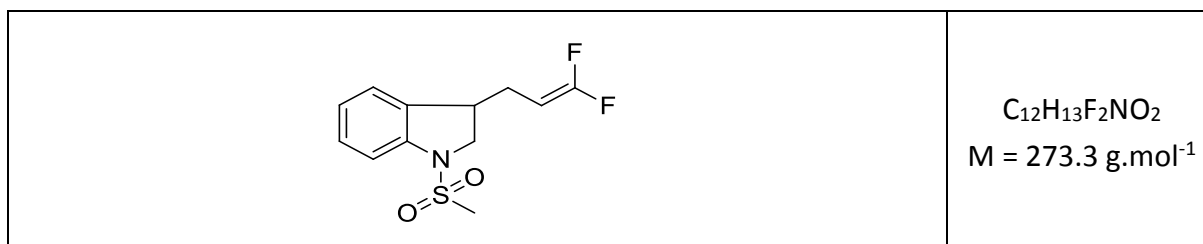
^{13}C NMR (δ , ppm) (CDCl₃, 100 MHz) 173.2, 142.9 (2C), 130.4-125.3 (m, 10C), 124.1 (q, $J = 280$ Hz), 57.6 (q, $J = 33$ Hz), 35.2, 30.8, 29.3 (3C), 29.1 (2C), 28.6, 25.5 (2C).

IR (σ , cm⁻¹, CCl₄) 2928, 2856, 1680, 1493, 1371, 1269, 1178, 1129.

HRMS (EI) Calcd for C₂₅H₃₁ClF₃NO : 453.2046 Found: 453.2035

3-(3,3-difluoroprop-2-en-1-yl)-1-methanesulfonyl-2,3-dihydro-1H-indole

II-19a



Following general procedure II-C with **II-15a** (80 mg, 0.24 mmol). **II-19a** (64 mg, 95%) was obtained as a white solid without purification.

$^1\text{H NMR}$ (δ , ppm) 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).
 (CDCl₃, 400 MHz)

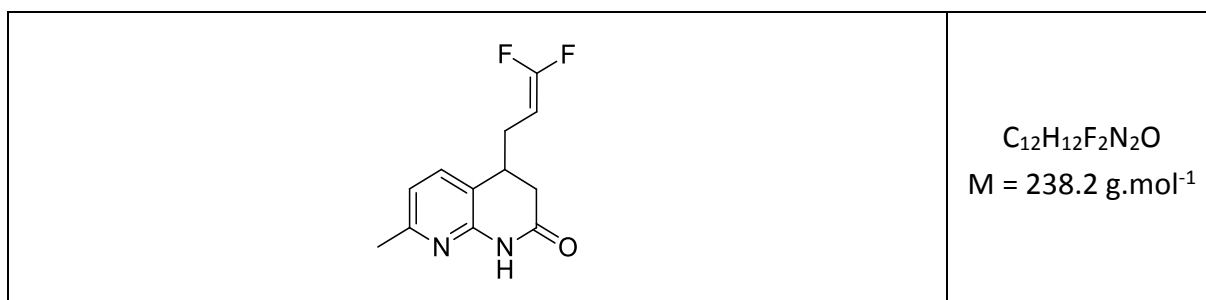
$^{13}\text{C NMR}$ (δ , ppm) 157.1 (t, $J = 288$ Hz), 141.8, 133.3, 128.7, 124.6, 123.7, 113.5, 74.7 (dd, $J = 23, 20$ Hz), 55.3, 39.7 (t, $J = 2$ Hz), 34.5, 27.3 (d, $J = 4$ Hz).
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 1746, 1480, 1460, 1364, 1166.

HRMS (EI) Calcd for C₁₂H₁₃F₂NO₂: 273.0635 Found: 273.0640

4-(3,3-difluoroprop-2-en-1-yl)-7-methyl-1,2,3,4-tetrahydro-1,8-naphthyridin-2-one

II-19b



Following general procedure II-C with **II-15b** (50.0 mg, 0.17 mmol). **II-19b** (40.4 mg, 100%) was obtained as a colorless oil without purification.

$^1\text{H NMR}$ (δ , ppm) 8.51 (bs, 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).
 (CDCl₃, 400 MHz)

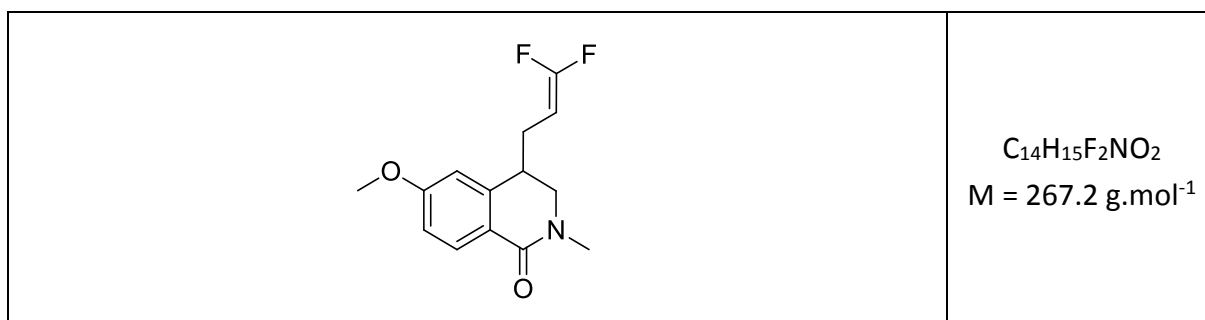
$^{13}\text{C NMR}$ (δ , ppm) 170.1, 158.4 (t, $J = 287$ Hz), 156.6, 149.5, 136.12, 118.2, 117.4, 74.6 (dd, $J = 24, 21$ Hz), 35.8, 34.9 (t, $J = 2$ Hz), 27.0 (d, $J = 4$ Hz), 23.6.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 3408, 2927, 1745, 1709, 1608, 1456, 1350, 1275, 1156.

HRMS (EI) Calcd for C₁₂H₁₂F₂N₂O : 238.0918 Found: 238.0925

4-(3,3-difluoroprop-2-en-1-yl)-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinolin-1-one

II-19c



Following general procedure II-C with **II-15c** (95 mg, 0.29 mmol). **II-19c** (75.1 mg, 97%) was obtained as a pale yellow oil without purification.

¹H NMR (δ, ppm) 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).
(CDCl₃, 400 MHz)

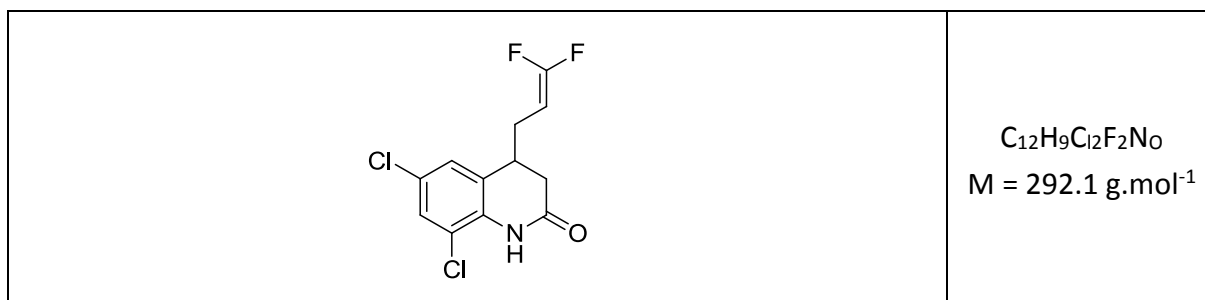
¹³C NMR (δ, ppm) 164.25, 162.21, 157.0 (dd, *J* = 288, 287 Hz), 142.7, 130.5, 121.5, 112.5, 111.8, 75.4 (dd, *J* = 23, 21 Hz), 55.3, 51.3, 37.9 (t, *J* = 2 Hz), 35.14, 26.5 (d, *J* = 4 Hz).
(CDCl₃, 100 MHz)

IR (σ, cm⁻¹, CCl₄) 2930, 1745, 1660, 1608, 1485, 1259.

HRMS (EI) Calcd for C₁₄H₁₅F₂NO₂: 267.1071 Found: 267.1069

6,8-dichloro-4-(3,3-difluoroprop-2-en-1-yl)-1,2,3,4-tetrahydroquinolin-2-one

II-19f



Following general procedure II-C with **II-15f** (130 mg, 0.38 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 70:30) to afford **II-19f** (55 mg, 50%) as an amorphous white solid. Mp : 136-138°C.

$^1\text{H NMR}$ (δ , ppm) 9.65 (bs, 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).
(CDCl_3 , 400 MHz)

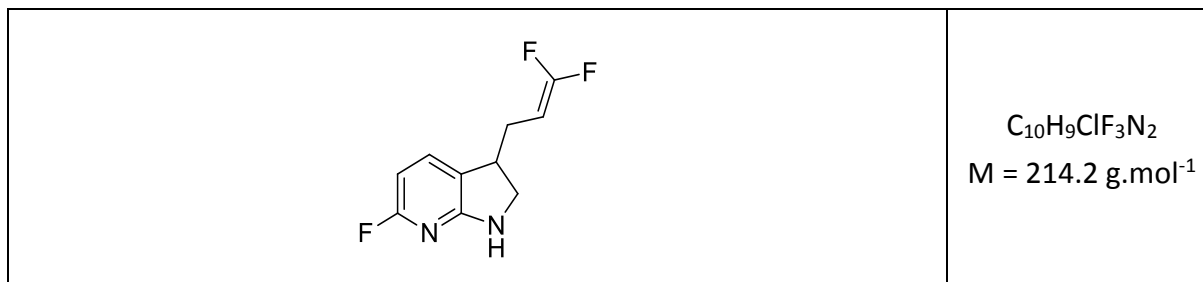
$^{13}\text{C NMR}$ (δ , ppm) 171.0, 155.8 (q, $J = 288$ Hz), 138.7, 134.1, 133.9, 124.0, 122.5, 114.9, 74.5 (dd, $J = 23, 21$ Hz), 34.2, 33.4, 25.7.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2952, 1745, 1691, 1601, 1578, 1394, 1373, 1317.

HRMS (EI) Calcd for : 291.0029 Found: 291.0024

3-(3,3-difluoroprop-2-en-1-yl)-6-fluoro-1H,2H,3H-pyrrolo[2,3-b]pyridine

II-23a



Following general procedure II-C with **II-22a**² (110 mg, 0.41 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 70:30) to afford **II-23a** (75 mg, 88%) as a colorless oil.

¹H NMR (δ , ppm) 7.30-7.22 (m, 1H), 6.07 (dd, $J = 7.7, 1.0$ Hz, 1H), 4.67 (bs, 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).
(CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 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).
(CDCl₃, 100 MHz)

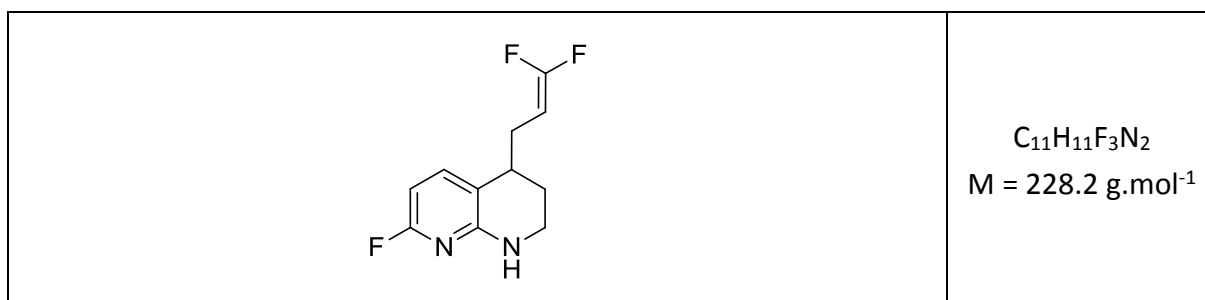
IR (σ , cm⁻¹, CCl₄) 3444, 2927, 1746, 1620, 1595, 1445.

HRMS (EI) Calcd for C₁₀H₉ClF₃N₂ : 214.0718 Found: 214.0722

² Obtained from X after deacetylation with K₂CO₃ (3 eq.) in refluxing methanol (3M) for 1 hour (98% yield)

1-[4-(3,3-difluoroprop-2-en-1-yl)-7-fluoro-1,2,3,4-tetrahydro-1,8-naphthyridin-1-yl]ethan-1-one

II-23b



Following general procedure II-C with **II-22b**³ (52 mg, 0.18 mmol). **II-23b** (35 mg, 83%) was obtained as an amorphous white solid without purification. Mp = 64-66 °C.

¹H NMR (δ, ppm) 7.25 (t, *J* = 8.0 Hz, 1H), 6.06 (dd, *J* = 7.9, 2.4 Hz, 1H), 5.29 (bs, 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).
(CDCl₃, 400 MHz)

¹³C NMR (δ, ppm) 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.
(CDCl₃, 100 MHz)

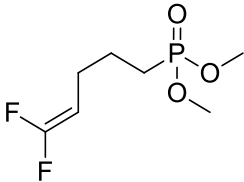
IR (σ, cm⁻¹, CCl₄) 3447, 3272, 2931, 1745, 1618, 1462, 1355, 1224.

HRMS (EI) Calcd for C₁₁H₁₁F₃N₂: 228.0874 Found: 228.0881

³ Obtained from X after deacetylation with K₂CO₃ (3 eq.) in refluxing methanol (3M) for 1 hour (100% yield)

dimethyl (5,5-difluoropent-4-en-1-yl)phosphonate

II-24a

	$C_7H_{13}F_2O_3P$ $M = 214.1 \text{ g}\cdot\text{mol}^{-1}$
-----------------------------------------------------------------------------------	-----------------------------------------------------------------

Following general procedure II-C with **II-18a** (150 mg, 0.57 mmol). The residue was purified by silica gel column chromatography (DCM/Methanol 95:5) to afford **II-24a** (98 mg, 80%) as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 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).
(CDCl_3 , 400 MHz)

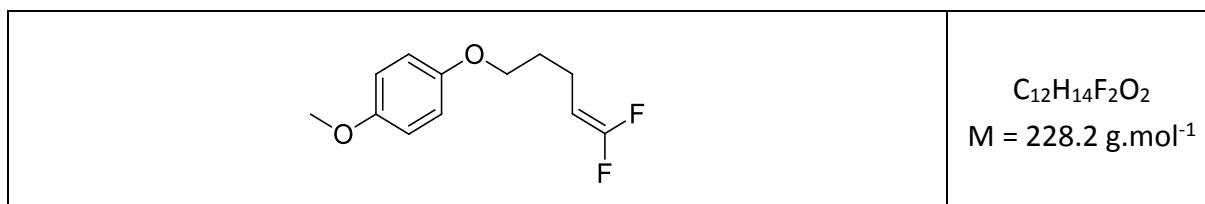
$^{13}\text{C NMR}$ (δ , ppm) 156.6 (t, $J = 287$ Hz), 76.9-76.3 (m), 52.3 (d, $J = 6$ Hz, 2C), 23.9 (d, $J = 142$ Hz), 22.9 (dd, $J = 18, 4$ Hz), 22.2.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2953, 1747, 1248, 1064, 1036.

HRMS (EI) Calcd for $C_7H_{13}F_2O_3P$: 214.0570 Found: 214.0567

1-[(5,5-difluoropent-4-en-1-yl)oxy]-4-methoxybenzene

II-24b



Following general procedure II-C with **II-18b** (210 mg, 0.74 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 97:3) to afford the product **II-24b** (153 mg, 90%) as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 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).
(CDCl_3 , 400 MHz)

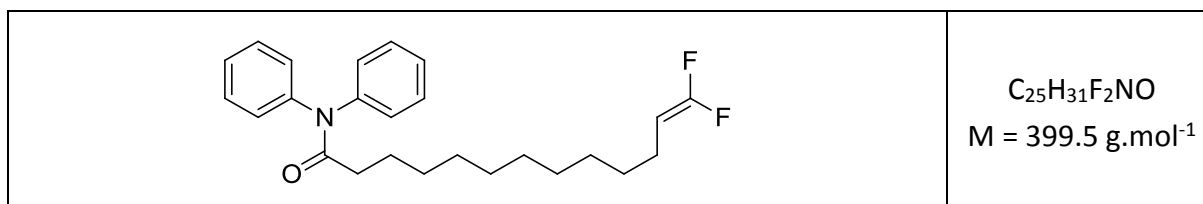
$^{13}\text{C NMR}$ (δ , ppm) 156.4 (dd, $J = 287, 285$ Hz), 153.9, 153.1, 115.5 (2C), 114.7 (2C), 77.5-77.0 (m), 67.6, 55.8, 29.1 (t, $J = 2$ Hz), 19.0 (d, $J = 4$ Hz).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2951, 1746, 1509, 1231.

HRMS (EI) Calcd for $C_{15}H_{18}ClF_3O_2S_2$: 228.0962 Found: 228.0964

13,13-difluoro-N,N-diphenyltridec-12-enamide

II-24c



Following general procedure II-C with **II-18c** (225 mg, 0.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20) to afford the product **II-24c** (100 mg, 50%) as a colorless oil.

$^1\text{H NMR}$ (δ , ppm) 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).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 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).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2928, 2856, 1746, 1680, 1594, 1493, 1369, 1271.

HRMS (EI) Calcd for $C_{25}H_{31}F_2NO$: 399.2374 Found: 399.2371

B. Chapitre III : Synthèse de difluorothiochromanes, une nouvelle famille de composés organo-fluorés

1. General procedure

General procedure III-A for the addition reaction

A solution of olefin (n mmol) and xanthate (between 1.5 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.

General procedure III-B for the cyclisation reaction

A solution of the xanthate adduct (n mmol) in AcOEt (40 n mL) was refluxed under a flow of nitrogen for 15 minutes. Lauroyl peroxide (DLP) 20 mol% was then 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 product as a mixture of two diastereoisomers.

General procedure III-C1 for the oxidation reaction

A solution of thioether (n mmol) in DCM (10n ml) was cooled to 0 °C and mCPBA (70%) (1.1n mmol) was added. The resulting solution was stirred until total consumption of the starting thioether and then quenched with Na₂S₂O₃ sat. The layers were portioned and the organic one was washed with water and brine. The solvents were evaporated to dryness. Flash column chromatography afforded the corresponding sulfoxide.

General procedure III-C2 for the oxidation and elimination reaction

A solution of thioether (n mmol) in DCM (10n ml) was cooled to 0 °C and mCPBA (70%) (1.1n mmol) was added. The resulting solution was stirred until total consumption of the starting thioether and then quenched with Na₂S₂O₃ sat. The layers were portioned and the organic one

was washed with water and brine. The solvents were evaporated to dryness to afford the corresponding sulfoxide. The latter was dissolved in diphenylether (10n ml) and heated up to 160 °C. The resulting solution was stirred until total consumption of the sulfoxide, then cooled to room temperature and purified on flash chromatography to yield the desired difluoro olefin.

General procedure III-D for the radical allylation⁴

A solution of olefin (2n mmol) and xanthate (n mmol) in AcOEt (n mL) was refluxed under a flux of nitrogen for 15 minutes. Lauroyl peroxide (DLP) 30 mol % was then added every hour until total conversion of the starting xanthate. The mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. Flash chromatography afforded the desired adduct as a mixture of E and Z isomers.

General procedure III-E for the preparation of fluoropyridine derivatives⁴

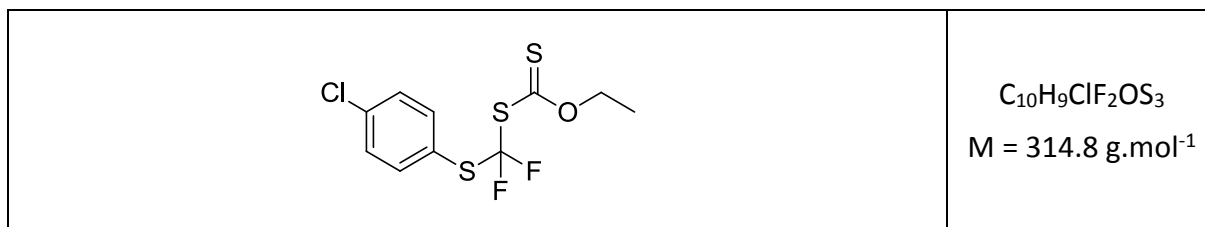
A solution of ketone (n mmol) in THF (6n mL) was cooled to -78 °C and vinyl magnesium bromide (0.7 M in THF) (1.2n mmol) was added dropwise over 15 min. The resulting solution was stirred until full consumption of the starting ketone and then quenched with NH₄Cl sat. The layers were partitioned and the organic one was washed with water and brine. The solvents were evaporated to dryness to afford the vinylic alcohol. A magnetically stirred round bottom flask was charged with the latter alcohol, 2,6-difluoropyridine (1.3n mmol) and dry DMSO (n mL). NaH (60% in mineral oil, 1.3n mmol) was added in one portion and the resulting suspension was heated up to 60 °C. The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and then quenched with water. Et₂O was added, the layers were partitioned and the aqueous one was extracted twice with Et₂O. The combined organic layers were washed with brine and dried over anhydrous MgSO₄. Removal of the solvent and purification on flash chromatography yielded the desired fluoropyridyl ether.

⁴ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

2. Experimental Procedures and spectroscopic data

ethyl ({{[(4-chlorophenyl)sulfanyl]difluoromethyl}sulfanyl)methanethioate

III-1



A magnetically stirred round bottom flask was charged with sodium 2-chloro-2,2-difluoroacetate (14.3 g, 94 mmol), sodium thiophenolate (23,6 g, 141 mmol), 170 ml of freshly distilled dioxane and was refluxed for 4 hours. Then 2N HCl (100 ml) was added, the layers were partitioned and the aqueous one was extracted twice with AcOEt. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The residue was heated in pentane and filtered to afford a mixture of **III-6** and dioxane in a 2:1 ratio (18.2 g, 68%).

A magnetically stirred round bottom flask was charged with a mixture of **III-6** and dioxane in a 2:1 ratio (16 g, 56 mmol), oxalyl chloride (14.7 mL, 168 mmol), 10 μ L of DMF and 60 mL of DCM. When the evolution of gas ceased (usually 3-4 hours), the mixture was diluted with cyclohexane (100 mL). DCM and the excess of oxalyl chloride were removed under reduced pressure (270 mbar, 40°C). The mixture was then cooled to 0°C and potassium *O*-ethyl xanthate salt (11.2 g, 70 mmol) was added over 5 minutes. After 6 hours and total conversion of the acyl chloride, the excess of potassium *O*-ethyl xanthate was filtered. The solution at refluxed temperature was irradiated with a halogen lamp for 12 hours. Then the solvent was evaporated under reduced pressure to afford **III-1** (16.5 g, 94%) as a white solid (14.0 g, 80% after recrystallisation from pentane).

1H NMR (δ , ppm) 7.56 (d, $J = 8.4$ Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 2H), 4.69 (q, $J = 7.1$ Hz, 2H), 1.48 (t, $J = 7.1$ Hz, 3H).
($CDCl_3$, 400 MHz)

^{13}C NMR (δ , ppm) 204.9, 137.9 (2C), 137.6, 130.2 (t, $J = 321$ Hz), 129.7 (2C), 124.5 (t, $J = 2$ Hz), 70.8, 13.6.
($CDCl_3$, 100 MHz)

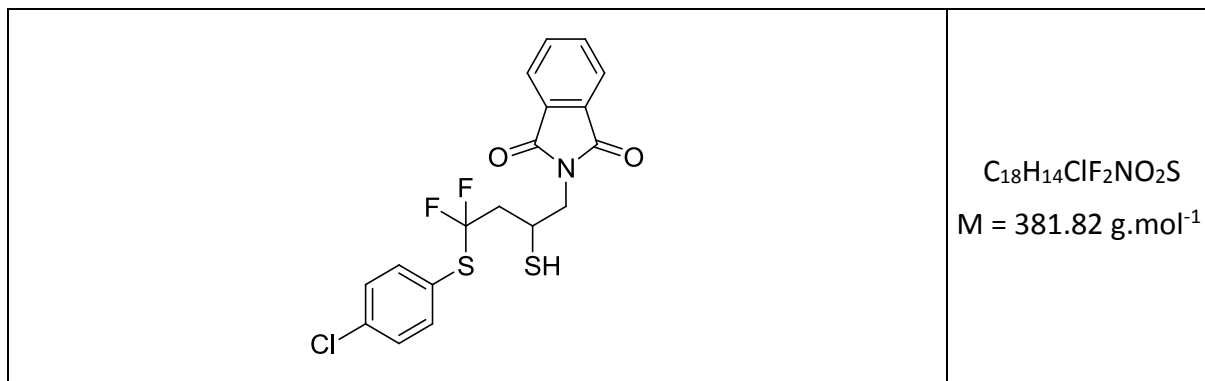
Chapitre III

IR (σ , cm^{-1} , CCl_4) 2990, 1574, 1477, 1264, 1243, 1115, 1095, 1033

HRMS (EI) Calcd for $\text{C}_{10}\text{H}_9\text{ClF}_2\text{OS}_3$: 313.9472 Found: 313.9471

2-(4-(4-chlorophenylthio)-4,4-difluorobutyl)phthalimide

III-11



A magnetically stirred round bottom flask was charged with **III-15a** (470 mg, 0.94 mmol), tris(trimethylsilyl)silane (349 mg, 1.41 mmol) in 3 ml of a 1:1 solution of toluene and cyclohexane. The solution was refluxed under a flow of nitrogen for 5 minutes then AIBN (8 mg, 0.05 mmol) was added. After 60 min and total consumption of the starting xanthate, 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 80:20) to afford the product **III-11** (150 mg, 42%) as an amorphous white solid⁵.

¹H NMR (δ , ppm) 7.92 – 7.87 (m, 2H), 7.80 – 7.76 (m, 2H), 7.55 – 7.51 (m, 2H), 7.35 – 7.31 (m, 2H), 3.77 (t, $J = 6.9$ Hz, 2H), 2.25 – 2.12 (m, 2H), 2.07 – 1.97 (m, 2H).
(CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 168.3 (2C), 137.4 (2C), 136.5, 134.1 (2C), 132.0 (2C), 129.4 (t, $J = 279$ Hz), 129.3 (2C), 125.23 (t, $J = 2$ Hz), 123.4 (2C), 37.0, 36.0 (t, $J = 24$ Hz), 22.7 (t, $J = 3$ Hz).
(CDCl₃, 100 MHz)

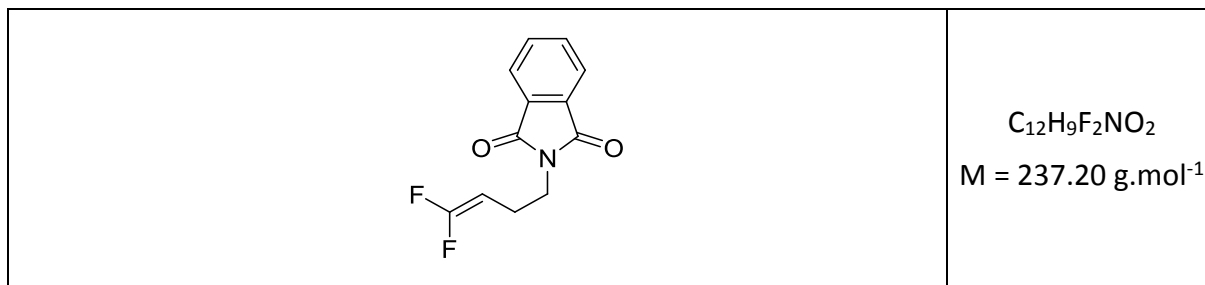
IR (σ , cm⁻¹, CCl₄) 2934, 1776, 1720, 1395

HRMS (EI) Calcd for C₁₈H₁₄ClF₂NO₂S : 381.0402 Found : 381.0395

⁵ Described with about 5% of cyclised product **23a**

2-(4,4-difluorobut-3-enyl)phthalimide

III-12



Following general procedure III-C, the reaction was carried out using **III-11** (60 mg, 0.16 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 95:5) to afford **III-12** (27 mg, 72%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.93 – 7.87 (m, 2H), 7.80 – 7.73 (m, 2H), 4.23 (dtd, $J = 24.9, 7.9, 2.1$ Hz, 1H), 3.78 (t, $J = 7.0$ Hz, 2H), 2.47 – 2.40 (m, 2H).
(CDCl_3 , 400 MHz)

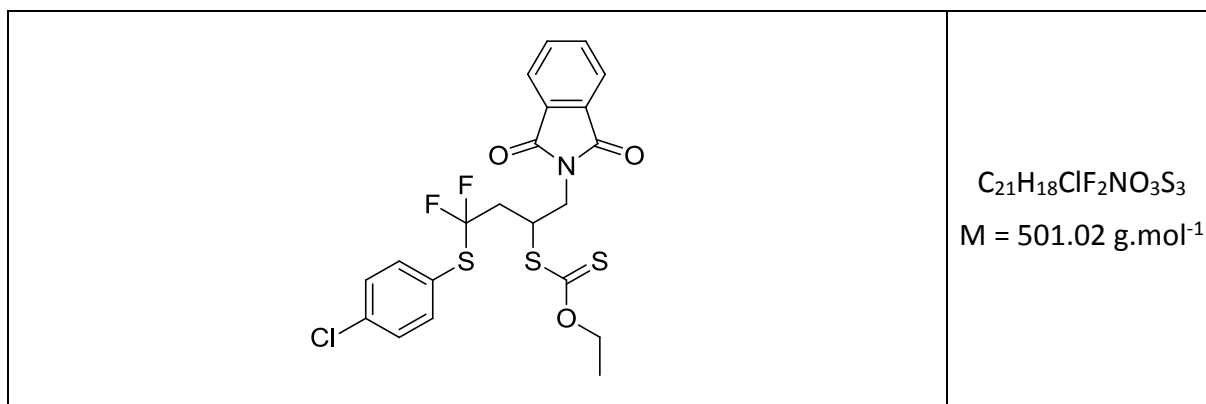
$^{13}\text{C NMR}$ (δ , ppm) 168.2 (2C), 157.1 (dd, $J = 289, 287$ Hz), 134.1 (2C), 132.0 (2C), 123.4 (2C), 74.7 (dd, $J = 24, 21$ Hz), 37.2 (t, $J = 3$ Hz), 21.9 (d, $J = 2$ Hz).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1776, 1748, 1721, 1395, 1364

HRMS (EI) Calcd for $C_{12}H_9F_2NO_2$: 237.0601 Found: 237.0605

ethyl ({4-[(4-chlorophenyl)sulfanyl]-1-(1,3-dioxo-2,3-dihydro-1H-isoindol-2-yl)-4,4-difluorobutan-2-yl}sulfanyl)methanethioate

III-15a



Following general procedure III-A, the reaction was carried out using N-allylphthalimide (93 mg, 0.5 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20 to 70:30) to afford the corresponding xanthate adduct **III-15a** (225 mg, 90%) as a pale yellow oil.

$^1\text{H NMR}$ (δ , ppm) 7.90 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.78 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.58 (d, $J = 8.5$ Hz, 2H), 7.36 (d, $J = 8.5$ Hz, 2H), 4.73 – 4.59 (m, 2H), 4.46 (dq, $J = 8.6, 6.4$ Hz, 1H), 4.13 (dd, $J = 14.1, 6.6$ Hz, 1H), 4.04 (dd, $J = 14.1, 8.6$ Hz, 1H), 2.83 – 2.54 (m, 2H), 1.47 (t, $J = 7.1$ Hz, 3H).
 (CDCl₃, 400 MHz)

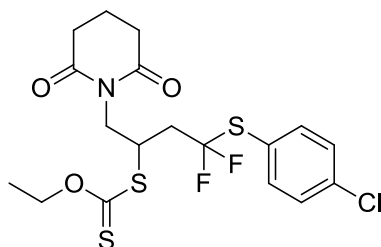
$^{13}\text{C NMR}$ (δ , ppm) 210.9, 168.0 (2C), 137.5 (2C), 136.7, 134.3 (2C), 131.7 (2C), 129.4 (2C), 128.4 (t, $J = 280$ Hz), 124.7 (t, $J = 2$ Hz), 123.6 (2C), 70.4, 43.7, 41.2 (t, $J = 24$ Hz), 40.4, 13.7.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2985, 2937, 1777, 1724, 1477, 1393, 1365, 1227, 1048

HRMS (EI) Calcd for C₂₁H₁₈ClF₂NO₃S₃: 501.0105 Found: 501.0108

ethyl ({4-[(4-chlorophenyl)sulfanyl]-1-(2,6-dioxopiperidin-1-yl)-4,4-difluorobutan-2-yl}sulfanyl)methanethioate

III-15b



$C_{18}H_{20}ClF_2NO_3S_3$
 $M = 468.0 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-A, the reaction was carried out using 1-(prop-2-en-1-yl)piperidine-2,6-dione (306 mg, 2 mmol), xanthate **III-1** (942 mg, 3 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 65:35) to afford the corresponding xanthate adduct **III-15b** (820 mg, 88%) as a white amorphous solid.

$^1\text{H NMR}$ (δ , ppm) 7.54 (d, $J = 8.5$ Hz, 2H), 7.35 (d, $J = 8.5$ Hz, 2H), 4.69-4.57 (m, 2H), 4.40-4.31 (m, 1H), 4.22-4.07 (m, 2H), 2.75-2.59 (m, 5H), 2.49 (dtd, $J = 22.8$, 11.0, 6.9 Hz, 1H), 1.89 (quint, $J = 6.6$ Hz, 2H), 1.43 (t, $J = 7.1$ Hz, 3H).
 (CDCl₃, 400 MHz)

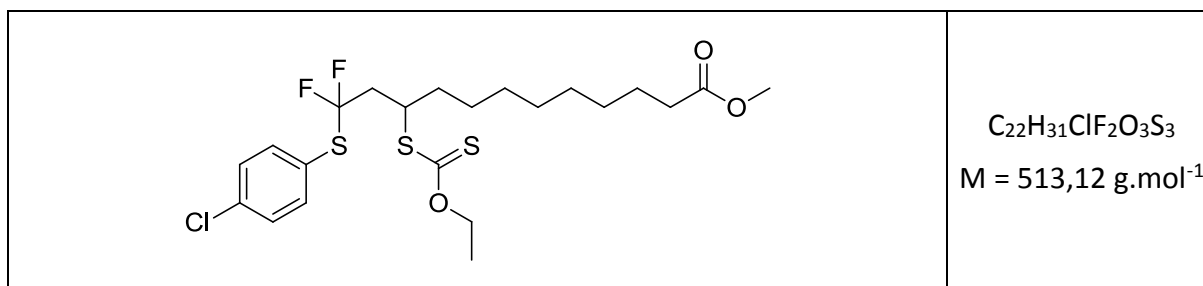
$^{13}\text{C NMR}$ (δ , ppm) 211.9, 172.4 (2C), 137.5 (2C), 136.6, 129.3 (2C), 128.4 (t, $J = 281$ Hz), 124.8 (t, $J = 2$ Hz), 70.3, 43.2, 41.8 (t, $J = 24$ Hz), 41.1, 32.7 (2C), 16.9, 13.6.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2961, 1733, 1687, 1477, 1351, 1225, 1166, 1049

HRMS (EI) Calcd for C₁₈H₂₀ClF₂NO₃S₃: 467.0262 Found: 467,0255

**methyl 12-[(4-chlorophenyl)sulfanyl]-10-[(ethoxymethanethioyl)sulfanyl]-
12,12-difluorododecanoate**

III-15c



Following general procedure III-A, the reaction was carried out using methyl undec-10-enoate (396 mg, 2 mmol), xanthate **III-1** (942 mg, 3 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 95:5) to afford the corresponding xanthate adduct **III-15c** (950 mg, 93%) as a colourless oil.

^1H NMR (δ , ppm) 7.58 (d, $J = 8.5$ Hz, 2H), 7.40 (d, $J = 8.5$ Hz, 2H), 4.69 (q, $J = 7.0$ Hz, 2H), 4.05 (tt, $J = 8.7, 4.8$ Hz, 1H), 3.70 (s, 3H), 2.78 – 2.62 (m, 1H), 2.52 (dddd, $J = 17.7, 15.2, 9.8, 8.2$ Hz, 1H), 2.34 (t, $J = 7.5$ Hz, 2H), 1.91 (ddt, $J = 15.1, 10.4, 4.9$ Hz, 1H), 1.77 – 1.60 (m, 3H), 1.46 (t+m, $J = 7.0$ Hz, 4H), 1.39 – 1.27 (m, 9H).

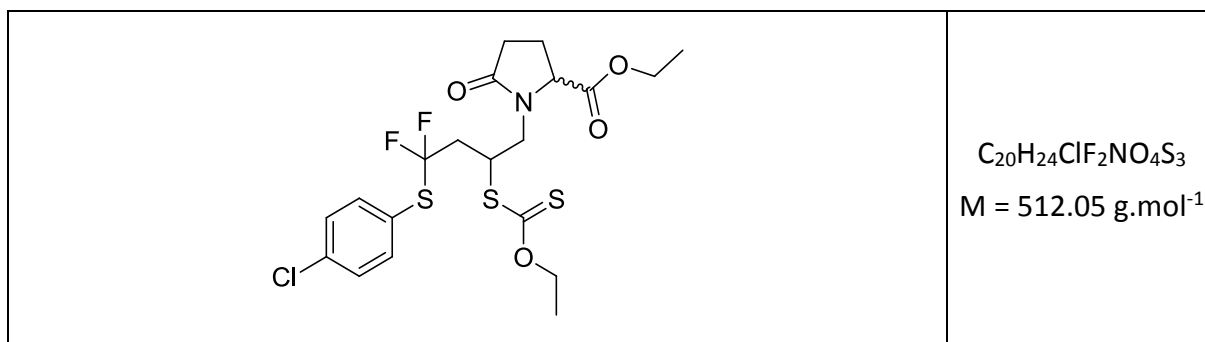
^{13}C NMR (δ , ppm) 213.0, 174.3, 137.5 (2C), 136.6, 129.3 (2C), 128.7 (t, $J = 281$ Hz), 125.0, 70.0, 51.5, 45.6, 43.2 (t, $J = 23$ Hz), 34.1, 33.3, 29.2, 29.1 (2C), 29.1, 26.6, 24.9, 13.8.

IR (σ , cm^{-1} , CCl_4) 2930, 2857, 1741, 1477, 1222, 1171, 1112, 1052

HRMS (EI) Calcd for $C_{22}H_{31}ClF_2O_3S_3$: 512.1092 Found: 512.1097

ethyl 1-{4-[(4-chlorophenyl)sulfanyl]-2-[(ethoxymethanethioyl)sulfanyl]-4,4-difluorobutyl}-5-oxopyrrolidine-2-carboxylate

III-15d



Following general procedure III-A, the reaction was carried out using ethyl 5-oxo-1-(prop-2-en-1-yl)pyrrolidine-2-carboxylate (99 mg, 0.5 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (DCM) to afford the corresponding xanthate adduct **III-15d** (225 mg, 88%) as a 1:1 mixture of diastereoisomers and as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.57 (d, $J = 8.5$ Hz, 2H), 7.45 – 7.33 (m, 2H), 4.72 – 4.64 (m, 2H), 4.50 (dd, $J = 8.9, 2.3$ Hz, 0.5H), 4.34 (dd, $J = 8.8, 3.1$ Hz, 0.5H), 4.32 – 4.18 (m, 2.5H), 4.14 – 4.02 (m, 1H), 3.95 (dd, $J = 14.7, 9.0$ Hz, 0.5H), 3.54 (dd, $J = 14.7, 5.6$ Hz, 0.5H), 3.17 (dd, $J = 12.9, 3.4$ Hz, 0.5H), 2.67 (td, $J = 15.6, 14.9, 6.7$ Hz, 1H), 2.61 – 2.28 (m, 4H), 2.19 – 2.09 (m, 1H), 1.46 (t, $J = 7.1$ Hz, 3H), 1.34 (t, $J = 7.1$ Hz, 1.5H), 1.33 (t, $J = 7.1$ Hz, 1.5H).

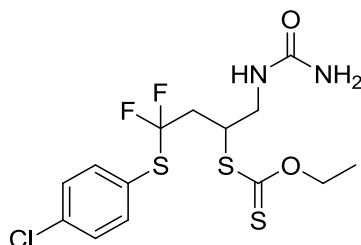
$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 212.7, 212.6, 175.9, 175.8, 171.7, 171.7, 137.6 (2C), 137.5 (2C), 136.7 (2C), 129.4 (2C), 129.4 (2C), 128.5 (t, $J = 280$ Hz), 128.2 (t, $J = 280$ Hz), 124.7 (2C), 70.5, 70.5, 61.8, 61.7, 59.9, 59.3, 45.2, 44.2, 44.1, 42.4, 41.3 (t, $J = 24$ Hz), 39.3 (t, $J = 24$ Hz), 29.2, 29.1, 23.3, 23.2, 14.3, 14.2, 13.8, 13.7.

IR (σ , cm⁻¹, CCl₄) 2984, 1747, 1709, 1477, 1411, 1226, 1050

HRMS (EI) Calcd for C₁₇H₁₉ClF₂NO₃S : 390.0742 Found: 390.0751

ethyl {[1-(carbamoylamino)-4-[(4-chlorophenyl)sulfanyl]-4,4-difluorobutan-2-yl]sulfanyl}methanethioate

III-15e

C₁₄H₁₇ClF₂O₂N₂S₃M = 414.9 g.mol⁻¹

Following general procedure III-A, the reaction was carried out using allylurea (50 mg, 0.5 mmol), ACS (140 mg, 0.6 mmol) xanthate **III-1** (342 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 100:0 to 0:100) to afford the corresponding xanthate adduct **III-15e** (164 mg, 79%) as a colourless oil.

¹H NMR (δ, ppm) 7.57 (d, *J* = 8.5 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 5.45 (t, *J* = 6.2 Hz, 1H), 4.79 (s, 2H), 4.69 (q, *J* = 7.1 Hz, 2H), 4.19 (quint, *J* = 5.9, 5.3 Hz, 1H), 3.71 (dt, *J* = 12.4, 6.1 Hz, 1H), 3.48 (dt, *J* = 14.3, 6.4 Hz, 1H), 2.73-2.52 (m, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).

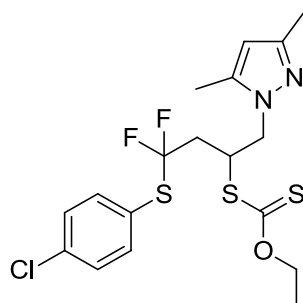
¹³C NMR (δ, ppm) 212.5, 158.6, 137.6 (2C), 136.7, 129.4 (2C), 128.6 (t, *J* = 281 Hz), 124.7 (t, *J* = 2 Hz), 70.6, 46.0, 43.2, 40.2 (t, *J* = 24 Hz), 13.7.

IR (σ, cm⁻¹, CCl₄) 1702, 1518, 1477, 1226, 1052

HRMS (EI) Calcd for C₁₄H₁₇ClF₂O₂N₂S₃ : 414.0109 Found: 414.0105

ethyl ({4-[(4-chlorophenyl)sulfanyl]-1-(3,5-dimethyl-1H-pyrazol-1-yl)-4,4-difluorobutan-2-yl}sulfanyl)methanethioate

III-15f



$C_{18}H_{21}ClF_2N_2OS_3$
 $M = 451.02 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-A, the reaction was carried out using 3,5-dimethyl-1-(prop-2-en-1-yl)-1H-pyrazole (68 mg, 0.5 mmol), ACS (140 mg, 0.6 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 80:20) to afford the corresponding xanthate adduct **III-15f** (150 mg, 66%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.53 (d, $J = 8.4 \text{ Hz}$, 2H), 7.37 (d, $J = 8.5 \text{ Hz}$, 2H), 5.83 (s, 1H), 4.76 – 4.61 (m, 2H), 4.46 (tt, $J = 7.6, 5.5 \text{ Hz}$, 1H), 4.37 (dd, $J = 14.3, 6.0 \text{ Hz}$, 1H), 4.29 (dd, $J = 14.3, 7.8 \text{ Hz}$, 1H), 2.79 (tdd, $J = 16.0, 13.6, 5.0 \text{ Hz}$, 1H), 2.61 (tdd, $J = 15.9, 12.7, 7.7 \text{ Hz}$, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.47 (t, $J = 7.1 \text{ Hz}$, 3H).
 (CDCl_3 , 400 MHz)

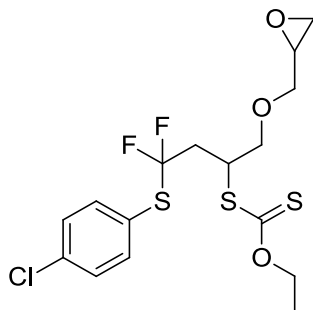
$^{13}\text{C NMR}$ (δ , ppm) 212.1, 148.1, 139.8, 137.4 (2C), 136.6, 129.4 (2C), 128.6 (t, $J = 280 \text{ Hz}$), 124.9 (t, $J = 2 \text{ Hz}$), 105.6, 70.4, 50.9, 44.9, 39.4 (t, $J = 24 \text{ Hz}$), 13.8, 13.5, 11.3.
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2926, 1477, 1226, 1112, 1095, 1055, 1014

HRMS (EI) Calcd for $C_{18}H_{21}ClF_2N_2OS_3$: 450.0473 Found: 450.0469

ethyl ({4-[(4-chlorophenyl)sulfanyl]-4,4-difluoro-1-(oxiran-2-ylmethoxy)butan-2-yl}sulfanyl)methanethioate

III-15g



$$\text{C}_{16}\text{H}_{19}\text{ClF}_2\text{O}_3\text{S}_3$$

$$M = 428.97 \text{ g}\cdot\text{mol}^{-1}$$

Following general procedure III-A, the reaction was carried out using Allyl glycidyl ether (57 mg, 0.5 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 90:1) to afford the corresponding xanthate adduct **III-15g** (196 mg, 91%) as a 1:1 mixture of diastereoisomers and as a colourless oil.

^1H NMR (δ , ppm) 7.59 (d, $J = 8.4$ Hz, 2H), 7.40 (d, $J = 8.5$ Hz, 2H), 4.69 (q, $J = 7.1$ Hz, 2H), 4.33 – 4.24 (m, 1H), 3.98 – 3.68 (m, 3H), 3.46 (ddd, $J = 11.7, 8.6, 5.9$ Hz, 1H), 3.20 – 3.14 (m, 1H), 2.92 – 2.76 (m, 2H), 2.64 (dt, $J = 5.2, 2.7$ Hz, 1H), 2.61 – 2.50 (m, 1H), 1.47 (t, $J = 7.1$ Hz, 3H).
(CDCl_3 , 400 MHz)

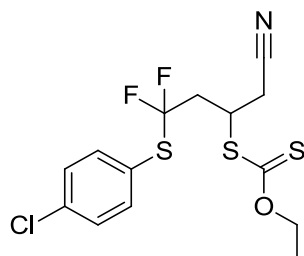
^{13}C NMR (δ , ppm) 212.7, 137.6 (2C), 136.6, 129.4 (2C), 128.6 (t, $J = 281$ Hz), 124.9 (t, $J = 2$ Hz), 71.8-71.7 (m, 2C), 70.3, 50.7, 45.2-45.0 (m, 1C), 44.1 (0.5C), 44.0 (0.5C) 39.3 (t, $J = 24$ Hz, 0.5C), 39.3 (t, $J = 24$ Hz, 0.5C), 13.8.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2991, 2925, 1477, 1389, 1223, 1015

HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{19}\text{ClF}_2\text{O}_3\text{S}_3$: 428.0153 Found: 428.0156

ethyl ({4-[(4-chlorophenyl)sulfanyl]-1-cyano-4,4-difluorobutan-2-yl}sulfanyl)methanethioate

III-15h



$C_{14}H_{14}ClF_2NOS_3$
 $M = 381.91 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-A, the reaction was carried out using Allyl cyanide (33 mg, 0.5 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20) to afford the corresponding xanthate adduct **III-15h** (150 mg, 79%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.59 (d, $J = 8.4$ Hz, 2H), 7.43 (d, $J = 8.5$ Hz, 2H), 4.72 (q, $J = 7.1$ Hz, 2H), 4.36 – 4.26 (m, 1H), 3.10 (dd, $J = 17.3, 5.0$ Hz, 1H), 3.02 (dd, $J = 17.4, 5.3$ Hz, 1H), 2.81 – 2.67 (m, 2H), 1.49 (t, $J = 7.1$ Hz, 3H).
 (CDCl_3 , 400 MHz)

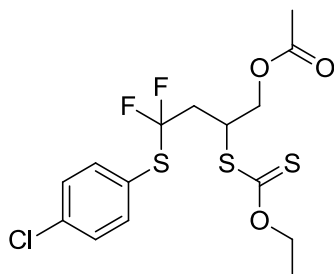
$^{13}\text{C NMR}$ (δ , ppm) 210.8, 137.6 (2C), 137.1, 129.6 (2C), 128.1 (t, $J = 280$ Hz), 124.1 (t, $J = 2$ Hz), 116.4, 70.9, 41.1, 40.9 (t, $J = 2$ Hz), 23.4, 13.8.
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2986, 1477, 1230, 1049

HRMS (EI) Calcd for $C_{11}H_9ClF_2NS$ ($[M-Xa]$): Found: 259.0025
 259.0034

4-[(4-chlorophenyl)sulfanyl]-2-[(ethoxymethanethioyl)sulfanyl]-4,4-difluorobutyl acetate

III-15i



$C_{15}H_{17}ClF_2O_3S_3$
 $M = 414.94 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-A, the reaction was carried out using Allyl acetate (50 mg, 0.5 mmol), xanthate III-1 (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 95:5) to afford the corresponding xanthate adduct III-15i (206 mg, 99%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.59 (d, $J = 8.4$ Hz, 2H), 7.41 (d, $J = 8.4$ Hz, 2H), 4.71 (q, $J = 7.1$ Hz, 2H), (CDCl₃, 400 MHz) 4.47 – 4.40 (m, 1H), 4.40 – 4.32 (m, 2H), 2.78 – 2.56 (m, 2H), 2.12 (s, 3H), 1.48 (t, $J = 7.1$ Hz, 3H).

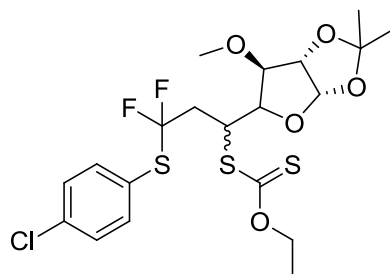
$^{13}\text{C NMR}$ (δ , ppm) 211.6, 170.4, 137.5 (2C), 136.8, 129.4 (2C), 128.3 (t, $J = 281$ Hz), 124.6 (CDCl₃, 100 MHz) (t, $J = 2$ Hz), 70.5, 64.7, 43.9, 39.6 (t, $J = 24$ Hz), 20.7, 13.8.

IR (σ , cm⁻¹, CCl₄) 2989, 1752, 1477, 1229, 1054

HRMS (EI) Calcd for C₁₅H₁₇ClF₂O₃S₃: 413.9996 Found: 414.0004

(±) ethyl ({1-[(3aR,5S,6R,6aR)-6-methoxy-2,2-dimethyl-tetrahydro-2H-furo[2,3-d][1,3]dioxol-5-yl]-3-[(4-chlorophenyl)sulfanyl]-3,3-difluoropropyl}sulfanyl)methanethioate

III-15j



$C_{20}H_{25}ClF_2O_5S_3$
 $M = 515.05 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-A, the reaction was carried out using (±)-(3aR,5R,6S,6aR)-5-ethenyl-6-methoxy-2,2-dimethyl-tetrahydro-2H-furo[2,3-d][1,3]dioxole (100 mg, 0.5 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 90:10) to afford the corresponding xanthate adduct **III-15j** (200 mg, 78%) as a 45:55 mixture of diastereoisomers and as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.58 (d, $J = 8.4$ Hz, 2H), 7.42 – 7.36 (m, 2H), 5.97 (d, $J = 3.8$ Hz, 0.45H), 5.96 (d, $J = 4.0$ Hz, 0.55H), 4.75 – 4.56 (m, 3.90H), 4.54 (dd, $J = 8.3, 3.3$ Hz, 0.55H), 4.36 (td, $J = 8.5, 4.3$ Hz, 0.55H), 3.89 (d, $J = 3.3$ Hz, 0.45H), 3.86 (d, $J = 3.3$ Hz, 0.55H), 3.43 (s, 1.65H), 3.41 (s, 1.35H), 2.98 – 2.67 (m, 1.55H), 2.62 – 2.47 (m, 0.45H), 1.54 (s, 1.35H), 1.53 (s, 1.65H), 1.47 (t, $J = 7.1$ Hz, 1.35H), 1.48 (t, $J = 7.1$ Hz, 1.65H), 1.37 (bs, 3H).
 (CDCl₃, 400 MHz)

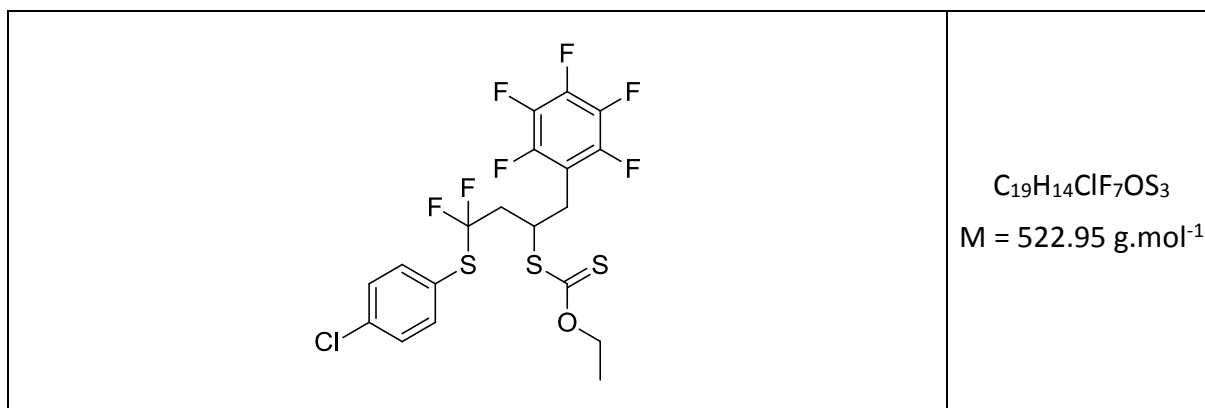
$^{13}\text{C NMR}$ (δ , ppm) Major : 212.3, 137.5 (2C), 136.5, 129.3 (2C), 128.7 (t, $J = 280$ Hz), 125.1, 111.9, 105.2, 84.0, 81.3, 80.3, 70.1, 57.8, 43.0, 39.9 (t, $J = 34$ Hz), 26.9, 26.3, 13.8.
 Minor : 212.2, 137.6 (2C), 136.4, 129.2 (2C), 128.7 (t, $J = 280$ Hz), 125.2, 112.0, 105.5, 85.4, 81.1, 79.5, 70.4, 57.5, 43.0, 38.0 (t, $J = 24$ Hz), 27.0, 26.4, 13.8.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2992, 2935, 1477, 1220, 1026

HRMS (EI) Calcd for C₂₀H₂₅ClF₂O₅S₃ : 514.0521 Found: 514.0497

ethyl ({4-[(4-chlorophenyl)sulfanyl]-4,4-difluoro-1-(pentafluorophenyl)butan-2-yl}sulfanyl)methanethioate

III-15k



Following general procedure III-A, the reaction was carried out using 1,2,3,4,5-pentafluoro-6-(prop-2-en-1-yl)benzene (104 mg, 0.5 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether) to afford the corresponding xanthate adduct **III-15k** (222 mg, 85%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.60 (d, $J = 8.4$ Hz, 2H), 7.42 (d, $J = 8.4$ Hz, 2H), 4.85 – 4.52 (m, 2H), 4.32 (ddt, $J = 10.5, 8.0, 5.3$ Hz, 1H), 3.38 (dd, $J = 14.4, 5.2$ Hz, 1H), 3.09 (dd, $J = 14.3, 10.6$ Hz, 1H), 2.83 (dddd, $J = 17.5, 15.4, 14.1, 5.2$ Hz, 1H), 2.57 (dddd, $J = 17.5, 15.4, 10.0, 8.0$ Hz, 1H), 1.46 (t, $J = 7.1$ Hz, 3H).
 (CDCl₃, 400 MHz)

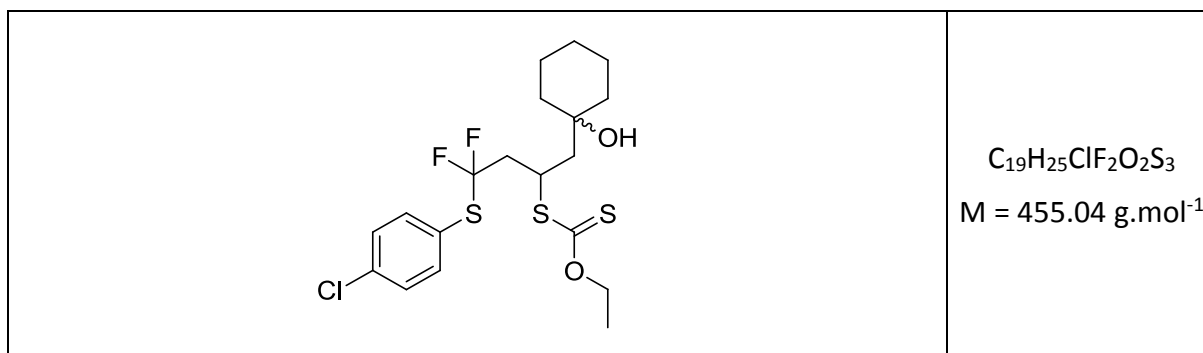
$^{13}\text{C NMR}$ (δ , ppm) 211.1, 137.5 (2C), 136.9, 129.5 (2C), 128.4 (t, $J = 281$ Hz), 124.6 (t, $J = 2$ Hz), 111.5-111.0 (m, 1C), 70.4, 44.5, 43.3 (t, $J = 24$ Hz), 26.6, 13.6
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2989, 1521, 1506, 1228, 1050

HRMS (EI) Calcd for C₁₉H₁₄ClF₇OS₃: 521.9784 Found: 521.9801

S-4-(4-chlorophenylthio)-4,4-difluoro-1-(1-hydroxycyclohexyl)butan-2-yl O-ethyl carbonodithioate

III-15I



Following general procedure III-A, the reaction was carried out using 1-allylcyclohexanol (70 mg, 0.5 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 90:10) to afford the corresponding xanthate adduct **III-15I** (200 mg, 88%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.60 – 7.56 (m, 2H), 7.43 – 7.38 (m, 2H), 4.70 (q, $J = 7.1$ Hz, 2H), 4.29 – 4.22 (m, 1H), 2.88 – 2.63 (m, 2H), 2.08 (dd, $J = 15.3, 4.9$ Hz, 1H), 1.91 (dd, $J = 15.3, 8.2$ Hz, 1H), 1.72 – 1.50 (m, 10H), 1.48 (t, $J = 7.1$ Hz, 3H).

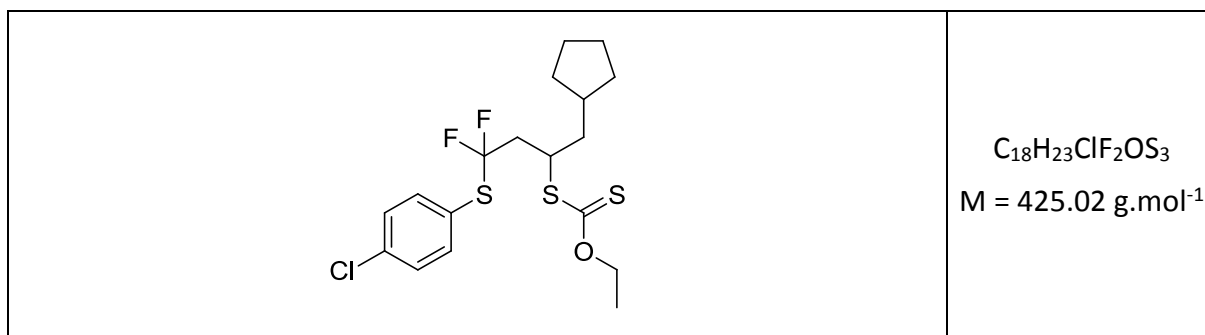
$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 212.5, 137.5 (2C), 136.6, 129.4 (2C), 128.7 (t, $J = 280$ Hz), 124.9 (t, $J = 2$ Hz), 71.5, 70.1, 45.1, 44.4 (t, $J = 22$ Hz), 40.8, 38.2, 37.5, 25.6, 22.1 (2C), 13.8.

IR (σ , cm⁻¹, CCl₄) 2936, 1477, 1221, 1051

HRMS (EI) Calcd for C₁₉H₂₅ClF₂O₂S₃ : 454.0673 Found: 454.0678

**S-4-(4-chlorophenylthio)-1-cyclopentyl-4,4-difluorobutan-2-yl O-ethyl
carbonodithioate**

III-15m



Following general procedure III-A, the reaction was carried out using allylcyclopentane (60 mg, 0.54 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 90:10) to afford the corresponding xanthate adduct **III-15m** (228 mg, 99%) as a colourless oil.

¹H NMR (δ, ppm) 7.61 – 7.56 (m, 2H), 7.43 – 7.38 (m, 2H), 4.70 (q, *J* = 7.1 Hz, 2H), 4.10 – 4.01 (m, 1H), 2.81 – 2.66 (m, 1H), 2.61 – 2.45 (m, 1H), 2.11 – 1.97 (m, 1H), 1.92 – 1.73 (m, 4H), 1.72 – 1.53 (m, 4H), 1.48 (t, *J* = 7.1 Hz, 3H), 1.26 – 1.13 (m, 2H).
(CDCl₃, 400 MHz)

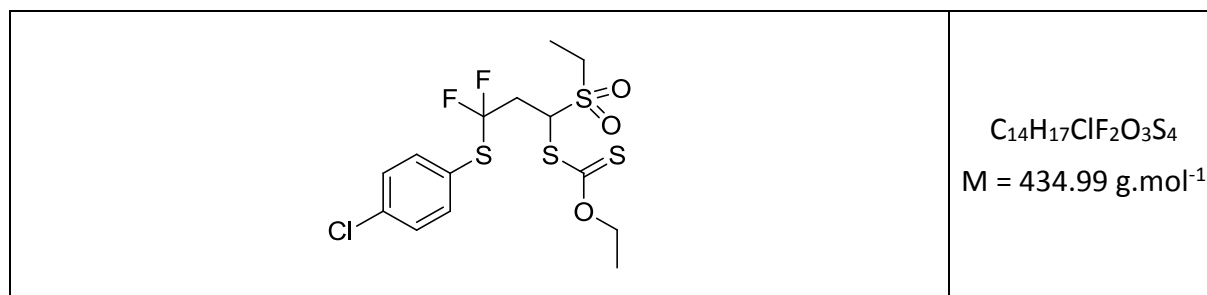
¹³C NMR (δ, ppm) 213.1, 137.5 (2C), 136.6, 129.4 (2C), 128.7 (t, *J* = 281 Hz), 125.0 (t, *J* = 2 Hz), 70.0, 45.0, 44.0 (t, *J* = 23 Hz), 39.5, 37.7, 32.8, 32.3, 25.1, 25.0, 13.8.
(CDCl₃, 100 MHz)

IR (σ, cm⁻¹, CCl₄) 2954, 1477, 1222, 1052

HRMS (EI) Calcd for C₁₈H₂₃ClF₂OS₃: 424.0568 Found: 424.0576

**SS-3-(4-chlorophenylthio)-1-(ethylsulfonyl)-3,3-difluoropropyl O-ethyl
carbonodithioate**

III-15n



Following general procedure III-A, the reaction was carried out using methylsulfonylene (68 mg, 0.56 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 70:30) to afford the corresponding xanthate adduct **III-15n** (217 mg, 89%) as a colourless oil.

^1H NMR (δ , ppm) 7.61 – 7.55 (m, 2H), 7.44 – 7.39 (m, 2H), 5.59 (dd, $J = 10.4, 1.7$ Hz, 1H), 4.76 (q, $J = 7.1$ Hz, 2H), 3.42 – 3.15 (m, 3H), 2.75 (tt, $J = 15.3, 10.4$ Hz, 1H), 1.53 – 1.46 (m, 6H).
(CDCl_3 , 400 MHz)

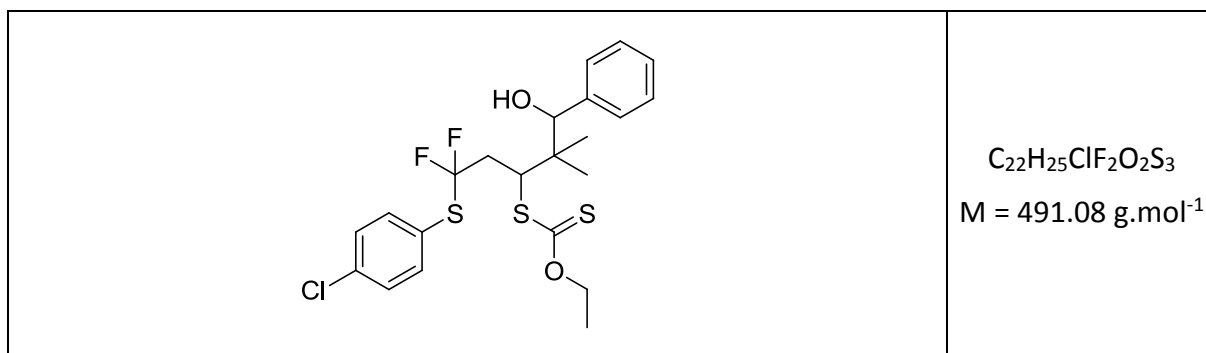
^{13}C NMR (δ , ppm) 208.8, 137.7 (2C), 137.0, 129.6 (2C), 127.6 (t, $J = 281$ Hz), 124.1 (t, $J = 2$ Hz), 72.2, 64.3, 44.4, 35.4 (t, $J = 25$ Hz), 13.8, 6.1.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1477, 1327, 1242, 1140, 1044

HRMS (EI) Calcd for $C_{14}H_{17}ClF_2O_3S_4$: 433.9717 Found: 433.9730

S-1-(4-chlorophenylthio)-1,1-difluoro-5-hydroxy-4,4-dimethyl-5-phenylpentan-3-yl O-ethyl carbonodithioate

III-15o



Following general procedure III-A, the reaction was carried out using (352 mg, 2 mmol), xanthate **III-1** (942 mg, 3 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 90:10) to afford the corresponding xanthate adduct **III-15o** (850 mg, 87%) as a 60:40 mixture of diastereoisomers and as a yellow oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.61 – 7.56 (m, 2H), 7.43 – 7.32 (m, 7H), 4.91 (d, $J = 3.2$ Hz, 0.6H), 4.81 (s, 0.4H), 4.77 – 4.69 (m, 2H), 4.60 (d, $J = 9.2$ Hz, 0.6H), 4.52 (d, $J = 9.5$ Hz, 0.4H), 3.15 – 3.01 (m, 0.4H), 2.90 – 2.76 (m, 0.6H), 2.75 – 2.72 (m, 0.6H), 2.71 – 2.48 (m, 1H), 1.95 – 1.91 (m, 0.4H), 1.49 (t, $J = 7.1$ Hz, 1.8H), 1.46 (t, $J = 7.1$ Hz, 1.2H), 1.07 (s, 6H).

$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) Major : 214.9, 140.7, 137.5 (2C), 136.5, 129.3 (2C), 129.0 (t, $J = 281$ Hz), 128.0 (2C), 127.7 (2C), 127.6, 125.1, 77.6, 70.8, 52.9, 43.1, 40.6 (t, $J = 22$ Hz), 21.8, 19.3, 13.8.

Minor : 212.9, 141.5, 137.5 (2C), 136.4, 129.3 (2C), 129.2 (t, $J = 281$ Hz), 127.9 (2C), 127.8 (2C), 127.6, 125.4, 78.3, 70.2, 52.9, 43.3, 41.1 (t, $J = 22$ Hz), 23.2, 20.0, 13.7.

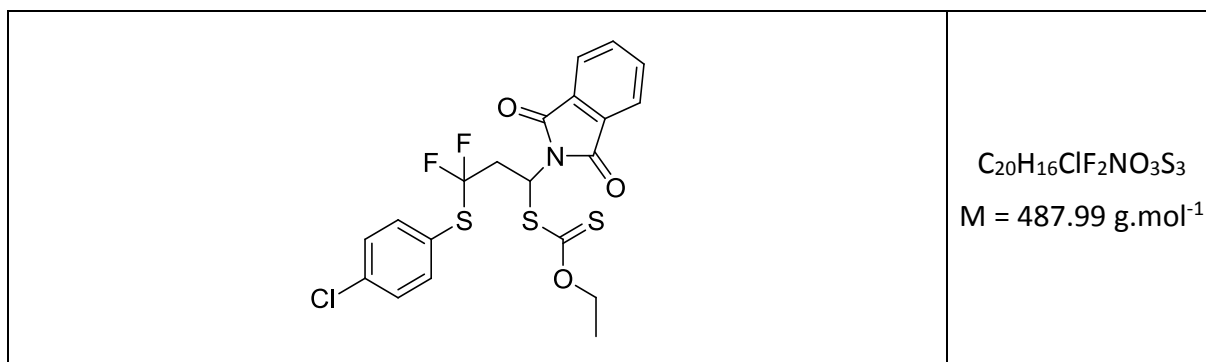
HRMS (EI)

Calcd for $C_{22}H_{25}ClF_2O_2S_3$: 490.0673

Found: 490.0678

S-3-(4-chlorophenylthio)-1-(1,3-dioxisoindolin-2-yl)-3,3-difluoropropyl O-ethyl carbonodithioate

III-15p



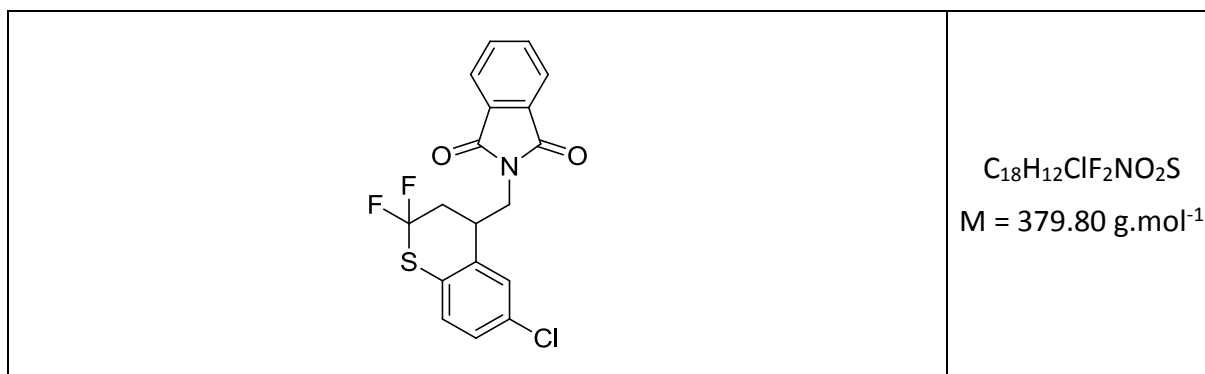
Following general procedure III-A, the reaction was carried out using *N*-vinylphthalimide (157 mg, 0.9 mmol), xanthate **III-1** (628 mg, 2 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20) to afford the corresponding xanthate adduct **III-15p** (300 mg, 68%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.95 – 7.89 (m, 2H), 7.82 – 7.77 (m, 2H), 7.54 – 7.49 (m, 2H), 7.38 – 7.33 (m, 2H), 6.70 (dd, $J = 11.4, 3.4$ Hz, 1H), 4.75 – 4.67 (m, 2H), 3.63 – 3.48 (m, 1H), 2.92 – 2.79 (m, 1H), 1.48 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 208.3, 165.3 (2C), 136.5 (2C), 135.8, 133.5 (2C), 130.5 (2C), 128.3 (2C), 126.3 (t, $J = 281$ Hz), 123.1 (t, $J = 2$ Hz), 122.75 (2C), 69.7, 50.8 (t, $J = 3$ Hz), 39.8 (t, $J = 24$ Hz), 12.7.

2-[(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methyl]-2,3-dihydro-1H-phthalimide

III-16a



Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15a** (224 mg, 0.45 mmol). The residue was purified by silica gel column chromatography (petroleum ether/DCM 50:50) to afford the corresponding thiochroman **III-16a** (86 mg, 50%) as a white amorphous solid.

$^1\text{H NMR}$ (δ , ppm) 7.93 – 7.87 (m, 2H), 7.82 – 7.77 (m, 2H), 7.24 (dd, $J = 8.3, 2.2$ Hz, 1H), 7.19 – 7.15 (m, 2H), 4.27 (ddd, $J = 13.7, 8.1, 2.4$ Hz, 1H), 3.99 (dd, $J = 13.7, 7.5$ Hz, 1H), 3.67 – 3.57 (m, 1H), 2.71 – 2.48 (m, 2H).
 (CDCl_3 , 400 MHz)

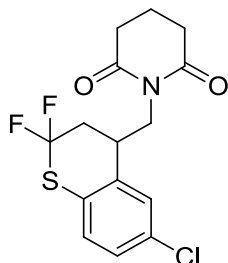
$^{13}\text{C NMR}$ (δ , ppm) 168.1 (2C), 135.2, 134.3 (2C), 132.1, 131.7 (2C), 129.6 (t, $J = 270$ Hz), 128.9 (t, $J = 2.2$ Hz), 128.5 – 128.4 (m, 2C), 128.2, 123.6 (2C), 39.6 (d, $J = 3.7$ Hz), 37.8 (t, $J = 23.6$ Hz), 37.3 (dd, $J = 5.3, 1.6$ Hz).
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2930, 1776, 1721, 1392, 1055

HRMS (EI) Calcd for $C_{18}H_{12}ClF_2NO_2S$: 379.0245 Found: 379.0244

1-[(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methyl]piperidine-2,6-dione

III-16b



$C_{15}H_{14}ClF_2NO_2S$
 $M = 345.79 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15b** (115 mg, 0.25 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 75:25) to afford the corresponding thiochroman **III-16b** (53 mg, 61%) as a white amorphous solid.

$^1\text{H NMR}$ (δ , ppm) 7.23 (dd, $J = 8.4, 2.2 \text{ Hz}$, 1H), 7.14 (d, $J = 8.5 \text{ Hz}$, 1H), 7.06 (d, $J = 2.2 \text{ Hz}$, 1H), 4.53 (ddd, $J = 12.2, 9.4, 2.6 \text{ Hz}$, 1H), 3.95 (dd, $J = 13.0, 6.5 \text{ Hz}$, 1H), 3.47 – 3.38 (m, 1H), 2.76 – 2.40 (m, 6H), 2.04 – 1.94 (m, 2H).
 (CDCl_3 , 400 MHz)

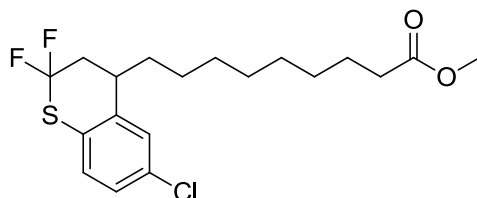
$^{13}\text{C NMR}$ (δ , ppm) 172.4 (2C), 135.5, 131.5, 129.9 (dd, $J = 268, 269 \text{ Hz}$), 129.2 (t, $J = 2 \text{ Hz}$), 128.3, 128.2 (dd, $J = 4, 2 \text{ Hz}$), 128.0, 40.0 (d, $J = 4 \text{ Hz}$), 37.8 (dd, $J = 24, 23 \text{ Hz}$), 36.6 (d, $J = 6 \text{ Hz}$), 32.8 (2C), 17.0
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2964, 1732, 1686, 1358, 1167

HRMS (EI) Calcd for $C_{15}H_{14}ClF_2NO_2S$: 345.0402 Found: 345.0410

methyl 9-(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)nonanoate

III-16c



$C_{19}H_{25}ClF_2O_2S$
 $M = 390,92 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15c** (338 mg, 0.66 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 95:5) to afford the corresponding thiochroman **III-16c** (80 mg, 31%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.26 (d, $J = 2.3 \text{ Hz}$, 1H), 7.23 (d, $J = 2.2 \text{ Hz}$, 1H), 7.14 (d, $J = 8.4 \text{ Hz}$, 1H),
 (CDCl₃, 400 MHz) 3.71 (s, 3H), 3.03 – 2.93 (m, 1H), 2.60 – 2.45 (m, 1H), 2.44 – 2.31 (m, 3H), 1.85 (d, $J = 11.2 \text{ Hz}$, 1H), 1.80 – 1.62 (m, 3H), 1.53 – 1.45 (m, 1H), 1.43 – 1.31 (m, 9H).

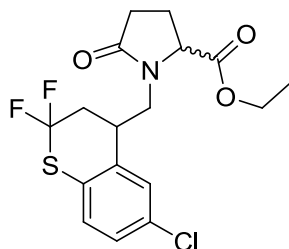
$^{13}\text{C NMR}$ (δ , ppm) 174.3, 139.6, 131.9, 130.8 (t, $J = 269 \text{ Hz}$), 128.6 (t, $J = 2 \text{ Hz}$), 128.2 (t, $J = 3 \text{ Hz}$),
 (CDCl₃, 100 MHz) 127.9, 127.3, 51.5, 39.2 (t, $J = 23 \text{ Hz}$), 38.2 (dd, $J = 4, 2 \text{ Hz}$), 34.1, 31.2, 29.5, 29.3, 29.2, 29.1, 27.0, 24.9.

IR (σ , cm⁻¹, CCl₄) 2931, 2857, 1741, 1464, 1199, 1173, 1051

HRMS (EI) Calcd for C₁₉H₂₅ClF₂O₂S: 390.1232 Found: 390.1235

ethyl 1-[(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methyl]-5-oxopyrrolidine-2-carboxylate

III-16d



$C_{17}H_{18}ClF_2NO_3S$
 $M = 389,84 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15d** (220 mg, 0.43 mmol). The residue was purified by silica gel column chromatography (DCM) to afford the corresponding thiochroman **III-16d** (62 mg, 37%) as a 1:1 mixture of diastereoisomers and as an amorphous white solid.

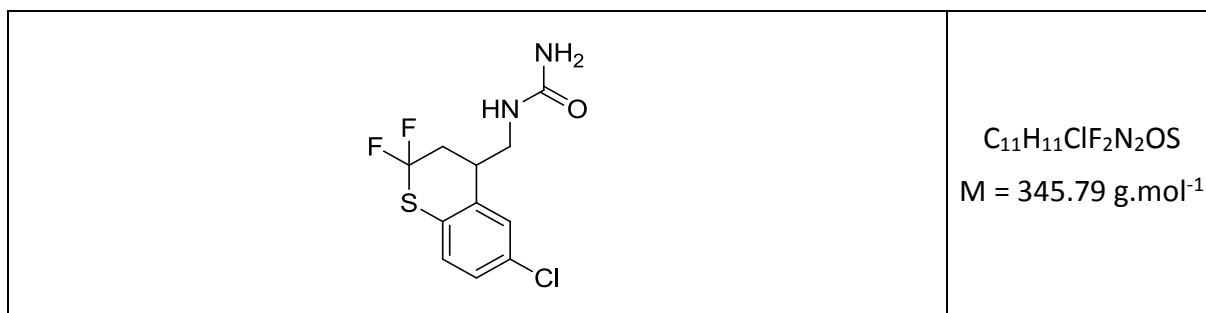
$^1\text{H NMR}$ (δ , ppm) 7.38 (d, $J = 2.3$ Hz, 1H), 7.28 (dd, $J = 8.4, 2.3$ Hz, 1H), 7.24 (dd, $J = 8.4, 2.2$ Hz, 1H), 7.19 (d, $J = 2.3$ Hz, 1H), 7.16 (d, $J = 8.4$ Hz, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 4.30 – 4.16 (m, 5H), 4.01 – 3.92 (m, 2H), 3.73 – 3.64 (m, 1H), 3.55 (dd, $J = 9.1, 2.3$ Hz, 1H), 3.53 – 3.46 (m, 1H), 3.39 (ddd, $J = 13.9, 9.4, 2.7$ Hz, 1H), 3.29 (ddd, $J = 14.3, 9.6, 1.8$ Hz, 1H), 2.64 – 2.35 (m, 9H), 2.31 – 2.06 (m, 3H), 1.31 (t, $J = 7.1$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H).
 (CDCl₃, 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 176.4, 176.0, 171.7, 171.5, 135.9, 135.0, 132.2, 132.0, 130.0 (t, $J = 269$ Hz), 129.6 (t, $J = 269$ Hz), 128.9, 128.7 (t, $J = 2$ Hz), 128.6, 128.4 (t, $J = 2$ Hz), 128.2 (2C), 128.1, 128.0 (t, $J = 3$ Hz), 61.8 (2C), 61.3 (d, $J = 3$ Hz), 61.0, 45.1 (d, $J = 3$ Hz), 43.6 (d, $J = 4$ Hz), 37.7 (t, $J = 23$ Hz), 36.5 (d, $J = 6$ Hz), 36.4, (t, $J = 23$ Hz) 36.2 (d, $J = 6$ Hz), 29.4, 29.3, 23.4, 23.3, 14.2, 14.1.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2931, 1747, 1705, 1199, 1181

HRMS (EI) Calcd for C₁₇H₁₈ClF₂NO₃S: 389.0664 Found: 389.0663

[(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methyl]urea	III-16e
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Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15e** (140 mg, 0.33 mmol), ACS (84 mg, 0.36 mmol). The residue was purified by silica gel column chromatography (ethyl acetate) to afford the corresponding thiochroman **III-16e** (45 mg, 47%) as an amorphous white solid.

¹H NMR (δ, ppm) 7.34 (d, *J* = 2.3 Hz, 1H), 7.25 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 5.06 (bs, 1H), 4.63 (bs, 2H), 3.69 – 3.58 (m, 1H), 3.47 – 3.36 (m, 2H), 2.70 (tdd, *J* = 15.2, 10.2, 4.9 Hz, 1H), 2.49 (dddd, *J* = 25.8, 14.7, 8.8, 3.9 Hz, 1H).
(CDCl₃, 400 MHz)

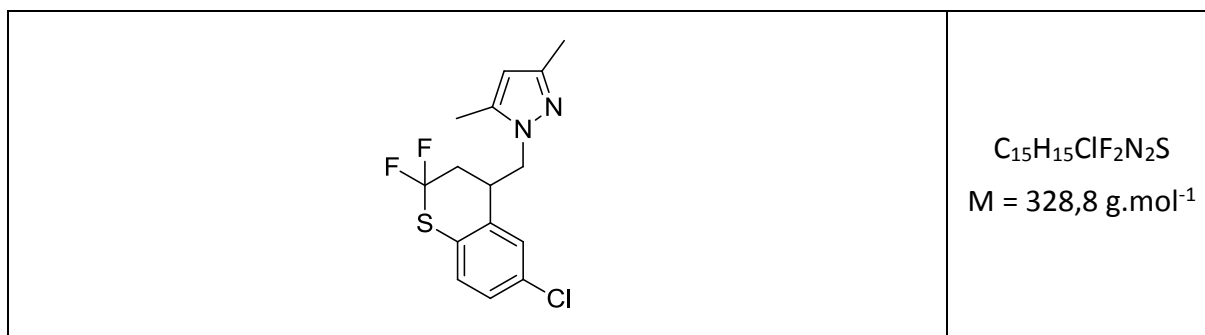
¹³C NMR (δ, ppm) 158.4, 135.5, 132.0, 130.1 (dd, *J* = 268, 269 Hz), 129.2, 128.5 (t, *J* = 2 Hz), 128.0, 127.8 (t, *J* = 3.0 Hz), 41.7 (d, *J* = 3.6 Hz), 38.5 (d, *J* = 6.4 Hz), 36.4 (t, *J* = 22.4 Hz).
(CDCl₃, 100 MHz)

IR (σ, cm⁻¹, CCl₄) 2928, 2359, 1702, 1515

HRMS (EI) Calcd for C₁₁H₁₁ClF₂N₂OS : 292.0249 Found: 292.0257

1-[(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methyl]-3,5-dimethyl-1H-pyrazole

III-16f



Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15f** (150 mg, 0.33 mmol), ACS (84 mg, 0.36 mmol). The residue was purified by silica gel column chromatography (DCM/ethyl acetate 95:5) to afford the corresponding thiochroman **III-16f** (55 mg, 51%) as a yellow oil.

^1H NMR (δ , ppm) 7.23 (dd, $J = 8.4, 2.3$ Hz, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 6.60 (d, $J = 2.3$ Hz, 1H), 5.76 (s, 1H), 4.31 – 4.17 (m, 2H), 3.91 – 3.82 (m, 1H), 2.71 (tdd, $J = 14.7, 7.2, 3.8$ Hz, 1H), 2.53 (dddd, $J = 29.7, 14.8, 7.3, 5.1$ Hz, 1H), 2.31 (s, 3H), 1.77 (s, 3H).
(CDCl_3 , 400 MHz)

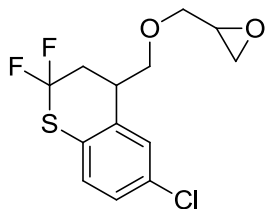
^{13}C NMR (δ , ppm) 148.5, 140.3, 134.2, 131.8, 129.8, 129.5 (t, $J = 269$ Hz), 128.2, 128.0 (d, $J = 2.9$ Hz), 127.4 (dd, $J = 3.6, 2.2$ Hz), 104.8, 49.5 (d, $J = 5.4$ Hz), 39.76 (d, $J = 7.6$ Hz), 36.72 (t, $J = 23$ Hz), 13.6, 10.3.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2929, 1467, 1075, 1060

HRMS (EI) Calcd for $C_{15}H_{15}ClF_2N_2S$: 328.0613 Found: 328.0612

2-[[[6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methoxy]methyl]oxirane

III-16g



$C_{13}H_{13}ClF_2O_2S$
 $M = 306,76 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15g** (125 mg, 0.3 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 90:10) to afford the corresponding thiocroman **III-16g** (53 mg, 57%) as a 1:1 mixture of diastereoisomers and as a colourless oil.

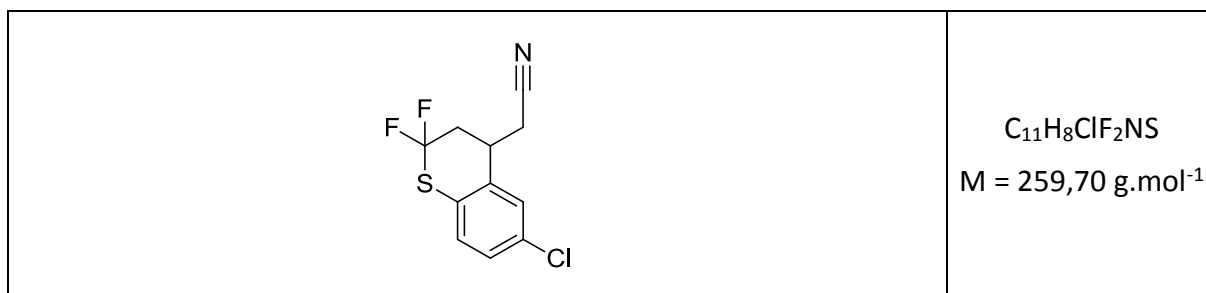
$^1\text{H NMR}$ (δ , ppm) 7.6 (t, $J = 2.7 \text{ Hz}$, 1H), 7.2 (dd, $J = 8.4, 2.2 \text{ Hz}$, 1H), 7.12 (d, $J = 8.4 \text{ Hz}$, 1H), 3.92 – 3.78 (m, 3H), 3.51 – 3.43 (m, 1H), 3.38 – 3.29 (m, 1H), 3.22 (dq, $J = 5.7, 3.0 \text{ Hz}$, 1H), 2.87 (td, $J = 4.6, 1.5 \text{ Hz}$, 1H), 2.68 – 2.54 (m, 3H).
 (CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 135.5, 135.4, 131.9 (2C), 129.9 (t, $J = 269 \text{ Hz}$, 2C), 129.0 (2C), 128.6 (2C), 127.9 (2C), 127.8 (2C), 72.0, 71.8, 71.3 (2C), 50.76 (d, $J = 3.7 \text{ Hz}$, 2C), 44.10 (d, $J = 7.0 \text{ Hz}$, 2C), 38.70 – 38.48 (m, 2C), 37.0 (t, $J = 23.1 \text{ Hz}$), 36.9 (t, $J = 23.1 \text{ Hz}$).
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2926, 1874, 1467, 1361, 1253, 1199, 1161 1100

HRMS (EI) Calcd for $C_{13}H_{13}ClF_2O_2S$: 306.0293 Found: 306.0287

2-(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)acetonitrile III-16h



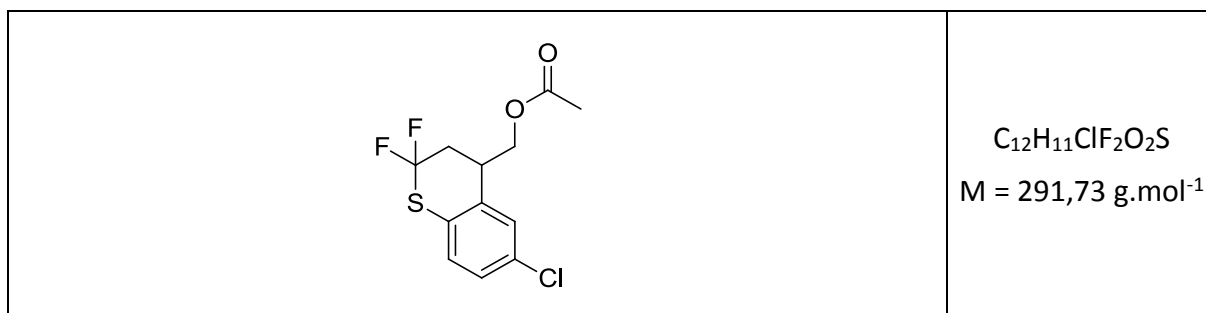
Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15h** (120 mg, 0.31 mmol). The residue was purified by silica gel column chromatography (petroleum ether/DCM 60:40) to afford the corresponding thiochroman **III-16h** (35 mg, 44%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.35 (d, $J = 2.2$ Hz, 1H), 7.34 – 7.30 (m, 1H), 7.18 (d, $J = 8.3$ Hz, 1H), 3.53 – 3.44 (m, 1H), 2.92 – 2.84 (m, 2H), 2.83 – 2.57 (m, 2H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 134.3, 132.6, 129.1 (t, $J = 269$ Hz), 128.9, 128.4 (m, 2C), 128.3 (t, $J = 2$ Hz), 117.2, 38.5 (t, $J = 24$ Hz), 35.4 (d, $J = 6$ Hz), 21.0 (d, $J = 4$ Hz).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2960, 2930, 1473, 1431, 1366, 1202, 1166, 1080, 1025

HRMS (EI) Calcd for $C_{11}H_8ClF_2NS$: 259.0034 Found: 259.0037

(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methyl acetate III-16i

Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15i** (200 mg, 0.48 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 95:5) to afford the corresponding thiochroman **III-16i** (66 mg, 47%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.31 (d, $J = 2.3$ Hz, 1H), 7.27 (dd, $J = 8.4, 2.3$ Hz, 1H), 7.15 (d, $J = 8.4$ Hz, 1H), 4.48 (ddd, $J = 11.2, 6.6, 1.8$ Hz, 1H), 4.37 (ddd, $J = 11.4, 7.5, 1.3$ Hz, 1H), 3.45 – 3.36 (m, 1H), 2.66 – 2.54 (m, 2H), 2.15 (s, 3H).
(CDCl_3 , 400 MHz)

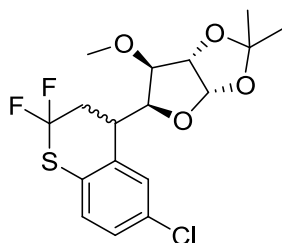
$^{13}\text{C NMR}$ (δ , ppm) 170.7, 134.5, 132.1, 129.6 (dd, $J = 270, 269$ Hz), 129.0 (dd, $J = 1, 2$ Hz), 128.5, 128.2, 128.1 (t, $J = 3.1$ Hz), 63.9 (d, $J = 3.5$ Hz), 37.5 (dd, $J = 4.9, 2.3$ Hz), 37.0 (t, $J = 23.5$ Hz), 20.8.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2930, 1751, 1470, 1431, 1366, 1230, 1037

HRMS (EI) Calcd for $C_{12}H_{11}ClF_2O_2S$: 292.0136 Found: 292.0141

(±) (3a*S*,5*S*,6*R*,6a*S*)-5-(6-chloro-2,2-difluoro-3,4-dihydro-2*H*-1-benzothiopyran-4-yl)-6-methoxy-2,2-dimethyl-tetrahydro-2*H*-furo[2,3-*d*][1,3]dioxole

III-16j



C₁₇H₁₉ClF₂O₄S
M = 391,73 g.mol⁻¹

Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15j** (180 mg, 0.35 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 95:5) to afford the corresponding thiochroman **III-16j** (64 mg, 46%) as a 1:1 mixture of diastereoisomers and as an amorphous white solid.

¹H NMR (δ, ppm) 7.43 (d, *J* = 2.3 Hz, 0.5H), 7.37 (d, *J* = 2.3 Hz, 0.5H), 7.27 (dd, *J* = 8.5, 2.3 Hz, 0.5H), 7.23 (dd, *J* = 8.4, 2.3 Hz, 0.5H), 7.16 – 7.10 (m, 1H), 5.98 (s, 0.5H), 5.97 (s, 0.5H), 4.69 (d, *J* = 4.0 Hz, 0.5H), 4.63 (d, *J* = 3.8 Hz, 0.5H), 4.54 (dt, *J* = 10.6, 2.4 Hz, 1H), 3.87 (d, *J* = 3.1 Hz, 0.5H), 3.65 – 3.58 (m, 0.5H), 3.53 (s, 1.5H), 3.49 (s, 1.5H), 3.45 – 3.39 (m, 0.5H), 3.37 (d, *J* = 2.8 Hz, 0.5H), 3.17 – 3.05 (m, 0.5H), 2.64 – 2.33 (m, 1.5H), 1.50 (s, 1.5H), 1.49 (s, 1.5H), 1.36 (s, 3H).

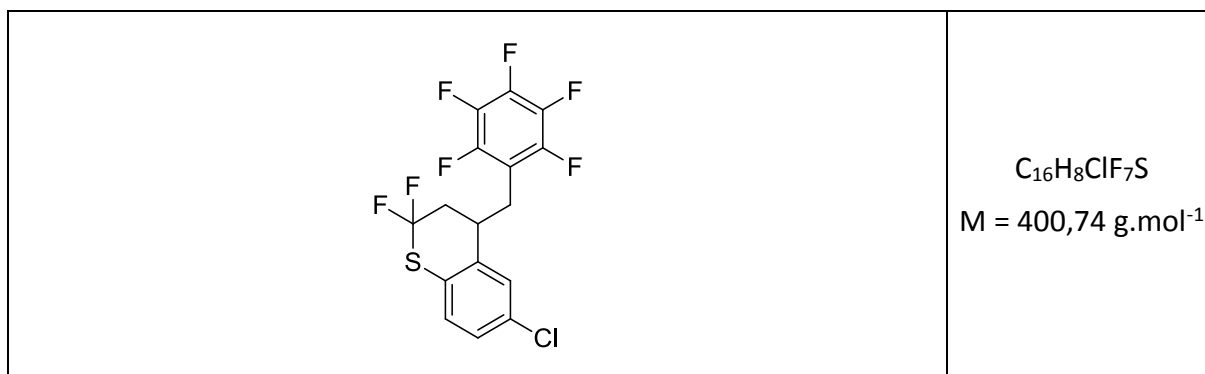
¹³C NMR (δ, ppm) 136.4, 134.4, 131.9, 131.7, 130.8, 130.6 (dd, *J* = 266, 269 Hz), 130.24 (t, *J* = 269 Hz), 130.1, 129.5, 128.3, 128.2, 128.1 (dd, *J* = 4.2, 1.9 Hz), 127.9, 127.77 (dd, *J* = 3.9, 2.3 Hz), 112.2, 111.6, 104.9, 104.8, 83.7 (d, *J* = 1.7 Hz), 83.1, 81.1, 80.8, 77.9 (d, *J* = 2.7 Hz), 76.9 (d, *J* = 2.8 Hz), 57.5, 56.9, 38.1 (d, *J* = 6.6 Hz), 37.3 (d, *J* = 8.1 Hz), 37.15 (t, *J* = 23 Hz), 35.9 (dd, *J* = 23.8, 22.4 Hz), 26.8, 26.7, 26.6, 26.2.

IR (σ, cm⁻¹, CCl₄) 2992, 2935, 1477, 1220, 1165, 1111, 1082, 1026

HRMS (EI) Calcd for C₁₇H₁₉ClF₂O₄S : 392.0661 Found: 392.0655

6-chloro-2,2-difluoro-4-[(pentafluorophenyl)methyl]-3,4-dihydro-2H-1-Benzothiopyran

III-16k



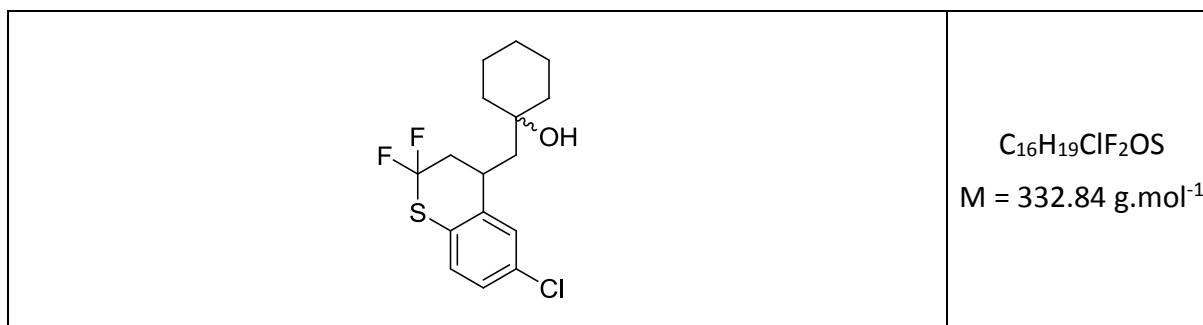
Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15k** (200 mg, 0.38 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 99.5:0.5) to afford the corresponding thiocroman **III-16k** (58 mg, 38 %) as a colourless oil.

1H NMR (δ , ppm) 7.28 (dd, $J = 8.4, 2.1$ Hz, 1H), 7.20 (d, $J = 8.4$ Hz, 1H), 7.01 (d, $J = 2.2$ Hz, 1H), 3.37 (ddt, $J = 25.7, 14.2, 4.5$ Hz, 2H), 3.09 (dd, $J = 13.2, 7.4$ Hz, 1H), 2.52 (dtdd, $J = 29.8, 14.6, 11.3, 5.1$ Hz, 2H).
 (CDCl₃, 400 MHz)

^{13}C NMR (δ , ppm) 136.6, 132.1, 129.8 (t, $J = 269$ Hz), 128.5-128.4 (m, 2C), 128.2, 128.0, 39.1 (t, $J = 23$ Hz), 38.2 (d, $J = 4$ Hz), 25.0
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2928, 2856, 1521, 1505

HRMS (EI) Calcd for C₁₆H₈ClF₇S : 399.9923 Found: 399.9928



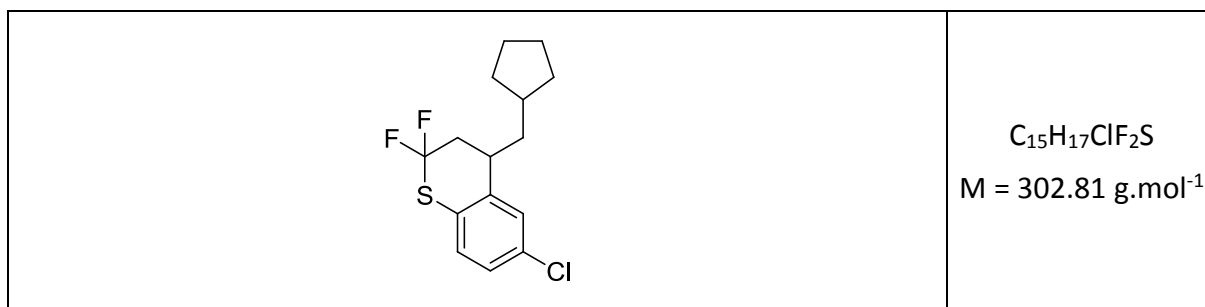
Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15I** (190 mg, 0.42 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 100:0 to 90:10) to afford the corresponding thiochroman **III-16I** (67 mg, 45%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.35 (d, $J = 2.1$ Hz, 1H), 7.21 (dd, $J = 8.4, 2.2$ Hz, 1H), 7.14 (d, $J = 8.3$ Hz, 1H), 3.43 – 3.34 (m, 1H), 2.82 – 2.55 (m, 2H), 2.04 – 1.94 (m, 2H), 1.75 – 1.43 (m, 9H), 1.41 – 1.32 (m, 2H).

$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 141.3, 132.2, 131.4 (t, $J = 239$ Hz), 128.6 – 128.5 (m, 2C), 128.1, 127.2, 71.7, 42.6, 40.7 (t, $J = 22$ Hz), 39.4, 37.0, 33.7 (dd, $J = 4, 2$ Hz), 25.7, 22.2 (2C).

6-chloro-4-(cyclopentylmethyl)-2,2-difluorothiochroman

III-16m



Following general procedure III-B, the reaction was carried out using xanthate adduct **III-15m** (200 mg, 0.47 mmol). The residue was purified by silica gel column chromatography (pentane 100%) to afford the corresponding thiochroman **III-16m** (30 mg, 21%) as a colourless oil.

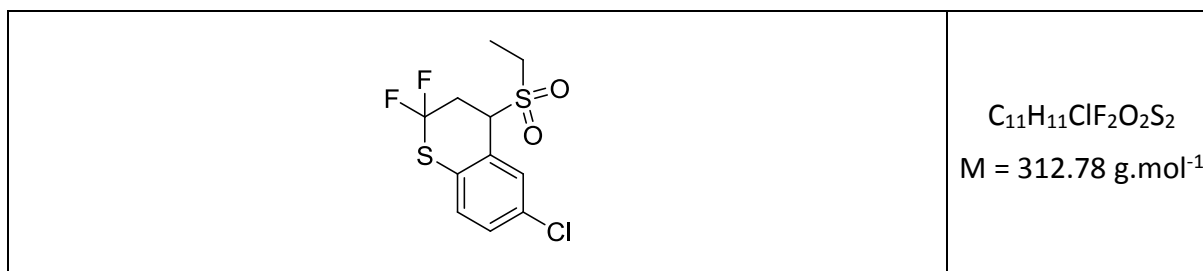
$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.27 (d, $J = 2.1$ Hz, 1H), 7.22 (dd, $J = 8.3, 2.2$ Hz, 1H), 7.15 (d, $J = 8.3$ Hz, 1H), 3.07 – 2.98 (m, 1H), 2.63 – 2.48 (m, 1H), 2.46 – 2.32 (m, 1H), 2.00 – 1.55 (m, 9H), 1.28 – 1.09 (m, 2H).

$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 140.1, 132.0, 131.0 (dd, $J = 252, 250$ Hz), 128.6, 128.3 (t, $J = 3$ Hz), 127.9, 127.3, 39.3 (t, $J = 22$ Hz), 37.6 (d, $J = 2$ Hz), 37.3 (dd, $J = 5, 2$ Hz), 37.2, 33.1, 32.3, 25.2, 25.1.

HRMS (EI) Calcd for C₁₅H₁₇ClF₂S : 302.0708 Found: 302.0700

6-chloro-4-(ethylsulfonyl)-2,2-difluorothiochroman

III-16n



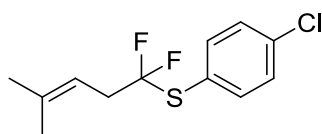
Following general procedure III-A, the reaction was carried out using xanthate adduct **III-15n** (200 mg, 0.46 mmol). The residue was purified by silica gel column chromatography (petroleum ether/EtOAc 90:10) to afford the corresponding thiochroman **III-16n** (25 mg, 17%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.79 (d, $J = 2.2$ Hz, 1H), 7.40 (dd, $J = 8.5, 2.2$ Hz, 1H), 7.21 (d, $J = 8.5$ Hz, 1H), 4.57 (dd, $J = 7.6, 4.7$ Hz, 1H), 3.51 – 3.38 (m, 1H), 3.12 – 3.02 (m, 1H), 3.01 – 2.89 (m, 1H), 2.86 – 2.76 (m, 1H), 1.35 (t, $J = 7.5$ Hz, 3H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 132.9, 131.9, 130.3, 129.6 (t, $J = 3$ Hz), 129.1 (dd, $J = 3, 2$ Hz), 126.9 (dd, $J = 273, 270.0$ Hz), 125.3, 63.9 (dd, $J = 5, 3$ Hz), 44.5 (d, $J = 4$ Hz), 35.9 (dd, $J = 28, 26$ Hz), 5.4.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4)

HRMS (EI) Calcd for $C_{11}H_{11}ClF_2O_2S_2$: 311.9857 Found: 311.9859

(4-chlorophenyl)(1,1-difluoro-4-methylpent-3-enyl)sulfane**III-17**

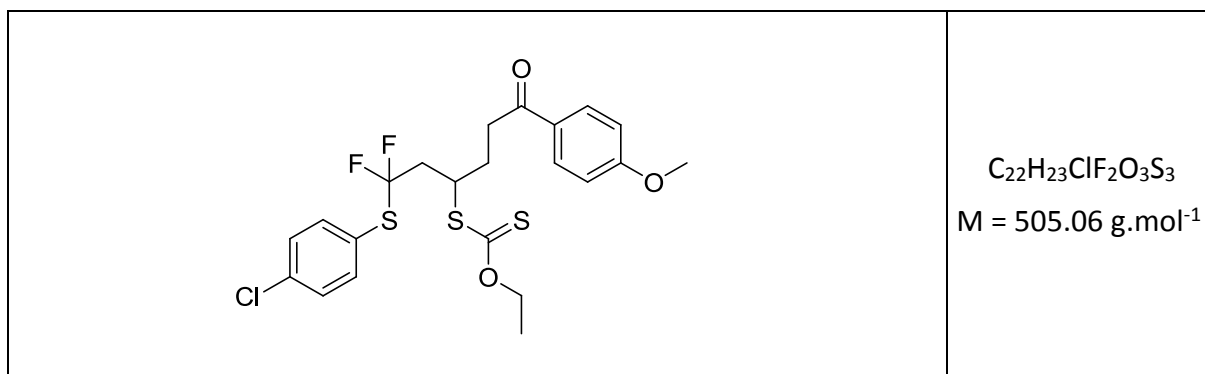
$C_{12}H_{13}ClF_2S$
 $M = 262.75 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-B, the reaction was carried out using **III-15o** (175 mg, 0.36 mmol). The residue was purified by silica gel column chromatography (petroleum ether 100%) to afford **III-17** (47 mg, 50%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.60 – 7.55 (m, 2H), 7.42 – 7.37 (m, 2H), 5.29 – 5.23 (m, 1H), 2.88 (td, J
 (CDCl₃, 400 MHz) = 14.4, 7.3 Hz, 2H), 1.83 (s, 3H), 1.69 (s, 3H).

**S-1-(4-chlorophenylthio)-1,1-difluoro-6-(4-methoxyphenyl)-6-oxohexan-3-yl
O-ethyl carbonodithioate**

III-21



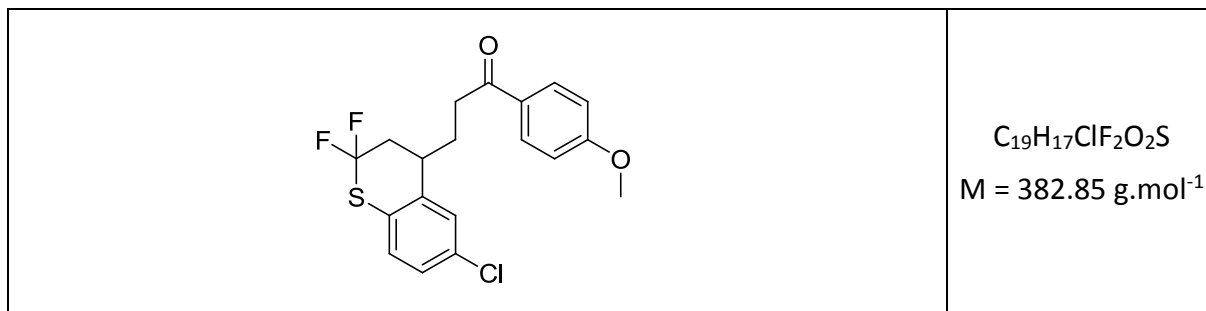
Following general procedure III-A, the reaction was carried out using 1-(3-methoxyphenyl)pent-4-en-1-one (570 mg, 3 mmol), xanthate **III-1** (1220 mg, 3.9 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 85:15) to afford the corresponding xanthate adduct **III-21** (1420 mg, 94%) as a pale yellow oil.

$^1\text{H NMR}$ (δ , ppm) 7.97 (d, $J = 8.8$ Hz, 2H), 7.59 (d, $J = 8.4$ Hz, 2H), 7.40 (d, $J = 8.4$ Hz, 2H), 6.97 (d, $J = 8.8$ Hz, 2H), 4.73 – 4.59 (m, 2H), 4.22 – 4.15 (m, 1H), 3.90 (s, 3H), 3.15 (t, $J = 7.4$ Hz, 2H), 2.85 – 2.70 (m, 1H), 2.65 – 2.53 (m, 1H), 2.53 – 2.43 (m, 1H), 2.15 – 2.02 (m, 1H), 1.45 (t, $J = 7.1$ Hz, 3H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 212.4, 197.2, 163.6, 137.6 (2C), 136.7, 130.3 (2C), 129.8, 129.4 (2C), 128.6 (t, $J = 275$ Hz), 124.9 (t, $J = 2$ Hz), 113.8 (2C), 70.3, 55.5, 45.3, 43.7 (t, $J = 24$ Hz), 35.4, 28.1, 13.8.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2961, 2937, 1682, 1603, 1510, 1477, 1230

HRMS (EI) Calcd for $C_{22}H_{23}ClF_2O_3S_3$: 504.066 Found: 504.0466

3-(6-chloro-2,2-difluorothiochroman-4-yl)-1-(4-methoxyphenyl)propan-1-one **III-22**

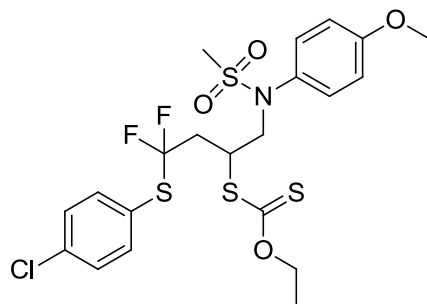
Following general procedure III-B, the reaction was carried out using xanthate adduct **III-21** (400 mg, 0.72 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 95:5) to afford the corresponding thiochroman **III-22** (180 mg, purity 80%, 35 %) as a 90:10 mixture of **III-22** and dexanthylated product.

$^1\text{H NMR}$ (δ , ppm) 7.99 (d, $J = 8.9$ Hz, 2H), 7.31 (d, $J = 2.2$ Hz, 1H), 7.24 (dd, $J = 8.4, 2.2$ Hz, 1H), 7.15 (d, $J = 8.4$ Hz, 1H), 7.00 (d, $J = 8.9$ Hz, 2H)
 (CDCl_3 , 400 MHz)

HRMS (EI) Calcd for $C_{19}H_{19}ClF_2NO_4S_4$: 555.0245 Found: 555.0246

ethyl ({4-[(4-chlorophenyl)sulfanyl]-4,4-difluoro-1-[N-(4-methoxyphenyl)methanesulfonamido]butan-2-yl)sulfanyl)methanethioate

III-24



$C_{21}H_{24}ClF_2NO_4S_4$
 $M = 556,13 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-A, the reaction was carried out using N-(4-methoxyphenyl)-N-(prop-2-en-1-yl)methanesulfonamide (241 mg, 1 mmol), xanthate **III-1** (470 mg, 1.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 75:25) to afford the corresponding xanthate adduct **III-24** (439 mg, 75%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.54 (d, $J = 8.4 \text{ Hz}$, 2H), 7.40 (d, $J = 8.4 \text{ Hz}$, 2H), 7.29 (d, $J = 9.0 \text{ Hz}$, 2H), 6.98 (d, $J = 9.0 \text{ Hz}$, 2H), 4.65 – 4.56 (m, 2H), 4.04 – 3.95 (m, 1H), 3.94 – 3.83 (m + s, 5H), 3.00 – 2.85 (m + s, 4H), 2.64 – 2.49 (m, 1H), 1.39 (t, $J = 7.1 \text{ Hz}$, 3H).
 (CDCl_3 , 400 MHz)

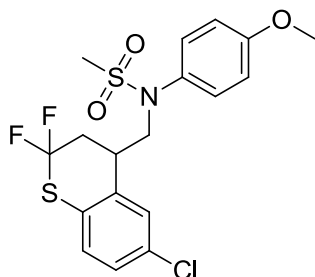
$^{13}\text{C NMR}$ (δ , ppm) 211.4, 159.7, 137.6 (2C), 136.7, 130.3, 130.2 (2C), 129.4 (2C), 128.4 (t, $J = 280 \text{ Hz}$), 124.8 (t, $J = 2 \text{ Hz}$), 114.8 (2C), 70.3, 55.6, 53.2, 42.9, 39.1 (t, $J = 24 \text{ Hz}$), 37.2, 13.7.
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2935, 1509, 1354, 1251, 1225, 1159, 1052

HRMS (EI) Calcd for $C_{21}H_{24}ClF_2NO_4S_4$: 555.0245 Found: 555.0246

N-[(6-chloro-2,2-difluoro-3,4-dihydro-2H-1-benzothiopyran-4-yl)methyl]-N-(4-methoxyphenyl)methanesulfonamide

III-25



$C_{18}H_{18}ClF_2NO_3S_2$
 $M = 433,92 \text{ g}\cdot\text{mol}^{-1}$

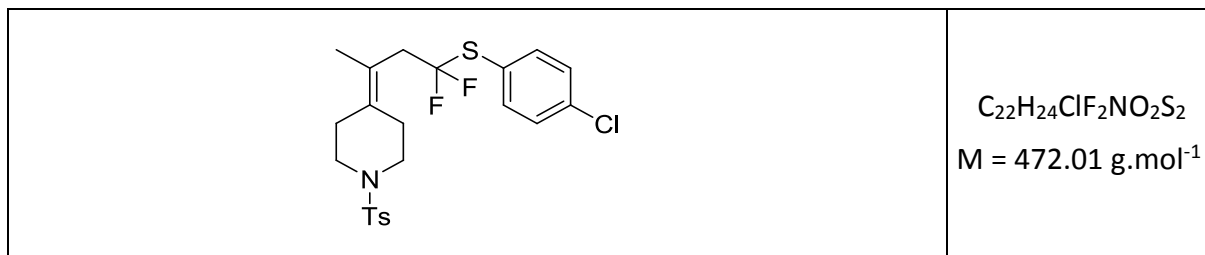
Following general procedure III-B, the reaction was carried out using xanthate adduct **III-24** (400 mg, 0.72 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 70:30) to afford the corresponding thiochroman **III-25** (110 mg, 35 %) as a white amorphous solid.

$^1\text{H NMR}$ (δ , ppm) 7.30 (d, $J = 8.9 \text{ Hz}$, 2H), 7.27 (d, $J = 2.2 \text{ Hz}$, 1H), 7.22 (dd, $J = 8.4, 2.2 \text{ Hz}$, 1H), 7.09 (d, $J = 8.4 \text{ Hz}$, 1H), 6.96 (d, $J = 8.8 \text{ Hz}$, 2H), 4.04 (dd, $J = 7.7, 1.5 \text{ Hz}$, 2H), 3.86 (s, 3H), 3.35 – 3.26 (m, 1H), 2.92 (s, 3H), 2.76 – 2.52 (m, 2H).
 (CDCl₃, 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 159.3, 135.4, 131.9, 131.6, 129.8 (t, $J = 270 \text{ Hz}$), 129.4 (2C), 128.7, 128.5, 128.2, 128.0, 114.9 (2C), 55.4, 52.5, 38.0 (d, $J = 5 \text{ Hz}$), 37.0 (t, $J = 23 \text{ Hz}$), 36.3.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2935, 1509, 1354, 1252, 1158, 1037

HRMS (EI) Calcd for C₁₈H₁₈ClF₂NO₃S₂: 433.0385 Found: 433.0378



Following general procedure III-D, the reaction was carried out using **III-29**⁶ (732 mg, 2 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10) to afford **III-30** (368 mg, 78%) as an amorphous solid.

¹H NMR (δ , ppm) 7.70 – 7.65 (m, 2H), 7.53 – 7.49 (m, 2H), 7.39 – 7.32 (m, 4H), 3.08 (t, $J = 5.6$ Hz, 4H), 2.92 (t, $J = 15.1$ Hz, 2H), 2.47 – 2.36 (m, 7H), 1.78 (s, 3H).
(CDCl₃, 400 MHz)

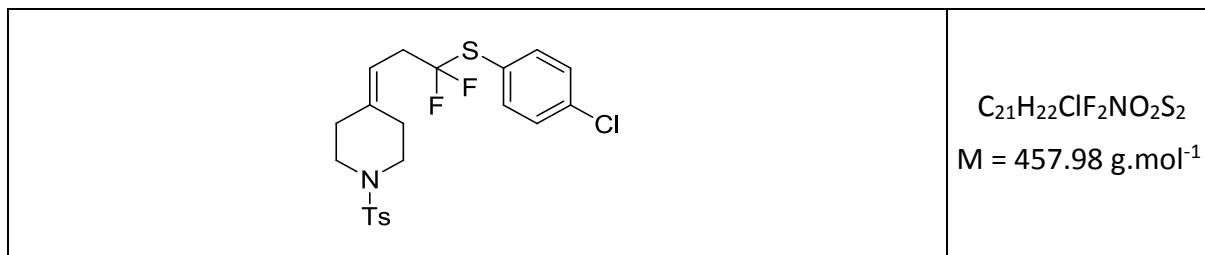
¹³C NMR (δ , ppm) 143.5, 137.31 (2C), 136.4, 133.7, 133.5, 129.7 (2C), 129.3 (2C), 129.1 (t, $J = 281$ Hz), 127.7 (2C), 125.3, 119.8 (t, $J = 2$ Hz), 47.0, 46.9, 42.7 (t, $J = 23$ Hz), 29.9, 29.4, 21.5, 19.5.
(CDCl₃, 100 MHz)

HRMS (EI) Calcd for C₂₂H₂₄ClF₂NO₂S₂: 471.0905 Found: 471.0904

⁶ Voir chapitre IV molécule **IV-16c** page 339

4-(3-(4-chlorophenylthio)-3,3-difluoropropylidene)-1-tosylpiperidine

III-34



Following general procedure III-D, the reaction was carried out using **III-33**⁷ (376 mg, 1 mmol), xanthate **III-1** (157 mg, 0.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 90:10) to afford **III-34** (190 mg, 84%) as an amorphous solid.

¹H NMR (δ , ppm) 7.71 – 7.65 (m, 2H), 7.54 – 7.48 (m, 2H), 7.39 – 7.32 (m, 4H), 5.29 (t, $J = 7.5 \text{ Hz}$, 1H), 3.15 – 3.04 (m, 4H), 2.83 (td, $J = 14.3, 7.5 \text{ Hz}$, 2H), 2.46 (s, 3H), 2.41 – 2.32 (m, 4H).

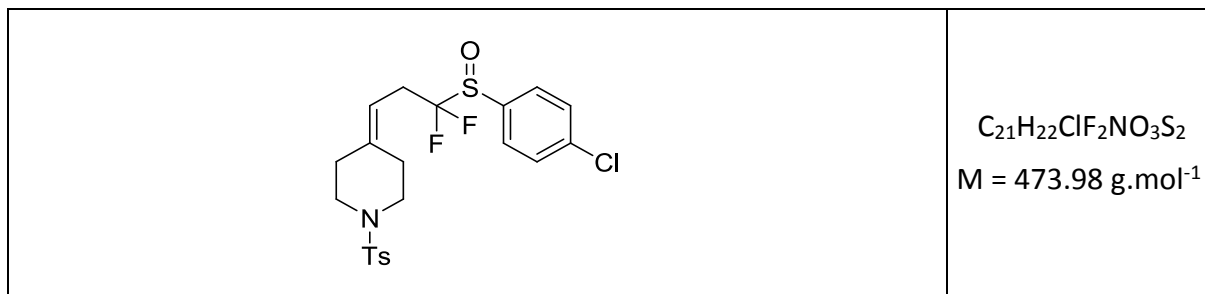
¹³C NMR (δ , ppm) 143.6, 139.6, 137.3 (2C), 136.5, 133.5, 129.7 (2C), 129.3 (2C), 128.9 (t, $J = 280 \text{ Hz}$), 127.6 (2C), 125.2, 114.1 (t, $J = 4 \text{ Hz}$), 47.6, 46.8, 36.8 (t, $J = 24 \text{ Hz}$), 35.4, 28.1, 21.5.

HRMS (EI) Calcd for $C_{21}H_{22}ClF_2NO_2S_2$: 457.0749 Found: 457.0749

⁷ Voir Chapitre IV molecule **IV-16a** page 332

4-(3-(4-chlorophenylsulfinyl)-3,3-difluoropropylidene)-1-tosylpiperidine

III-34bis



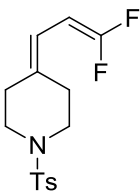
Following general procedure III-C1, the reaction was carried out using **III-34** (153 mg, 0.34 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the corresponding xanthate adduct **III-34bis** (158 mg, 99%) as an amorphous solid.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.68 – 7.65 (m, 2H), 7.64 (m, 2H), 7.58 – 7.53 (m, 2H), 7.34 (m, 2H), 5.22 (t, $J = 7.5$ Hz, 1H), 3.20 – 2.97 (m, 5H), 2.68 (m, 1H), 2.45 (s, 3H), 2.42 – 2.28 (m, 4H).

$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 143.6, 141.6, 139.1, 135.0, 133.5, 129.7 (2C), 129.6 (2C), 127.6 (2C), 127.3 (2C), 127.2 (dd, $J = 302, 287$ Hz), 111.5 (dd, $J = 6, 3$ Hz), 47.5, 46.8, 35.5, 28.9 (dd, $J = 21, 20$ Hz), 28.1, 21.5.

4-(3,3-difluoroallylidene)-1-tosylpiperidine

III-35

	$C_{15}H_{17}F_2NO_2S$ $M = 313.36 \text{ g}\cdot\text{mol}^{-1}$
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A magnetically stirred round bottom flask was charged with **III-34bis** (100 mg, 0.21 mmol), diphenylether (2.1 ml) and heated up to 160 °C. The resulting solution was stirred until total consumption of the sulfoxide (30 min), then cooled to room temperature and purified on flash chromatography (petroleum ether / ethyl acetate 90:10) to afford **III-35** (61 mg, 94%) as an amorphous white solide.

¹H NMR (δ , ppm) 7.66 (d, $J = 8.2$ Hz, 2H), 7.34 (d, $J = 8.2$ Hz, 2H), 5.72 (d, $J = 11.3$ Hz, 1H), 5.02 (ddd, $J = 23.7, 11.3, 2.0$ Hz, 1H), 3.10 – 3.03 (m, $J = 12.7, 6.4$ Hz, 4H), 2.45 (s, 3H), 2.39 – 2.33 (m, 4H).
(CDCl₃, 400 MHz)

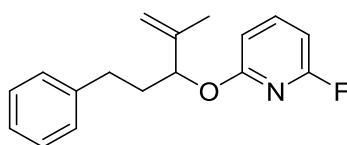
¹³C NMR (δ , ppm) 157.0 (dd, $J = 296, 290$ Hz), 143.7, 135.6 (dd, $J = 11, 3$ Hz), 133.2, 129.7 (2C), 127.6 (2C), 113.1 (d, $J = 2$ Hz), 77.6 (dd, $J = 26, 15$ Hz), 47.7, 46.9, 35.2, 28.1, 21.5.
(CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2927, 1704, 1362, 1167

HRMS (EI) Calcd for C₁₅H₁₇F₂NO₂S: 313.0948 Found: 313.0956

2-fluoro-6-(2-methyl-5-phenylpent-1-en-3-yloxy)pyridine

III-37



$C_{17}H_{18}FNO$
 $M = 271.33 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with 2-bromopropene (907 mg, 7.5 mmol), 6 mL of THF and cooled to -78°C . $t\text{BuLi}$ (1.8 M, 15 mmol) was added over 10 minutes and the solution was allowed to warm to room temperature for 1 minute. The reaction was cooled to -78°C and a solution of dihydrocinnamaldehyde (800 μl , 6 mmol) in THF (6 mL) was added slowly. The solution was stirred until total consumption of the starting ketone and then quenched with NH_4Cl sat. The layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were washed with brine and dried over anhydrous MgSO_4 to afford the corresponding allylic alcohol (~quantitative).

Following literature procedure,⁸ a magnetically stirred round bottom flask was charged with the latter alcohol (6 mmol), 2,6-difluoropyridine (560 μl , 7.8 mmol) and dry DMSO (6 mL). NaH (60% in mineral oil) (312 mg, 7.8 mmol) was added in one portion and the resulting suspension was heated up to 60°C . The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and the quenched with water. Et₂O was added, the layers were partitioned and the aqueous one was extracted twice with Et₂O. The combined organic layers were washed with brine and dried over anhydrous MgSO_4 . Removal of the solvent and purification on flash chromatography (petroleum ether / dichloromethane 70:30) yielded the desired fluoropyridyl ether **III-37** (1.1 mg, 67% over two steps) as a colourless oil.

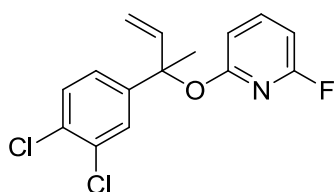
¹H NMR (δ , ppm) 7.68 (q, $J = 8.1$ Hz, 1H), 7.35 – 7.30 (m, 2H), 7.27 – 7.21 (m, 3H), 6.65 (dd, $J = 8.0, 1.6$ Hz, 1H), 6.49 (dd, $J = 7.8, 2.6$ Hz, 1H), 5.46 (dd, $J = 7.6, 5.4$ Hz, 1H), 5.10 (bs, 1H), 4.99 – 4.97 (m, 1H), 2.85 – 2.67 (m, 2H), 2.24 – 2.13 (m, 1H), 2.13 – 2.01 (m, 1H), 1.84 (s, 3H).
 (CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 162.6 (d, $J = 14$ Hz), 162.1 (d, $J = 240$ Hz), 143.6, 142.6 (d, $J = 8$ Hz), 141.8, 128.4 (4C), 125.9, 112.9, 107.4 (d, $J = 5$ Hz), 100.1 (d, $J = 36.0$ Hz), 78.5, 34.9, 31.8, 18.3.
 (CDCl₃, 100 MHz)

⁸ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

2-(2-(3,4-dichlorophenyl)but-3-en-2-yloxy)-6-fluoropyridine

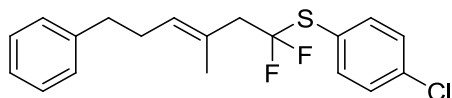
III-39



$C_{15}H_{12}Cl_2FNO$
 $M = 312.17 \text{ g}\cdot\text{mol}^{-1}$

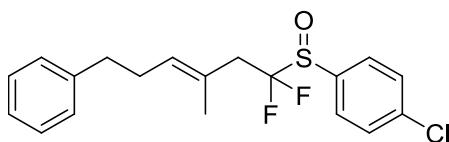
Following general procedure IV-E, the reaction was carried out using 1-(3,4-dichlorophenyl)ethanone (1.89 g, 10 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 98:2) to afford the corresponding fluoropyridine derivative **III-39** (1.12 g, 36 %) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.65 (q, $J = 8.1 \text{ Hz}$, 1H), 7.57 (d, $J = 2.2 \text{ Hz}$, 1H), 7.42 (d, $J = 8.4 \text{ Hz}$, 1H),
 (CDCl₃, 400 MHz) 7.31 (dd, $J = 8.4, 2.2 \text{ Hz}$, 2H), 6.67 (dd, $J = 8.0, 1.5 \text{ Hz}$, 1H), 6.44 (dd, $J = 7.8, 2.8 \text{ Hz}$, 1H), 6.44 (dd, $J = 17.4, 10.8 \text{ Hz}$, 1H), 5.39 (d, $J = 17.4 \text{ Hz}$, 1H),
 5.33 (d, $J = 10.8 \text{ Hz}$, 1H), 2.02 (s, 3H).

(4-chlorophenyl)(1,1-difluoro-3-methyl-6-phenylhex-3-enyl)sulfane**III-40**
 $C_{19}H_{19}ClF_2S$
 $M = 352.87 \text{ g}\cdot\text{mol}^{-1}$

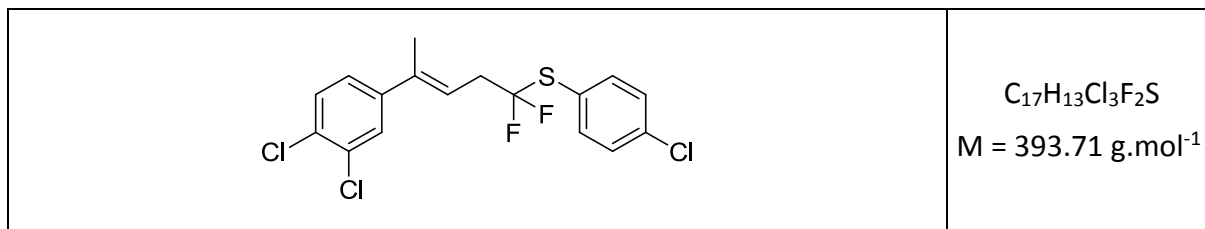
Following general procedure III-D, the reaction was carried out using **III-37** (271 mg, 1 mmol), xanthate **III-1** (157 mg, 0.5 mmol). The residue was purified by silica gel column chromatography (petroleum ether/dichloromethane 80:20) to afford **III-40** (133 mg, 71%) as a 7:3 E/Z ratio and as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) $7.64 - 7.56$ (m, 2H), $7.45 - 7.34$ (m, 4H), $7.33 - 7.25$ (m, 3H), 5.61 (t, $J = 7.2$ Hz, 0.3H), 5.51 (t, $J = 7.1$ Hz, 0.7H), $2.99 - 2.84$ (m, 2H), $2.83 - 2.73$ (m, 2H), $2.53 - 2.39$ (m, 2H), 1.93 (s, 0.9H), 1.79 (s, 2.1H).
 (CDCl₃, 400 MHz)

1-chloro-4-(1,1-difluoro-3-methyl-6-phenylhex-3-enylsulfinyl)benzene**III-42**
 $C_{19}H_{19}ClF_2OS$
 $M = 368.87 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-C1, the reaction was carried out using **III-40** (130 mg, 0.34 mmol). The residue was purified by silica gel column chromatography (petroleum ether/dichloromethane 50:50) to afford the corresponding sulfoxide **III-42** (90 mg, 72%) as an amorphous solid.

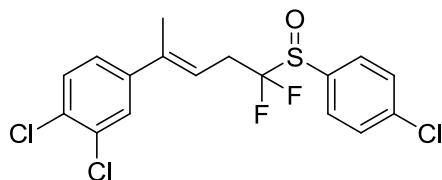
$^1\text{H NMR}$ (δ , ppm) 7.69 (m, 2H), $7.62 - 7.57$ (m, 2H), $7.35 - 7.29$ (m, 2H), $7.26 - 7.15$ (m, 3H), 5.59 (t, $J = 7.2$ Hz, 0.3H), 5.53 (t, $J = 7.1$ Hz, 0.7H), $3.11 - 2.94$ (m, 1.2H), $2.75 - 2.55$ (m, 2.8H), $2.47 - 2.38$ (m, 1.4H), $2.34 - 2.24$ (m, 0.6H), 1.83 (s, 0.9H), 1.69 (s, 2.1H).
 (CDCl₃, 400 MHz)

(E)-(4-chlorophenyl)(4-(3,4-dichlorophenyl)-1,1-difluoropent-3-enyl)sulfane**III-41**

Following general procedure III-D, the reaction was carried out using **III-39** (614 mg, 2 mmol), xanthate **III-1** (314 mg, 1 mmol). The residue was purified by silica gel column chromatography (petroleum ether 100%) to afford **III-41** (100 mg, 26%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.61 – 7.57 (m, 2H), 7.53 (d, $J = 2.2$ Hz, 1H), 7.44 (d, $J = 8.4$ Hz, 1H), 7.42 – 7.39 (m, 2H), 7.28 (dd, $J = 8.4, 2.2$ Hz, 1H), 5.87 (td, $J = 7.4, 1.3$ Hz, 1H), 3.10 (td, $J = 14.1, 7.4$ Hz, 2H), 2.07 (s, 3H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 142.9, 138.3, 137.4 (2C), 136.5, 132.5, 131.3, 130.2, 129.4 (2C), 129.2 (t, $J = 280$ Hz), 127.9, 125.3 – 125.2 (m, 2C), 118.9 (t, $J = 4$ Hz), 38.5 (t, $J = 24$ Hz), 16.25.
(CDCl_3 , 100 MHz)

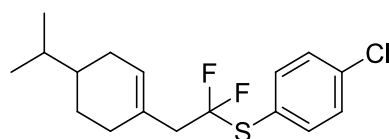
(E)-1,2-dichloro-4-(5-(4-chlorophenylsulfinyl)-5,5-difluoropent-2-en-2-yl)benzene**III-43**

$C_{17}H_{13}Cl_3F_2OS$
 $M = 409.71 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-C1, the reaction was carried out using **III-41** (100 mg, 0.24 mmol). The residue was purified by silica gel column chromatography (petroleum ether/dichloromethane 50:50) to afford the corresponding sulfoxide **III-43** (100 mg, 96%) as an amorphous solid.

$^1\text{H NMR}$ (δ , ppm) 7.71 (d, $J = 8.3$ Hz, 2H), 7.59 (d, $J = 8.5$ Hz, 2H), 7.46 (d, $J = 2.1$ Hz, 1H), 7.42 (d, $J = 8.4$ Hz, 1H), 7.22 (dd, $J = 8.4, 2.0$ Hz, 1H), 5.75 (t, $J = 7.0$ Hz, 1H), 3.38 – 3.20 (m, 1H), 3.06 – 2.89 (m, 1H), 2.08 (s, 3H).
 (CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 142.6, 140.2, 139.1, 135.1, 132.5, 131.5, 130.2, 129.6 (2C), 127.8, 127.5 (dd, $J = 301, 287$ Hz), 127.4 (2C), 125.2, 116.2 (dd, $J = 6, 3$ Hz), 30.6 (t, $J = 21$ Hz), 16.3.
 (CDCl_3 , 100 MHz)

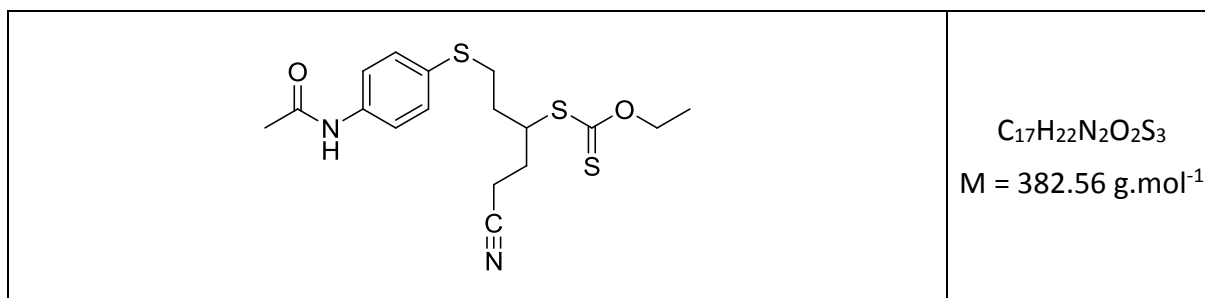
(4-chlorophenyl)(1,1-difluoro-2-(4-isopropylcyclohex-1-enyl)ethyl)sulfane**III-53**

$C_{17}H_{21}ClF_2S$
 $M = 330,10 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-A, the reaction was carried out using sabinen (75%) (181 mg, 1mmol) and xanthate **III-1** (157 mg, 0.5 mmol) to afford 180 mg (80%) of a mixture of five and six membered ring adducts (respectively **III-48** and **III-49**). A magnetically stirred round bottom flask was charged with this mixture, an aqueous solution of hypophosphorous acid (50% wt) (244 mg, 2.0 mmol), triethylamine (242 mg, 2.4 mmol) in 4 ml of dioxane. The solution was refluxed under a flow of nitrogen for 5 minutes then AIBN (6.5 mg, 0.04 mmol) was added every hour until TLC showed total consumption of the starting adducts. 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) to afford the product **III-53** (80 mg, 61%) as a colourless oil.

1H NMR (δ , ppm) 7.58 (d, $J = 8.5$ Hz, 2H), 7.39 (d, $J = 8.5$ Hz, 2H), 5.71 (bs, 1H), 2.85 (t, $J = 15.0$ Hz, 2H), 2.28 – 2.10 (m, 3H), 1.91 – 1.79 (m, 2H), 1.61 – 1.49 (m, $J = 13.4, 6.7$ Hz, 1H), 1.41 – 1.23 (m, 2H), 0.97 (d, $J = 6.7$ Hz, 3H), 0.96 (d, $J = 6.8$ Hz, 3H).
 ($CDCl_3$, 400 MHz)

^{13}C NMR (δ , ppm) 140.9 (2C), 139.7, 132.8, 132.8 (t, $J = 281$ Hz), 132.8, 132.7 (2C), 129.4 (t, $J = 2$ Hz), 50.7 (t, $J = 23$ Hz), 43.1, 35.7, 33.2, 32.8, 29.9, 23.5, 23.2.
 ($CDCl_3$, 100 MHz)



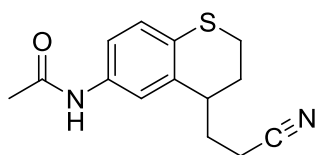
Following general procedure III-A, the reaction was carried out using **III-54** (221 mg, 1 mmol), cyanomethyl xanthate (322 mg, 2 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 60:40) to afford the corresponding xanthate adduct **III-56** (265 mg, 69%).

$^1\text{H NMR}$ (δ , ppm) 7.58 (s, 1H), 7.52 – 7.48 (m, 2H), 7.38 – 7.34 (m, 2H), 4.69 (q, $J = 7.1$ Hz, 2H), 4.06 – 3.95 (m, 1H), 3.13 – 3.03 (m, 1H), 3.02 – 2.92 (m, 1H), 2.51 (t, $J = 7.5$ Hz, 2H), 2.21 (s, 3H), 2.17 – 2.07 (m, 1H), 2.06 – 1.93 (m, 3H), 1.48 (t, $J = 7.1$ Hz, 3H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 212.5, 168.5, 137.0, 131.5 (2C), 130.1, 120.5 (2C), 119.1, 70.6, 48.9, 33.6, 31.9, 30.8, 24.6, 15.0, 13.8.
(CDCl_3 , 100 MHz)

N-(4-(2-cyanoethyl)thiochroman-6-yl)acetamide

III-58



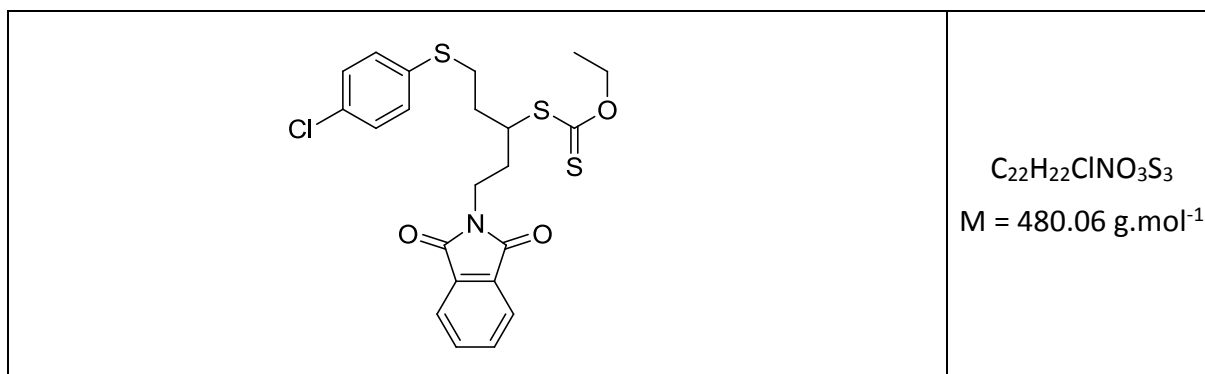
$C_{14}H_{16}N_2OS$
 $M = 260.35 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure III-B, the reaction was carried out using xanthate adduct **III-56** (230 mg, 0.6 mmol). The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 50:50) to afford the corresponding thiocroman **III-58** (40 mg, 20% - purity 80%) as an amorphous solid.

$^1\text{H NMR}$ (δ , ppm) 7.58 (bs, 1H), 7.32 (d, $J = 2.3$ Hz, 1H), 7.27 (dd, $J = 8.4, 2.3$ Hz, 1H), 7.09 (d, $J = 8.4$ Hz, 1H), 3.12 (td, $J = 12.4, 4.5$ Hz, 1H), 3.04 – 2.96 (m, 2H), 2.45 – 2.39 (m, 2H), 2.19 (s, 3H), 2.10 – 2.00 (m, 3H), 1.95 – 1.87 (m, 1H).
 (CDCl_3 , 400 MHz)

**S-1-(4-chlorophenylthio)-5-(1,3-dioxisoindolin-2-yl)pentan-3-yl O-ethyl
carbonodithioate**

III-57

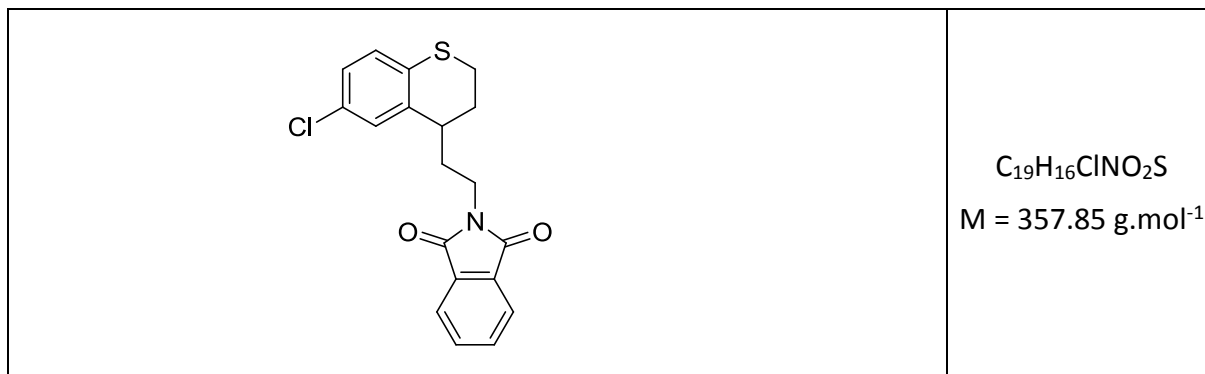


Following general procedure III-A, the reaction was carried out using **III-55** (540 mg, 2 mmol), *N*-phthalimidemethyl xanthate (281 mg, 2 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 80:20) to afford the corresponding xanthate adduct **III-57** (425 mg, 66%) as a mixture of and starting xanthate in a 3:1 ratio.

$^1\text{H NMR}$ (δ , ppm) $7.91 - 7.87$ (m, 2H), $7.79 - 7.75$ (m, 2H), $7.34 - 7.27$ (m, 4H), 4.64 (q, $J = 7.1$ Hz, 2H), $3.91 - 3.81$ (m, 3H), $3.15 - 2.99$ (m, 2H), $2.23 - 1.95$ (m, 4H), 1.43 (t, $J = 7.1$ Hz, 3H).
 (CDCl₃, 400 MHz)

2-(2-(6-chlorothiochroman-4-yl)ethyl)isoindoline-1,3-dione

III-59



Following general procedure III-B, the reaction was carried out using xanthate adduct **III-57** (0.58 mmol). The residue was purified by silica gel column chromatography (petroleum ether/dichloromethane 70:30) to afford the corresponding thiocroman **III-59** (111 mg, 45 %) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.93 – 7.87 (m, 2H), 7.80 – 7.74 (m, 2H), 7.20 (d, $J = 0.9$ Hz, 1H), 7.10 – 7.04 (m, 2H), 3.84 – 3.79 (m, 2H), 3.22 (td, $J = 12.1, 4.1$ Hz, 1H), 3.02 (dt, $J = 12.3, 4.6$ Hz, 1H), 2.95 – 2.87 (m, 1H), 2.34 – 2.26 (m, 1H), 2.15 – 1.92 (m, 3H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 168.4 (2C), 138.3, 134.1 (2C), 132.1 (2C), 131.1, 129.4, 129.3, 128.0, 126.9, 123.3 (2C), 35.7, 35.4, 32.3, 25.6, 22.8.
(CDCl_3 , 100 MHz)

HRMS (EI) Calcd for $C_{19}H_{16}ClNO_2S$: 357.0590 Found: 357.0597

C. Chapitre IV : Synthèse et utilisation d'un nouveau précurseur du radical 1-chloro-1,1-difluorométhane

1. General procedures

General procedure IV-A for the radical addition

A solution of olefin (n mmol) and xanthate (1.5 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.

General procedure IV-B for the radical reduction

To a solution of xanthate adduct (n mmol) in a 1:1 mixture of toluene and cyclohexane (1.6n mL) was added tris(trimethylsilyl)silane (1.2n mmol) and the solution was refluxed under a flow of nitrogen for 15 minutes. AIBN (0.1n mmol) was then added every hour until total conversion of the starting xanthate was observed (typically 1-2 hours). The mixture was cooled to room temperature and the solvent evaporated under reduced pressure. Flash column chromatography afforded the desired product.

General procedure IV-C for the one pot radical addition-cyclisation

A solution of olefin (n mmol) and xanthate (1.5 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 (typically 2-3 hours). The reaction mixture was cooled to room temperature, diluted with AcOEt (9 n mL) then refluxed under a flow of nitrogen for 15 minutes. Lauroyl peroxide (DLP) 25 mol% was then added every hour until total conversion of the xanthate adduct was observed (typically 5 portions of DLP). The mixture was cooled to room temperature and the solvent evaporated under reduced pressure. Flash column chromatography afforded the desired product.

General procedure IV-D for the preparation of fluoropyridine derivatives⁹

A solution of ketone (n mmol) in THF ($6n$ mL) was cooled to -78 °C and vinyl magnesium bromide (0.7 M in THF) ($1.2n$ mmol) was added dropwise over 15 min. The resulting solution was stirred until full consumption of the starting ketone and then quenched with NH_4Cl sat. The layers were partitioned and the organic one was washed with water and brine. The solvents were evaporated to dryness to afford the vinylic alcohol. A magnetically stirred round bottom flask was charged with the latter alcohol, 2,6-difluoropyridine ($1.3n$ mmol) and dry DMSO (n mL). NaH (60% in mineral oil, $1.3n$ mmol) was added in one portion and the resulting suspension was heated up to 60 °C. The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and then quenched with water. 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 purification on flash chromatography yielded the desired fluoropyridyl ether.

General procedure IV-E1 for the radical allylation¹⁰

A solution of olefin ($2n$ mmol) and xanthate (n mmol) in AcOEt (n mL) was refluxed under a flux of nitrogen for 15 minutes. Lauroyl peroxide (DLP) 30 mol % was then added every hour until total conversion of the starting xanthate. The mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. Flash chromatography afforded the desired adduct as a mixture of E and Z isomers.

General procedure IV-E2 for the radical allylation¹¹

A mixture of olefin and xanthate ($2n$ mmol) in AcOEt ($2.9 n$ mL) was refluxed under a flow of nitrogen for 15 minutes. Lauroyl peroxide (DLP) 40% mol was then added every hour until 80 mol% (2 hours). The reaction medium was cooled to room temperature and $0.2n$ mmol of olefin were added. The mixture was then refluxed for 15 minutes and DLP 40 mol% was added every hour until full conversion of the starting xanthate. The reaction medium was cooled to room temperature and after removal of the solvent the residue was purified by flash column chromatography to afford the desired enol ether.

⁹ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

¹⁰ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

¹¹ Debien, L.; Quiclet-Sire, B.; Zard, S. Z. *Org. Lett.* **2011**, *13*, 5676

General procedure IV-F1 for the radical elimination

A solution of Chlorodifluoro derivative (n mmol) and DBU (30n mmol) was heated at 120 °C under an argon atmosphere (2-6 hours) until total conversion and then quenched with NH₄Cl sat. EtOAc was added, the layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous MgSO₄. Removal of the solvent (and purification on flash chromatography) yielded the desired difluoro olefin.

General procedure IV-F2 for the radical elimination

A solution of Chlorodifluoro derivative (n mmol) and DBU (30n mmol) was heated at 45 °C under an argon atmosphere (2 hours) until total conversion and then quenched with NH₄Cl sat. EtOAc was added, the layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous MgSO₄. Removal of the solvent (and purification on flash chromatography) yielded the desired difluoro olefin.

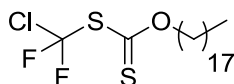
General procedure IV-F3 for the radical elimination

A solution of Chlorodifluoro derivative (n mmol) and DBU (30n mmol) was heated at 90 °C under an argon atmosphere (14 hours or specified) until total conversion and then quenched with NH₄Cl sat. EtOAc was added, the layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous MgSO₄. Removal of the solvent (and purification on flash chromatography) yielded the desired indole derivatives.

2. Experimental Procedures and Spectroscopic Data

S-chlorodifluoromethyl O-octadecyl carbonodithioate

IV-1



$C_{20}H_{37}ClF_2OS_2$
 $M = 431.08 \text{ g}\cdot\text{mol}^{-1}$

See page 383 for a diagram of the apparatus used for this reaction.¹² Thionyl chloride (22 mL, 303 mmol) was slowly added from a dropwise funnel to a solution of chlorodifluoroacetic acid (19.25 mL, 228 mmol) in dry DMF (115 mL) at 0 °C. The solution was then heated in an oil bath to 40 °C with stirring. Chlorodifluoroacetic chloride was produced as a gas (bp 26 °C), which was condensed via a dry ice cooled condenser to another flask containing a solution of sodium *O*-octadecyl carbonodithioate (28.44 g, 77 mmol) in dry cyclohexane (308 mL). The temperature of the oil bath was gradually increased from 40 to 60 °C to maintain a steady rate of chlorodifluoroacetic chloride production. After 3 hours, the dry ice condenser was replaced by a classic water condenser and the solution of acyl xanthate (flashy yellow) was irradiated with a 250W tungsten halogen lamp until total conversion of the acyl xanthate was observed by TLC. The solution was cooled to room temperature and 250 mL of the solvent were evaporated under reduced pressure. The residue was purified on silica gel column chromatography (petroleum ether 100%) to afford xanthate **IV-1** (20.4 g, 61%) as a yellow liquid.¹³

¹H NMR (δ , ppm) 4.70 (t, $J = 6.5$ Hz, 2H), 1.93 – 1.85 (m, 2H), 1.54 – 1.44 (m, 2H), 1.44 – 1.26 (m, 28H), 0.94 (t, $J = 6.7$ Hz, 3H).
 (CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 202.8, 127.8 (t, $J = 332$ Hz) 75.3, 32.0, 29.8 (4C), 29.7 (3C), 29.6, 29.5, 29.5, 29.4, 29.1, 28.0, 25.7, 22.7, 14.1.
 (CDCl₃, 100 MHz)

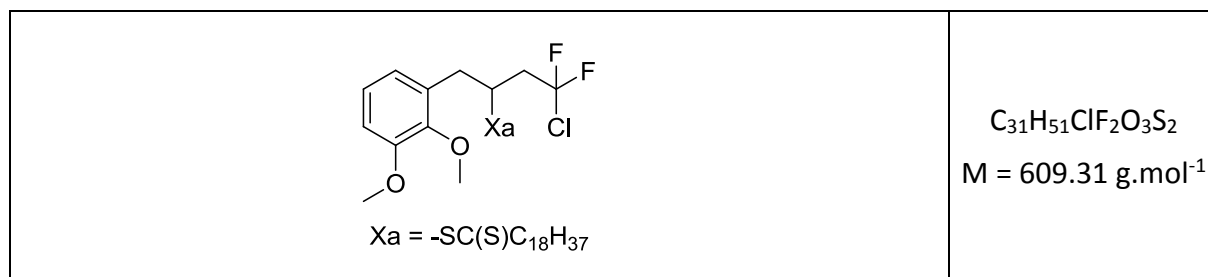
IR (σ , cm⁻¹, CCl₄) 2927, 2855, 1269, 1115, 1037

¹² Li, Y.; Miller, S.J. *J. Org. Chem.* **2011**, *76*, 9785.

¹³ The same reaction was carried out with 10 mmol of *O*-octadecyl carbonodithioate and **3** was obtained with 81% yield.

**S-4-chloro-1-(2,3-dimethoxyphenyl)-4,4-difluorobutan-2-yl O-octadecyl
carbonodithioate**

IV-5



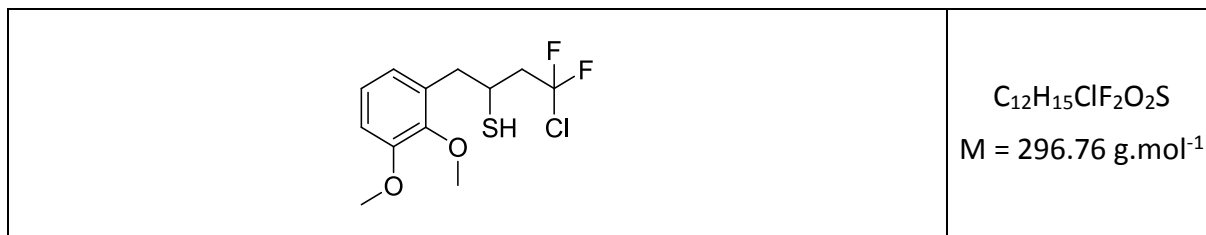
Following general procedure IV-A, the reaction was carried out using 1-allyl-2,3-dimethoxybenzene (534 mg, 3.00 mmol), xanthate **IV-1** (1.94 g, 4.50 mmol) and two portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 95:5) to afford the corresponding xanthate adduct **IV-5** (1.73 mg, 95%).

¹H NMR (δ, ppm) 7.06 (t, *J* = 7.9 Hz, 1H), 6.92 – 6.87 (m, 2H), 4.65 – 4.53 (m, 2H), 4.40 – 4.31 (m, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.30 (dd, *J* = 14.0, 6.6 Hz, 1H), 3.00 (dd, *J* = 14.0, 8.7 Hz, 1H), 2.95 – 2.70 (m, 2H), 1.88 – 1.79 (m, 2H), 1.50 – 1.25 (m, 30H), 0.97 – 0.90 (m, 3H).
(CDCl₃, 400 MHz)

¹³C NMR (δ, ppm) 212.4, 152.8, 147.5, 131.1, 128.6 (t, *J* = 294 Hz), 123.9, 122.7, 111.4, 74.3, 60.6, 55.7, 45.7, 45.5 (t, *J* = 24 Hz), 33.9, 32.0, 29.8 – 29.7 (8C), 29.6, 29.5, 29.4, 29.3, 28.2, 26.0, 22.8, 14.2.
(CDCl₃, 100 MHz)

4-chloro-1-(2,3-dimethoxyphenyl)-4,4-difluorobutane-2-thiol

IV-6



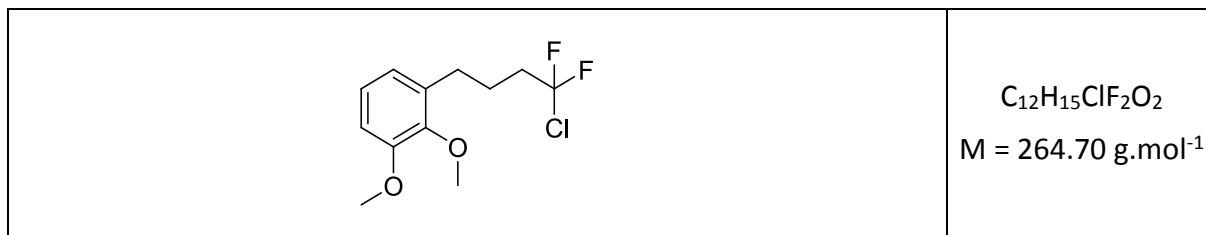
A magnetically stirred round bottom flask was charged with **IV-5** (913 mg, 1.5 mmol), ethylenediamine (400 μL , 6 mmol) and 20 mL of a 1:1 mixture of Et_2O and EtOH . The reaction mixture was stirred until total conversion of the starting xanthate and then quenched with HCl 1N. Et_2O was added, the 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 yielded the desired thiol **IV-6** (355 mg, 80%).

^1H NMR (δ , ppm) 7.07 (t, $J = 7.9$ Hz, 1H), 6.90 (d, $J = 8.2$ Hz, 1H), 6.82 (d, $J = 7.6$ Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.68 – 3.59 (m, 1H), 3.17 (dd, $J = 13.5, 6.4$ Hz, 1H), 2.85 (dd, $J = 13.5, 8.4$ Hz, 1H), 2.79 – 2.57 (m, 2H), 1.88 (d, $J = 5.5$ Hz, 1H).

^{13}C NMR (δ , ppm) 153.1, 147.7, 131.9, 129.2 (t, $J = 293$ Hz), 124.2, 123.1, 111.7, 60.9, 56.00, 49.7 (t, $J = 23$ Hz), 39.7, 35.4.

1-(4-chloro-4,4-difluorobutyl)-2,3-dimethoxybenzene

IV-8



Following general procedure IV-A, the reaction was carried out using 1-allyl-2,3-dimethoxybenzene (534 mg, 3.00 mmol), xanthate **IV-1** (1.94 g, 4.50 mmol) and two portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 95:5) to afford the corresponding xanthate adduct **IV-5** (1.73 mg, 95%).

Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-5** (457 mg, 0.75 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding reduced product **IV-8** (170 mg, 86%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.00 (t, $J = 7.9$ Hz, 1H), 6.80 (d, $J = 8.2$ Hz, 1H), 6.75 (d, $J = 7.6$ Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 2.71 (t, $J = 7.5$ Hz, 2H), 2.37 – 2.23 (m, 2H), 1.97 – 1.86 (m, 2H).
(CDCl_3 , 400 MHz)

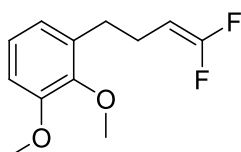
$^{13}\text{C NMR}$ (δ , ppm) 153.4, 147.8, 135.2, 130.6 (t, $J = 292$ Hz), 124.6, 122.4, 111.3, 61.2, 56.3, 42.0 (t, $J = 24$ Hz), 29.3, 24.8 (t, $J = 3$ Hz).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2935

HRMS (EI) Calcd for $C_{12}H_{15}ClF_2O_2$: 264.0729 Found: NF

1-(4,4-difluorobut-3-enyl)-2,3-dimethoxybenzene

IV-9



$C_{12}H_{14}F_2O_2$
 $M = 228.24 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-F1, the reaction was carried out using **IV-8** (60 mg, 0.23 mmol) to afford **IV-9** (42 mg, 80%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.04 (t, $J = 7.9$ Hz, 1H), 6.84 (d, $J = 8.1$ Hz, 1H), 6.81 (d, $J = 7.6$ Hz, 1H),
 (CDCl₃, 400 MHz) 4.23 (dtd, $J = 25.5, 7.8, 2.3$ Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 2.75 (t, $J = 7.7$ Hz, 2H), 2.37 – 2.28 (m, 2H).

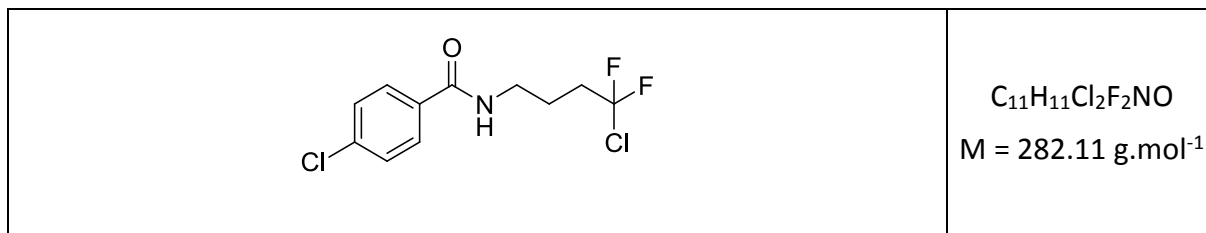
$^{13}\text{C NMR}$ (δ , ppm) 156.3 (dd, $J = 287, 285$ Hz), 152.8, 147.2, 134.8, 123.9, 121.9, 110.48,
 (CDCl₃, 100 MHz) 77.7 (dd, $J = 22, 21$ Hz), 60.7, 55.7, 29.9 (t, $J = 2$ Hz), 23.3 (d, $J = 2$ Hz).

IR (σ , cm⁻¹, CCl₄) 2935, 1746, 1596, 1481, 1271, 1224, 1085

HRMS (EI) Calcd for C₁₂H₁₄F₂O₂: 228.0962 Found: 228.0969

4-chloro-N-(4-chloro-4,4-difluorobutyl)benzamide

IV-11



Following general procedure IV-A, the reaction was carried out using *N*-allyl-4-chlorobenzamide (391 mg, 2 mmol), xanthate **IV-1** (1.29 g, 3.00 mmol) and three portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding xanthate adduct **IV-13c** (1.10 g, 87%).

Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-13c** (1.06 g, 1.69 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding reduced product **IV-11** (440 mg, 92%) as a white amorphous solid.

¹H NMR (δ, ppm) 7.70 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 6.24 (bs, 1H), 3.59 – 3.48 (m, 2H), 2.46 – 2.32 (m, 2H), 2.00 – 1.87 (m, 2H).
(CDCl₃, 400 MHz)

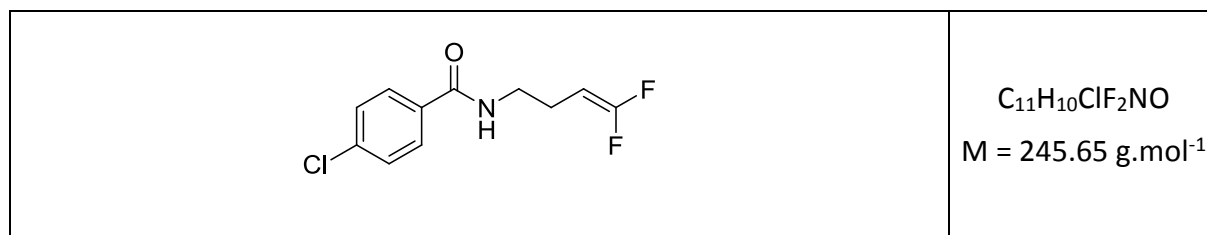
¹³C NMR (δ, ppm) 166.7, 138.0, 132.6, 129.6 (t, *J* = 292 Hz), 129.0 (2C), 128.3 (2C), 39.4 (t, *J* = 25 Hz), 38.8, 23.9 (t, *J* = 3 Hz).
(CDCl₃, 100 MHz)

IR (σ, cm⁻¹, CCl₄) 1677, 1515, 1483

HRMS (EI) Calcd for C₁₁H₁₁Cl₂F₂NO : 282.0186 Found: 282.0179

4-chloro-N-(4,4-difluorobut-3-enyl)benzamide

IV-12



Following general procedure IV-F1, the reaction was carried out using **IV-11** (140 mg, 0.50 mmol) to afford the desired difluoro olefin **IV-12** (115 mg, 94%) as an amorphous white solid.

1H NMR (δ , ppm) 7.70 (d, $J = 8.3$ Hz, 2H), 7.41 (d, $J = 8.4$ Hz, 2H), 6.24 (bs, 1H), 3.59 – 3.48 (m, 2H), 2.46 – 2.32 (m, 2H), 2.00 – 1.87 (m, 2H).
($CDCl_3$, 400 MHz)

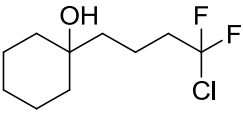
^{13}C NMR (δ , ppm) 167.8, 157.1 (dd, $J = 288, 287$ Hz), 137.8, 132.9, 128.9 (2C), 128.3 (2C), 75.1 (dd, $J = 23, 21$ Hz), 39.5 (t, $J = 3$ Hz), 22.9 (d, $J = 4$ Hz).
($CDCl_3$, 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1747, 1677, 1596, 1516, 1484

HRMS (EI) Calcd for $C_{11}H_{10}ClF_2NO$: 245.0419 Found: 245.0425

1-(4-chloro-4,4-difluorobutyl)cyclohexanol

IV-14b

	$C_{10}H_{17}ClF_2O$ $M = 226.69 \text{ g}\cdot\text{mol}^{-1}$
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Following general procedure A, the reaction was carried out using 1-allylcyclohexanol (140 mg, 1.00 mmol), xanthate **IV-1** (657 mg, 1.50 mmol) and two portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding xanthate adduct **IV-13b** (560 mg, 97%).

Following procedure B, the reaction was carried out using the latter xanthate adduct **IV-13b** (512 mg, 0.88 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding reduced product **IV-14b** (170 mg, 86%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 2.34 (tt, $J = 13.0, 8.0$ Hz, 2H), 1.80 – 1.70 (m, 2H), 1.66 – 1.43 (m, 11H), (CDCl₃, 400 MHz) 1.39 – 1.27 (m, 2H).

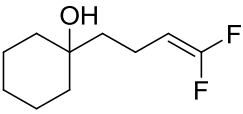
$^{13}\text{C NMR}$ (δ , ppm) 129.4 (t, $J = 292$ Hz), 70.6, 41.7 (t, $J = 24$ Hz), 40.5, 36.8 (2C), 25.2, 21.6 (2C), 16.5 (t, $J = 3$. Hz).

IR (σ , cm⁻¹, CCl₄) 2935, 2856, 1207, 1106

HRMS (EI) Calcd for C₁₀H₁₇ClF₂O : 226.0936 Found: 226.0934

1-(4,4-difluorobut-3-enyl)cyclohexanol

IV-15b

	$C_{10}H_{16}F_2O$ $M = 190.23 \text{ g}\cdot\text{mol}^{-1}$
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Following general procedure F1, the reaction was carried out using **IV-14b** (65 mg, 0.28 mmol) to afford **IV-15b** (51 mg, 93%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 4.19 (dtd, $J = 25.5, 7.8, 2.5$ Hz, 1H), 2.17 – 2.05 (m, 2H), 1.67 – 1.43 (m, 12H), 1.36 – 1.28 (m, 1H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 156.1 (dd, $J = 287, 285$ Hz), 78.4 (dd, $J = 22, 21$ Hz), 71.2, 41.9, 37.3 (2C), 25.8, 22.2 (2C), 16.1 (d, $J = 4$ Hz).
(CDCl_3 , 100 MHz)

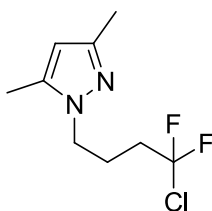
IR (σ , cm^{-1} , CCl_4) 2935, 2856, 1747

HRMS (EI) Calcd for $C_{10}H_{14}F_2$: 172.1064

Found: 172.1054

1-(4-chloro-4,4-difluorobutyl)-3,5-dimethyl-1H-pyrazole

IV-14d



$C_9H_{13}ClF_2N_2$
 $M = 222.66 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-A, the reaction was carried out using 1-allyl-3,5-dimethyl-1H-pyrazole (136 mg, 1 mmol), xanthate **IV-1** (657 mg, 1.5 mmol), camphor sulfonic acid (328 mg, 1.40 mmol) and three portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20 then diethyl ether / triethylamine 90:10) to afford the corresponding xanthate adduct **IV-13d** (540 mg, 95%).

Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-13d** (500 mg, 0.87 mmol) and camphor sulfonic acid (245 mg, 1.04 mmol). The mixture was then cooled to room temperature and quenched with saturated NaHCO_3 . EtOAc was added and the layers were partitioned and the aqueous one was extracted twice with EtOAc. 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 corresponding reduced product **IV-14d** (140 mg, 72%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 5.82 (s, 1H), 4.06 (t, $J = 7.0$ Hz, 2H), 2.41 – 2.29 (m, 2H), 2.25 (s, 3H), 2.24 (s, 3H), 2.18 – 2.09 (m, 2H).
 (CDCl_3 , 400 MHz)

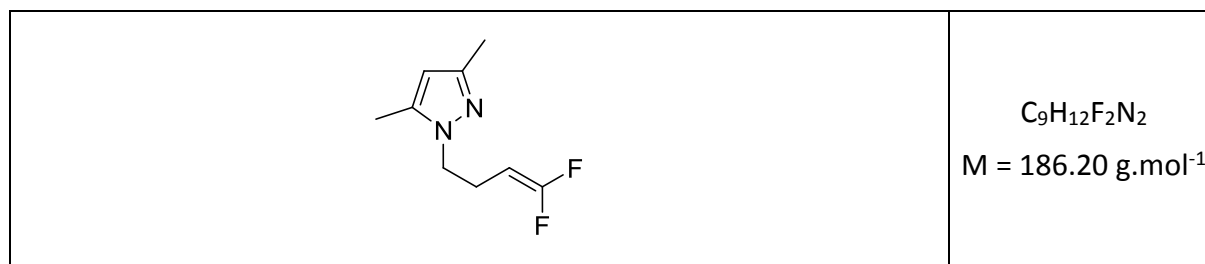
$^{13}\text{C NMR}$ (δ , ppm) 147.7, 138.6, 129.6 (t, $J = 292$ Hz), 105.3, 46.9, 39.0 (t, $J = 25$ Hz), 24.3, 13.5, 11.0.
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2930, 1462, 1423, 1212, 1191, 1105

HRMS (EI) Calcd for $C_{19}H_{13}ClF_2N_2$: 222.0735 Found: 222.0735

1-(4,4-difluorobut-3-enyl)-3,5-dimethyl-1H-pyrazole

IV-15d



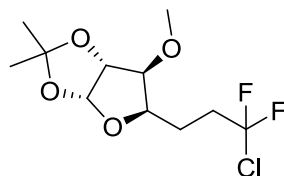
Following general procedure IV-F1, the reaction was carried out using **IV-14d** (59 mg, 0.26 mmol) to afford **IV-15d** (42 mg, 85%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 5.87 (s, 1H), 4.19 (dtd, $J = 25.2, 7.9, 1.9$ Hz, 1H), 4.08 (t, $J = 7.1$ Hz, 2H), 2.57 – 2.50 (m, 2H), 2.31 – 2.23 (m, 2H), 2.29 (s, 3H), 2.28 (s, 3H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 156.9 (dd, $J = 289, 287$ Hz), 147.3, 139.4, 105.3, 74.5 (dd, $J = 24, 21$ Hz), 47.7, 23.6 (d, $J = 4$ Hz), 13.2, 11.0.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2927, 2855, 1746, 1544

HRMS (EI) Calcd for $C_9H_{12}F_2N_2$: 186.0969 Found: 186.0949

(3aR,5R,6S,6aR)-5-(3-chloro-3,3-difluoropropyl)-6-methoxy-2,2-dimethyltetrahydrofuro[3,2-d][1,3]dioxole**IV-14e**

$C_{11}H_{17}ClF_2O_4$
 $M = 286.70 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-A, the reaction was carried out using (3aR,5R,6S,6aR)-6-methoxy-2,2-dimethyl-5-vinyltetrahydrofuro[3,2-d][1,3]dioxole (200 mg, 1.00 mmol), xanthate **IV-1** (646 mg, 1.50 mmol) and two portions of lauroyl peroxyde. The crude mixture was used in the next step without any purification.

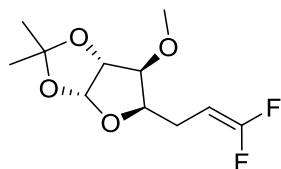
Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-13e** (~1 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding reduced product **IV-14e** (215 mg, 75% over two steps) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.92 (d, $J = 3.9$ Hz, 1H), 4.63 (d, $J = 3.9$ Hz, 1H), 4.21 (ddd, $J = 8.4, 5.0, 3.3$ Hz, 1H), 3.63 (d, $J = 3.2$ Hz, 1H), 3.46 (s, 3H), 2.66 – 2.49 (m, 1H), 2.48 – 2.32 (m, 1H), 2.15 – 2.04 (m, 1H), 1.99 – 1.87 (m, 1H), 1.53 (s, 3H), 1.36 (s, 3H).
 (CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 130.4 (t, $J = 292$ Hz), 112.1, 105.3, 85.2, 82.1, 79.2, 58.4, 39.5 (t, $J = 25$ Hz), 27.3, 26.7, 22.9.
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2992, 2936, 1455, 1373, 1214, 1194, 1123, 1058

HRMS (EI) Calcd for $C_{10}H_{14}ClF_2O_4$: 271.0549 Found: 271.0548

(3aR,5R,6S,6aR)-5-(3,3-difluoroallyl)-6-methoxy-2,2-dimethyltetrahydrofuro[3,2-d][1,3]dioxole**IV-15e**

$C_{11}H_{16}F_2O_4$
 $M = 250.24 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-F1, the reaction was carried out using **IV-14e** (63 mg, 0.22 mmol) to afford **IV-15e** (50 mg, 91%) as a colourless oil.

$^1\text{H NMR}$ (δ , ppm) 5.92 (d, $J = 3.9$ Hz, 1H), 4.61 (d, $J = 3.9$ Hz, 1H), 4.28 (dtd, $J = 25.2, 8.0, 2.3$ Hz, 1H), 4.16 (td, $J = 7.2, 3.1$ Hz, 1H), 3.61 (d, $J = 3.1$ Hz, 1H), 3.45 (s, 3H), 2.48 – 2.32 (m, 2H), 1.53 (s, 3H), 1.36 (s, 3H).
 (CDCl₃, 400 MHz)

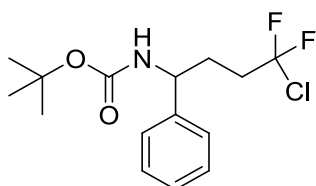
$^{13}\text{C NMR}$ (δ , ppm) 156.8 (dd, $J = 288, 285$ Hz), 111.4, 107.8, 84.1, 81.4, 79.4 (dd, $J = 3, 2$ Hz), 74.4 (dd, $J = 25, 20$ Hz), 57.8, 26.7, 26.1, 21.37 (d, $J = 5$ Hz).
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2992, 2935, 1750, 1373, 1321, 1247, 1190, 1083

HRMS (EI) Calcd for C₁₁H₁₆F₂O₄: 250.1017 Found: 250.1027

tert-butyl 4-chloro-4,4-difluoro-1-phenylbutylcarbamate

IV-14f



$C_{15}H_{20}ClF_2NO_2$
 $M = 319.77 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-A, the reaction was carried out using *tert*-butyl 1-phenylallylcarbamate (233 mg, 1.00 mmol), xanthate **IV-1** (646 mg, 1.50 mmol) and two portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding xanthate adduct **IV-13f** (640 mg, 95%).

Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-13f** (615 mg, 0.92 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford the corresponding reduced product **IV-14f** (240 mg, 95%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.39 – 7.26 (m, 5H), 4.85 (bs, 1H), 4.68 (bs, 1H), 2.45 – 2.18 (m, 2H), 2.16 – 1.99 (m, 2H), 1.42 (s, 9H).
 (CDCl₃, 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 155.9, 142.1, 130.3 (t, $J = 292 \text{ Hz}$), 129.7 (2C), 128.6, 127.0 (2C), 80.6, 54.6, 39.8 (t, $J = 25 \text{ Hz}$), 31.1, 29.1 (3C).
 (CDCl₃, 100 MHz)

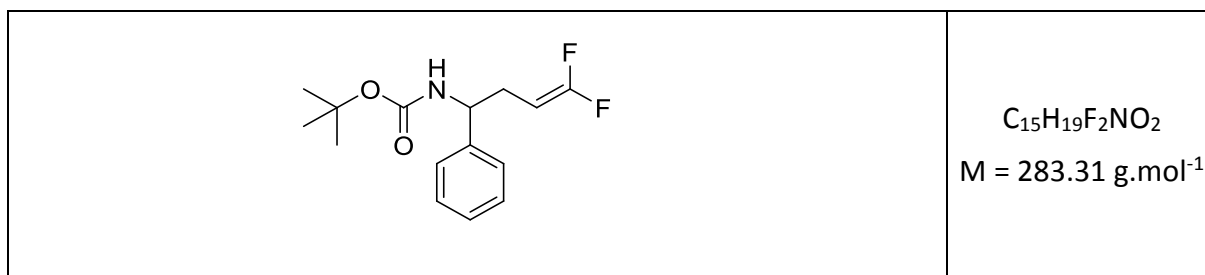
IR (σ , cm⁻¹, CCl₄) 1719, 1489, 1168

MS (CI) $m/z = 284 \text{ (M+H}^+)$, $301 \text{ (M+NH}_4^+)$

HRMS (EI) Calcd for $C_{15}H_{20}ClF_2NO_2$: 319.1151 Found: NF

tert-butyl 4,4-difluoro-1-phenylbut-3-enylcarbamate

IV-15f



Following general procedure IV-F1, the reaction was carried out using **IV-14f** (60 mg, 0.19 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20) to afford **IV-15f** (32 mg, 60%) as an amorphous white solid.

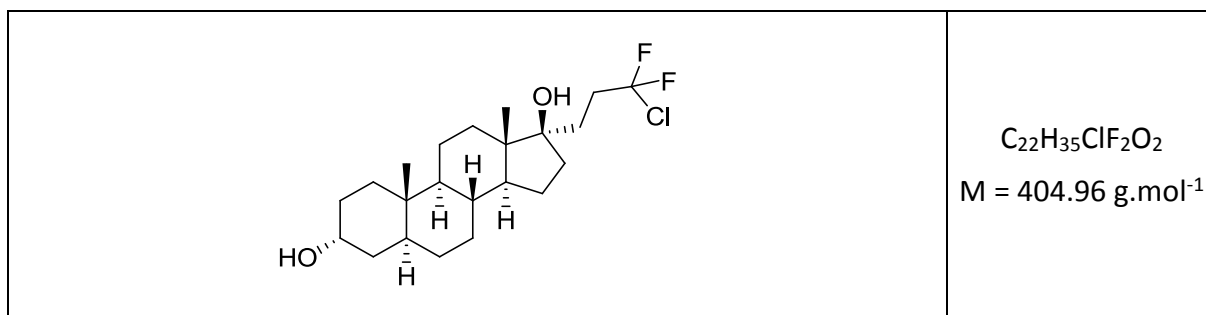
$^1\text{H NMR}$ (δ , ppm) 7.37 – 7.23 (m, 5H), 4.82 (bs, 1H), 4.70 (bs, 1H), 4.09 (dtd, $J = 25.1, 7.9, 2.2$ Hz, 1H), 2.49 – 2.43 (m, 2H), 1.42 (s, 9H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 157.0 (dd, $J = 288, 287$ Hz), 155.2, 141.4, 128.7 (2C), 127.6, 126.3 (2C), 79.8, 74.36 (dd, $J = 24, 20$ Hz) 54.3, 29.8, 28.4 (3C).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1747, 1720, 1543, 1490, 1168

MS (CI) $m/z = 320$ ($\text{M}+\text{H}^+$), 337 ($\text{M}+\text{NH}_4^+$)

HRMS (EI) Calcd for $C_{15}H_{20}ClF_2NO_2$: 283.1384 Found: NF

(3R,5S,8R,9S,10S,13S,14S,17R)-17-(3-chloro-3,3-difluoropropyl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthrene-3,17-diol**IV-14g**

Following general procedure IV-A, the reaction was carried out using (3R,5S,8R,9S,10S,13S,14S,17R)-10,13-dimethyl-17-vinylhexadecahydro-1H-cyclopenta[a]phenanthrene-3,17-diol (318 mg, 1.00 mmol), xanthate **IV-1** (646 mg, 1.5 mmol) and three portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford the corresponding xanthate adduct **IV-13g** (500 mg, 67%).

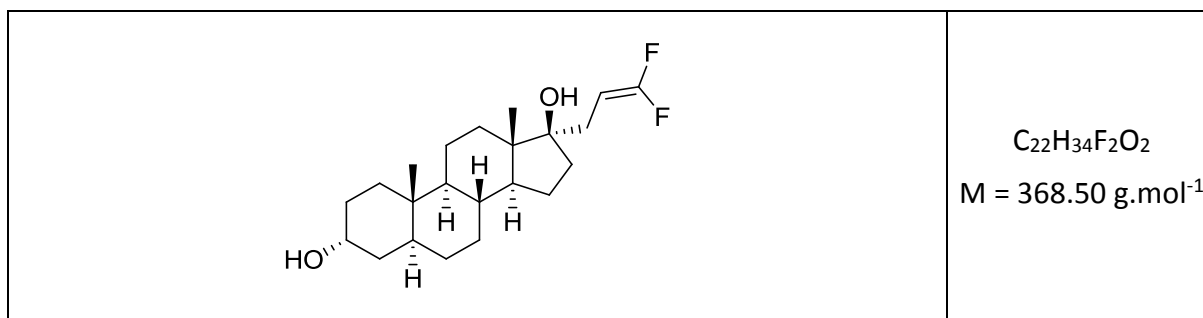
Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-13g** (494 mg, 0.66 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford the corresponding reduced product **IV-14g** (185 mg, 67%) as an amorphous white solid.

¹H NMR (δ , ppm) 3.69 – 3.59 (m, 1H), 2.72 – 2.55 (m, 1H), 2.55 – 2.37 (m, 1H), 1.95 – 1.81 (m, 3H), 1.80 – 0.93 (m, 24H), 0.91 (s, 3H), 0.87 (s, 3H), 0.73 – 0.64 (m, 1H).
(CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 130.8 (t, $J = 292$ Hz), 82.6, 71.3, 54.2, 50.6, 46.6, 44.9, 38.2, 37.1 (t, $J = 24$ Hz), 37.0, 36.4, 35.6, 35.0, 31.8, 31.7, 31.5, 30.2, 28.6, 23.7, 20.9, 14.4, 12.4.
(CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2933, 2859, 1543, 1039

HRMS (EI) Calcd for C₂₂H₃₅ClF₂O₂: 404.2294 Found: 404.2305

(3R,5S,8R,9S,10S,13S,14S,17R)-17-(3,3-difluoroallyl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthrene-3,17-diol**IV-15g**

Following general procedure IV-F1, the reaction was carried out using **IV-14g** (59 mg, 0.15 mmol). The residue was purified by silica gel column chromatography (EtOAc) to afford **IV-15g** (48 mg, 89%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 4.40 (dddd, $J = 25.9, 9.0, 6.5, 2.6$ Hz, 1H), 3.67 – 3.57 (m, 1H), 2.26 – 2.09 (m, 2H), 1.95 – 1.80 (m, 2H), 1.80 – 0.92 (m, 21H), 0.90 (s, 3H), 0.86 (s, 3H), 0.72 – 0.61 (m, 1H).
(CDCl_3 , 400 MHz)

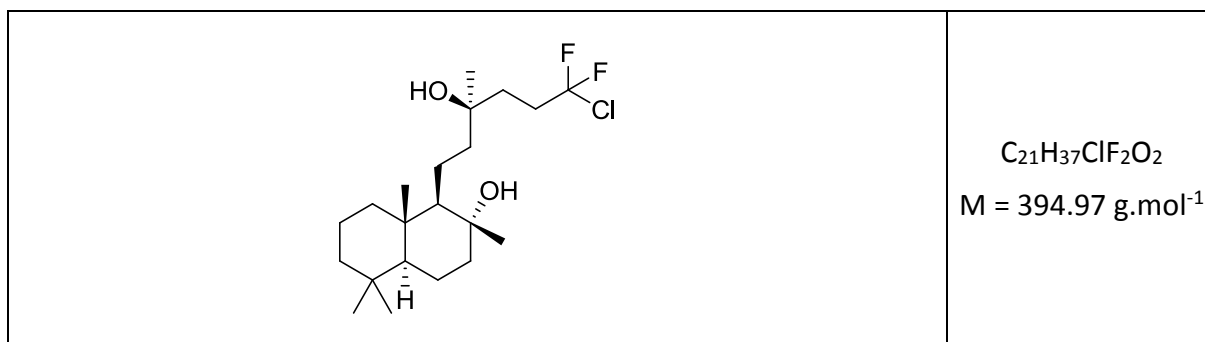
$^{13}\text{C NMR}$ (δ , ppm) 157.1 (dd, $J = 287, 285$ Hz), 83.0 (t, $J = 2$ Hz), 74.6 (dd, $J = 23, 20$ Hz), 71.3, 54.3, 50.7, 46.3, 44.9, 38.2, 37.1, 36.4, 35.6, 35.1, 31.8, 31.6, 31.5, 30.4 (d, $J = 4$ Hz), 28.6, 23.6, 20.9, 14.4, 12.4.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2928, 2855, 1746

HRMS (EI) Calcd for $C_{22}H_{34}F_2O_2$: 368.2527 Found: 368.2534

**(1R,2R,4aS,8aS)-1-((R)-6-chloro-6,6-difluoro-3-hydroxy-3-methylhexyl)-
2,5,5,8a-tetramethyldecahydronaphthalen-2-ol**

IV-14h



Following general procedure IV-A, the reaction was carried out using sclareol (308 mg, 1.00 mmol), xanthate **IV-1** (646 mg, 1.50 mmol) and two portions of lauroyl peroxyde. The crude mixture was used in the next step without any purification.

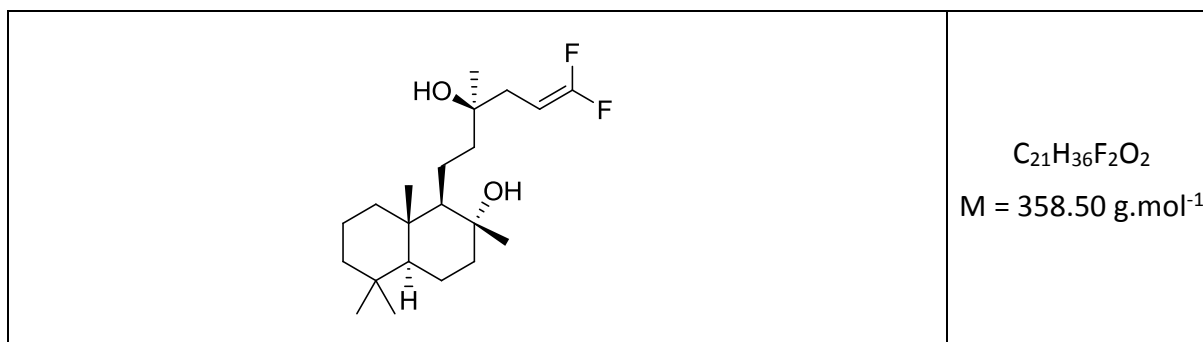
Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-13h** (~1 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20 to 50:50) to afford the corresponding reduced product **IV-14h** (220 mg, 56% over two steps) as an amorphous white powder.

¹H NMR (δ, ppm) 2.46 (m, 2H), 2.25 (bs, 2H), 1.88 (dt, *J* = 12.1, 3.1 Hz, 1H), 1.76 (dd, *J* = 9.5, 7.4 Hz, 2H), 1.73 – 1.55 (m, 6H), 1.52 – 1.25 (m, 6H), 1.23 (s, 3H), 1.22 (s, 3H), 1.21 – 1.16 (m, 1H), 1.01 – 0.95 (m, 2H), 0.91 (s, 3H), 0.84 (s, 3H), 0.83 (s, 3H).
(CDCl₃, 400 MHz)

¹³C NMR (δ, ppm) 130.6 (t, *J* = 291 Hz), 75.2, 71.8, 61.7, 56.0, 44.6, 44.4, 41.9, 39.7, 39.2, 36.9 (t, *J* = 23 Hz), 36.3, 33.4, 33.3, 25.7, 24.4, 21.5, 20.5, 18.8, 18.41, 15.4.
(CDCl₃, 100 MHz)

IR (σ, cm⁻¹, CCl₄) 3434, 2937, 2870, 1389, 1090

HRMS (EI) Calcd for C₂₁H₃₇ClF₂O₂ : 394.2450 Found: 394.2440

(1R,2R,4aS,8aS)-1-((R)-6,6-difluoro-3-hydroxy-3-methylhex-5-enyl)-2,5,5,8a-tetramethyldecahydronaphthalen-2-ol**IV-15h**

Following general procedure IV-F1, the reaction was carried out using **IV-14h** (50 mg, 0.13 mmol) to afford **IV-15h** (37 mg, 81%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 4.33 (dtd, $J = 25.5, 8.1, 2.7 \text{ Hz}$, 1H), 2.15 (dt, $J = 8.1, 1.5 \text{ Hz}$, 2H), 1.88 (dt, $J = 12.1, 3.1 \text{ Hz}$, 1H), 1.74 – 1.52 (m, 6H), 1.52 – 1.26 (m, 6H), 1.21 (s, 6H), 1.20 – 1.17 (m, 1H), 1.00 – 0.95 (m, 2H), 0.91 (s, 3H), 0.83 (s, 3H), 0.83 (s, 3H).¹⁴

$^{13}\text{C NMR}$ (δ , ppm) 156.9 (dd, $J = 287, 285 \text{ Hz}$), 75.0, 74.3 (dd, $J = 23, 20 \text{ Hz}$), 72.8 (t, $J = 2. \text{ Hz}$), 61.8, 56.0, 44.3, 44.2, 42.0, 39.6, 39.2, 36.3 (d, $J = 3 \text{ Hz}$), 33.4, 33.3, 25.6, 24.3, 21.5, 20.5, 18.8, 18.4, 15.4.

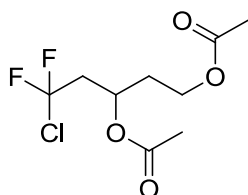
IR (σ , cm^{-1} , CCl_4) 3428, 2928, 1870, 1747, 1459, 1389

HRMS (EI) Calcd for $C_{21}H_{36}F_2O_2$: 358,2683 Found: 358.2686

¹⁴ Alcoholic hydrogens not visible in nmr

5-chloro-5,5-difluoropentane-1,3-diyl diacetate

IV-14i



$C_9H_{13}ClF_2O_4$
 $M = 258.65 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-A,¹⁵ the reaction was carried out using vinyl acetate (340 mg, 4 mmol), xanthate **IV-1** (862 mg, 2 mmol) and four portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 85:15) to afford the corresponding xanthate adduct **IV-13i** (dimer) (650 mg, 55%).

Following general procedure IV-B, the reaction was carried out using the latter xanthate adduct **IV-13i** (640 mg, 1.10 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20 to 40:60) to afford the corresponding reduced product **IV-14i** (200 mg, 70%) as a pale yellow oil.

¹H NMR (δ , ppm) 5.47 – 5.38 (m, 1H), 4.18 – 4.12 (m, 2H), 2.75 (dddd, $J = 15.3, 13.9, 11.0, 7.9 \text{ Hz}$, 1H), 2.60 (dddd, $J = 15.3, 13.9, 13.0, 4.0 \text{ Hz}$, 1H), 2.10 (s, 6H), 2.07 – 1.94 (m, 2H).
 (CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 170.9, 169.9, 127.7 (t, $J = 293 \text{ Hz}$), 65.7 (t, $J = 3 \text{ Hz}$), 60.0, 45.7 (t, $J = 24 \text{ Hz}$), 33.1, 21.0, 20.9.
 (CDCl₃, 100 MHz)

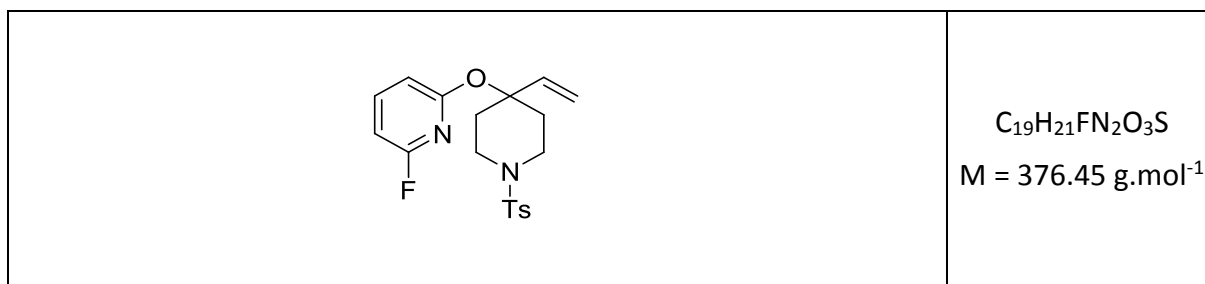
IR (σ , cm⁻¹, CCl₄) 1751, 1366, 1227, 1111

HRMS (EI) Calcd for C₉H₁₃ClF₂O₄ : 258.0470 Found: 258.0470

¹⁵ The olefin/xanthate ratio was changed for this example

2-fluoro-6-(1-tosyl-4-vinylpiperidin-4-yloxy)pyridine

IV-16a



Following general procedure IV-D, the reaction was carried out using 1-tosyl-piperidin-4-one (2.26 g, 6.30 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford the corresponding fluoropyridine derivative **IV-16a** (1.70 g, 45 %) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.69 (d, $J = 8.3$ Hz, 2H), 7.59 (dd, $J = 16.4, 8.0$ Hz, 1H), 7.35 (d, $J = 8.0$ Hz, 2H), 6.49 – 6.42 (m, $J = 7.8, 2.3$ Hz, 2H), 6.18 (dd, $J = 17.7, 11.0$ Hz, 1H), 5.24 (d, $J = 11.6$ Hz, 1H), 5.20 (d, $J = 5.0$ Hz, 1H), 3.62 (dt, $J = 11.8, 3.3$ Hz, 2H), 2.80 (td, $J = 11.9, 2.5$ Hz, 2H), 2.62 – 2.54 (m, 2H), 2.47 (s, 3H), 2.00 (ddd, $J = 14.2, 12.1, 4.5$ Hz, 2H).

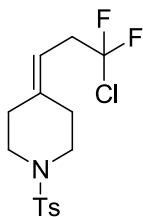
$^{13}\text{C NMR}$ (δ , ppm) 161.4 (d, $J = 161.4$ Hz), 161.3 (d, $J = 240$ Hz), 143.4, 142.4 (d, $J = 8$ Hz), 140.7, 133.1, 129.7 (2C), 127.7 (2C), 115.5, 108.9 (d, $J = 5$ Hz), 100.7 (d, $J = 36$ Hz), 78.9, 42.1 (2C), 34.6 (2C), 21.6.

IR (σ , cm^{-1} , CCl_4) 2929, 1731, 1608, 1574, 1452, 1440, 1360, 1231, 1169

HRMS (EI) Calcd for $C_{19}H_{21}FN_2O_3S$: 376.1257 Found: NF

4-(3,3-difluoroallylidene)-1-tosylpiperidine

IV-17a

	$C_{15}H_{18}ClF_2NO_2S$ $M = 349.82 \text{ g}\cdot\text{mol}^{-1}$
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Following general procedure IV-E1, the reaction was carried out using olefin **IV-16a** (752 mg, 2.00 mmol), xanthate **IV-1** (438 mg, 1.00 mmol) and five portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 90:10) to afford **IV-17a** (270 mg, 77%).

$^1\text{H NMR}$ (δ , ppm) 7.67 (d, $J = 8.1$ Hz, 2H), 7.36 (d, $J = 7.9$ Hz, 2H), 5.28 (t, $J = 7.5$ Hz, 1H), 3.09 (dt, $J = 9.4, 5.8$ Hz, 4H), 2.99 (td, $J = 12.7, 7.5$ Hz, 2H), 2.46 (s, 3H), 2.40 – 2.35 (m, 4H).
(CDCl_3 , 400 MHz)

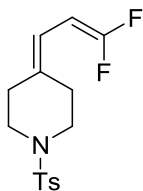
$^{13}\text{C NMR}$ (δ , ppm) 143.7, 140.7, 133.3, 129.8 (2C), 128.8 (t, $J = 292$ Hz), 127.6 (2C), 113.4 (t, $J = 4$ Hz), 47.6, 46.8, 39.8 (t, $J = 25$ Hz), 35.3, 28.1, 21.6.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2926, 2847, 1361, 1250, 1168, 1103, 1018

HRMS (EI) Calcd for $C_{15}H_{17}F_2NO_2S$: 349.0715 Found: 349.0719

4-(3,3-difluoroallylidene)-1-tosylpiperidine

IV-20a

	$C_{15}H_{17}F_2NO_2S$ $M = 313.36 \text{ g}\cdot\text{mol}^{-1}$
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Following general procedure IV-F2, the reaction was carried out using **IV-17a** (40 mg, 0.11 mmol) to afford **IV-20a** (29 mg, 81%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.66 (d, $J = 8.2$ Hz, 2H), 7.34 (d, $J = 8.2$ Hz, 2H), 5.72 (d, $J = 11.3$ Hz, 1H), 5.02 (ddd, $J = 23.7, 11.3, 2.0$ Hz, 1H), 3.10 – 3.03 (m, $J = 12.7, 6.4$ Hz, 4H), 2.45 (s, 3H), 2.39 – 2.33 (m, 4H).
(CDCl_3 , 400 MHz)

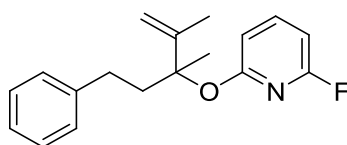
$^{13}\text{C NMR}$ (δ , ppm) 157.0 (dd, $J = 296, 290$ Hz), 143.7, 135.6 (dd, $J = 11, 3$ Hz), 133.2, 129.7 (2C), 127.6 (2C), 113.1 (d, $J = 2$ Hz), 77.6 (dd, $J = 26, 15$ Hz), 47.7, 46.9, 35.2, 28.1, 21.5.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2927, 1704, 1362, 1167

HRMS (EI) Calcd for $C_{15}H_{17}F_2NO_2S$: 313.0948 Found: 313.0956

2-(2,3-dimethyl-5-phenylpent-1-en-3-yloxy)-6-fluoropyridine

IV-16b



$C_{18}H_{20}FNO$
 $M = 285.36 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with 2-bromopropen (670 μL , 7.50 mmol), 6 mL of Et_2O and cooled to -78°C . $t\text{BuLi}$ (1.8 M, 15 mmol) was added over 10 minutes and the solution was allowed to warm to room temperature for 1 minute. The reaction was cooled to -78°C and a solution of 4-phenylbutan-2-one (888 g, 6.00 mmol) in Et_2O (6 mL) was added slowly. The solution was stirred until total consumption of the starting ketone and then quenched with NH_4Cl sat. 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 to afford the corresponding allylic alcohol (~quantitative).

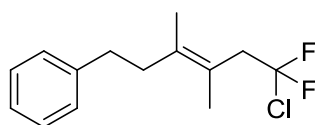
Following literature procedure,¹⁶ a magnetically stirred round bottom flask was charged with the latter alcohol (1.14 g, 6.00 mmol), 2,6-difluoropyridine (863 μL , 12 mmol) and dry DMSO (6 mL). NaH (60% in mineral oil) (360 mg, 9 mmol) was added in one portion and the resulting suspension was heated up to 50°C . The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and then quenched with water. 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 purification by flash chromatography (petroleum ether/diethyl ether 99:1) yielded the desired fluoropyridyl ether **IV-16b** (1.42 g, 83% over two steps) as colourless oil.

$^1\text{H NMR}$ (δ , ppm) 7.65 (q, $J = 8.1 \text{ Hz}$, 1H), 7.35 – 7.28 (m, 2H), 7.25 – 7.18 (m, 3H), 6.65 (d, $J = 8.0 \text{ Hz}$, 1H), 6.48 (dd, $J = 7.8, 2.7 \text{ Hz}$, 1H), 5.08 (s, 1H), 5.03 (s, 1H), 2.72 – 2.65 (m, 2H), 2.44 – 2.34 (m, 1H), 2.31 – 2.20 (m, 1H), 1.83 (s, 3H), 1.79 (s, 3H).

¹⁶ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

(6-chloro-6,6-difluoro-3,4-dimethylhex-3-enyl)benzene

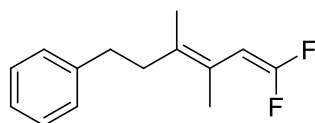
IV-17b



$C_{14}H_{17}ClF_2$
 $M = 258.73 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-E1, the reaction was carried out using olefin **IV-16b** (570 mg, 2 mmol), xanthate **IV-1** (538 mg, 1.22 mmol) and five portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether 100%) to afford **IV-17b** (314 mg, 84%) as colourless oil and as a mixture of (Z) and (E) isomers in a 3:7 ratio.

$^1\text{H NMR}$ (δ , ppm) 7.37 – 7.30 (m, 2H), 7.27 – 7.20 (m, 3H), 3.12 (t, $J = 14.1 \text{ Hz}$, 1.4H), 3.00 (t, $J = 14.1 \text{ Hz}$, 0.6H), 2.77 – 2.69 (m, 2H), 2.43 (t, $J = 7.9 \text{ Hz}$, 2H), 1.80 (s, 3.9H), 1.72 (s, 2.1H).
 (CDCl_3 , 400 MHz)

(6,6-difluoro-3,4-dimethylhexa-3,5-dienyl)benzene**IV-20b**

$C_{14}H_{16}F_2$
 $M = 222.27 \text{ g}\cdot\text{mol}^{-1}$

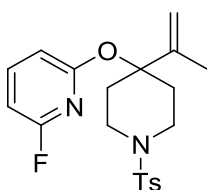
Following general procedure IV-F2, the reaction was carried out using **IV-17b** (50 mg, 0.19 mmol). Crude ^1H NMR revealed a conversion of 85%. Compound **IV-20b** appeared as a mixture of (Z) and (E) isomers in a 3:7 ratio.¹⁷

^1H NMR (δ , ppm) Isomer E :
 (CDCl_3 , 400 MHz) 7.36 – 7.30 (m, 2H), 7.26 – 7.20 (m, 3H), 5.10 (dd, $J = 27.3, 5.0$ Hz, 1H),
 2.76 – 2.68 (m, 2H), 2.47 – 2.39 (m, 2H), 1.78 (s, 3H), 1.77 (s, 3H).

¹⁷ We were not able to separate this compound from unpolar impurities.

2-fluoro-6-(4-(prop-1-en-2-yl)-1-tosylpiperidin-4-yloxy)pyridine

IV-16c



$C_{20}H_{23}F_2N_2O_3S$
 $M = 390.47 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with 2-bromopropen (670 μl , 7.50 mmol), 6 mL of Et_2O and cooled to -78°C . $t\text{BuLi}$ (1.8 M, 15 mmol) was added over 10 minutes and the solution was allowed to warm to room temperature for 1 minute. The reaction was cooled to -78°C and a solution of 1-tosyl-piperidin-4-one (1.52 g, 6.00 mmol) in Et_2O (6 mL) was added slowly. The solution was stirred until total consumption of the starting ketone and then quenched with NH_4Cl sat. 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 to afford the corresponding allylic alcohol (~quantitative).

Following literature procedure,¹⁸ a magnetically stirred round bottom flask was charged with the latter alcohol (1.18 g, 4.00 mmol), 2,6-difluoropyridine (367 μl , 5.10 mmol) and dry DMSO (4 mL). NaH (60% in mineral oil) (204 mg, 5.10 mmol) was added in one portion and the resulting suspension was heated up to 60°C . The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and then quenched with water. 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 purification by flash chromatography yielded the desired fluoropyridyl ether **IV-16c** (1000 mg, 45% over two steps) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.69 (d, $J = 8.3$ Hz, 2H), 7.58 (dd, $J = 16.3, 8.0$ Hz, 1H), 7.34 (d, $J = 8.1$ Hz, 2H), 6.48 – 6.42 (m, 2H), 5.00 (s, 1H), 4.97 (s, 1H), 3.72 (d, $J = 11.6$ Hz, 2H), 2.71 (td, $J = 12.4, 2.1$ Hz, 2H), 2.60 (dd, $J = 14.7, 2.0$ Hz, 2H), 2.47 (s, 3H), 1.98 (td, $J = 13.6, 4.6$ Hz, 2H), 1.72 (s, 3H).
 (CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 161.5 (d, $J = 240$ Hz), 161.2 (d, $J = 14$ Hz), 146.8, 143.4, 142.5 (d, $J = 8$ Hz), 133.7, 129.7 (2C), 127.7 (2C), 112.4, 108.2 (d, $J = 5$ Hz), 100.7 (d, $J = 36$ Hz), 80.5, 42.1 (2C), 33.8 (2C), 21.5, 18.7.
 (CDCl_3 , 100 MHz)

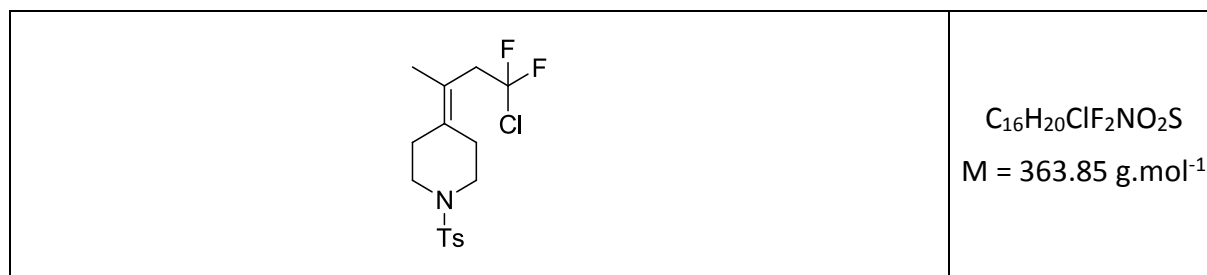
¹⁸ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

IR (σ , cm^{-1} , CCl_4) 1608, 1574, 1440, 1360, 1328, 1321, 1168

HRMS (EI) Calcd for $\text{C}_{20}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_3\text{S}$: 390.1413 Found: 390.1402

4-(4-chloro-4,4-difluorobutan-2-ylidene)-1-tosylpiperidine

IV-17c



Following general procedure IV-E1, the reaction was carried out using olefin **IV-16c** (600 mg, 1.53 mmol), xanthate **IV-1** (337 mg, 0.77 mmol) and five portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-17c** (190 mg, 68%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.63 (d, $J = 7.9$ Hz, 2H), 7.31 (d, $J = 7.9$ Hz, 2H), 3.10 – 2.95 (m, 6H), 2.42 (s, 3H), 2.41 – 2.35 (m, 4H), 1.74 (s, 3H).
(CDCl_3 , 400 MHz)

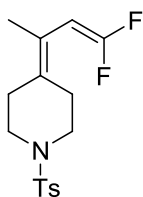
$^{13}\text{C NMR}$ (δ , ppm) 143.6, 134.7, 133.2, 129.7 (2C), 129.0 (t, $J = 294$ Hz), 127.7 (2C), 119.1, 47.0, 46.9, 45.6 (t, $J = 24$ Hz), 29.9, 29.4, 21.6, 19.4.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2926, 1363, 1168

HRMS (EI) Calcd for $C_{16}H_{20}ClF_2NO_2S$: 363.0871 Found: 363.0866

4-(4,4-difluorobut-3-en-2-ylidene)-1-tosylpiperidine

IV-20c



$C_{16}H_{19}F_2NO_2S$
 $M = 327.39 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-F2, the reaction was carried out using **IV-17c** (55 mg, 0.15 mmol) to afford after filtration through a silica plug (solvent: AcOEt) **IV-20c** (45 mg, 91%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.67 (d, $J = 8.0$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 4.97 (dd, $J = 26.6, 4.3$ Hz, 1H), 3.07 – 3.00 (m, 4H), 2.50 – 2.34 (m, 7H), 1.79 (s, 3H).
 (CDCl_3 , 400 MHz)

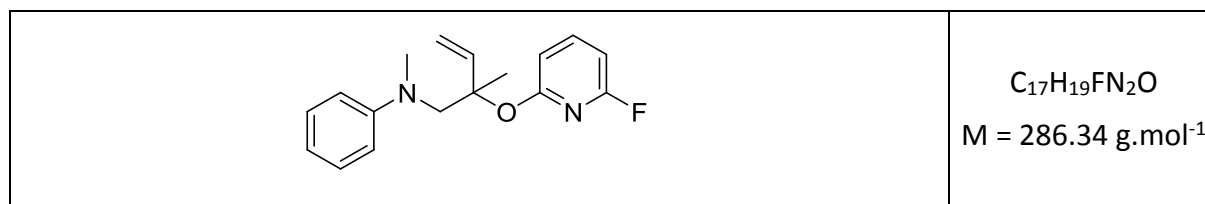
$^{13}\text{C NMR}$ (δ , ppm) 155.6 (dd, $J = 296, 287$ Hz), 143.6, 133.0, 131.8 (dd, $J = 6, 3$ Hz), 129.7 (2C), 127.7 (2C), 118.3 (t, $J = 5$ Hz), 80.9 (dd, $J = 27, 15$ Hz), 47.0 (2C), 29.9, 29.0, 21.6, 16.75.
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2929, 1716, 1363, 1169

HRMS (EI) Calcd for $C_{16}H_{19}F_2NO_2S$: 327.1105 Found: 327.1107

N-(2-(6-fluoropyridin-2-yloxy)-2-methylbut-3-enyl)-N-methylaniline

IV-16d

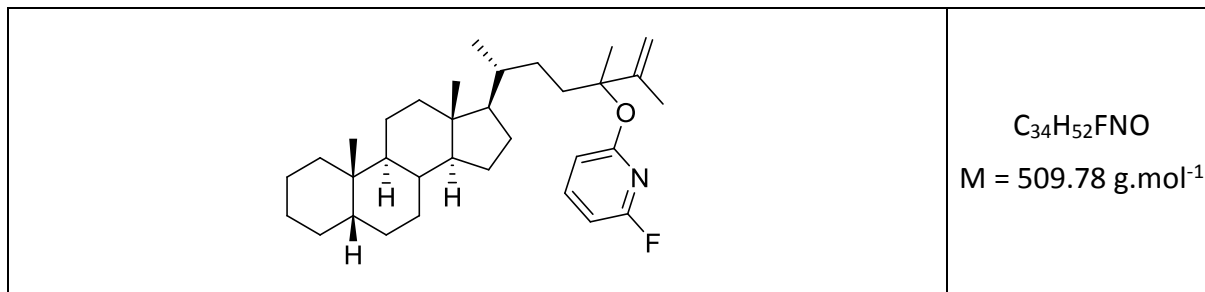


Following general procedure IV-D, the reaction was carried out using 1-(methyl(phenyl)amino)propan-2-one (1.2 g, 7.35 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 90:10) to afford the corresponding fluoropyridine derivative **IV-16d** (700 g, 33 %).

$^1\text{H NMR}$ (δ , ppm) 7.66 (q, $J = 8.1$ Hz, 1H), 7.32 (m, 2H), 6.94 (d, $J = 8.4$ Hz, 2H), 6.79 (t, $J = 7.2$ Hz, 1H), 6.64 (d, $J = 8.0$ Hz, 1H), 6.51 (dd, $J = 7.8, 2.4$ Hz, 1H), 6.26 (dd, $J = 17.6, 11.0$ Hz, 1H), 5.38 (d, $J = 17.6$ Hz, 1H), 5.30 (d, $J = 11.0$ Hz, 1H), 3.87 (d, $J = 15.5$ Hz, 1H), 3.82 (d, $J = 15.4$ Hz, 1H), 3.14 (s, 3H), 1.81 (s, 3H).
 (CDCl_3 , 400 MHz)

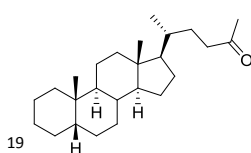
2-((6R)-6-((5S,9S,10S,13R,14S,17R)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2,3-dimethylhept-1-en-3-yloxy)-6-fluoropyridine

IV-16e



A magnetically stirred round bottom flask was charged with 2-bromopropene (273 μL , 3.07 mmol), 3 mL of THF and cooled to -78°C . $t\text{BuLi}$ (1.72 M, 6.14 mmol) was added over 10 minutes and the solution was allowed to warm to room temperature for 1 minute. The reaction was cooled to -78°C and a solution of ketone¹⁹ (1.00 g, 2.79 mmol) in THF (3 mL) was added slowly. The solution was stirred until total consumption of the starting ketone and then quenched with NH_4Cl sat. The layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were washed with brine and dried over anhydrous MgSO_4 to afford the corresponding allylic alcohol (~quantitative).

Following literature procedure,²⁰ a magnetically stirred round bottom flask was charged with the latter alcohol (2.79 mmol), 2,6-difluoropyridine (400 μl , 5.58 mmol) and dry DMSO (3 mL). NaH (60% in mineral oil) (145 mg, 3.63 mmol) was added in one portion and the resulting suspension was heated up to 60°C . The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and the quenched with water. 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 purification on flash chromatography (petroleum ether / diethyl ether 97:3) yielded the desired fluoropyridyl ether **IV-16e** (926 mg, 67% over two steps) as an amorphous white solid.



²⁰ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

Chapitre IV

¹H NMR²¹ (δ , ppm) 7.67 – 7.57 (m, 1H), 6.62 (d, J = 8.0 Hz, 1H), 6.45 (dd, J = 7.8, 2.8 Hz, 1H), 5.02 – 4.96 (m, 2H), 1.77 (s, 3H), 1.68 (s, 1.5H), 1.68 (s, 1.5H), 0.96 (s, 3H), 0.94 (d, J = 6.7 Hz, 3H), 0.67 (s, 3H).
(CDCl₃, 400 MHz)

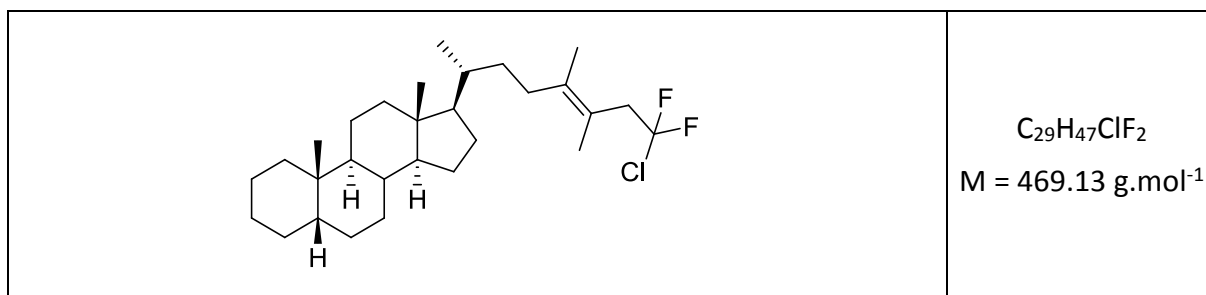
¹³C NMR (δ , ppm) 162.1 (d, J = 15 Hz), 161.7 (d, J = 239 Hz), 148.7, 142.1 (d, J = 8 Hz), 111.5, 108.3 (d, J = 5 Hz), 99.9 (d, J = 36 Hz), 85.8, 56.6, 55.8
(CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2925, 2863, 1611, 1572, 1439, 1231

HRMS (EI) Calcd for C₃₄H₅₂FNO : 509.4033 Found: NF

²¹ Only characteristic protons are reported

(5S,9S,10S,13R,14S,17R)-17-((R,E)-8-chloro-8,8-difluoro-5,6-dimethyloct-5-en-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthrene **IV-17e**



Following general procedure IV-E1, the reaction was carried out using olefin **IV-16e** (700 mg, 1.40 mmol), xanthate **IV-1** (306 mg, 0.70 mmol) and five portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether 100%) to afford **IV-17e** (246 mg, 77%) as an amorphous white solid and as a mixture of (Z) and (E) isomers in a 1:3 ratio.

$^1\text{H NMR}^{22}$ (δ , ppm) 3.11 (m, 2H), 1.82 (s, 3H), 1.76 (s, 3H), 0.98 (s, 3H), 0.70 (s, 3H).

(CDCl_3 , 400 MHz)

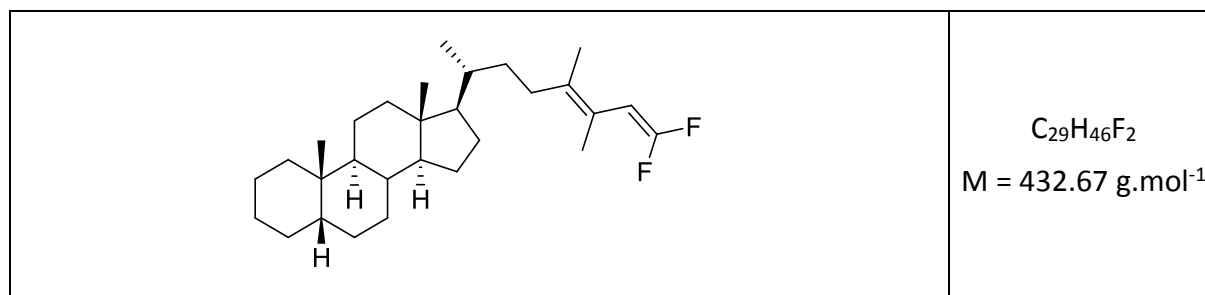
$^{13}\text{C NMR}$ (δ , ppm) 137.9, 129.9 (t, $J = 293 \text{ Hz}$), 118.5, 56.7, 56.0, 46.5 (t, $J = 23 \text{ Hz}$), 43.8, 42.8, 40.6, 40.3, 37.7, 35.9, 35.8, 35.4, 33.8, 31.47, 28.4, 27.6, 27.3, 27.1, 26.6, 24.3 (2C), 21.4, 20.9, 19.3, 19.2, 18.8, 12.1.

(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2931, 2863, 1450, 1377; 1199, 1090

HRMS (EI) Calcd for $C_{29}H_{47}ClF_2$: 468.3334 Found: 468.3332

²² Only characteristic protons are reported

(5S,9S,10S,13R,14S,17R)-17-((R,E)-8,8-difluoro-5,6-dimethylocta-5,7-dien-2-yl)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthrene**IV-20d**

Following general procedure IV-F2, the reaction was carried out using **IV-17e** (210 mg, 0.45 mmol) to afford **IV-20d** (180 mg, 93%) as an amorphous white solid and as a mixture of (Z) and (E) isomers in a 1:3 ratio.²³

¹H NMR²⁴ (δ , ppm) 5.10 (dd, $J = 27.4, 5.2$ Hz, 1H), 1.85 (s, 3H), 1.72 (s, 3H), 1.01 (d, $J = 6.5$ Hz, 3H), 0.96 (s, 3H), 0.69 (s, 3H).
(CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 155.2 (dd, $J = 297, 285$ Hz), 135.3 (dd, $J = 7, 4$ Hz), 117.8 (t, $J = 5$ Hz), 82.0 (dd, $J = 27, 14$ Hz), 56.7, 56.0, 43.8, 42.8, 40.6, 40.3, 37.6, 36.0, 35.9, 35.4, 34.0, 31.2, 28.4, 27.6, 27.3, 27.1, 26.6, 24.3 (2C), 21.4, 20.9, 19.4, 18.8, 16.4 (d, $J = 5$ Hz), 12.1.
(CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2931, 2863, 1716, 1450, 1376, 1347, 1203

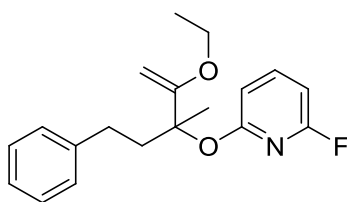
HRMS (EI) Calcd for C₂₉H₄₆F₂ : 432.3568 Found: 432.3577

²³ In this example the organic phase washed twice with aqueous HCl 1N during the work-up

²⁴ Only characteristic protons of the major diastereoisomer are reported

2-(2-ethoxy-3-methyl-5-phenylpent-1-en-3-yloxy)-6-fluoropyridine

IV-18a



$C_{19}H_{22}FNO_2$
 $M = 311.42 \text{ g}\cdot\text{mol}^{-1}$

Following literature procedure,²⁵ a magnetically stirred round bottom flask was charged with vinyl ethyl ether (2.8 mL, 30.00 mmol), 6 mL of THF and cooled to $-78 \text{ }^\circ\text{C}$. $t\text{BuLi}$ (1.7 M, 14.40 mmol) was added slowly and the solution was allowed to warm to room temperature for 10 minutes. The reaction was cooled to $-78 \text{ }^\circ\text{C}$ and a solution of 4-phenylbutan-2-one (888 mg, 6.00 mmol) in THF (6 mL) was added slowly. The solution was stirred until total consumption of the starting ketone and then quenched with NH_4Cl sat. 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 to afford the corresponding allylic alcohol (~quantitative).

Following literature procedure,²⁶ a magnetically stirred round bottom flask was charged with the latter alcohol (1.32 mg, 6 mmol), 2,6-difluoropyridine (650 μL , 9.00 mmol) and dry DMSO (4.5 mL). NaH (60% in mineral oil) (288 mg, 7.2 mmol) was added in one portion and the resulting suspension was heated up to $60 \text{ }^\circ\text{C}$. The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and the quenched with water. 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 purification by flash chromatography (petroleum ether/diethyl ether 95:5) yielded the desired fluoropyridyl ether **IV-18a** (850 mg, 45% over two steps) as colourless oil.

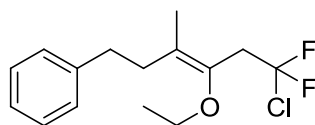
$^1\text{H NMR}$ (δ , ppm) 7.65 (q, $J = 8.2 \text{ Hz}$, 1H), 7.34 – 7.27 (m, 2H), 7.23 – 7.18 (m, 3H), 6.67 (d, $J = 8.0 \text{ Hz}$, 1H), 6.49 (dd, $J = 7.8, 2.4 \text{ Hz}$, 1H), 4.39 (s, 1H), 4.12 (s, 1H), (CDCl₃, 400 MHz) 3.84 – 3.71 (m, 2H), 2.73 – 2.66 (m, 2H), 2.51 – 2.32 (m, 2H), 1.81 (s, 3H), 1.26 (t, $J = 6.7 \text{ Hz}$, 3H).

²⁵ Debien, L; Quiclet-Sire, B; Zard, S. Z. *Org. Lett.* **2011**, *13*, 5676

²⁶ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

Chapitre IV

¹³C NMR (δ , ppm) 163.4, 161.9 (d, $J = 16$ Hz), 161.6 (d, $J = 239$ Hz), 142.5, 142.0 (d, $J = 8$ Hz), 128.4 (2C), 128.3 (2C), 125.6, 108.9 (d, $J = 5$ Hz), 100.1 (d, $J = 36$ Hz), 83.4, 81.5, 63.1, 40.8, 30.3, 23.5, 14.4.
(CDCl₃, 100 MHz)

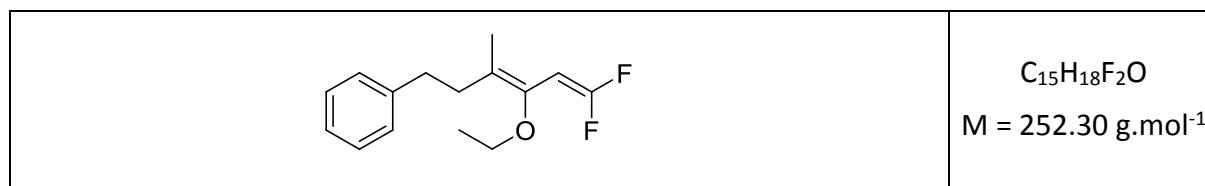
(6-chloro-4-ethoxy-6,6-difluoro-3-methylhex-3-enyl)benzene**IV-19a**

$C_{15}H_{19}ClF_2O$
 $M = 288.76 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-E2, the reaction was carried out using olefin **IV-18a** (630 then 100 mg, 2.0 + 0.3 mmol), xanthate **IV-1** (438 mg, 1 mmol) and five portions of lauroyl peroxyde. The residue was dissolved in 5 mL of ethyl acetate, 2.5 mL of aqueous HCl (2N) was added and the mixture was stirred for 1 hour.²⁷ The layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Removal of the solvent and purification on flash chromatography (petroleum ether/diethyl ether 90:10) afford **IV-19a** (195 mg, 68%) as a colourless oil and as a mixture of (Z) and (E) isomers in a 35:65 ratio.

1H NMR (δ , ppm) 7.36 – 7.31 (m, 2H), 7.27 – 7.19 (m, 3H), 3.67 (q, $J = 7.0$ Hz, 0.7H), 3.56 (q, $J = 7.0$ Hz, 1.3H), 3.23 (t, $J = 13.1$ Hz, 1.3H), 2.99 (t, $J = 13.1$ Hz, 0.7H), 2.78 – 2.72 (m, 2H), 2.54 – 2.48 (m, 1.3H), 2.38 – 2.31 (m, 0.7H), 1.84 (s, 1.05H), 1.75 (s, 1.95H), 1.27 (d, $J = 7.0$ Hz, 3H).

²⁷ Selective deprotection of the starting enol ether

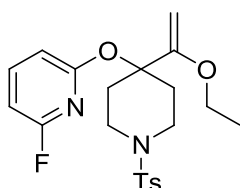
(4-ethoxy-6,6-difluoro-3-methylhexa-3,5-dienyl)benzene**IV-20e**

Following general procedure IV-F2, the reaction was carried out using **IV-19a** (50 mg, 0.17 mmol). The residue was purified by silica gel column chromatography (petroleum ether/diethyl ether 95:5) to afford **IV-20e** (38 mg, 90%) as a colourless oil and as a mixture of (Z) and (E) isomers in a 35:65 ratio.

¹H NMR (δ, ppm) 7.36 – 7.30 (m, 2H), 7.27 – 7.20 (m, 3H), 4.92 (dd, *J* = 25.4, 3.4 Hz, 0.65H), 4.78 (dd, *J* = 25.1, 4.0 Hz, 0.35H), 3.67 (q, *J* = 7.0 Hz, 0.7H), 3.54 (q, *J* = 7.0 Hz, 1.3H), 2.78 – 2.70 (m, 2H), 2.55 – 2.48 (m, 1.3H), 2.37 – 2.32 (m, 0.7H), 1.82 (s, 1.05H), 1.71 (s, 1.95H), 1.25 (t, *J* = 7.0 Hz, 1H).

2-(4-(1-ethoxyvinyl)-1-tosylpiperidin-4-yloxy)-6-fluoropyridine

IV-18b

C₂₁H₂₅FN₂O₄S

M = 420.4976

g.mol⁻¹

Following literature procedure,²⁸ a magnetically stirred round bottom flask was charged with vinyl ethyl ether (2.8 mL, 30.00 mmol), 6mL of THF and cooled to -78 °C. ^tBuLi (1.7 M, 14.40 mmol) was added slowly and the solution was allowed to warm to room temperature for 10 minutes. The reaction was cooled to -78 °C and a solution of 1-tosyl-piperidin-4-one (1.52 g, 6.00 mmol) in THF (6 mL) was added slowly. The solution was stirred until total consumption of the starting ketone and then quenched with NH₄Cl sat. The layers were partitioned and the aqueous one was extracted twice with Et₂O. The combined organic layers were washed with brine and dried over anhydrous MgSO₄ to afford the corresponding allylic alcohol (1460 mg, 4.50 mmol).

Following literature procedure,²⁹ a magnetically stirred round bottom flask was charged with the latter alcohol (1460 mg, 4.50 mmol), 2,6-difluoropyridine (650 µl, 9.00 mmol) and dry DMSO (4.5 mL). NaH (60% in mineral oil) (200 mg, 5.00 mmol) was added in one portion and the resulting suspension was heated up to 60 °C. The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and the quenched with water. Et₂O was added, the layers were partitioned and the aqueous one was extracted twice with Et₂O. The combined organic layers were washed with brine and dried over anhydrous MgSO₄. Removal of the solvent and purification by flash chromatography (petroleum ether / ethyl acetate 80:20) yielded the desired fluoropyridyl ether **IV-18b** (1.26 mg, 50% over two steps) as an amorphous white solid.

¹H NMR (δ, ppm) (CDCl₃, 400 MHz) 7.69 (d, *J* = 8.3 Hz, 2H), 7.58 (q, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.49 (dd, *J* = 7.9, 1.3 Hz, 1H), 6.44 (dd, *J* = 7.8, 2.7 Hz, 1H), 4.18 (d, *J* = 3.1 Hz, 1H), 4.03 (d, *J* = 3.1 Hz, 1H), 3.71 – 3.66 (m, 2H), 3.64 (q, *J* = 7.0 Hz, 2H), 2.76 (td, *J* = 12.1, 2.4 Hz, 2H), 2.64 – 2.57 (m, 2H), 2.46 (s, 3H), 2.14 – 2.05 (m, 2H), 1.14 (t, *J* = 7.0 Hz, 3H).

²⁸ Debien, L; Quiclet-Sire, B; Zard, S. Z. *Org. Lett.* **2011**, *13*, 5676

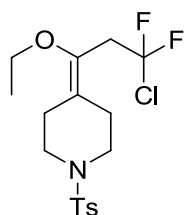
²⁹ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

Chapitre IV

¹³C NMR (δ , ppm) 162.2, 161.4 (d, $J = 239.7$ Hz), 161.3 (d, $J = 14.5$ Hz), 143.4, 142.2 (d, $J = 7.9$ Hz), 133.6, 129.7 (2C), 127.7 (2C), 108.8 (d, $J = 5.2$ Hz), 100.8 (d, $J = 36.0$ Hz), 82.5, 79.1, 63.1, 42.1 (2C), 33.6 (2C), 21.6, 14.1.

4-(3-chloro-1-ethoxy-3,3-difluoropropylidene)-1-tosylpiperidine

IV-19b



$C_{17}H_{22}ClF_2NO_3S$
 $M = 393.88 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-E2, the reaction was carried out using olefin **IV-18b** (672 then 126 mg, 1.60 + 0.40 mmol), xanthate **IV-1** (350 mg, 0.80 mmol) and five portions of lauroyl peroxyde. The residue was dissolved in 5 mL of ethyl acetate, 2.5 mL of aqueous HCl (2N) was added and the mixture was stirred for 1 hour.³⁰ The layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Removal of the solvent and purification on flash chromatography (petroleum ether / ethyl acetate 80:20) afford **IV-19b** (170 mg, 86%).

1H NMR (δ , ppm) 7.64 (d, $J = 8.1$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 3.63 (q, $J = 7.0$ Hz, 2H), 3.16 (t, $J = 13.0$ Hz, 2H), 3.06 – 2.99 (m, 4H), 2.51 (t, $J = 5.7$ Hz, 2H), 2.43 (s, 3H), 2.32 (t, $J = 5.6$ Hz, 2H), 1.23 (t, $J = 7.0$ Hz, 3H).
 (CDCl₃, 400 MHz)

^{13}C NMR (δ , ppm) 143.7, 139.8 (t, $J = 2.5$ Hz), 133.1, 129.7 (2C), 127.9 (t, $J = 293.9$ Hz), 127.6 (2C), 124.2, 65.7, 46.9 (2C), 39.5 (t, $J = 25.1$ Hz), 28.6, 26.3, 21.5, 15.2.
 (CDCl₃, 100 MHz)

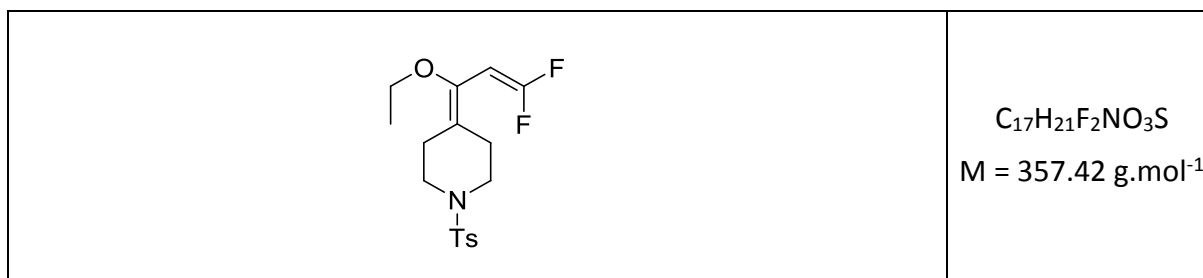
IR (σ , cm⁻¹, CCl₄) 2929, 1717, 1362, 1168

HRMS (EI) Calcd for $C_{17}H_{22}ClF_2NO_3S$: 393.0977 Found: NF

³⁰ Selective deprotection of the starting enol ether

4-(1-ethoxy-3,3-difluoroallylidene)-1-tosylpiperidine

IV-20f



Following general procedure IV-F2, the reaction was carried out using **IV-19b** (90 mg, 0.23 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford **IV-20f** (37 mg, 45%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.67 (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 4.82 (dd, $J = 24.7, 3.1$ Hz, 1H), 3.65 (q, $J = 7.0$ Hz, 2H), 3.03 (t, $J = 5.4$ Hz, 4H), 2.54 (t, $J = 5.8$ Hz, 2H), 2.47 (s, 3H), 2.29 (t, $J = 5.4$ Hz, 2H), 1.23 (t, $J = 7.0$ Hz, 3H).
(CDCl_3 , 400 MHz)

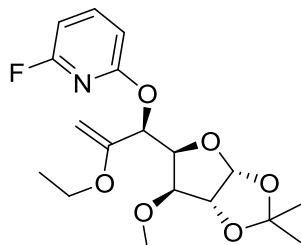
$^{13}\text{C NMR}$ (δ , ppm) 156.0 (dd, $J = 298, 290$ Hz), 143.6, 138.0 (dd, $J = 8, 5$ Hz), 133.1, 129.7 (2C), 127.7 (2C), 121.0 (dd, $J = 6, 3$ Hz), 75.0 (dd, $J = 28, 15$ Hz), 66.1, 47.0, 46.9, 28.4, 26.0, 21.6, 15.04.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2929, 1741, 1716, 1362, 1168

HRMS (EI) Calcd for $C_{17}H_{21}F_2NO_3S$: 357.1210 Found: NF

2-((S)-2-ethoxy-1-((3aR,5S,6S,6aR)-6-methoxy-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)allyloxy)-6-fluoropyridine

IV-18c

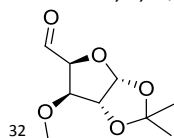


$C_{18}H_{24}FNO_6$
 $M = 369.38 \text{ g}\cdot\text{mol}^{-1}$

Following literature procedure,³¹ a magnetically stirred round bottom flask was charged with vinyl ethyl ether (3.36 mL, 35.00 mmol), 7 mL of THF and cooled to -78°C . $t\text{BuLi}$ (1.7 M, 16.80 mmol) was added slowly and the solution was allowed to warm to room temperature for 10 minutes. The reaction was cooled to -78°C and a solution of aldehyde³² (1.41 g, 7.00 mmol) in THF (7 mL) was added slowly. The solution was stirred until total consumption of the starting aldehyde and then quenched with NH_4Cl sat. 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 to afford the corresponding allylic alcohol.

Following literature procedure,³³ a magnetically stirred round bottom flask was charged with the latter alcohol (crude residue), 2,6-difluoropyridine (1 mL, 14.00 mmol) and dry DMSO (7 mL). NaH (60% in mineral oil) (360 mg, 9.1 mmol) was added in one portion. The reaction mixture was stirred until total conversion of the starting alcohol, cooled to room temperature and the quenched with water. 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 purification on flash chromatography (petroleum ether / diethyl ether 80:20) yielded the desired fluoropyridyl ether **IV-18c** (1.29 mg, 50% over two steps) as an amorphous white solid.

³¹ Debien, L; Quiclet-Sire, B; Zard, S. Z. *Org. Lett.* **2011**, *13*, 5676



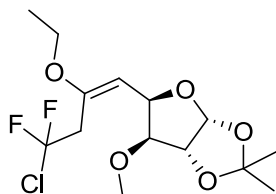
³² this aldehyde was prepared from diacetone D-glucose in three steps according to literature procedures: (a) Yan, S.; Klemm, D. *Tetrahedron* **2002**, *58*, 10065. (b) Petitou, M.; Sinay, P. *Eur. J. Org. Chem.* **2002**, *67*, 3595

³³ Charrier, N.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2008**, *130*, 8898.

Chapitre IV

¹H NMR (δ, ppm) (CDCl ₃ , 400 MHz)	7.72 – 7.64 (m, 1H), 6.67 (dd, <i>J</i> = 8.0, 0.9 Hz, 1H), 6.50 (dd, <i>J</i> = 7.8, 2.3 Hz, 1H), 5.96 (d, <i>J</i> = 3.6 Hz, 1H), 5.68 (d, <i>J</i> = 9.7 Hz, 1H), 4.69 (dd, <i>J</i> = 9.7, 3.1 Hz, 1H), 4.58 (d, <i>J</i> = 3.7 Hz, 1H), 4.53 (d, <i>J</i> = 2.0 Hz, 1H), 4.24 (d, <i>J</i> = 1.5 Hz, 1H), 3.88 – 3.75 (m, 3H), 3.16 (s, 3H), 1.55 (s, 3H), 1.36 (s, 3H), 1.32 (t, <i>J</i> = 7.0 Hz, 3H).
¹³C NMR (δ, ppm) (CDCl ₃ , 100 MHz)	161.9 (d, <i>J</i> = 241 Hz), 161.7 (d, <i>J</i> = 14 Hz), 157.3, 142.7 (d, <i>J</i> = 8 Hz), 111.9, 107.1 (d, <i>J</i> = 5 Hz), 105.5, 100.7 (d, <i>J</i> = 36 Hz), 87.7, 83.5, 81.6, 78.6, 73.5, 63.2, 57.8, 27.0, 26.6, 14.3.
IR (σ, cm ⁻¹ , CCl ₄)	2992, 2935, 1737, 1620, 1578, 1450, 1327, 1233, 1080, 1021
HRMS (EI)	Calcd for [C ₁₅ H ₁₇ FNO ₆] ⁺ : 326.1040 ³⁴ Found: 326.1037

³⁴ Enol ether deprotected and loss of CH₃.

(3a*S*,5*S*,6*R*,6a*S*)-5-((*E*)-4-chloro-2-ethoxy-4,4-difluorobut-1-enyl)-6-methoxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole**IV-19c**

$C_{14}H_{21}ClF_2O_5$
 $M = 342.76 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-E2, the reaction was carried out using olefin **IV-18c** (630 then 63 mg, 1.70 + 0.17 mmol), xanthate **IV-1** (373 mg, 0.85 mmol) and five portions of lauroyl peroxyde to afford a mixture of the desired product and starting olefin (76% yield). 120 mg of the residue were dissolved in 1 mL of ethyl acetate, 0.5 mL of acetic acid and 0.1 mL of water were added and the mixture was stirred at 35 °C for 6 hour.³⁵ Removal of the solvent and purification by flash chromatography (petroleum ether / ethyl acetate 90:10) afforded **IV-19c** (40 mg, 85%). Overall yield : 64%

¹H NMR (δ , ppm) 5.91 (d, $J = 3.9$ Hz, 1H), 4.98 (d, $J = 9.3$ Hz, 1H), 4.79 (dd, $J = 9.3, 3.0$ Hz, 1H), 4.63 (dd, $J = 8.5, 3.9$ Hz, 1H), 3.89 – 3.79 (m, 2H), 3.60 (d, $J = 3.0$ Hz, 1H), 3.52 – 3.40 (m, 4H), 3.14 (dt, $J = 15.0, 12.6$ Hz, 1H), 1.55 (s, 3H), 1.36 (s, 3H), 1.34 (t, $J = 7.0$ Hz, 3H).
 (CDCl₃, 400 MHz)

¹³C NMR (δ , ppm) 151.8 (t, $J = 3$ Hz), 127.6 (t, $J = 294$ Hz), 111.4, 104.3, 96.7, 85.6, 82.0, 76.7, 63.3, 58.2, 43.9 (t, $J = 26$ Hz), 26.9, 26.2, 14.3.
 (CDCl₃, 100 MHz)

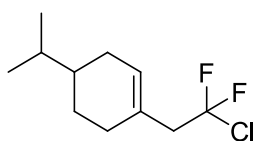
IR (σ , cm⁻¹, CCl₄) 2992, 2936, 1728, 1374, 1083, 1025

HRMS (EI) Calcd for C₁₄H₂₁ClF₂O₅ : 342.1046 Found: NF

³⁵ Selective deprotection of the starting enol ether

1-(2-chloro-2,2-difluoroethyl)-4-isopropylcyclohex-1-ene

IV-21



$C_{11}H_{17}ClF_2$
 $M = 222.70 \text{ g}\cdot\text{mol}^{-1}$

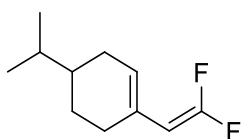
Following general procedure III-A, the reaction was carried out using sabinen (75%) (360 mg, 2mmol) and xanthate **IV-1** (438 mg, 1 mmol) to afford 260 mg (45%) of a mixture of five and six membered ring adducts. A magnetically stirred round bottom flask was charged with this mixture, an aqueous solution of hypophosphorous acid (50% wt) (296 mg, 2.0 mmol), triethylamine (249 mg, 2.4 mmol) in 4.5 ml of dioxane. The solution was refluxed under a flow of nitrogen for 5 minutes then AIBN (7 mg, 0.04 mmol) was added every hour until TLC showed total consumption of the starting adducts. 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) to afford the product **IV-21** (75 mg, 75%) as a colourless oil.

1H NMR (δ , ppm) 5.73 (bs, 1H), 2.96 (t, $J = 13.9$ Hz, 2H), 2.24 – 2.07 (m, 3H), 1.89 – 1.73 (m, 2H), 1.58 – 1.45 (m, 1H), 1.38 – 1.19 (m, 2H), 0.94 (d, $J = 6.3$ Hz, 3H), 0.93 (d, $J = 6.6$ Hz, 3H).
 ($CDCl_3$, 400 MHz)

^{13}C NMR (δ , ppm) 129.9, 129.3 (t, $J = 293$ Hz), 128.6 (t, $J = 2$ Hz), 49.7 (t, $J = 24$ Hz), 39.5, 32.2, 29.6, 29.2, 26.3, 19.9, 19.6.
 ($CDCl_3$, 100 MHz)

1-(2,2-difluorovinyl)-4-isopropylcyclohex-1-ene

IV-22



$C_{11}H_{16}F_2$
 $M = 186.24 \text{ g}\cdot\text{mol}^{-1}$

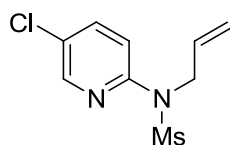
Following general procedure IV-F2, the reaction was carried out using **IV-21** (30 mg, 0.13 mmol) to afford **IV-22** (22 mg, 88%) as colourless liquid.³⁶

¹H NMR (δ , ppm) 5.67 (bs, 1H), 4.85 (dd, $J = 27.5, 4.1$ Hz, 1H), 2.44 – 1.77 (m, 7H), 1.55 – 1.44 (m, 1H), 0.95 – 0.90 (m, 6H).
 (CDCl₃, 400 MHz)

³⁶ This compound is extremely volatile. As we tried to evaporate traces of solvent for good ¹³C NMR, we lost it.

N-allyl-N-(5-chloropyridin-2-yl)methanesulfonamide

IV-24f



C₉H₁₁ClN₂O₂S
M = 246.71 g.mol⁻¹

A magnetically stirred round bottom flask was charged with 5-chloropyridin-2-amine (2.56 g, 20 mmol) and pyridine (10 mL). Methanesulfonyl chloride (2 mL, 26 mmol) was then added drop wise and the solution was stirred for 2 hours. Water (30 mL) was added and the solution was heated to reflux. The mixture was allowed to cool to room temperature, the precipitate filtered off and dry under reduced pressure to afford the desired N-(5-chloropyridin-2-yl)methanesulfonamide,³⁷ which was used without any purification. A magnetically stirred round bottom flask was charged with the latter compound, allylbromide (3.2 mL, 30 mmol) and DMF (60 mL). NaH (1.2 g, 30 mmol) was added portion wise and the mixture was stirred for 1 hours. The medium was quenched with water, EtOAc was added, the layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous MgSO₄ and the solvent was evaporated to dryness. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford the desired olefin **IV-24f** (3.6 g, 73%) as a brown oil.

¹H NMR (δ, ppm) 8.42 (d, *J* = 2.6 Hz, 1H), 7.71 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.38 (d, *J* = 8.7 Hz, 1H), 5.97 – 5.87 (m, 1H), 5.30 (d, *J* = 17.1 Hz, 1H), 5.21 (d, *J* = 10.2 Hz, 1H), 4.53 (d, *J* = 5.8 Hz, 2H), 3.13 (s, 3H).
(CDCl₃, 400 MHz)

¹³C NMR (δ, ppm) 151.3, 147.1, 138.0, 132.7, 129.4, 121.2, 118.9, 51.2, 39.6.
(CDCl₃, 100 MHz)

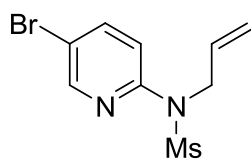
IR (σ, cm⁻¹, CCl₄) 1579, 1462, 1360, 1165

HRMS (EI) Calcd for C₉H₁₁ClN₂O₂S : 246.0230 Found: 246.0234

³⁷ Toluene was added for an easier removal of the water.

N-allyl-N-(5-bromopyridin-2-yl)methanesulfonamide

IV-24g



$C_9H_{11}BrN_2O_2S$
 $M = 291.16 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with 5-bromopyridin-2-amine (3.46 g, 20 mmol) and pyridine (10 mL). Methanesulfonyl chloride (2 mL, 26 mmol) was then added drop wise and the solution was stirred for 2 hours. Water (30 mL) was added and the solution was heated to reflux. The mixture was allowed to cool to room temperature, the precipitate filtered off and dry under reduced pressure to afford the desired N-(5-bromopyridin-2-yl)methanesulfonamide,³⁸ which was used without any purification. A magnetically stirred round bottom flask was charged with the latter compound, allylbromide (3.2 mL, 30 mmol) and DMF (60 mL). NaH (1.2 g, 30 mmol) was added portion wise and the mixture was stirred for 1 hours. The medium was quenched with water, EtOAc was added, the layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated to dryness. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford the desired olefin **IV-24g** (3.5 g, 60%) as a brown oil.

1H NMR (δ , ppm) 8.50 (d, $J = 2.5$ Hz, 1H), 7.84 (dd, $J = 8.6, 2.5$ Hz, 1H), 7.31 (d, $J = 8.6$ Hz, 1H), 5.96 – 5.85 (m, 1H), 5.29 (dd, $J = 17.2, 1.3$ Hz, 1H), 5.20 (dd, $J = 10.2, 1.1$ Hz, 1H), 4.52 (d, $J = 5.8$ Hz, 2H), 3.13 (s, 3H).
 (CDCl₃, 400 MHz)

^{13}C NMR (δ , ppm) 151.7, 149.3, 140.8, 132.6, 121.3, 118.9, 117.5, 51.1, 39.7.
 (CDCl₃, 100 MHz)

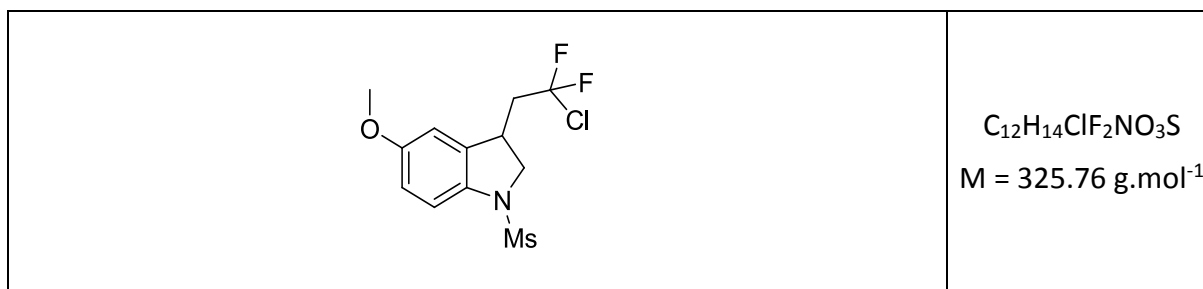
IR (σ , cm⁻¹, CCl₄) 1574, 1460, 1361, 1165, 1008

HRMS (EI) Calcd for $C_9H_{11}BrN_2O_2S$: 289.9725 Found: 289.9729

³⁸ Toluene was added for an easier removal of the water.

3-(2-chloro-2,2-difluoroethyl)-5-methoxy-1-(methylsulfonyl)indoline

IV-26a



Following general procedure IV-C, the reaction was carried out with *N*-allyl-*N*-(4-methoxyphenyl)methanesulfonamide (241 mg, 1.00 mmol) and xanthate **IV-1** (646 mg, 1.50 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 80:20 to 60:40) to afford **IV-26a** (215 mg, 75%) as an amorphous solid.

$^1\text{H NMR}$ (δ , ppm) 7.39 (d, $J = 8.7$ Hz, 1H), 6.84 (d, $J = 8.8$ Hz, 1H), 6.80 (s, 1H), 4.31 – 4.23 (m, 1H), 3.84 (s, 3H), 3.83 – 3.75 (m, 2H), 2.98 – 2.83 (s + m, 4H), 2.70 – 2.56 (m, 1H).
(CDCl_3 , 400 MHz)

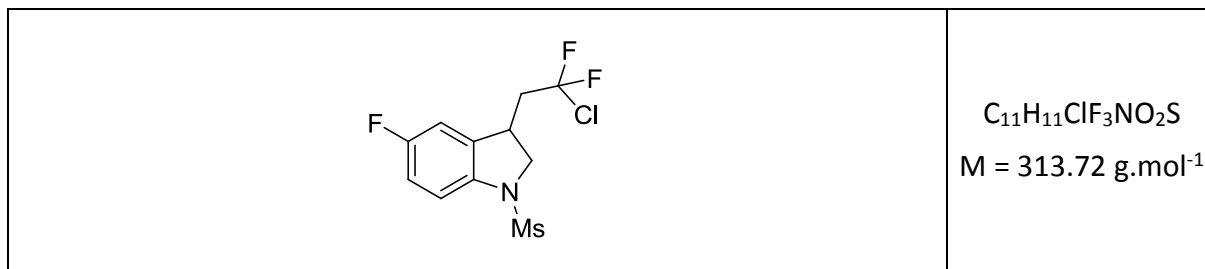
$^{13}\text{C NMR}$ (δ , ppm) 157.1, 135.0, 133.7, 128.6 (t, $J = 292$ Hz), 115.2, 113.9, 110.6, 56.6, 55.8, 46.3 (t, $J = 24.0$ Hz), 36.0, 34.3.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1489, 1364, 1166

HRMS (EI) Calcd for $C_{12}H_{14}ClF_2NO_3S$: 325.0351 Found: 325.0353

3-(2-chloro-2,2-difluoroethyl)-5-fluoro-1-(methylsulfonyl)indoline

IV-26b



Following general procedure IV-C, the reaction was carried out with *N*-allyl-*N*-(4-fluorophenyl)methanesulfonamide (284 mg, 1.24 mmol) and xanthate **IV-1** (801 mg, 1.86 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-26b** (280 mg, 72%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.42 (dd, $J = 8.7, 4.4$ Hz, 1H), 7.04 – 6.96 (m, 2H), 4.34 – 4.24 (m, 1H), 3.88 – 3.77 (m, 2H), 2.94 (s, 3H), 2.94 – 2.81 (m, 1H), 2.73 – 2.58 (m, 1H).

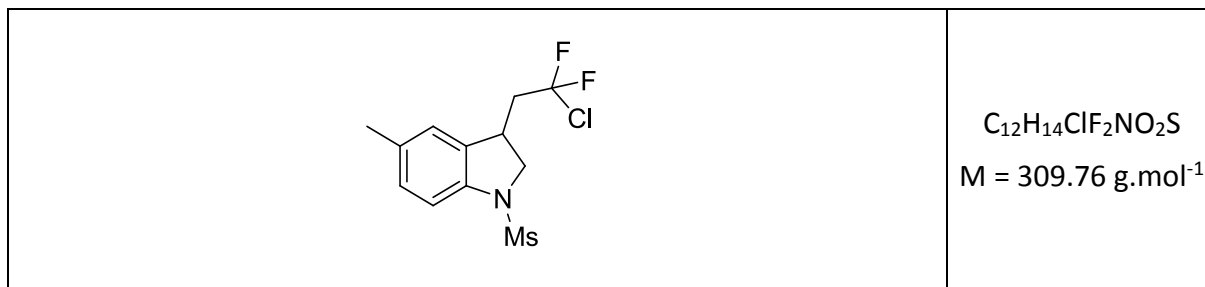
$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 159.8 (d, $J = 244$ Hz), 137.7 (d, $J = 2$ Hz), 134.0 (d, $J = 8$ Hz), 128.4 (t, $J = 292$ Hz), 115.8 (d, $J = 23$ Hz), 115.0 (d, $J = 8$ Hz), 112.0 (d, $J = 25$ Hz), 56.6 (t, $J = 2$ Hz), 46.1 (t, $J = 24$ Hz), 35.8, 34.7.

IR (σ , cm⁻¹, CCl₄) 1486, 1367, 1168

HRMS (EI) Calcd for C₁₁H₁₁ClF₃NO₂S : 313.0151 Found: 313.0153

3-(2-chloro-2,2-difluoroethyl)-5-methyl-1-(methylsulfonyl)indoline

IV-26c



Following general procedure IV-C, the reaction was carried out with *N*-allyl-*N*-p-tolyl methanesulfonamide (225 mg, 1.00 mmol) and xanthate **IV-1** (646 mg, 1.50 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-26c** (285 mg, 92%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.35 (d, $J = 8.2$ Hz, 1H), 7.11 (d, $J = 8.3$ Hz, 1H), 7.06 (s, 1H), 4.30 – 4.20 (m, 1H), 3.84 – 3.74 (m, 2H), 3.00 – 2.84 (s + m, 4H), 2.69 – 2.53 (m, 1H), 2.37 (s, 3H).
(CDCl_3 , 400 MHz)

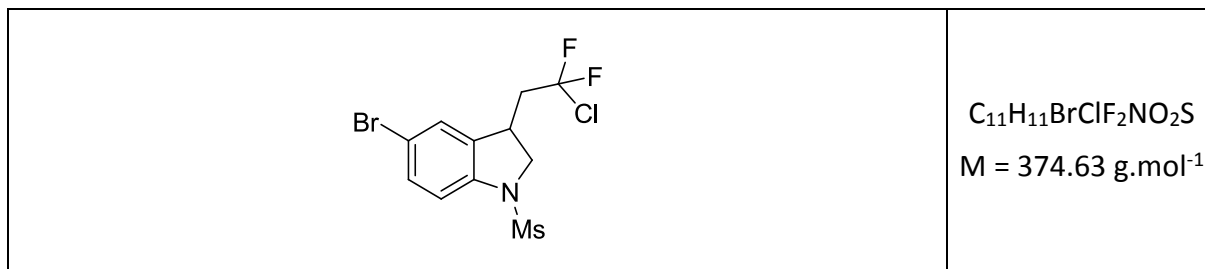
$^{13}\text{C NMR}$ (δ , ppm) 139.3, 134.0, 132.1, 129.1, 128.7 (t, $J = 292$ Hz), 125.0, 113.8, 56.4, 46.4 (t, $J = 46$ Hz), 35.7, 34.4, 20.9.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1489, 1365, 1167

HRMS (EI) Calcd for $C_{12}H_{14}ClF_2NO_2S$: 309.0402 Found: 309.0404

5-bromo-3-(2-chloro-2,2-difluoroethyl)-1-(methylsulfonyl)indoline

IV-26d



Following general procedure IV-C, the reaction was carried out with *N*-allyl-*N*-(4-bromophenyl)methanesulfonamide (290 mg, 1.00 mmol) and xanthate **IV-1** (646 mg, 1.50 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-26d** (314 mg, 84%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 7.42 (dd, $J = 8.5, 1.9 \text{ Hz}$, 1H), 7.37 (d, $J = 1.8 \text{ Hz}$, 1H), 7.34 (d, $J = 8.6 \text{ Hz}$, 1H), 4.31 – 4.23 (m, 1H), 3.87 – 3.78 (m, 2H), 2.95 (s, 3H), 2.95 – 2.82 (m, 1H), 2.65 (m, 1H).
(CDCl_3 , 400 MHz)

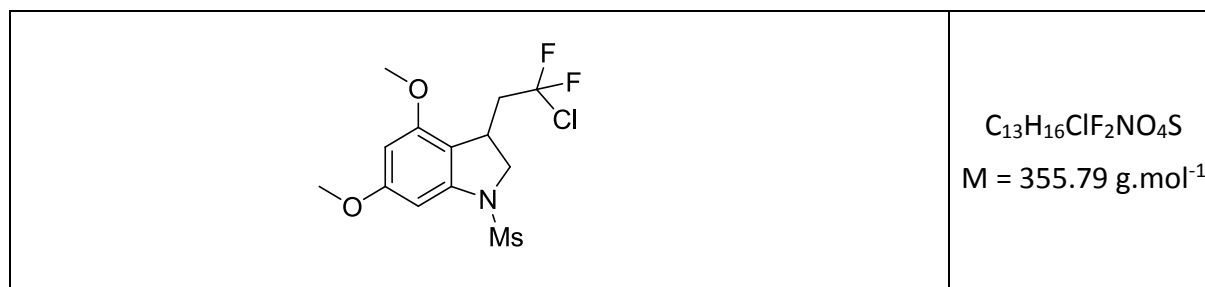
$^{13}\text{C NMR}$ (δ , ppm) 140.9, 134.2, 132.1, 128.4 (t, $J = 292 \text{ Hz}$), 127.7, 116.6, 115.2, 56.3, 46.2 (t, $J = 24 \text{ Hz}$), 35.6, 35.0.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1478, 1368, 1169, 1120

HRMS (EI) Calcd for $C_{11}H_{11}BrClF_2NO_2S$: 372.9350 Found: 372.9354

3-(2-chloro-2,2-difluoroethyl)-4,6-dimethoxy-1-(methylsulfonyl)indoline

IV-26e



Following general procedure IV-C, the reaction was carried out with *N*-allyl-*N*-(3,5-dimethoxyphenyl)methanesulfonamide (119 mg, 0.44 mmol) and xanthate **IV-1** (284 mg, 0.66 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-26e** (105 mg, 67%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 6.70 (d, $J = 1.9$ Hz, 1H), 6.22 (d, $J = 1.9$ Hz, 1H), 4.11 (dd, $J = 10.9, 9.3$ Hz, 1H), 4.00 (dd, $J = 10.9, 4.8$ Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.83 – 3.77 (m, 1H), 3.21 – 3.07 (m, 1H), 2.95 (s, 3H), 2.44 (tdd, $J = 15.0, 10.8, 8.4$ Hz, 1H).

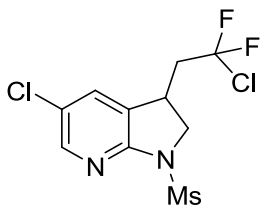
$^{13}\text{C NMR}$ (δ , ppm) (CDCl₃, 100 MHz) 162.5, 157.0, 143.6, 129.1 (t, $J = 293$ Hz), 110.7, 94.3, 91.7, 56.2, 55.8, 55.5, 44.6 (t, $J = 23$ Hz), 34.7, 33.6.

IR (σ , cm⁻¹, CCl₄) 1604, 1364, 1205, 1167, 1110

HRMS (EI) Calcd for C₁₃H₁₆ClF₂NO₄S : 355.0457 Found: 355.0451

5-chloro-3-(2-chloro-2,2-difluoroethyl)-1-(methylsulfonyl)-2,3-dihydro-1H-pyrrolo[2,3-b]pyridine

IV-26f



$C_{10}H_{10}Cl_2F_2N_2O_2S$
 $M = 331.17 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-C, the reaction was carried out with **IV-14f** (246 mg, 1.00 mmol) and xanthate **IV-1** (646 mg, 1.50 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford **IV-26f** (120 mg, 36%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 8.22 (dd, $J = 2.3, 0.9 \text{ Hz}$, 1H), 7.53 (dd, $J = 2.2, 1.3 \text{ Hz}$, 1H), 4.44 – 4.35 (m, 1H), 3.97 (dd, $J = 10.5, 7.0 \text{ Hz}$, 1H), 3.86 – 3.77 (m, 1H), 3.38 (s, 4H), 2.93 – 2.79 (m, 1H), 2.79 – 2.64 (m, 1H).
 (CDCl₃, 400 MHz)

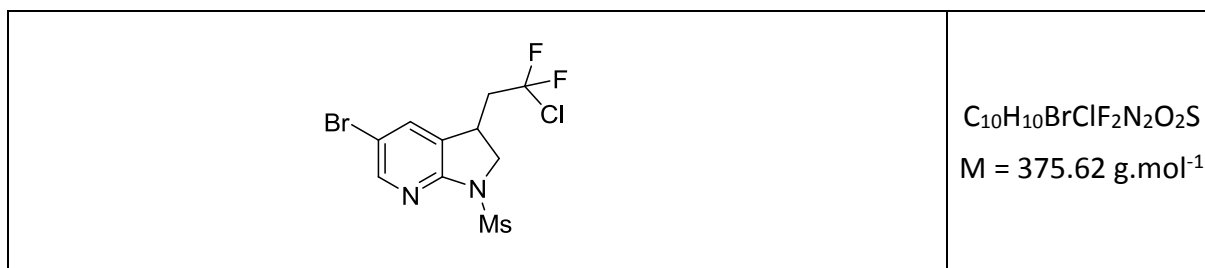
$^{13}\text{C NMR}$ (δ , ppm) 154.5, 146.6, 133.3, 128.2 (t, $J = 292 \text{ Hz}$), 126.8, 126.4, 53.9, 45.9 (t, $J = 24 \text{ Hz}$), 40.0, 33.4 (t, $J = 3 \text{ Hz}$).
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 2928, 1439, 1354, 1167

HRMS (EI) Calcd for C₁₀H₁₀F₂Cl₂N₂O₂S : 329.2808 Found: 329.9804

5-bromo-3-(2-chloro-2,2-difluoroethyl)-1-(methylsulfonyl)-2,3-dihydro-1H-pyrrolo[2,3-b]pyridine

IV-26g



Following general procedure IV-C, the reaction was carried out with **IV-14g** (291 mg, 1.00 mmol) and xanthate **IV-1** (646 mg, 1.50 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford **IV-26g** (130 mg, 35%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 8.29 – 8.28 (m, 1H), 7.66 – 7.64 (m, 1H), 4.36 (t, $J = 9.8$ Hz, 1H), 3.94 (dd, $J = 10.3, 7.2$ Hz, 1H), 3.85 – 3.76 (m, 1H), 3.35 (s, 3H), 2.92 – 2.79 (m, 1H), 2.76 – 2.63 (m, 1H).
 (CDCl₃, 400 MHz)

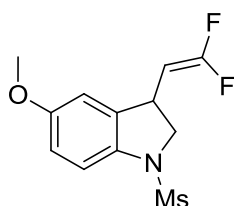
$^{13}\text{C NMR}$ (δ , ppm) 154.9, 148.7, 135.9, 128.2 (t, $J = 292$ Hz), 127.4, 113.9, 53.8, 45.8 (t, $J = 24$ Hz), 39.9, 33.4.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 1437, 1354, 1223, 1167, 1116

HRMS (EI) Calcd for C₁₀H₁₀BrClF₂N₂O₂S : 373.9303 Found: 373.9315

3-(2,2-difluorovinyl)-5-methoxy-1-(methylsulfonyl)indoline

IV-27a



$C_{12}H_{13}F_2NO_3S$
 $M = 289.30 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with **IV-26a** (20 mg, 0.06 mmol), DBU (450 mg, 3.00 mmol) and was stirred at 35 °C for 8 hours. The medium was quenched with saturated NH_4Cl , EtOAc was added, the layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated to dryness. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford a mixture (14.2 mg, 80%) of **IV-27a** and **IV-28a** in a 92:8 ratio.

1H NMR (δ , ppm) 7.38 (d, $J = 8.8$ Hz, 1H), 6.83 (dd, $J = 8.8, 2.6$ Hz, 1H), 6.76 (d, $J = 2.6$ Hz, 1H), 4.43 – 4.33 (m, 1H), 4.30 – 4.22 (m, 2H), 3.84 (s, 3H), 3.66 – 3.57 (m, 1H), 2.89 (s, 3H).
 (CDCl₃, 400 MHz)

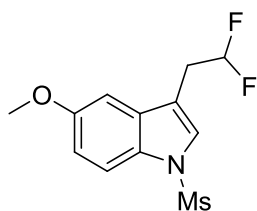
^{13}C NMR (δ , ppm) 157.4 (t, $J = 290$ Hz), 157.2, 134.8, 134.5, 115.3, 114.0, 110.9, 79.2 (dd, $J = 24, 18$ Hz), 56.6 (t, $J = 3$ Hz), 55.8, 35.4 (d, $J = 5$ Hz), 34.2.
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 1743, 1489, 1363, 1168

HRMS (EI) Calcd for $C_{12}H_{13}F_2NO_3S$: 289.0584 Found: 289.0586

3-(2,2-difluoroethyl)-5-methoxy-1-(methylsulfonyl)-1H-indole

IV-28a



$C_{12}H_{13}F_2NO_3S$
 $M = 289.30 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with **IV-26a** (100 mg, 0.31 mmol), DBU (1.4 g, 9.3 mmol) and was stirred at 70 °C for 5 hours. The medium was quenched with saturated NH_4Cl and EtOAc was added. The layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated to dryness. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-28a** (30 mg, 34%).³⁹

1H NMR (δ , ppm) 7.85 (d, $J = 9.8$ Hz, 1H), 7.41 (s, 1H), 7.08 – 7.04 (m, 2H), 6.07 (tt, $J = 56.4, 4.4$ Hz, 1H), 3.93 (s, 3H), 3.28 (tdd, $J = 17.0, 4.3, 0.7$ Hz, 2H), 3.12 (s, 3H).
 (CDCl₃, 400 MHz)

^{13}C NMR (δ , ppm) 156.8, 131.6, 129.7, 125.7, 115.7 (t, $J = 241$ Hz), 114.3, 114.1, 113.3 (t, $J = 6$ Hz), 102.1, 55.8, 40.6, 30.5 (t, $J = 24$ Hz).
 (CDCl₃, 100 MHz)

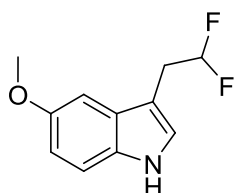
IR (σ , cm⁻¹, CCl₄) 1477, 1379, 1233, 1177, 1118, 1063, 1038

HRMS (EI) Calcd for $C_{12}H_{13}F_2NO_3S$: 289.0584 Found: 289.0580

³⁹ Described with about 15% of **13a**

3-(2,2-difluoroethyl)-5-methoxy-1H-indole

IV-30a



$C_{11}H_{11}F_2NO$
 $M = 211.21 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-F3, the reaction was carried out using **IV-26a** (10 mg, 0.03 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 90:10) to afford **IV-30a** (5 mg, 77%).

$^1\text{H NMR}$ (δ , ppm) 8.07 (bs, 1H), 7.33 (d, $J = 8.9$ Hz, 1H), 7.17 (d, $J = 2.3$ Hz, 1H), 7.08 (d, $J = 2.3$ Hz, 1H), 6.94 (dd, $J = 8.9, 2.3$ Hz, 1H), 6.02 (tt, $J = 57.0, 4.6$ Hz, 1H), 3.92 (s, 3H), 3.32 (td, $J = 17.1, 4.5$ Hz, 2H).
 (CDCl₃, 400 MHz)

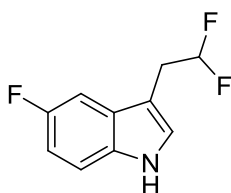
$^{13}\text{C NMR}$ (δ , ppm) 154.4, 131.2, 127.9, 124.2, 116.7 (t, $J = 241$ Hz), 112.7, 112.0, 106.7 (t, $J = 7$ Hz), 100.4, 55.9, 30.9 (t, $J = 23$ Hz).
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 3490, 2928, 1489, 1222, 1118, 1060

HRMS (EI) Calcd for C₁₁H₁₁F₂NO : 211.0809 Found: 211.0809

3-(2,2-difluoroethyl)-5-fluoro-1H-indole

IV-30b



$C_{10}H_8F_3N$
 $M = 199.17 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-F3, the reaction was carried out using **IV-26b** (50 mg, 0.16 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 90:10) to afford **IV-30b** (20 mg, 63%).

^1H NMR (δ , ppm) 8.17 (bs, 1H), 7.35 (dd, $J = 8.8, 4.3$ Hz, 1H), 7.30 (dd, $J = 9.6, 2.2$ Hz, 1H), 7.23 (d, $J = 2.2$ Hz, 1H), 7.02 (td, $J = 9.0, 2.5$ Hz, 1H), 6.01 (tt, $J = 56.9, 4.5$ Hz, 1H), 3.30 (td, $J = 17.3, 4.5$ Hz, 2H).
 (CDCl₃, 400 MHz)

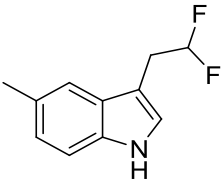
^{13}C NMR (δ , ppm) 158.1 (d, $J = 235$ Hz), 132.6, 128.0 (d, $J = 10$ Hz), 125.3, 116.5 (t, $J = 241$ Hz), 111.9 (d, $J = 10$ Hz), 110.9 (d, $J = 26$ Hz), 107.1 (td, $J = 7, 5$ Hz), 103.8 (d, $J = 24$ Hz), 30.8 (t, $J = 23$ Hz).
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 3488, 2973, 1587, 1488, 1455, 1118, 1060

HRMS (EI) Calcd for C₁₀H₈F₃N : 199.0609 Found: 199.0601

3-(2,2-difluoroethyl)-5-methyl-1H-indole

IV-30c

	$C_{11}H_{11}F_2N$ $M = 195.21 \text{ g}\cdot\text{mol}^{-1}$
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Following general procedure IV-F3, the reaction was carried out using **IV-26c** (60 mg, 0.19 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 90:10) to afford **IV-30c** (23 mg, 62%).

$^1\text{H NMR}$ (δ , ppm) 8.08 (bs, 1H), 7.45 (s, 1H), 7.33 (d, $J = 8.2$ Hz, 1H), 7.14 (s, 1H), 7.11 (d, $J = 8.2$ Hz, 1H), 6.03 (tt, $J = 57.0, 4.6$ Hz, 1H), 3.33 (td, $J = 17.2, 4.5$ Hz, 2H), 2.53 (s, 3H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 134.4, 129.2, 127.7, 124.1, 123.7, 118.3, 116.7 (t, $J = 241$ Hz), 111.0, 106.4 (t, $J = 7$ Hz), 30.8 (t, $J = 23$ Hz), 21.6.
(CDCl_3 , 100 MHz)

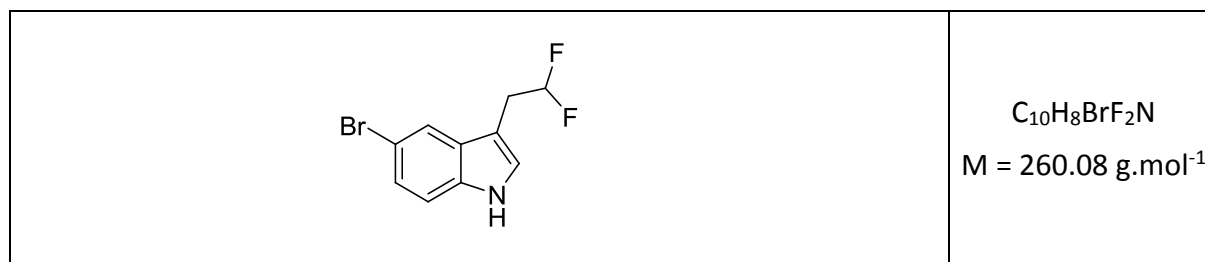
IR (σ , cm^{-1} , CCl_4) 3489, 2973, 2922, 1393, 1379, 1118, 1055

HRMS (EI) Calcd for $C_{11}H_{11}F_2N$: 195.0860 Found: 195.0834⁴⁰

⁴⁰ 195.0834 is the closest mass found. Error = 18 ppm

5-bromo-3-(2,2-difluoroethyl)-1H-indole

IV-30d



Following general procedure IV-F3, the reaction was carried out using **IV-26d** (80 mg, 0.22 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 90:10) to afford **IV-30d** (35 mg, 63%).

$^1\text{H NMR}$ (δ , ppm) 8.20 (bs, 1H), 7.79 (t, $J = 4.6$ Hz, 1H), 7.36 (dd, $J = 8.6, 1.8$ Hz, 1H), 7.30 (d, $J = 8.6$ Hz, 1H), 7.19 (d, $J = 2.3$ Hz, 1H), 6.01 (tt, $J = 56.8, 4.5$ Hz, 1H), 3.30 (td, $J = 17.3, 4.5$ Hz, 2H).
(CDCl_3 , 400 MHz)

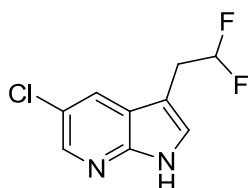
$^{13}\text{C NMR}$ (δ , ppm) 134.7, 129.3, 125.3, 124.8, 121.4, 116.3 (t, $J = 241$ Hz), 113.2, 112.7, 106.6 (t, $J = 7$ Hz), 30.6 (t, $J = 23$ Hz).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 3485, 2973, 1459, 13984, 1118, 1096, 1058

HRMS (EI) Calcd for $C_{10}H_8BrF_2N$: 258.9808 Found: 258.9810

5-chloro-3-(2,2-difluoroethyl)-1H-pyrrolo[2,3-b]pyridine

IV-30f



$C_9H_7ClF_2N_2$
 $M = 216.61 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-F3 (reaction time: 2 hours), the reaction was carried out using **IV-26f** (33 mg, 0.10 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-30f** (18 mg, 71%) as an amorphous white solid.

1H NMR (δ , ppm) 10.10 (bs, 1H), 8.34 (d, $J = 2.1$ Hz, 1H), 7.98 (d, $J = 1.3$ Hz, 1H), 7.37 (d, $J = 1.6$ Hz, 1H), 6.01 (tt, $J = 56.7, 4.3$ Hz, 1H), 3.30 (td, $J = 17.5, 4.3$ Hz, 2H).
 (CDCl₃, 400 MHz)

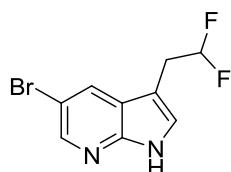
^{13}C NMR (δ , ppm) 146.9, 142.0, 127.0, 126.0, 124.1, 121.1, 116.2 (t, $J = 242$ Hz), 105.2 (t, $J = 6$ Hz), 30.9 (t, $J = 23$ Hz).
 (CDCl₃, 100 MHz)

IR (σ , cm⁻¹, CCl₄) 3476, 2925, 1471, 1396, 1118, 1060

HRMS (EI) Calcd for C₉H₇ClF₂N₂: 216.0266 Found: 216.0266

5-bromo-3-(2,2-difluoroethyl)-1H-pyrrolo[2,3-b]pyridine

IV-30g



$C_9H_7BrF_2N_2$
 $M = 261.07 \text{ g}\cdot\text{mol}^{-1}$

Following general procedure IV-F3 (reaction time: 2 hours), the reaction was carried out using **IV-26c** (70 mg, 0.19 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-30g** (30.5 mg, 63%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 11.02 (s, 1H), 8.42 (d, $J = 2.0$ Hz, 1H), 8.13 (d, $J = 2.0$ Hz, 1H), 7.36 (s, 1H), 6.01 (tt, $J = 56.7, 4.3$ Hz, 1H), 3.30 (td, $J = 17.5, 4.1$ Hz, 2H).
 (CDCl_3 , 400 MHz)

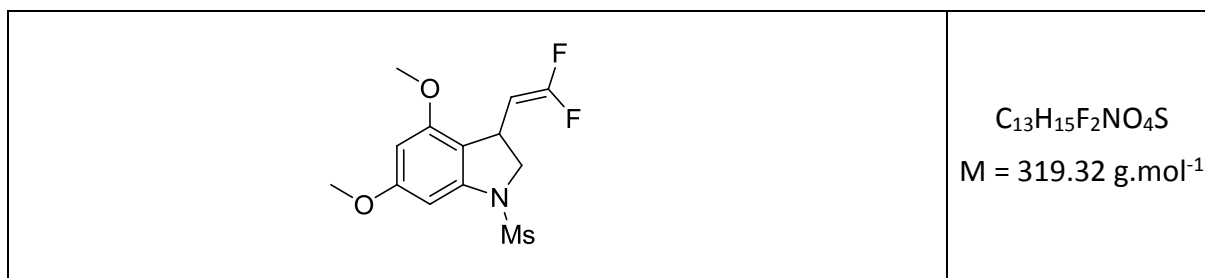
$^{13}\text{C NMR}$ (δ , ppm) 147.2, 143.50, 129.9, 126.0, 122.0, 116.2 (t, $J = 241$ Hz), 111.7, 104.9 (t, $J = 6$ Hz), 30.9 (t, $J = 23$ Hz).
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 3475, 2925, 1470, 1396, 1118, 1062

HRMS (EI) Calcd for $C_9H_7BrF_2N_2$: 259.9761 Found: 259.9756

3-(2,2-difluorovinyl)-4,6-dimethoxy-1-(methylsulfonyl)indoline

IV-27b



Following general procedure IV-F3, the reaction was carried out using **IV-26b** (51 mg, 0.14 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 90:10) to afford **IV-27b** (42 mg, 91%) as an amorphous white solid.

$^1\text{H NMR}$ (δ , ppm) 6.69 (d, $J = 2.0$ Hz, 1H), 6.21 (d, $J = 2.0$ Hz, 1H), 4.40 – 4.30 (m, 1H), 4.20 – 4.10 (m, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.82 – 3.77 (m, 1H), 2.94 (s, 3H).
(CDCl_3 , 400 MHz)

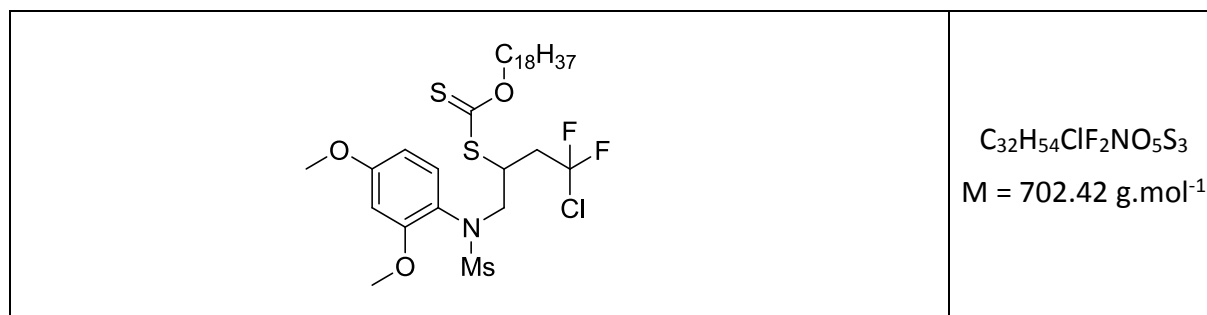
$^{13}\text{C NMR}$ (δ , ppm) 162.4, 157.3, 156.3 (dd, $J = 290, 288$ Hz), 143.3, 111.5, 94.4, 91.7, 80.3 (dd, $J = 22, 18$ Hz), 57.23 (t, $J = 3$ Hz), 55.8, 55.5, 34.6, 32.1 (d, $J = 6$ Hz).
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1743, 1604, 1363, 1205, 1168

HRMS (EI) Calcd for $C_{13}H_{15}F_2NO_4S$: 319.0690 Found: 319.0686

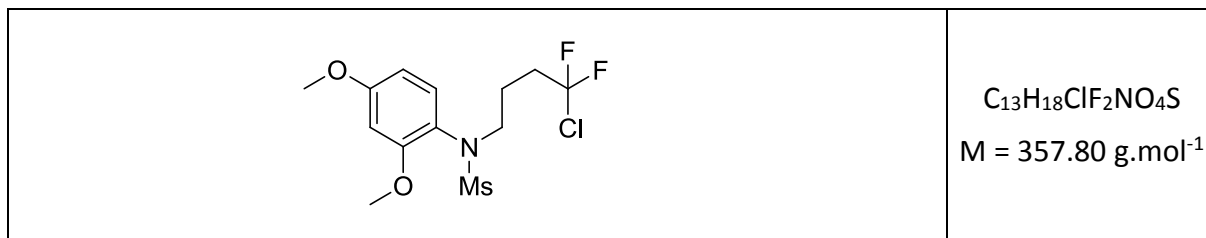
S-4-chloro-1-(N-(2,4-dimethoxyphenyl)methylsulfonamido)-4,4-difluorobutan-2-yl O-octadecyl carbonodithioate

IV-33



Following general procedure IV-A, the reaction was carried out using *N*-allyl-*N*-(2,4-dimethoxyphenyl)methanesulfonamide (271 mg, 1.00 mmol), xanthate **IV-1** (646 mg, 1.5 mmol) and two portions of lauroyl peroxyde. The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford the corresponding xanthate adduct **IV-33** (680 mg, 96%).

$^1\text{H NMR}$ (δ , ppm) (CDCl₃, 400 MHz) 7.34 – 7.29 (m, 1H), 6.60 – 6.52 (m, 2H), 4.58 – 4.41 (m, 2H), 3.92 – 3.83 (m, 7H), 3.38 – 3.21 (m, 1H), 2.95 (s, 3H), 2.81 – 2.57 (m, 1H), 1.72 (s, 2H), 1.41 – 1.23 (m, 32H), 0.92 (t, $J = 6.9 \text{ Hz}$, 3H).

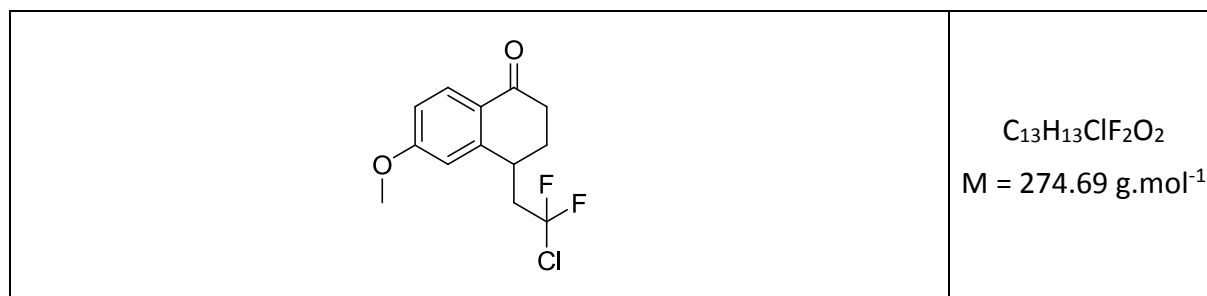
N-(4-chloro-4,4-difluorobutyl)-N-(2,4-dimethoxyphenyl)methanesulfonamide **IV-34**


Following general procedure IV-C, the reaction was carried out with *N*-allyl-*N*-(2,4-dimethoxyphenyl)methanesulfonamide (271 mg, 1.00 mmol) and xanthate **IV-1** (646 mg, 1.50 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 80:20) to afford **IV-27c** as the major product.

¹H NMR (δ, ppm) 7.28 (d, *J* = 9.3 Hz, 1H), 6.56 – 6.54 (m, 2H), 3.90 (s, 3H), 3.87 (s, 3H), (CDCl₃, 400 MHz) 3.77 – 3.60 (m, 2H), 2.95 (s, 3H), 2.56 – 2.41 (m, 2H), 1.82 – 1.72 (m, 2H).

4-(2-chloro-2,2-difluoroethyl)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one

IV-36



Following general procedure IV-C, the reaction was carried out with 1-(4-methoxyphenyl)pent-4-en-1-one (191 mg, 1.00 mmol) and xanthate **IV-1** (646 mg, 1.50 mmol). The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 85:15) to afford **IV-36** (130 mg, 50%) as an amorphous white solid.

^1H NMR (δ , ppm) 8.07 (d, $J = 8.7$ Hz, 1H), 6.92 (dd, $J = 8.8, 2.5$ Hz, 1H), 6.80 (d, $J = 2.4$ Hz, 1H), 3.92 (s, 3H), 3.50 – 3.43 (m, 1H), 2.85 – 2.62 (m, 5H), 2.42 – 2.22 (m, 2H).
(CDCl_3 , 400 MHz)

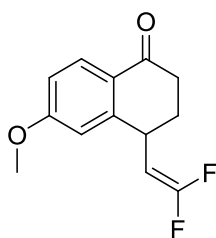
^{13}C NMR (δ , ppm) 196.0, 164.0, 147.9, 130.3, 129.2 (t, $J = 293$ Hz), 125.6, 113.6, 112.6, 55.6, 45.9 (t, $J = 23$ Hz), 34.2 (dd, $J = 3, 1$ Hz), 33.9, 26.6.
(CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 1685, 1601, 1268, 1254

HRMS (EI) Calcd for $C_{13}H_{13}ClF_2O_2$: 274.0572 Found: 274.0573

4-(2,2-difluorovinyl)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one

IV-37



$C_{13}H_{12}F_2O_2$
 $M = 238.23 \text{ g}\cdot\text{mol}^{-1}$

A magnetically stirred round bottom flask was charged with **IV-36** (22 mg, 0.08 mmol), DBU (600 mg, 4.00 mmol) and was stirred at 35 °C for 8 hours. The medium was quenched with saturated NH_4Cl and EtOAc was added. The layers were partitioned and the aqueous one was extracted twice with EtOAc. The combined organic layers were dried over anhydrous MgSO_4 and the solvent was evaporated to dryness. The residue was purified by silica gel column chromatography (petroleum ether / diethyl ether 85:15) to afford a mixture (13 mg, 58%) of **IV-37** and **IV-36** in a 85:15 ratio.

$^1\text{H NMR}$ (δ , ppm) 8.09 (d, $J = 8.7 \text{ Hz}$, 1H), 6.92 (dd, $J = 8.7, 2.6 \text{ Hz}$, 1H), 6.80 (s, 1H), 4.43 (ddd, $J = 24.4, 10.2, 2.2 \text{ Hz}$, 1H), 3.92 (s, 3H), 3.90 – 3.82 (m, 1H), 2.84 – 2.61 (m, 2H), 2.36 – 2.27 (m, 1H), 2.10 – 1.99 (m, 1H).
 (CDCl_3 , 400 MHz)

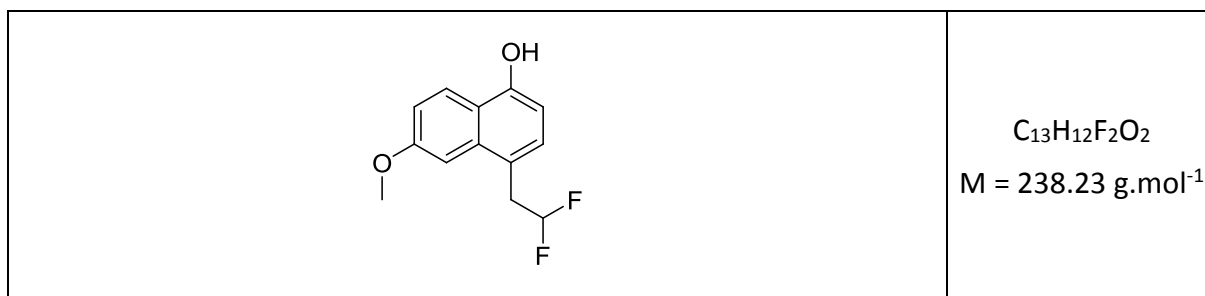
$^{13}\text{C NMR}$ (δ , ppm) 196.1, 164.0, 157.1 (t, $J = 289 \text{ Hz}$), 147.23, 130.1, 125.7, 113.2, 112.6, 81.1 (dd, $J = 22, 19 \text{ Hz}$), 55.6, 37.0, 34.1 (d, $J = 5 \text{ Hz}$), 30.2.
 (CDCl_3 , 100 MHz)

IR (σ , cm^{-1} , CCl_4) 2942, 1741, 1685, 1600, 1268,

HRMS (EI) Calcd for $C_{13}H_{12}F_2O_2$: 238.0805 Found: 238.0802

4-(2,2-difluoroethyl)-6-methoxynaphthalen-1-ol

IV-38



Following general procedure IV-F3, the reaction was carried out using **IV-36** (20 mg, 0.73 mmol). The residue was purified by silica gel column chromatography (petroleum ether / ethyl acetate 85:15) to afford **IV-38** (9 mg, 52%).

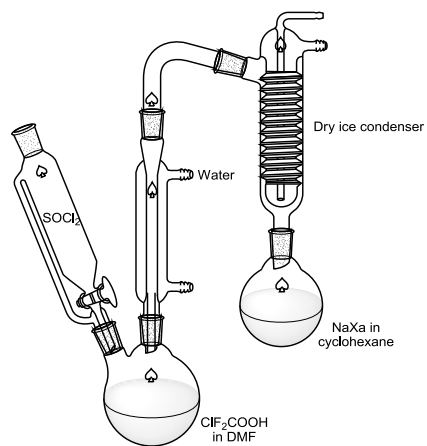
$^1\text{H NMR}$ (δ , ppm) 8.23 (d, $J = 9.8$ Hz, 1H), 7.28 – 7.21 (m, 3H), 6.69 (d, $J = 7.7$ Hz, 1H), 6.08 (tt, $J = 56.8, 4.7$ Hz, 1H), 5.30 (s, 1H), 4.00 (s, 3H), 3.52 (td, $J = 16.6, 4.6$ Hz, 2H).
(CDCl_3 , 400 MHz)

$^{13}\text{C NMR}$ (δ , ppm) 158.6, 151.6, 134.8, 129.2, 124.4, 120.0 (2C), 117.2, 116.7 (t, $J = 242$ Hz), 106.3, 102.6, 55.4, 37.7 (t, $J = 23$ Hz).
(CDCl_3 , 100 MHz)

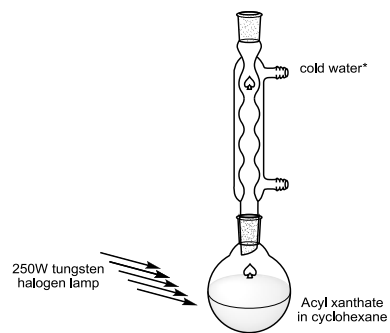
IR (σ , cm^{-1} , CCl_4) 3607, 1632, 1606, 1467, 1220, 1055, 1029

HRMS (EI) Calcd for $C_{13}H_{12}F_2O_2$: 238.0805 Found: 238.0808

Apparatus used for the synthesis of IV-1



STEP 1



STEP 2

* caution : the reflux of cyclohexane can be very strong when irradiating.
Make sure the water is cold enough and use a very efficient condenser

