Organic & Biomolecular Chemistry

PAPER



Cite this: Org. Biomol. Chem., 2015, **13**, 717

Received 23rd July 2014, Accepted 29th August 2014 DOI: 10.1039/c4ob01547a

www.rsc.org/obc

Introduction

Short and efficient synthesis of fluorinated $\delta\text{-lactams}\dagger$

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The diastereoselective synthesis of fluorinated δ -lactams has been achieved through an efficient five step process. The route can tolerate a range of functionalities, and provides a quick route for the generation of new fluorinated medicinal building blocks.

Fluorination has been used to increase the potency and 'druglike' nature of active compounds for many years, making organofluorine compounds a cornerstone in medicinal chemistry.¹ Fluorination has also been extensively used to alter the basicity of *N*-heterocycles, and as a tool through which hydrogen bonding can be probed and assessed.² As such, new ways to selectively incorporate fluorine atoms into different substructures is an ever expanding area of research.^{1,2}

δ-Lactams on the other hand are also present widely in medicinal chemistry and natural systems. For instance, aripiprazole 1 is used currently for the treatment of schizophrenia and bipolar disorders (Fig. 1).³

Thus, it is not surprising that considerable time and efforts have been directed towards the synthesis of fluorinated δ -lactams.^{4–6} However to date, there are a relatively small number of examples and few general routes available to enable synthesis of compound libraries to drive structure–activity relationship understanding in medicinal chemistry programmes.

Herein, we would like to report a short and efficient route to the synthesis of fluorinated $\delta\text{-lactams}$ starting from

Fig. 1 Aripiprazole 1.

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‡The author to whom crystallographic data questions should be addressed. §Ian Sword Reader of Organic Chemistry. commercial aldehydes. The methodology is amenable for the generation of a wide range of δ -lactams, and has the potential to allow entry into several different classes of *N*-heterocyclic compounds.

Results and discussion

Our initial studies towards the synthesis of fluorinated δ -lactams began with benzaldehyde, which upon amino allylation under Kobayashi conditions afforded amine 3.⁷ Amide coupling of amine 3 with 2-fluoroacrylic acid 4 then afforded the desired diene 5 in 85% yield over the 2 steps (Scheme 1).

Amide 5 was then treated with a range of metathesis catalysts in an attempt to induce ring closure (Scheme 2), however only a complex mixture of cross metathesis products resulted, with no desired cyclised product 6 being detected.

The lack of cyclisation could be attributed to the interaction of the ruthenium catalyst with the amide group which prevents



Scheme 1 Formation of dialkene 5 from benzaldehyde 2.



Scheme 2 Attempted RCM reaction with dialkene 5.



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Table 1 Synthesis of α , β -unsaturated lactams **9a**-i with isolated yields for the intermediates **7a**-j and **8a**-j

R ^{-CHO} 1. PMB-NH ₂ PMB-NH 2. MgBr R HBTU R Grubbs II 7 R B R 9									
R	Yield		Yield		Yield				
Ph	95%	7a	63%	8a	Quant	9a			
4-MeOPh	80%	7 b	66%	8b	Quant	9b			
4-CF ₃ Ph	66%	7c	45%	8c	Quant	9c			
1-Naphthyl	99%	7 d	31%	8d	Quant	9d			
4-BrPh	97%	7e	54%	8e	99%	9e			
i-Butyl	76%	7 f	74%	8f	85%	9f			
Cyclohexyl	74%	7g	70%	8g	89%	9g			
2-Furyl	83%	7ĥ	28%	8ĥ	64%	9ĥ			
N-Ts 2-pyrrole	85%	7i	50%	8i	77%	9i			
2-Pyridyl	73%	7j	68%	8j	_	9j			

the ring closing metathesis from taking place, in a situation similar to that reported by Vilar and co-workers.⁸

To test this hypothesis, the route was altered to incorporate a protecting group on the amide to prevent the amide from interacting with the Ru catalyst. The protecting group of choice was the *p*-methoxybenzyl group due to its electron donating properties, and the ease of removal *via* oxidative cleavage.⁹

Thus, reaction of *p*-methoxybenzylamine with benzaldehyde yielded the corresponding imine which upon allyl Grignard addition produced the secondary amine **7a** in near quantitative yield. HBTU promoted coupling between the amine **7a** and 2-fluoroacrylic acid **4** and then proceeded to generate the desired amide **8a** in good yield.

Gratifyingly, PMB protection of the amide unit allowed the ring closing metathesis reaction to proceed smoothly to yield the unsaturated lactam **9a** in quantitative yield (Table 1).

With the benzaldehyde example working efficiently, the scope of the methodology was explored (Table 1). Electron donating and electron withdrawing substituents on the aromatic ring were both tested with good results in all cases through the four step sequence. The electron withdrawing analogue being slightly less efficient in the first three steps, however, the RCM reaction produced the desired unsaturated lactam **9c** in quantitative yield.

Aliphatic substrates are also well tolerated, and afforded the corresponding fluorinated lactams **9f**, **9g** cleanly and in good yield over the 4 step sequence.

Finally, furan, pyrrole and pyridine frameworks were also explored due to their widespread use in medicinal and biological chemistry. Furfural and *N*-tosylpyrrole carboxaldehyde proceeded to generate the structurally interesting fluorinated δ -lactams **9h**, **9i** in good yield. In the case of the pyridine unit, the amino allylation and amide coupling proceeded in reasonable yields, affording intermediates **7j** and **8j** respectively. Unfortunately, the ring closing metathesis failed to generate the desired fluorinated δ -lactam **9j** under any of the conditions attempted. This was rationalised in the same manner as the previous example (Scheme 2), where an unprotected nitrogen atom was thought to bind to the Ru catalyst.

Table 2 Synthesis of δ-lactams 11a-g								
PMB	F CAN MeCN/H ₂ O		2 Pd/C HeOH	:				
R	Yield		Yield					
Ph 4-MeOPh 4-CF ₃ Ph Naph 4-BrPh i-Butyl Cvclohexyl	94% 40% 47% 61% 72% 97% 79%	10a 10b 10c 10d 10e 10f 10g	98% 83% Quant Quant Quant Quant Ouant	11a 11b 11c 11d 11e 11f 11g				

With the fluorinated ring system in place, the removal of the *p*-methoxybenzyl protecting group and reduction of the olefin unit were explored. Removal of the PMB group was achieved with cerium ammonium nitrate to yield the desired fluoro-pyridones **10a-g** in variable yields (Table 2). Unfortunately, treatment of the furyl and pyrrole substituted pyridones **9h-i** with CAN failed to yield the desired unprotected pyridones, resulting instead in substrate decomposition.

Hydrogenation of the fluoro-olefin unit, on the other hand, proceeded in near quantitative yield in most cases, and with complete diastereoselectivity to yield the desired fluorinated δ -lactams **11a–g**. The only exception was the brominated analogue **10e**, which unsurprisingly yielded the unbrominated lactam **11a** upon hydrogenation in excellent yield.

The *syn* selectivity of hydrogenation, and hence the stereochemistry of the newly formed C3 stereocentre, is dictated by the C6 substituent. The relative stereochemistry was corroborated by X-ray crystallography (Fig. 2).¹⁰

The bromo-lactam intermediate **10e**, on the other hand, presented us with an opportunity to further explore the scope of the fluoro-lactam intermediates as medicinal chemistry building blocks. Thus treatment of fluoro-lactam **10e** under Suzuki–Miyaura conditions with phenylboronic acid generated the tricyclic unit **12** in near quantitative yield.¹¹

Alkene reduction under standard conditions then generated the desired fluoro-lactam unit **13** in excellent yield and with complete diastereocontrol (Scheme 3).



Fig. 2 Crystal structure of fluorinated δ -lactam, 11a.



Scheme 3 Cross-coupling and reduction of α,β -unsaturated lactam 10e to generate δ -lactam 13.

Conclusions

In conclusion, we have developed a fast and reliable approach to the synthesis of a number of fluorinated δ -lactams in an efficient 5 step process. Work is now underway to expand the methodology to allow access to other fluorinated ring systems including pyridines and pyrroles as well as developing an enantioselective variant of this methodology.

Experimental

All reactions were performed in oven-dried glassware under an inert argon atmosphere unless otherwise stated. Tetrahydrofuran (THF), diethyl ether, toluene and dichloromethane were purified through a solvent purification system. Petroleum ether refers to the fraction boiling between 40 and 60 °C. All reagents were used as received, unless otherwise stated. Solvents were evaporated under reduced pressure at 40 °C unless otherwise stated. IR spectra were recorded as thin films on NaCl plates using a Fourier Transform spectrometer. Only significant absorptions (ν_{max}) are reported in wavenumbers (cm⁻¹). Proton magnetic resonance spectra (¹H NMR), fluorine magnetic resonance spectra (¹⁹F NMR) and carbon magnetic resonance spectra (13C NMR) were recorded at 400 MHz, 377 MHz and 100 MHz or at 500 MHz, 470 MHz and 125 MHz respectively. ¹³C NMR spectra were recorded with 1H noise decoupling. Chemical shifts (δ) are reported in parts per million (ppm) and are referenced to the residual solvent peak. The order of citation in parentheses is (1) the number of equivalent nuclei (by integration), (2) multiplicity (s = singlet, d =doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, m = multiplet, b = broad), (3) and the coupling constant (J) quoted in hertz to the nearest 0.1 Hz. High resolution mass spectra were obtained by electrospray (EI) chemical ionisation (CI) mass spectrometry operating at a resolution of 15 000 full widths at half height. Flash chromatography was performed using silica gel (40-63 micron) as the stationary phase. TLC was performed on aluminium sheets pre-coated with silica (Silica Gel 60 F254) unless otherwise stated. The plates were visualised by the quenching of UV fluorescence $(\lambda_{\text{max}} 254 \text{ nm})$ and/or by staining with either anisaldehyde, potassium permanganate, iodine or cerium ammonium molybdate followed by heating.

1-Phenylbut-3-en-1-ylamine, 3¹²

Benzaldehyde (0.21 g, 2.0 mmol) was dissolved in methanol (4 mL) and the resulting solution was cooled to -78 °C. NH₃ (*ca.* 4 mL) was condensed into the solution, and the resulting reaction mixture was warmed to -10 °C and stirred until the excess ammonia had evaporated (3 h). Allylboronic pinacol ester (0.76 mL, 4.0 mmol) was added and the reaction was stirred for 2 h. The reaction vessel was then allowed to warm up to room temperature and stirred for a further 1 h. Aq. HCl (6 M) was added slowly to the solution until pH 1 and the mixture was extracted with diethyl ether (3 × 20 mL). The

aqueous phase was collected, and aq. NaOH (2 M) was added slowly until pH 14. The aqueous solution was extracted with CH_2Cl_2 (3 × 20 mL). The combined CH_2Cl_2 phases were then dried (Na₂SO₄), filtered and evaporated *in vacuo* to yield amine 3 as a colourless oil (0.28 g, 1.9 mmol, 95%) which was of sufficient purity to enable the substance to be used without further purification.

¹H (CDCl₃, 400 MHz) δ : 7.27–7.15 (5H, m), 5.68–5.63 (1H, m), 5.06–5.00 (2H, m), 3.91 (1H, dd, J_{HH} = 8.0, 5.2 Hz) 2.40–2.27 (2H, m), 1.60 (2H, br s). ¹³C (CDCl₃, 125 MHz) δ : 145.8, 135.4, 128.4, 127.9, 126.4, 117.7, 55.4, 44.2.

2-Fluoroacrylic acid, 4¹³

Commercially available 2-fluoroacrylic acid methyl ester (0.87 mL, 9.6 mmol) was dissolved in $EtOH-H_2O$ (8.7:1.3, 10 mL). Aq. NaOH (2 M) was then added dropwise until pH 11 was reached, and the resulting mixture was stirred for 30 min. After which, the solution was evaporated to dryness under vacuum to yield the sodium salt as a white solid. Diethyl ether (20 mL) was added to the salt, followed by aq. HCl (6 M) dropwise until the solid dissolved. The layers were then separated, and the aqueous layer was extracted with diethyl ether (10 mL). The organics were combined, dried over sodium sulfate and evaporated *in vacuo* to yield the desired acid 4 as a white solid (0.74 g, 8.0 mmol, 87%) with no need for further purification.

¹H (CDCl₃, 400 MHz) δ : 11.51 (1H, br s), 5.92 (1H, dd, J_{HF} = 42.8, J_{HH} = 3.6 Hz), 5.52 (1H, dd, J_{HF} = 12.4, J_{HH} = 3.2 Hz). ¹⁹F (CDCl₃, 470 MHz) δ : -118.3. ¹³C (CDCl₃, 125 MHz) δ : 165.4 (d, J_{CF} = 46.3 Hz), 151.3 (d, J_{CF} = 323.8 Hz), 105.2 (d, J_{CF} = 18.8 Hz).

2-Fluoro-N-(1-phenyl-but-3-enyl)-propenamide, 5

A solution of 2-fluoroacrylic acid 4 (0.41 g, 4.6 mmol) in CH_2Cl_2 (25 mL) was treated with HBTU (2.59 g, 6.5 mmol) and was then cooled down to 0 °C. DIPEA (1.19 mL, 6.5 mmol) and amine 3 (0.80 g, 5.4 mmol) were sequentially added, and the reaction was stirred at room temperature until completion by TLC analysis (1 h). The solvent was removed under reduced pressure, and the resulting residue was purified by flash column chromatography (0–5% EtOAc in petroleum ether) to yield amide 5 as a white solid (0.89 g, 4.0 mmol, 89%). m.p. 63–65 °C.

¹H (CDCl₃, 400 MHz) δ: 7.28–7.16 (5H, m), 6.48 (1H, br s), 5.66–5.55 (2H, m), 5.09–5.03 (4H, m), 2.55 (2H, t, J_{HH} = 6.8 Hz). ¹⁹F (CDCl₃, 470 MHz) δ: -121.3. ¹³C (CDCl₃, 125 MHz) δ: 158.8 (d, J_{CF} = 30.0 Hz), 156.2 (d, J_{CF} = 268.8 Hz) 140.8, 133.4, 128.8, 127.7, 126.5, 118.3, 99.1 (d, J_{CF} = 15.0 Hz), 52.6, 40.3. m/z[CI (+ve)] 220.3 [M + H]⁺, HRMS found [M + H]⁺ 220.1135, C₁₃H₁₅FNO requires 220.1138. IR (thin film) ν_{max} = 3338, 1651, 1529, 1190 cm⁻¹.

1-(Toluene-4'-sulfonyl)-1H-pyrrol-2-carboxaldehyde¹⁴

Pyrrole-2-carboxyaldehyde (1.00 g, 10.5 mmol) was dissolved in THF (20 mL) and the solution was cooled down to 0 °C. NaH (0.62 g, 60% in oil, 15.0 mmol) was added slowly, and the resulting mixture was stirred at 0 °C for 10 min. Tosyl chloride

(3.0 g, 15.0 mmol) was added, and the reaction mixture was stirred for a further 15 min at 0 °C before being allowed to warm up to room temperature and stirred overnight. The reaction mixture was quenched with H₂O (20 mL), and extracted with CH₂Cl₂ (2 × 25 mL). The combined organics were then dried (Na₂SO₄) and the solvent was removed *in vacuo*. The resulting crude residue was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the tosylated pyrrole as a white solid (2.47 g, 9.9 mmol, 94%).

¹H (CDCl₃, 400 MHz) δ : 10.01 (1H, s), 7.83 (2H, d, J_{HH} = 8.3 Hz), 7.65 (1H, dd, J_{HH} = 3.0, 1.8 Hz), 7.35 (2H, d, J_{HH} = 8.3 Hz), 7.12 (1H, dd, J_{HH} = 3.7, 1.8 Hz), 6.43 (1H, br appt, J_{HH} = 3.4 Hz), 2.45 (3H, s). ¹³C (CDCl₃, 125 MHz) δ : 178.9, 145.9, 135.3, 133.6, 130.1, 129.5, 127.6, 124.4, 112.4, 21.7.

General procedure A: synthesis of PMB protected allylic amines from aldehydes

Na₂SO₄ (2 g) was dried under vacuum in a round bottom flask for 10 min. The aldehyde (1 eq.) was then added, followed by toluene (15 mL) and 4-methoxybenzylamine (1.1 eq.). The resulting reaction mixture was then heated to reflux for 3 h. The reaction was then cooled down to room temperature, and the solid residue was filtered off. The solution was concentrated under vacuum and the residue was re-dissolved in anhydrous diethyl ether (20 mL). The solution was placed under argon and was cooled down to 0 °C. The solution was then treated dropwise with allylmagnesium bromide (1.5 eq.) and the resulting mixture was allowed to warm up to room temperature overnight. The reaction was quenched with water (20 mL) and extracted with diethyl ether (3×20 mL). The combined organic extracts were dried over sodium sulfate, and evaporated under reduced pressure. The crude residue was purified by flash column chromatography to afford the corresponding allylic amine.

4'-Methoxy-N-(1-phenyl-3-butenyl)benzylamine, 7a¹⁵

Following general procedure A, benzaldehyde (0.95 mL, 9.4 mmol) was reacted with 4-methoxybenzylamine (1.4 mL, 10.4 mmol) and allylmagnesium bromide (14.3 mL 1.0 M in THF, 14.3 mmol). The crude residue was purified by flash column chromatography (0–2.5% EtOAc in petroleum ether) to yield the expected amine 7a (2.39 g, 8.9 mmol, 95% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.40–7.36 (4H, m,), 7.30–7.28 (1H, m), 7.20 (2H, d, J_{HH} = 8.6 Hz), 6.88 (2H, d, J_{HH} = 8.6 Hz), 5.75–5.70 (1H, m), 5.11–5.70 (2H, m), 3.83 (3H, s), 3.71 (1H, dd, J_{HH} = 7.8, 5.9 Hz), 3.64 (1H, d, J_{HH} = 13.2 Hz), 3.49 (1H, d, J_{HH} = 13.2 Hz,), 2.44–2.41 (2H, m), 1.73 (1H, br s). ¹³C (CDCl₃, 125 MHz) δ: 158.5, 143.9, 135.5, 132.8, 129.3 (2C), 128.4 (2C), 127.3 (2C), 127.0 (2C), 117.5, 113.7, 61.5, 55.3, 50.8, 43.1.

4'-Methoxy-N-[1-(4"-methoxyphenyl)-3-butenyl]benzylamine, 7b¹⁶

Following general procedure A, 4-methoxybenzaldehyde (0.84 mL, 7.3 mmol) was reacted with 4-methoxybenzylamine (1.1 mL, 8.0 mmol) and allylmagnesium bromide (11.0 mL

1.0 M in THF, 11.0 mmol). The crude residue was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the expected amine 7**b** (1.67 g, 5.6 mmol, 77% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ : 7.30 (2H, d, J_{HH} = 8.8 Hz), 7.19 (2H, d, J_{HH} = 8.6 Hz), 6.92 (2H, d, J_{HH} = 8.8 Hz), 6.87 (2H, d, J_{HH} = 8.6 Hz), 5.75–5.68 (1H, m), 5.12–5.04 (2H, m), 3.85 (3H, s) 3.82 (3H, s), 3.68–3.60 (2H, m), 3.47 (1H, d, J_{HH} = 12.9 Hz), 2.43–2.39 (2H, m). ¹³C (CDCl₃, 125 MHz) δ : 158.6, 158.5, 135.9, 135.6 (2C), 132.8, 129.3 (2C), 128.3 (2C), 117.4, 113.7 (2C), 60.81, 55.3, 55.2, 50.7, 43.2.

4'-Methoxy-*N*-[1-(4"-trifluoromethanephenyl)-3-butenyl]benzylamine, 7c

Following general procedure A, 4-(trifluoromethyl)benzaldehyde (0.78 mL, 5.7 mmol) was reacted with 4-methoxybenzylamine (0.83 mL, 6.3 mmol) and allylmagnesium bromide (8.6 mL 1.0 M in THF, 8.6 mmol). The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the expected amine 7c (1.27 g, 3.8 mmol, 66% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.62 (2H, d, J_{HH} = 8.2 Hz), 7.51 (2H, d, J_{HH} = 8.2 Hz), 7.18 (2H, d, J_{HH} = 8.8 Hz), 6.88 (2H, d, J_{HH} = 8.8 Hz), 5.75–5.65 (1H, m), 5.12–5.08 (2H, m), 3.83 (3H, s), 3.77 (1H, dd, J_{HH} = 7.6, 5.6 Hz), 3.64 (1H, d, J_{HH} = 13.2 Hz), 3.45 (1H, d, J_{HH} = 13.2 Hz), 2.45–2.34 (2H, m). ¹⁹F (CDCl₃, 377 MHz) δ: -62.3. ¹³C (CDCl₃, 125 MHz) δ: 158.7, 148.2, 134.8, 132.4, 129.8 (2C), 127.7 (2C), 125.7, 125.4 (2C), 125.3, 118.2, 113.8 (2C), 61.2, 55.3, 44.2, 33.6. *m*/*z* [CI (+ve)] 336.1 [M + H]⁺. HRMS found [M + H]⁺ 336.1572, C₁₉H₂₁F₃NO requires 336.1575. IR (thin film) ν_{max} = 2935, 1612, 1512, 1323, 1246, 1120, 1066 cm⁻¹.

4'-Methoxy-N-[1-(naphthalen-1"-yl)-3-butenyl]benzylamine, 7d

Following general procedure A, 1-naphthaldehyde (0.86 mL, 6.40 mmol) was reacted with 4-methoxybenzylamine (0.84 mL, 7.0 mmol) and allylmagnesium bromide (9.6 mL 1.0 M in THF, 9.6 mmol). The crude product was purified by flash column chromatography (0–10% diethyl ether in petroleum ether) to yield the desired amine 7d (2.03 g, 6.3 mmol, 99% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 8.10 (1H, appd, J_{HH} = 7.4 Hz), 7.81–7.79 (1H, m), 7.72–7.67 (2H, m), 7.44–7.38 (3H, m), 7.09 (2H, d, J_{HH} = 8.6 Hz), 6.76 (2H, d, J_{HH} = 8.6 Hz), 5.75–5.67 (1H, m), 5.05–4.97 (2H, m), 3.71 (3H, s), 3.60 (1H, d, J_{HH} = 13.0 Hz), 3.44 (1H, d, J_{HH} = 13.0 Hz), 2.59–2.54 (1H, m), 2.41–2.35 (1H, m). ¹³C (CDCl₃, 125 MHz) δ: 158.7, 139.7, 138.9, 135.8, 134.1, 132.9, 131.7, 129.4 (2C), 129.0, 127.4, 125.7, 125.3, 123.9, 123.1, 117.7, 113.8 (2C), 56.9, 55.4, 51.1, 42.2. *m/z* [CI (+ve)] 318.2 [M + H]⁺, HRMS found [M + H]⁺ 318.1862, C₂₂H₂₄NO requires 318.1858. IR (thin film) ν_{max} = 2960, 1511, 1246, 1035 cm⁻¹.

4'-Methoxy-N-[1-(4"-bromophenyl)-3-butenyl]benzylamine, 7e

Following general procedure A, 4-bromobenzaldehyde (1 g, 5.4 mmol) was reacted with 4-methoxybenzylamine (0.74 mL,

5.4 mmol) and allylmagnesium bromide (8.1 mL 1.0 M in THF, 8.1 mmol). The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the desired amine 7e (1.82 g, 5.25 mmol, 97% yield) as a pale yellow oil.

¹H (CDCl₃, 500 MHz) δ : 7.48 (2H, d, J_{HH} = 8.4 Hz), 7.27 (2H, d, J_{HH} = 8.4 Hz), 7.15 (2H, d, J_{HH} = 9.1 Hz), 6.87 (2H, d, J_{HH} = 9.1 Hz), 5.72–5.63 (1H, m), 5.10–5.05 (2H, m), 3.82 (3H, s), 3.66 (1H, dd, J_{HH} = 7.8, 6.3 Hz), 3.61 (1H, d, J_{HH} = 13.1 Hz), 3.46 (1H, d, J_{HH} = 13.1 Hz), 2.40–2.35 (2H, m). ¹³C (CDCl₃, 125 MHz) δ : 158.7, 143.3, 135.1, 132.6, 131.6 (2C), 129.3 (2C), 129.1 (2C), 120.4, 117.9, 113.9 (2C), 60.7, 55.3, 50.9, 42.7. m/z [CI (+ve)] 345.8 M⁺, HRMS found [M + H]⁺ 346.0804, C₁₈H₂₁⁷⁹BrNO requires 346.0807. IR (thin film) ν_{max} = 2945, 2835, 1511, 1245, 1035, 1009 cm⁻¹.

4'-Methoxy-N-(1-isobutyl-3-butenyl)benzylamine, 7f

Following general procedure A, isovaleraldehyde (1.25 mL, 11.6 mmol) was reacted with 4-methoxybenzylamine (1.7 mL, 12.7 mmol) and allylmagnesium bromide (17.4 mL 1.0 M in THF, 17.4 mmol). The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield **7f** (2.06 g, 8.4 mmol, 76% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.26 (2H, d, J_{HH} = 8.8 Hz), 6.86 (2H, d, J_{HH} = 8.8 Hz), 5.82–5.70 (1H, m), 5.14–5.00 (2H, m), 3.81 (3H, s), 3.73 (1H, quint, J_{HH} = 6.4 Hz), 2.70–2.65 (1H, m), 2.25–2.03 (2H, m), 1.62 (1H, appsept, J_{HH} = 6.8 Hz), 1.46–1.23 (2H, m), 0.90 (3H, d, J_{HH} = 6.6 Hz), 0.87 (3H, d, J_{HH} = 6.6 Hz). ¹³C (CDCl₃, 100 MHz) δ: 158.5, 135.8, 133.0, 129.3 (2C), 118.7, 113.7 (2C), 55.3, 54.0, 50.5, 41.2, 38.6, 24.7, 22.5. *m*/*z* [CI (+ve)] 248.2 [M + H]⁺, HRMS found [M + H]⁺ 248.2018, C₁₆H₂₆NO requires 248.2014. IR (thin film) ν_{max} = 2953, 2906, 1612, 1512, 1464, 1246 cm⁻¹.

4'-Methoxy-N-(1-cyclohexyl-3-butenyl)benzylamine, 7g

Following general procedure A, cyclohexanecarboxaldehyde (1.08 mL, 8.87 mmol) was reacted with 4-methoxybenzylamine (1.2 mL, 9.8 mmol) and allylmagnesium bromide (13.3 mL 1.0 M in THF, 13.3 mmol). The crude product was purified by flash column chromatography (0–2.5% diethyl ether in petroleum ether) to yield the desired amine 7g (1.81 g, 6.6 mmol, 74% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.26 (2H, d, J_{HH} = 8.6 Hz), 6.87 (2H, d, J_{HH} = 8.6 Hz), 5.85–5.75 (1H, m), 5.11–5.06 (2H, m), 3.82 (3H, s), 3.71 (2H, s), 2.42–2.38 (1H, m), 2.32–2.26 (1H, m), 2.16–2.09 (1H, m), 1.81–1.70 (4H, m), 1.47–1.43 (1H, m), 1.31–1.18 (4H, m,), 1.10–1.00 (2H, m). ¹³C (CDCl₃, 125 MHz) δ: 158.5, 136.8, 133.3, 129.3 (2C), 116.8, 113.7 (2C), 61.1, 55.3, 51.3, 40.6, 35.3, 29.4, 28.9, 26.8, 26.7, 26.7. *m*/z [CI (+ve)] 274.2 [M + H]⁺, HRMS found [M + H]⁺ 274.2171, C₁₈H₂₈NO requires 274.2168. IR (thin film) ν_{max} = 2924, 1511, 1246, 1037 cm⁻¹.

4'-Methoxy-N-[1-(furan-2"-yl)-3-butenyl]benzylamine, 7h

Following general procedure A, 2-furaldehyde (0.86 mL, 10.4 mmol) was reacted with 4-methoxybenzylamine (1.3 mL, 11.4 mmol) and allylmagnesium bromide (15.6 mL 1.0 M in

THF, 15.6 mmol). The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the desired amine 7h (2.21 g, 8.59 mmol, 83% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.42 (1H, dd, J_{HH} = 1.8, 0.8 Hz), 7.23 (2H, d, J_{HH} = 8.7 Hz), 6.88 (2H, d, J_{HH} = 8.7 Hz), 6.36 (1H, dd, J_{HH} = 3.7, 1.8 Hz), 6.21 (1H, d, J_{HH} = 3.7 Hz), 5.79–5.62 (1H, m), 5.14–5.06 (2H, m), 3.83 (3H, s), 3.79 (1H, t, J_{HH} = 6.8 Hz), 3.72 (1H, d, J_{HH} = 13.0 Hz), 3.56 (1H, d, J_{HH} = 13.0 Hz), 2.58–2.53 (2H, m). ¹³C (CDCl₃, 125 MHz) δ: 158.6, 156.3, 141.5, 134.9, 132.4, 129.4 (2C), 117.5, 113.8 (2C), 109.9, 106.6, 55.3, 54.7, 50.5, 39.3. m/z [CI (+ve)] 258.2 [M + H]⁺, HRMS found [M + H]⁺ 258.1492, C₁₆H₂₀NO₂ requires 258.1494. IR (thin film) ν_{max} = 2930, 2850, 1511, 1441, 1246, 1035 cm⁻¹.

4'-Methoxy-*N*-[1-(1"-(toluene-4"'-sulfonyl)-1*H*-pyrrol-2"-yl)-3butenyl]benzylamine, 7i

Following general procedure A, 1-(toluene-4'-sulfonyl)-1*H*-pyrrol-2-carboxaldehyde (1 g, 4.02 mmol) was reacted with 4-methoxybenzylamine (0.53 mL, 4.4 mmol) and allylmagnesium bromide (6.0 mL 1.0 M in THF, 6.0 mmol). The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired amine 7i (1.4 g, 3.42 mmol, 85% yield) as a brown oil.

¹H (CDCl₃, 500 MHz) δ: 7.62 (2H, d, J_{HH} = 8.3 Hz), 7.36 (1H, dd, J_{HH} = 3.2, 1.7 Hz), 7.25 (2H, d, J_{HH} = 8.3 Hz), 7.15 (2H, d, J_{HH} = 8.6 Hz), 6.84 (2H, d, J_{HH} = 8.6 Hz), 6.35–6.33 (1H, m), 6.30 (1H, t, J_{HH} = 3.3 Hz), 5.73–5.63 (1H, m), 5.05–4.98 (2H, m), 4.22 (1H, dd, J_{HH} = 7.3, 5.1 Hz), 3.84 (3H, s), 3.43 (1H, d, J_{HH} = 12.6 Hz), 3.25 (1H, d, J_{HH} = 12.6 Hz), 2.47–2.30 (2H, m), 2.41 (3H, s). ¹³C (CDCl₃, 125 MHz) δ: 158.6, 144.9, 137.6, 136.7, 135.0, 132.6, 129.9 (2C), 129.1 (2C), 126.7 (2C), 123.1, 117.5, 114.1 (2C), 112.7, 111.6, 55.3, 54.0, 50.1, 40.7, 21.7. *m/z* [ESI] 433.1 [M + Na]⁺, HRMS found [M + Na]⁺ 433.1539, C₂₃H₂₆N₂O₃SNa requires 433.1556. IR (thin film) ν_{max} = 2975, 1512, 1247, 1172 cm⁻¹.

4'-Methoxy-N-[1-(pyridin-2"-yl)-3-butenyl]benzylamine, 7j

Following general procedure A, pyridine-2-carboxaldehyde (0.89 mL, 9.30 mmol) was reacted with 4-methoxybenzylamine (1.2 mL, 10.2 mmol) and allylmagnesium bromide (14.0 mL 1.0 M in THF, 14.0 mmol). The crude product was purified by flash column chromatography (0–25% diethyl ether in petroleum ether) to yield the desired amine 7j (1.82 g, 6.78 mmol, 73% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 8.51 (1H, dq, J_{HH} = 4.8, 0.9 Hz), 7.58 (1H, td, J_{HH} = 7.7, 1.8 Hz), 7.30 (1H, d, J_{HH} = 7.7 Hz), 7.12 (2H, d, J_{HH} = 8.6 Hz), 7.08 (1H, ddd, J_{HH} = 7.4, 4.8, 1.1 Hz), 6.76 (2H, d, J_{HH} = 8.6 Hz), 5.70–5.60 (1H, m), 4.99–4.92 (2H, m), 3.75 (1H, dd, J_{HH} = 7.8, 5.9 Hz), 3.71 (3H, s), 3.54 (1H, d, J_{HH} = 12.9 Hz), 3.43 (1H, d, J_{HH} = 12.9 Hz), 2.50–2.43 (1H, m), 2.39–2.32 (1H, m). ¹³C (CDCl₃, 125 MHz) δ: 163.3, 158.5, 149.4, 136.3, 135.3, 132.6, 129.3 (2C), 121.9 (2C), 117.5, 113.7 (2C), 62.8, 55.3, 51.1, 41.6. m/z [CI (+ve)] 269.1 [M + H]⁺, HRMS found [M + H]⁺ 269.1653, C₁₇H₂₁N₂O requires 269.1654. IR (thin film) ν_{max} = 2836, 1512, 1247, 905 cm⁻¹.

General procedure B: amide coupling of allylic amine

2-Fluoroacrylic acid (1.5 eq.) and HBTU (1.5 eq.) were dry mixed and then dissolved in CH_2Cl_2 (20 mL). DIPEA (1.5 eq.) was added followed by the corresponding amine (1 eq.). The resulting solution was stirred and refluxed for 17 h. The reaction was cooled down to room temperature and the solvent was then evaporated under reduced pressure. The crude material was purified by flash column chromatography.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-(1-phenyl-3-butenyl)acrylamide, 8a

Amine 7a (0.5 g, 1.8 mmol) was coupled with 2-fluoroacrylic acid (0.25 g, 2.8 mmol) using HBTU (1.1 g, 2.8 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the desired dialkene 8a (0.38 g, 1.10 mmol, 63% yield) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) & 7.36–7.32 (5H, m), 6.97 (2H, d, $J_{HH} = 8.6$ Hz), 6.76 (2H, d, $J_{HH} = 8.3$ Hz), 5.75–5.66 (1H, m), 5.35 (1H, br s), 5.26 (1H, br s), 5.08–4.99 (3H, m), 4.47 (1H, d, $J_{HH} = 15.7$ Hz), 4.16 (1H, br s), 3.78 (3H, s), 2.74 (2H, br s). ¹⁹F (CDCl₃, 470 MHz) & -102.4, -114.2. ¹³C (CDCl₃, 125 MHz) & 163.3 (d, $J_{CF} = 30.0$ Hz), 158.7, 158.2 (d, $J_{CF} = 271.3$), 138.1, 134.2, 134.1 (2C), 129.2 (2C), 128.6 (2C) 128.1 (2C), 118.1, 113.6 (2C), 99.4 (d, $J_{CF} = 16.3$ Hz), 55.2 (2C), 35.7, 33.5. m/z [EI (+ve)] 339.2 [M]⁺, HRMS found [M]⁺ 339.1639, C₂₁H₂₂FNO₂ requires 339.1635. IR (thin film) $\nu_{max} = 2937$, 1637, 1512, 1417, 1246, 1176, 1033 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-[1-(4"'-methoxyphenyl)-3-butenyl]acrylamide, 8b

Amine 7b (0.55 g, 1.8 mmol) was coupled with 2-fluoroacrylic acid (0.25 g, 2.8 mmol) using HBTU (1.1 g, 2.8 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the desired dialkene **8b** (0.44 g, 1.2 mmol, 66%) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.27 (2H, d, J_{HH} = 8.6 Hz), 6.98 (2H, d, J_{HH} = 8.6 Hz), 6.89 (2H, d, J_{HH} = 8.4 Hz), 6.77 (2H, d, J_{HH} = 8.4 Hz), 5.74–5.64 (1H, m), 5.35 (1H, br s), 5.23 (1H, br s), 5.07–4.92 (3H, m), 4.46 (1H, d, J_{HH} = 15.5 Hz), 4.14 (1H, br s), 3.83 (3H, s), 3.78 (3H, s), 2.69 (2H, br s). ¹⁹F (CDCl₃, 470 MHz) δ: -102.1, -104.2. ¹³C (CDCl₃, 125 MHz) δ: 163.2 (d, J_{CF} = 30.0 Hz), 159.4, 159.3, 158.7, 158.5 (d, J_{CF} = 271.3), 134.2, 134.1, 129.8 (2C), 129.2 (2C), 118.0, 113.9 (2C), 113.6 (2C), 99.2 (d, J_{CF} = 15.0 Hz), 65.9, 55.3, 55.2, 36.04, 33.5. m/z [EI (+ve)] 369.2 [M]⁺, HRMS found [M]⁺ 369.1743, C₂₂H₂₄FNO₃ requires 369.1740. IR (thin film) ν_{max} = 2933, 2837, 1635, 1512, 1246, 1178, 1033 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-[1-(4"'-trifluoromethanephenyl)-3-butenyl]acrylamide, 8c

Amine 7c (0.64 g, 1.8 mmol) was coupled with 2-fluoroacrylic acid (0.25 g, 2.8 mmol) using HBTU (1.1 g, 2.8 mmol) following general procedure B. The crude product was purified

by flash column chromatography (0-5% diethyl ether in petroleum ether) to yield the desired dialkene **8c** (0.33 g, 0.80 mmol, 45%) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ : 7.57 (2H, d, J_{HH} = 8.0 Hz), 7.44 (2H, d, J_{HH} = 8.0 Hz), 6.98 (2H, d, J_{HH} = 8.4 Hz), 6.76 (2H, d, J_{HH} = 8.4 Hz), 5.76–5.66 (1H, m), 5.41 (1H, d, J_{HH} = 3.2 Hz), 5.29 (1H, d, J_{HH} = 3.2 Hz), 5.14–5.09 (3H, m), 4.43 (1H, d, J_{HH} = 15.6 Hz), 4.34 (1H, br. s), 3.80 (3H, s), 2.79 (2H, br. s). ¹⁹F (CDCl₃, 377 MHz) δ : -62.3, -102.5, -104.4. ¹³C (CDCl₃, 125 MHz) δ : 163.4 (d, J_{CF} = 29.8 Hz), 159.0, 158.0 (d, J_{CF} = 273.0 Hz), 142.5, 139.0, 137.8, 133.9, 129.9, 129.2 (2C), 128.8 (2C), 125.3 (2C), 125.0, 122.9, 118.5, 113.7 (2C), 99.8 (d, J_{CF} = 12.5 Hz), 59.8, 55.2, 35.4. m/z [EI (+ve)] 407.1 [M]⁺, HRMS found [M]⁺ 407.1504, C₂₂H₂₁F₄NO₂ requires 407.1508. IR (thin film) ν_{max} = 2939, 1639, 1514, 1415, 1325, 1246, 1120, 1068 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-[1-(naphthalen-1"'-yl)-3-butenyl]acrylamide, 8d

Amine 7d (0.5 g, 1.5 mmol) was coupled with 2-fluoroacrylic acid (0.21 g, 2.3 mmol) using HBTU (0.89 g, 2.3 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the desired dialkene 8d (0.21 g, 0.53 mmol, 36%) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 8.07 (1H, d, J_{HH} = 8.4 Hz), 7.87 (1H, br d, J_{HH} = 8.4 Hz), 7.82 (1H, t, J_{HH} = 4.6 Hz), 7.59–7.51 (2H, m), 7.44 (2H, d, J_{HH} = 5.0 Hz), 6.76 (2H, d, J_{HH} = 8.3 Hz), 6.63 (2H, d, J_{HH} = 8.3 Hz), 6.57 (1H, br s), 5.87–5.76 (1H, m), 5.32 (1H, br d, J_{HF} = 47.8 Hz), 5.14–5.05 (3H, m), 4.40 (1H, br d, J_{HH} = 16.2 Hz), 3.91 (1H, dd, J_{HH} = 16.2, 1.7 Hz), 3.75 (3H, s), 2.77 (2H, appt, J_{HH} = 6.7 Hz). ¹⁹F (CDCl₃, 377 MHz) δ: -103.7, -103.8. ¹³C (CDCl₃, 100 MHz) δ: 162.9 (d, J_{CF} = 30.4 Hz), 158.7, 158.2 (d, J_{CF} = 263.3 Hz), 134.7, 133.9, 132.6, 132.5, 129.2, 128.8, 128.6 (2C), 126.9, 126.5, 124.7, 124.6, 123.4, 117.7, 114.4, 113.4 (2C), 99.9 (d, J_{CF} = 15.8 Hz), 55.2 (2C), 54.1, 36.3. m/z [EI (+ve)] 389.2 [M]⁺. HRMS found [M]⁺ 389.1794, C₂₅H₂₄FNO₂ requires 389.1791. IR (thin film) ν_{max} = 2970, 1632, 1513, 1246, 1176 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-[1-(4"'-bromophenyl)-3-butenyl]acrylamide, 8e

Amine 7e (0.50 g, 1.4 mmol) was coupled with 2-fluoroacrylic acid (0.19 g, 2.2 mmol) using HBTU (0.82 g, 2.2 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–5% diethyl ether in petroleum ether) to yield the desired dialkene 8e (0.24 g, 0.57 mmol, 41%) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ: 7.47 (2H, d, J_{HH} = 8.1 Hz), 7.21 (2H, d, J_{HH} = 8.1 Hz), 6.99 (2H, d, J_{HH} = 8.6 Hz), 6.79 (2H, d, J_{HH} = 8.6 Hz), 5.74–5.63 (1H, m), 5.40–5.25 (2H, m,), 5.19–5.05 (3H, m), 4.44 (1H, d, J_{HH} = 16.0 Hz), 4.25 (1H, m), 3.81 (3H, s), 2.74–2.69 (2H, m). ¹⁹F (CDCl₃, 470 MHz) δ: -102.3, -104.2. ¹³C (CDCl₃, 125 MHz) δ: 163.3 (d, J_{CF} = 29.4 Hz), 158.9, 157.9 (d, J_{CF} = 273.3 Hz), 137.3, 133.9, 131.6 (2C), 130.3 (2C), 129.1 (2C), 129.0, 122.0, 118.3, 113. 7 (2C), 99.6 (d, J_{CF} = 15.6 Hz), 55.3 (2C), 35.6, 23.9. m/z [EI (+ve)] 417.0 [M]⁺, HRMS found

 $[M]^+$ 417.0739, C₂₁H₂₁⁷⁹BrFNO₂ requires 417.0740. IR (thin film) ν_{max} = 2940, 1639, 1513, 1247, 1176 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-(1-isobutyl-3-butenyl)acrylamide, 8f

Amine 7f (0.27 g, 1.1 mmol) was coupled with 2-fluoroacrylic acid (0.25 g, 2.8 mmol) using HBTU (1.1 g, 2.8 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–2.5% diethyl ether in petroleum ether) to yield the desired dialkene 8f (0.26 g, 0.81 mmol, 74%) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ: 7.27 (2H, d, J_{HH} = 8.0 Hz), 6.85 (2H, d, J_{HH} = 7.2 Hz), 5.73–5.62 (1H, m), 5.26 (1H, br s), 5.15 (1H, br s), 5.13–5.02 (2H, m), 4.54–4.39 (2H, m), 4.19–4.01 (1H, m), 3.81 (3H, s), 2.33–2.19 (2H, m), 1.52–1.16 (3H, m), 0.85 (3H, d, J_{HH} = 6.4 Hz,), 0.74 (3H, d, J_{HH} = 6.0 Hz). ¹⁹F (CDCl₃, 377 MHz) δ: -102.4 (dd, J_{FH} = 47.5, 16.2 Hz), -103.6 (dd, J_{FH} = 46.5, 15.1 Hz). ¹³C (CDCl₃, 125 MHz) δ: 163.6 (d, J_{CF} = 30.1 Hz), 158.7, 158.3 (d, J_{CF} = 270.0 Hz), 135.4, 134.3, 130.3, 129.2 (2C), 118.0, 113.8 (2C), 98.5, 57.2, 55.3, 44.1, 42.0, 38.9, 24.6, 22.7. m/z [CI (+ve)] 320.2 [M + H]⁺, HRMS found [M + H]⁺ 320.2025, C₁₉H₂₇FNO₂ requires 320.2026. IR (thin film) ν_{max} = 2958, 1637, 1514, 1246 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-(1-cyclohexyl-3-butenyl)acrylamide, 8g

Amine 7g (0.48 g, 1.8 mmol) was coupled with 2-fluoroacrylic acid (0.24 g, 2.6 mmol) using HBTU (1.0 g, 2.6 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–2.5% diethyl ether in petroleum ether) to yield the desired dialkene **8g** (0.44 g, 1.3 mmol, 70%) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ : 7.32 (2H, d, J_{HH} = 8.6 Hz), 6.84 (2H, d, J_{HH} = 8.6 Hz), 5.63–5.56 (1H, m), 5.27–4.91 (4H, m), 4.43 (2H, s), 3.81 (3H, s), 3.69 (1H, br t, J_{HH} = 9.3 Hz), 2.51–2.44 (1H, m), 2.33–2.25 (1H, m), 1.85–1.51 (5H, m), 1.20–1.05 (2H, m), 0.97–0.81 (4H, m). ¹⁹F (CDCl₃, 470 MHz) δ : –102.7. ¹³C (CDCl₃, 125 MHz) δ : 164.6 (d, J_{CF} = 30.0 Hz), 158.7, 158.2 (d, J_{CF} = 270.0 Hz), 134.6, 130.1, 129.8 (2C), 117.7, 113.7 (2C), 98.5 (d, J_{CF} = 15.0 Hz), 64.7, 55.3, 44.8, 40.9, 35.1, 30.5, 30.4, 26.3, 26.1, 26.0. m/z [CI (+ve)] 346.3 [M + H]⁺, HRMS found [M + H]⁺ 346.2176, C₂₁H₂₉FNO₂ requires 346.2182. IR (thin film) ν_{max} = 2924, 2852, 1635, 1513, 1442, 1246 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-[1-(furan-2'''-yl)-3-butenyl]acrylamide, 8h

Amine 7h (0.5 g, 1.9 mmol) was coupled with 2-fluoroacrylic acid (0.26 g, 2.9 mmol) using HBTU (1.1 g, 2.9 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–10% diethyl ether in petroleum ether) to yield the desired dialkene 8h (0.18 g, 0.54 mmol, 28%) as a yellow oil.

¹H (CDCl₃, 400 MHz) δ : 7.36 (1H, br s), 7.00 (2H, d, J_{HH} = 8.6 Hz), 6.77 (2H, d, J_{HH} = 8.6 Hz), 6.35–6.25 (2H, m), 5.72–5.64 (1H, m), 5.38–5.24 (2H, m), 5.10–5.05 (3H, m), 4.55 (1H, d, J_{HH} = 15.7 Hz), 4.27 (1H, m), 3.80 (3H, s), 2.65–2.59 (2H, m).

¹⁹F (CDCl₃, 470 MHz) δ: -103.5, -105.3. ¹³C (CDCl₃, 125 MHz) δ: 163.1 (d, J_{CF} = 29.4 Hz), 158.6, 157.6 (d, J_{CF} = 267.8 Hz), 151.9, 142.4, 133.1, 129.2 (2C), 118.7, 114.2, 113.6 (2C), 110.3, 109.2, 99.3, 57.7, 55.2, 44.4, 23.8. m/z [EI (+ve)] 329.2 [M]⁺, HRMS found [M]⁺ 329.1427, C₁₉H₂₀FNO₃ requires 329.1428. IR (thin film) ν_{max} = 2956, 1699, 1513, 1246, 1117 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-[1-(1"'-(toluene-4""-sulfonyl)-1*H*-pyrrol-2"'-yl)-3-butenyl]acrylamide, 8i

Amine 7i (0.66 g, 1.6 mmol) was coupled with 2-fluoroacrylic acid (0.22 g, 2.4 mmol) using HBTU (0.92 g, 2.4 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–15% EtOAc in petroleum ether) to yield the desired dialkene **8i** (0.39 g, 0.81 mmol, 50%) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.72 (2H, br s), 7.39 (1H, br s), 7.31 (2H, d, J_{HH} = 8.3 Hz), 7.00 (2H, d, J_{HH} = 8.6 Hz), 6.81 (2H, d, J_{HH} = 8.6 Hz), 6.26–6.12 (2H, m), 5.75–5.65 (1H, m), 5.50–5.08 (3H, m), 4.81–4.53 (3H, m), 4.09 (1H, d, J_{HH} = 6.0 Hz), 3.81 (3H, s), 2.49–2.41 (5H, m). ¹⁹F (CDCl₃, 470 MHz) δ: -103.9. ¹³C (CDCl₃, 125 MHz) δ: 162.4 (d, J_{CF} = 29.4 Hz), 159.3, 157.9 (d, J_{CF} = 276.8 Hz), 145.2, 143.4, 137.0, 135.9, 133.8, 130.0 (2C), 129.7 (2C), 129.3, 127.2 (2C), 117.8, 117.4, 114.0, 113.5 (2C), 98.9, 60.4, 55.2, 51.8, 46.7, 21.6. m/z [EI (+ve)] 482.1 [M]⁺, HRMS found [M]⁺ 482.1676, C₂₆H₂₇FN₂O₂S requires 482.1676. IR (thin film) ν_{max} = 2975, 1652, 1511, 1247 cm⁻¹.

2'-Fluoro-*N*-(4"-methoxybenzyl)-*N*-[1-(pyridin-2"'-yl)-3-butenyl]acrylamide, 8j

Amine 7j (0.5 g, 1.86 mmol) was coupled with 2-fluoroacrylic acid (0.25 g, 2.8 mmol) using HBTU (1.1 g, 2.8 mmol) following general procedure B. The crude product was purified by flash column chromatography (0–25% diethyl ether in petroleum ether) to yield the desired dialkene 8j (0.42 g, 1.24 mmol, 67%) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 8.55 (1H, s), 7.63 (1H, dt, J_{HH} = 7.7, 1.8 Hz), 7.37 (1H, br s), 7.19 (1H, br s), 6.93 (2H, d, J_{HH} = 8.6 Hz), 6.70 (2H, d, J_{HH} = 8.6 Hz), 5.76–5.65 (1H, m), 5.47–5.02 (5H, m), 4.59 (2H, s), 3.76 (3H, s), 3.04–2.95 (1H, m), 2.89–2.80 (1H, m). ¹⁹F (CDCl₃, 377 MHz) δ: –102.5, –105.1. ¹³C (CDCl₃, 125 MHz) δ: 163.4 (d, J_{CF} = 29.4 Hz), 158.5, 158.0 (d, J_{CF} = 271.5 Hz), 157.7, 149.0, 136.6, 134.4, 129.7 (2C), 128.7, 124.1, 122.9, 118.3, 113.5 (2C), 99.5 (d, J_{CF} = 16.5 Hz), 62.5, 59.5, 55.1, 35.0. m/z [CI (+ve)] 341.1 [M + H]⁺, HRMS found [M + H]⁺ 341.1669, C₂₀H₂₂FN₂O₂ requires 341.1665. IR (thin film) ν_{max} = 1638, 1513, 1415, 1207, 1176 cm⁻¹.

General procedure C: ring-closing metathesis of fluorinated dialkene

A solution of the dialkene (1 eq.) in toluene (0.0025 g ml⁻¹) was treated with Grubbs 2nd generation catalyst (2.5 mol%) and the resulting mixture was heated to 100 °C until completion as indicated by TLC analysis (1–4 hours). The reaction was cooled down to room temperature, the solvent was removed under reduced pressure and the crude material was purified by flash column chromatography.

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3-Fluoro-1-(4'-methoxybenzyl)-6-phenyl-5, 6-dihydro-1*H*-pyridin-2-one, 9a

Dialkene **8a** (0.11 g, 0.32 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9a** (0.10 g, 0.32 mmol, quantitative yield) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ : 7.40–7.34 (3H, m), 7.19 (2H, d, $J_{HH} = 7.2$ Hz), 7.15 (2H, d, $J_{HH} = 8.6$ Hz), 6.86 (2H, d, $J_{HH} = 8.6$ Hz), 5.77 (1H, m), 5.54 (1H, d, $J_{HH} = 14.8$ Hz), 4.57 (1H, dd, $J_{HH} = 7.7$, 2.6 Hz), 3.83 (3H, s), 3.51 (1H, d, $J_{HH} = 14.8$ Hz), 2.99–2.93 (1H, m), 2.50–2.44 (1H, m). ¹⁹F (CDCl₃, 470 MHz) δ : –126.8. ¹³C (CDCl₃, 125 MHz) δ : 159.8 (d, $J_{CF} = 30.0$ Hz), 159.2, 149.4 (d, $J_{CF} = 251.1$ Hz), 139.4, 129.6 (2C), 129.0, 128.9 (2C), 128.0, 126.4 (2C), 114.1 (2C), 109.5 (d, $J_{CF} = 14.6$ Hz), 57.0, 55.3, 47.2, 29.4 (d, $J_{CF} = 6.0$ Hz). m/z [EI (+ve)] 311.2 [M]⁺. HRMS found [M]⁺ 311.1318, C₁₉H₁₈FNO₂ requires 311.1322. IR (thin film) $\nu_{max} = 2933$, 2837, 1651, 1512, 1247, 1176, 1031 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-(4"-methoxyphenyl)-5,6dihydro-1*H*-pyridin-2-one, 9b

Dialkene **8b** (0.22 g, 0.58 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9b** (0.19 g, 0.58 mmol, quantitative yield) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ: 7.05 (2H, d, J_{HH} = 8.8 Hz), 7.00 (2H, d, J_{HH} = 8.8 Hz), 6.80 (2H, d, J_{HH} = 8.8 Hz), 6.77 (2H, d, J_{HH} = 8.8 Hz), 5.70–5.66 (1H, m), 5.66 (1H, d, J_{HH} = 14.8 Hz), 4.41 (1H, dd, J_{HH} = 7.6, 3.2 Hz), 3.74 (3H, s), 3.84 (3H, s), 3.39 (1H, d, J_{HH} = 14.8 Hz), 2.84–2.79 (1H, m), 2.37–2.32 (1H, m). ¹⁹F (CDCl₃, 470 MHz) δ: -126.7. ¹³C (CDCl₃, 125 MHz) δ: 159.7 (d, J_{CF} = 30.2 Hz), 159.4, 159.2, 149.4 (d, J_{CF} = 252.5 Hz), 131.2, 129.6 (2C), 129.0, 127.6 (2C), 114.2 (2C), 114.1 (2C), 109.6 (d, J_{CF} = 13.8 Hz), 56.6, 55.4, 55.3, 47.1, 29.6 (d, J_{CF} = 5.0 Hz). m/z [EI (+ve)] 341.1 [M]⁺. HRMS found [M]⁺ 341.1420, C₂₀H₂₀FNO₃ requires 341.1427. IR (thin film) ν_{max} = 2951, 2837, 1651, 1512, 1462, 1247, 1178, 1033 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-(4"-trifluoromethanephenyl)-5,6-dihydro-1*H*-pyridin-2-one, 9c

Dialkene **8c** (0.20 g, 0.49 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9c** (0.18 g, 0.49 mmol, quantitative yield) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ : 7.64 (2H, d, J_{HH} = 8.0 Hz), 7.30 (2H, d, J_{HH} = 8.4 Hz), 7.14 (2H, d, J_{HH} = 8.6 Hz), 6.85 (2H, d, J_{HH} = 8.6 Hz), 5.78–5.75 (1H, m), 5.52 (1H, d, J_{HH} = 14.8 Hz), 4.62 (1H, dd, J_{HH} = 7.6, 2.0 Hz), 3.82 (3H, s), 3.53 (1H, d, J_{HH} = 14.8 Hz), 3.05–2.98 (1H, m), 2.48–2.43 (1H, m). ¹⁹F (CDCl₃, 470 MHz) δ : -62.3, -126.1. ¹³C (CDCl₃, 125 MHz) δ : 159.6 (d, J_{CF} = 30.1 Hz), 159.4, 149.4 (d, J_{CF} = 253.8 Hz), 143.5, 130.6, 130.3, 129.6 (2C), 128.5, 126.8 (2C), 124.9 (2C), 114.2 (2C), 109.3 (d, J_{CF} = 15.0 Hz), 56.7, 55.3, 47.5, 29.2 (d, J_{CF} = 6.3 Hz).

m/z [EI (+ve)] 379.0 [M]⁺, HRMS found [M]⁺ 379.1198, C₂₀H₁₇F₄NO₂ requires 379.1195. IR (thin film) ν_{max} = 2970, 1737, 1654, 1512, 1413, 1327, 1249, 1112, 1068 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-(naphthalen-1"-yl)-5,6-dihydro-1*H*-pyridin-2-one, 9d

Dialkene **8d** (0.14 g, 0.36 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–15% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9d** (0.13 g, 0.36 mmol, quantitative yield) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ: 7.97–7.94 (1H, m), 7.88 (1H, d, $J_{HH} = 8.2$ Hz), 7.78–7.75 (1H, m), 7.56–7.53 (2H, m), 7.49 (1H, br t, $J_{HH} = 7.7$ Hz), 7.34 (1H, d, $J_{HH} = 7.2$ Hz), 7.15 (2H, d, $J_{HH} = 8.5$ Hz), 6.86 (2H, d, $J_{HH} = 8.5$ Hz), 5.74–7.69 (1H, m), 5.61 (1H, d, $J_{HH} = 14.8$ Hz), 5.39 (1H, br d, $J_{HH} = 8.3$ Hz), 3.83 (3H, s), 3.47 (1H, d, $J_{HH} = 14.8$ Hz), 3.12–3.04 (1H, m), 2.70–2.62 (1H, m). ¹⁹F (CDCl₃, 377 MHz) δ: -127.5. ¹³C (CDCl₃, 125 MHz) δ: 160.5 (d, $J_{CF} = 31.2$ Hz), 159.2, 149.1 (d, $J_{CF} = 255.0$ Hz), 134.4, 133.5, 130.2, 129.7, 129.5 (2C), 129.1, 128.8, 126.7, 125.8, 125.3, 123.9 121.9, 114.1 (2C), 109.9 (d, $J_{CF} = 14.7$ Hz), 55.3, 53.7, 47.4, 27.8 (d, $J_{CF} = 5.5$ Hz). m/z [EI (+ve)] 361.2 [M]⁺. HRMS found [M]⁺ 361.1480, C₂₃H₂₀FNO₂ requires 361.1478. IR (thin film) $\nu_{max} = 2932$, 1652, 1511, 1244, 1200 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-(4"-bromophenyl)-5,6-dihydro-1*H*-pyridin-2-one, 9e

Dialkene **8e** (0.17 g, 0.41 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–15% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9e** (0.15 g, 0.39 mmol, 96%) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ : 7.51 (2H, d, J_{HH} = 8.5 Hz), 7.14 (2H, d, J_{HH} = 8.6 Hz), 7.05 (2H, d, J_{HH} = 8.5 Hz), 6.87 (2H, d, J_{HH} = 8.6 Hz), 5.79–5.74 (1H, m), 5.50 (1H, d, J_{HH} = 14.6 Hz), 4.52 (1H, dd, J_{HH} = 7.6, 2.4 Hz), 3.83 (3H, s), 3.51 (1H, d, J_{HH} = 14.6 Hz), 3.00–2.91 (1H, m), 2.46–2.38 (1H, m). ¹⁹F (CDCl₃, 377 MHz) δ : -126.3. ¹³C (CDCl₃, 100 MHz) δ : 159.6 (d, J_{CF} = 31.0 Hz), 159.3, 149.3 (d, J_{CF} = 253.0 Hz), 138.5, 132.1 (2C), 129.6 (2C) 128.6, 128.1 (2C), 122.0, 114.2 (2C), 109.4 (d, J_{CF} = 15.0 Hz), 56.5, 55.3, 47.3, 29.3 (d, J_{CF} = 6.0 Hz). m/z [CI (+ve)] 391.7 [M + H]⁺, HRMS found [M + H]⁺ 390.0489, C₁₉H₁₈⁷⁹BrFNO₂ requires 390.0505. IR (thin film) ν_{max} = 2950, 1653, 1512, 1247, 1217 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-isobutyl-5, 6-dihydro-1*H*-pyridin-2-one, 9f

Dialkene **8f** (0.23 g, 0.71 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9f** (0.17 g, 0.60 mmol, 85%) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ : 7.14 (2H, d, J_{HH} = 8.4 Hz), 6.79 (2H, d, J_{HH} = 8.8 Hz), 5.77–5.71 (1H, m), 5.27 (1H, d, J_{HH} = 14.8 Hz), 3.73 (3H, s), 3.66 (1H, d, J_{HH} = 14.8 Hz), 3.31–3.26 (1H, m), 2.48–2.44 (1H, m), 2.14–2.07 (1H, m), 1.72–1.65 (1H, m),

1.43–1.39 (1H, m), 1.27–1.17 (1H, m), 0.85 (3H, d, J_{HH} = 6.8 Hz), 0.76 (3H, d, J_{HH} = 6.8 Hz). ¹⁹F (CDCl₃, 470 MHz) δ : –127.6. ¹³C (CDCl₃, 125 MHz) δ : 159.2, 158.7 (d, J_{CF} = 31.3 Hz), 149.6 (d, J_{CF} = 252.5 Hz), 129.5, 129.4 (2C), 114.1 (2C), 109.8 (d, J_{CF} = 13.8 Hz), 55.3, 52.1, 46.9, 39.6, 25.1, 24.6 (d, J_{CF} = 5.0 Hz), 23.6, 21.5. m/z [EI (+ve)] 291.2 [M]⁺. HRMS found [M]⁺ 291.1629, C₁₇H₂₂FNO₂ requires 291.1635. IR (thin film) ν_{max} = 2955, 1651, 1512, 1249, 1201 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-cyclohexane-5, 6-dihydro-1*H*-pyridin-2-one, 9g

Dialkene **8g** (0.35 g, 1.06 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9g** (0.30 g, 0.94 mmol, 89%) as a colourless oil.

¹H (CDCl₃, 400 MHz) & 7.23 (2H, d, $J_{HH} = 8.8$ Hz), 6.87 (2H, d, $J_{HH} = 8.8$ Hz), 5.83–5.79 (1H, m), 5.49 (1H, d, $J_{HH} = 14.9$ Hz), 3.83 (3H, s), 3.79 (1H, d, $J_{HH} = 14.9$ Hz), 3.18 (1H, br t, $J_{HH} = 6.8$ Hz), 2.54–2.45 (1H, m), 2.36–2.28 (1H, m), 1.86–1.63 (6H, m), 1.29–1.07 (4H, m), 1.00–0.94 (1H, m). ¹⁹F (CDCl₃, 470 MHz) & -128.2. ¹³C (CDCl₃, 125 MHz) & 159.2, 159.0 (d, $J_{CF} = 31.1$ Hz), 149.5 (d, $J_{CF} = 253.2$ Hz, *CF*), 129.7, 129.3 (2C), 114.1 (2C), 110.6 (d, $J_{CF} = 14.2$ Hz), 59.0, 55.3, 48.7, 40.8, 30.3, 30.2, 26.4, 26.3, 26.2, 22.8 (d, $J_{CF} = 5.5$ Hz). m/z [CI (+ve)] 318.2 [M + H]⁺, HRMS found [M + H]⁺ 318.1871, C₁₉H₂₅FNO₂ requires 318.1869. IR (thin film) $\nu_{max} = 2925$, 2850, 1645, 1511, 1247, 1198 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-(furan-2"-yl)-5,6-dihydro-1*H*-pyridin-2-one, 9h

Dialkene **8h** (0.37 g, 1.1 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9h** (0.21 g, 0.69 mmol, 62%) as a colourless oil.

¹H (CDCl₃, 400 MHz) δ: 7.40 (1H, dd, J_{HH} = 1.7, 0.6 Hz), 7.22 (2H, d, J_{HH} = 8.6 Hz), 6.90 (2H, d, J_{HH} = 8.6 Hz), 6.36 (1H, dd, J_{HH} = 3.2, 1.8 Hz), 6.19 (1H, br d, J_{HH} = 3.2 Hz), 5.91–5.86 (1H, m), 5.48 (1H, d, J_{HH} = 14.8 Hz), 4.59 (1H, dd, J_{HH} = 7.0, 2.5 Hz), 3.84 (3H, s), 3.75 (1H, d, J_{HH} = 14.8 Hz), 2.84–2.75 (1H, m), 2.67–2.59 (1H, m). ¹⁹F (CDCl₃, 470 MHz) δ: -126.3. ¹³C (CDCl₃, 125 MHz) δ: 159.4 (d, J_{CF} = 30.0 Hz), 152.2, 149.1 (d, J_{CF} = 252.5 Hz), 142.5, 131.0, 129.6 (2C), 128.9, 114.2 (2C), 110.3, 110.1 (d, J_{CF} = 16.5 Hz), 107.5, 55.3, 51.6, 47.4, 26.2 (d, J_{CF} = 5.9 Hz). m/z [EI (+ve)] 301.2 [M]⁺. HRMS found [M]⁺ 301.1111, C₁₇H₁₆FNO₃ requires 301.1114. IR (thin film) ν_{max} = 2957, 2364, 1654, 1513, 1415, 1248, 1117 cm⁻¹.

3-Fluoro-1-(4'-methoxybenzyl)-6-(1"-(toluene-4"'-sulfonyl)-1*H*-pyrrol-2"-yl)-5,6-dihydro-1*H*-pyridin-2-one, 9i

Dialkene **8i** (0.23 g, 0.47 mmol) was subjected to general procedure C. The crude product was purified by flash column chromatography (0–30% EtOAc in petroleum ether) to yield the desired α , β -unsaturated lactam **9i** (0.16 g, 0.36 mmol, 77%) as a pale yellow oil.

¹H (CDCl₃, 400 MHz) δ: 7.50 (2H, d, J_{HH} = 8.5 Hz), 7.37 (1H, dd, J_{HH} = 1.7, 1.5 Hz), 7.30 (2H, d, J_{HH} = 8.5 Hz), 6.89 (2H, d, J_{HH} = 8.6 Hz), 6.83 (2H, d, J_{HH} = 8.6 Hz), 6.28 (1H, t, J_{HH} = 3.3 Hz), 6.16–6.15 (1H, m), 5.76–5.72 (1H, m), 5.30 (1H, d, J_{HH} = 15.0 Hz), 4.95 (1H, d, J_{HH} = 7.2 Hz), 3.85 (3H, s), 3.12 (1H, d, J_{HH} = 15.0 Hz), 2.94–2.87 (1H, m), 2.71–2.65 (1H, m), 2.47 (3H, s). ¹⁹F (CDCl₃, 377 MHz) δ: –127.9. ¹³C (CDCl₃, 125 MHz) δ: 159.6 (d, J_{CF} = 30.0 Hz), 159.1, 148.8 (d, J_{CF} = 252.5 Hz), 145.4, 136.1, 132.5, 130.3 (2C), 128.9 (2C), 128.8, 126.4 (2C), 124.8, 114.8, 114.0 (2C), 112.0, 109.8 (d, J_{CF} = 15.0 Hz), 55.3, 51.9, 47.4, 27.0 (d, J_{CF} = 6.3 Hz), 21.7. m/z [ESI (+ve)] 477.1 [M + Na]⁺, HRMS found [M + Na]⁺ 477.1259, C₂₄H₂₃FN₂O₄SNa requires 477.1255. IR (thin film) ν_{max} = 2955, 1630, 1515, 1447, 1276, 1205 cm⁻¹.

General procedure D: removal of the *p*-methoxybenzyl protecting group

The cyclic amide (1 eq.) was dissolved in a MeCN-H₂O (8:2, 4 mL) mixture and ceric ammonium nitrate was added portionwise. The resulting solution was stirred at room temperature until completion indicated by TLC analysis (7 h). The reaction was quenched with aq. sat. NaHCO₃ (10 mL) and extracted with diethyl ether (3 × 10 mL). The organics were combined, dried (Na₂SO₄) and evaporated *in vacuo*. The crude material was purified by flash column chromatography.

3-Fluoro-6-phenyl-5,6-dihydro-1*H*-pyridin-2-one, 10a

α,β-Unsaturated lactam **9a** (96 mg, 0.31 mmol) was subjected to general procedure D using 0.45 g of ceric ammonium nitrate (2.7 eq., 0.86 mmol). The crude product was purified by flash column chromatography (0–30% EtOAc in petroleum ether) to yield the desired dihydropyridone **10a** (60 mg, 0.29 mmol, 94%) as a white solid. m.p. 109–111 °C.

¹H (CDCl₃, 400 MHz) δ : 7.45–7.37 (5H, m), 6.09 (1H, ddd, $J_{HF} = 11.1$ Hz, $J_{HH} = 5.9$, 3.3 Hz), 5.62 (1H, br s), 4.82 (1H, dd, $J_{HH} = 11.6$, 5.8 Hz), 2.74–2.60 (2H, m). ¹⁹F (CDCl₃, 470 MHz) δ : -129.9. ¹³C (CDCl₃, 125 MHz) δ : 161.2 (d, $J_{CF} = 32.8$ Hz), 149.1 (d, $J_{CF} = 253.2$ Hz), 139.9, 129.2 (2C), 128.8, 126.4 (2C), 113.5 (d, $J_{CF} = 13.8$ Hz), 56.1, 31.2 (d, $J_{CF} = 5.0$ Hz). m/z [EI (+ve)] 191.1 [M]⁺, HRMS found [M]⁺ 191.0748, C₁₁H₁₀FNO requires 191.0746. IR (thin film) $\nu_{max} = 2356$, 1705, 1670, 1248 cm⁻¹.

3-Fluoro-6-(4'-methoxyphenyl)-5,6-dihydro-1*H*-pyridin-2-one, 10b

 α ,β-Unsaturated lactam **9b** (0.14 g, 0.42 mmol) was subjected to general procedure D using 1.3 g of ceric ammonium nitrate (5.5 eq., 2.3 mmol). The crude product was purified by flash column chromatography (0–25% EtOAc in petroleum ether) to yield the desired dihydropyridone **10b** (37 mg, 0.17 mmol, 40%) as a yellow solid. m.p. 133–135 °C.

¹H (CDCl₃, 400 MHz) δ : 7.21 (2H, d, J_{HH} = 8.6 Hz), 6.84 (2H, d, J_{HH} = 8.6 Hz), 6.01–6.97 (1H, m), 5.57 (1H, br s), 4.67 (1H, dd, J_{HH} = 12.1, 5.6 Hz,), 3.81 (3H, s), 2.60–2.46 (2H, m). ¹⁹F (CDCl₃, 470 MHz) δ : –130.0. ¹³C (CDCl₃, 125 MHz) δ : 161.1 (d, J_{CF} = 31.3 Hz), 159.8, 149.8 (d, J_{CF} = 253.8 Hz), 131.9, 127.6 (2C), 114.4 (2C), 113.6 (d, J_{CF} = 13.8 Hz), 55.6, 55.4, 31.2 (d, J_{CF} = 5.3 Hz). m/z [CI (+ve)] 222.1 [M + H]⁺, HRMS found [M + H]⁺ 222.0929, C₁₂H₁₃FNO₂ requires 222.09230. IR (thin film) ν_{max} = 1695, 1630, 1250 cm⁻¹.

3-Fluoro-6-(4'-trifluoromethanephenyl)-5,6-dihydro-1*H*-pyridin-2-one, 10c

α,β-Unsaturated lactam **9c** (0.16 g, 0.42 mmol) was subjected to general procedure D using 1.1 g of ceric ammonium nitrate (4.9 eq., 2.1 mmol). The crude product was purified by flash column chromatography (0–20% EtOAc in petroleum ether) to yield the desired dihydropyridone **10c** (50 mg, 0.20 mmol, 47%) as a white solid. m.p. 104–105 °C.

¹H (CDCl₃, 500 MHz) δ : 7.60 (2H, d, J_{HH} = 8.2 Hz), 7.43 (2H, d, J_{HH} = 8.2 Hz), 5.99 (1H, ddd, J_{HF} = 11.8 Hz, J_{HH} = 5.5, 3.6 Hz), 5.93 (1H, br s), 4.80 (1H, dd, J_{HH} = 10.5, 6.1 Hz), 2.67–2.53 (2H, m). ¹⁹F (CDCl₃, 470 MHz) δ : -62.4, -129.1. ¹³C (CDCl₃, 125 MHz) δ : 161.1 (d, J_{CF} = 31.3 Hz), 149.6 (d, J_{CF} = 253.8 Hz), 144.0, 131.1, 130.9, 126.8 (2C), 126.1 (2C), 113.2 (d, J_{CF} = 13.8 Hz), 55.4, 30.9 (d, J_{CF} = 5.0 Hz). m/z [EI (+ve)] 259.1 [M]⁺, HRMS found [M]⁺ 259.0623, C₁₂H₉F₄NO requires 259.0620. IR (thin film) ν_{max} = 1720, 1705, 1680, 1305, 1180 cm⁻¹.

3-Fluoro-6-(naphthalen-1'-yl)-5,6-dihydro-1*H*-pyridin-2-one, 10d

 α ,β-Unsaturated lactam **9d** (0.11 g, 0.30 mmol) was subjected to general procedure D using 0.97 g of ceric ammonium nitrate (5.9 eq., 1.8 mmol). The crude product was purified by flash column chromatography (0–15% EtOAc in petroleum ether) to yield the desired dihydropyridone **10d** (37 mg, 0.15 mmol, 51%) as a yellow solid. m.p. 135–137 °C.

¹H (CDCl₃, 400 MHz) δ : 7.96 (1H, d, J_{HH} = 8.1 Hz), 7.85 (1H, br d, J_{HH} = 7.9 Hz), 7.79 (1H, d, J_{HH} = 8.1 Hz), 7.55–7.41 (4H, m), 6.04 (1H, dt, J_{HF} = 11.0 Hz, J_{HH} = 4.6 Hz), 5.74 (1H, br s), 5.56 (1H, t, J_{HH} = 8.5 Hz), 2.81–2.76 (2H, m). ¹⁹F (CDCl₃, 470 MHz) δ : -129.6. ¹³C (CDCl₃, 125 MHz) δ : 161.2 (d, J_{CF} = 33.0 Hz), 149.6 (d, J_{CF} = 252.5 Hz), 135.3, 134.1, 130.0, 129.4, 129.2, 126.9, 126.2, 125.5, 123.9, 122.1, 113.7 (d, J_{CF} = 12.5 Hz), 52.3, 29.7 (d, J_{CF} = 5.0 Hz). m/z [EI (+ve)] 241.1 [M]⁺, HRMS found [M]⁺ 241.0902, C₁₅H₁₂FNO requires 241.0903. IR (thin film) ν_{max} = 1715, 1797, 1320, 1180 cm⁻¹.

3-Fluoro-6-(4'-bromophenyl)-5,6-dihydro-1H-pyridin-2-one, 10e

 α ,β-Unsaturated lactam **9e** (0.19 g, 0.47 mmol) was subjected to general procedure D using 0.98 g of ceric ammonium nitrate (3.8 eq., 1.8 mmol). The crude product was purified by flash column chromatography (0–20% EtOAc in petroleum ether) to yield the desired dihydropyridone **10e** (92 mg, 0.34 mmol, 72%) as a white solid. m.p. 199–200 °C.

¹H (CDCl₃, 400 MHz) δ : 7.56 (2H, d, J_{HH} = 8.1 Hz), 7.27 (2H, d, J_{HH} = 8.1 Hz), 6.09 (1H, dt, J_{HF} = 10.9 Hz, J_{H} = 4.7 Hz), 5.58 (1H, br s), 4.79 (1H, t, J_{HH} = 8.5 Hz), 2.67–2.62 (2H, m). ¹⁹F (CDCl₃, 470 MHz) δ : –129.6. ¹³C (CDCl₃, 125 MHz) δ : 161.0 (d, J_{CF} = 31.2 Hz), 149.6 (d, J_{CF} = 253.2 Hz), 138.9, 132.3 (2C), 128.0 (2C), 122.7, 113.3 (d, J_{CF} = 13.8 Hz), 55.5, 31.0 (d, J_{CF} = 5.0 Hz). m/z [CI (+ve)] 269.8 [M + H]⁺, HRMS found [M + H]⁺ 269.9945, $C_{11}H_{10}^{79}BrFNO$ requires 269.9930. IR (thin film) $\nu_{max} = 1705, 1685, 1205, 1010 \text{ cm}^{-1}$.

3-Fluoro-6-isobutyl-5,6-dihydro-1H-pyridin-2-one, 10f

α,β-Unsaturated lactam **9f** (0.13 g, 0.44 mmol) was subjected to general procedure D using 0.91 g of ceric ammonium nitrate (3.8 eq., 1.7 mmol). The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired dihydropyridone **10f** (70 mg, 0.4 mmol, 92%) as a white solid. m.p. 61–63 °C.

¹H (CDCl₃, 500 MHz) δ: 6.07 (1H, ddd, J_{HF} = 11.1 Hz, J_{HH} = 5.9, 3.3 Hz), 5.59 (1H, br s, N*H*), 3.76–3.72 (1H, m), 2.49–2.40 (1H, m), 2.34–2.25 (1H, m), 1.74–1.63 (1H, m), 1.59–1.51 (1H, m), 1.45–1.36 (1H, m), 0.97 (3H, d, J_{HH} = 6.6 Hz), 0.96 (3H, d, J_{HH} = 6.6 Hz). ¹⁹F (CDCl₃, 470 MHz) δ: -130.1. ¹³C (CDCl₃, 100 MHz) δ: 161.2 (d, J_{CF} = 28.0 Hz), 149.7 (d, J_{CF} = 253.0 Hz), 113.7 (d, J_{CF} = 13.0 Hz), 49.3, 44.0, 28.3 (d, J_{CF} = 5.0 Hz), 24.4, 22.6, 22.2. *m*/*z* [CI (+ve)] 172.1 [M + H]⁺, HRMS found [M + H]⁺ 172.1144, C₉H₁₅FNO requires 172.1138. IR (thin film) ν_{max} = 3219, 2934, 2906, 1696, 1669, 1264, 1206 cm⁻¹.

3-Fluoro-6-cyclohexane-5,6-dihydro-1H-pyridin-2-one, 10g

α,β-Unsaturated lactam **9g** (0.22 g, 0.70 mmol) was subjected to general procedure D using 1.3 g of ceric ammonium nitrate (3.3 eq., 2.3 mmol). The crude product was purified by flash column chromatography (0–10% EtOAc in petroleum ether) to yield the desired dihydropyridone **10g** (0.11 g, 0.55 mmol, 79%) as a white solid. m.p. 108–110 °C.

¹H (CDCl₃, 400 MHz) δ : 5.98 (1H, dt, J_{HF} = 11.4 Hz, J_{HH} = 4.3 Hz), 5.54 (1H, br s), 3.35 (1H, br q, J_{HH} = 7.7 Hz), 2.32–2.29 (2H, m), 1.74–1.61 (5H, m), 1.43–1.32 (1H, m), 1.19–0.97 (3H, m), 0.95–0.92 (2H, m). ¹⁹F (CDCl₃, 470 MHz) δ : -130.5. ¹³C (CDCl₃, 125 MHz) δ : 161.3 (d, J_{CF} = 31.3 Hz), 149.6 (d, J_{CF} = 252.5 Hz), 114.0 (d, J_{CF} = 13.8 Hz), 56.0, 41.4, 28.8, 28.7, 26.1, 25.9 (d, J_{CF} = 5.0 Hz), 24.9, 24.8. m/z [CI (+ve)] 198.1 [M + H]⁺, HRMS found [M + H]⁺ 198.1295, C₁₁H₁₇FNO requires 198.1294. IR (thin film) ν_{max} = 2927, 2855, 1691, 1652, 1208, 1199 cm⁻¹.

General procedure E: hydrogenation of α , β -unsaturated lactams

A solution of dihydropyridone (1 eq.) in MeOH (2 mL) was treated with palladium activated charcoal (10% by weight) and the suspension was stirred under a H_2 atmosphere until completion indicated by TLC analysis (1–4 hours). The resulting mixture was filtered through celite, dried (Na₂SO₄) and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography.

3-Fluoro-6-phenyl-piperidin-2-one, 11a

Dihydropyridone **10a** (43 mg, 0.22 mmol) was subjected to general procedure E. The crude product was purified by flash column chromatography (0–30% EtOAc in petroleum ether) to yield the desired δ -lactam **11a** (32 mg, 0.17 mmol, 75%) as a white solid. m.p. 149–151 °C.

¹H (CDCl₃, 400 MHz) δ : 7.45–7.32 (5H, m), 5.93 (1H, br s), 4.95 (1H, dt, J_{HF} = 46.27 Hz, J_{HH} = 5.28 Hz), 4.61–4.60 (1H, m), 2.28–2.24 (1H, m), 2.17–2.03 (3H, m). ¹⁹F (CDCl₃, 470 MHz) δ : –180.3. ¹³C (CDCl₃, 125 MHz) δ : 167.5 (d, J_{CF} = 20.1 Hz), 141.4, 129.0 (2C), 128.4, 126 1 (2C), 85.7 (d, J_{CF} = 175.1 Hz), 57.3, 27.3 (d, J_{CF} = 3.7 Hz), 26.2 (d, J_{CF} = 20.0 Hz). m/z [EI (+ve)] 193.1 [M]⁺. HRMS found [M]⁺ 193.0904, C₁₁H₁₂FNO requires 193.0903. IR (thin film) ν_{max} = 3194, 2066, 2958, 1666, 1329 cm⁻¹.

3-Fluoro-6-(4'-methoxyphenyl)-piperidin-2-one, 11b

Dihydropyridone **10b** (24 mg, 0.11 mmol) was subjected to general procedure E. The crude product was purified by flash column chromatography (0–50% EtOAc in petroleum ether) to yield the desired δ -lactam **11b** (14 mg, 0.06 mmol, 58%) as a white solid. m.p. 159–161 °C.

¹H (CDCl₃, 400 MHz) & 7.25 (2H, d, J_{HH} = 8.6 Hz), 6.94 (2H, d, J_{HH} = 8.6 Hz), 5.83 (1H, s), 4.94 (1H, dt, J_{HF} = 47.1 Hz, J_{HH} = 4.6 Hz), 4.56–4.51 (1H, m), 3.84 (3H, s), 2.34–2.24 (1H, m), 2.13–1.96 (3H, m). ¹⁹F (CDCl₃, 470 MHz) & -184.8. ¹³C (CDCl₃, 125 MHz) & 167.2 (d, J_{CF} = 22.1 Hz), 159.6, 133.4, 127.3 (2C), 114.4 (2C), 85.7 (d, J_{CF} = 176.1 Hz), 57.0, 55.4, 27.4 (d, J_{CF} = 4.6 Hz), 26.4 (d, J_{CF} = 21.2 Hz). m/z [EI (+ve)] 223.1 [M]⁺. HRMS found [M]⁺ 223.0999, C₁₂H₁₄FNO₂ requires 223.1009. IR (thin film) ν_{max} = 2930, 1695, 1510, 1230 cm⁻¹.

3-Fluoro-6-(4'-trifluoromethanephenyl)-piperidin-2-one, 11c

Dihydropyridone **10c** (29 mg, 0.11 mmol) was subjected to general procedure E. The crude product was purified by flash column chromatography (0–40% EtOAc in petroleum ether) to yield the desired δ -lactam **11c** (29 mg, 0.11 mmol, quantitative yield) as a white solid. m.p. 122–124 °C.

¹H (CDCl₃, 400 MHz) δ: 7.60 (2H, d, J_{HH} = 8.2 Hz), 7.38 (2H, d, J_{HH} = 8.2 Hz), 5.93 (1H, s), 4.86 (1H, dt, J_{HF} = 47.1 Hz, J_{HH} = 5.0 Hz), 4.59 (1H, br t, J_{HH} = 5.7 Hz), 2.22–2.12 (1H, m), 2.11–1.89 (3H, m). ¹⁹F (CDCl₃, 470 MHz) δ: -62.4, -185.0. ¹³C (CDCl₃, 125 MHz) δ: 167.4 (d, J_{CF} = 22.3 Hz), 145.4, 130.9, 130.6, 126.6 (2C), 126.1 (2C), 85.5 (d, J_{CF} = 176.5 Hz), 57.0, 27.2 (d, J_{CF} = 4.2 Hz), 26.1 (d, J_{CF} = 21.0 Hz). m/z [EI (+ve)] 261.1 [M]⁺. HRMS found [M]⁺ 261.0773, C₁₂H₁₁F₄NO requires 261.0777. IR (thin film) ν_{max} = 3005, 2970, 1675, 1430 cm⁻¹.

3-Fluoro-6-(naphthalen-1'-yl)-piperidin-2-one, 11d

Dihydropyridone **10d** (38 mg, 0.15 mmol) was subjected to general procedure E. The crude product was purified by flash column chromatography (0–40% EtOAc in petroleum ether) to yield the desired δ -lactam **11d** (29 mg, 0.12 mmol, 81%) as a white solid. m.p. 144–147 °C.

¹H (CDCl₃, 400 MHz) δ : 7.99–7.93 (2H, m), 7.87 (1H, d, $J_{HH} = 8.0$ Hz), 7.62–7.51 (4H, m), 6.02 (1H, s), 5.48–5.46 (1H, m), 5.02 (1H, dt, $J_{HF} = 46.9$ Hz, $J_{HH} = 5.7$ Hz), 2.43–2.33 (1H, m), 2.28–2.23 (3H, m). ¹⁹F (CDCl₃, 377 MHz) δ : –186.1. ¹³C (CDCl₃, 100 MHz) δ : 168.3 (d, $J_{CF} = 19.9$ Hz), 136.6, 134.0, 129.8, 129.4, 128.9, 126.8, 126.0, 125.4, 123.7, 121.9, 85.8 (d, $J_{CF} = 177.0$ Hz), 53.3, 25.9 (d, $J_{CF} = 6.0$ Hz), 25.7 (d, $J_{CF} = 20.0$ Hz). m/z [CI (+ve)] 244.0 [M + H]⁺, HRMS found [M + H]⁺ 244.1137, C₁₅H₁₅FNO requires 244.1138. IR (thin film) $\nu_{max} = 3240, 2900, 1650, 1110$ cm⁻¹.

3-Fluoro-6-isobutyl-piperidin-2-one, 11f

Dihydropyridone **10f** (39 mg, 0.23 mmol) was subjected to general procedure E. The crude product was purified by flash column chromatography (0–20% EtOAc in petroleum ether) to yield the desired δ -lactam **11f** (40 mg, 0.23 mmol, quantitative yield) as a white solid. m.p. 78–81 °C.

¹H (CDCl₃, 400 MHz) δ: 6.00 (1H, s), 4.80 (1H, dt, J_{HF} = 48.6 Hz, J_{HH} = 4.5 Hz), 3.40–3.37 (1H, m), 2.16–2.13 (1H, m), 1.96–1.89 (1H, m), 1.81–1.77 (1H, m), 1.64–1.58 (2H, m), 1.40–1.31 (2H, m), 0.87 (3H, d, J_{HH} = 6.6 Hz), 0.85 (3H, d, J_{HH} = 6.6 Hz). ¹⁹F (CDCl₃, 470 MHz) δ: -185.0. ¹³C (CDCl₃, 125 MHz) δ: 167.4 (d, J_{CF} = 20.0 Hz), 86.3 (d, J_{CF} = 173.8 Hz), 50.8, 45.6, 26.5 (d, J_{CF} = 21.3 Hz), 24.3, 24.0 (d, J_{CF} = 3.7 Hz), 22.6, 22.3. m/z [CI (+ve)] 174.1 [M + H]⁺, HRMS found [M + H]⁺ 174.1300, C₉H₁₇FNO requires 174.1294. IR (thin film) ν_{max} = 2950, 2935, 1630 cm⁻¹.

3-Fluoro-6-cyclohexane-piperidin-2-one, 11g

Dihydropyridone **10g** (80 mg, 0.40 mmol) was subjected to general procedure E. The crude product was purified by flash column chromatography (0–20% EtOAc in petroleum ether) to yield the desired δ -lactam **11g** (81 mg, 0.40 mmol, quantitative yield) as a white solid. m.p. 148–159 °C.

¹H (CDCl₃, 500 MHz) & 5.93 (1H, s), 4.74 (1H, dt, J_{HF} = 47.2 Hz, J_{HH} = 4.4 Hz), 3.13–3.09 (1H, m), 2.21–2.13 (1H, m), 1.90–1.79 (1H, m), 1.74–1.62 (7H, m), 1.35–1.30 (1H, m), 1.22–1.14 (2H, m), 1.11–1.03 (1H, m), 0.99–0.89 (2H, m). ¹⁹F (CDCl₃, 470 MHz) & -184.6. ¹³C (CDCl₃, 125 MHz) & 167.4 (d, J_{CF} = 19.9 Hz), 86.0 (d, J_{CF} = 173.7 Hz), 57.8, 42.6, 28.6, 28.4, 26.9 (d, J_{CF} = 21.3 Hz), 26.2, 26.0, 25.9, 20.2 (d, J_{CF} = 3.4 Hz). m/z [EI (+ve)] 199.1 [M]⁺. HRMS found [M]⁺ 199.1376, C₁₁H₁₈FNO requires 199.1372. IR (thin film) ν_{max} = 2926, 2870, 1664, 1410 cm⁻¹.

3-Fluoro-6-(4'-phenylphenyl)-5,6-dihydro-1H-pyridin-2-one, 12

Dihydropyridone **10e** (98 mg, 0.36 mmol) was dissolved in a mixture of toluene (12 mL) and H₂O (2 mL). K₂CO₃ (0.11 g, 0.79 mmol), PhB(OH)₂ (88 mg, 0.72 mmol) and Pd(PPh₃)₄ (84 mg, 20 mol%) were then sequentially added and the resulting solution was heated at 90 °C for 16 h. The reaction was cooled down to room temperature and was filtered through celite and the celite was washed with EtOAc (30 mL). The organic layer was washed with H₂O (1 × 10 mL) and brine (1 × 10 mL) and then dried (Na₂SO₄) and evaporated *in vacuo*. The crude residue was purified by flash column chromatography (0–20% EtOAc in petroleum ether) to yield the desired cross-coupled product **12** (87 mg, 0.33 mmol, 90%) as a white solid. m.p. 199–201 °C.

¹H NMR (CDCl₃, 400 MHz) δ : 7.58 (2H, d, J_{HH} = 8.0 Hz), 7.52 (2H, d, J_{HH} = 8.0 Hz), 7.40–7.31 (5H, m), 6.02 (1H, ddd, J_{HH} = 11.0, 5.8, 3.3 Hz), 5.59 (1H, s), 4.77 (1H, dd, J_{HH} = 11.3, 6.0 Hz), 2.70–2.55 (2H, m). ¹⁹F (CDCl₃, 377 MHz) δ : –129.8. ¹³C (CDCl₃, 100 MHz) δ : 161.0 (d, J_{CF} = 31.1 Hz), 149.9 (d, J_{CF} = 253.6 Hz), 141.8, 140.2, 138.9, 128.9 (2C), 127.8 (2C), 127.7, 127.1 (2C), 126.8 (2C), 113.5 (d, J_{CF} = 14.0 Hz), 55.8, 31.1 (d, J_{CF} = 5.7 Hz). m/z [EI (+ve)] 267.1 [M]⁺, HRMS found [M]⁺ 267.1058, C₁₇H₁₄FNO requires 267.1059. IR (thin film) ν_{max} = 2358, 1693, 1658, 1258, 1198 cm⁻¹.

3-Fluoro-6-(4'-phenylphenyl)-piperidin-2-one, 13

Dihydropyridone **12** (34 mg, 0.13 mmol) was subjected to general procedure E. The crude product was purified by flash column chromatography (0–40% EtOAc in petroleum ether) to yield the desired δ -lactam **13** (34 mg, 0.13 mmol, quantitative) as a white solid. m.p. 171–173 °C.

¹H (CDCl₃, 400 MHz) δ: 7.64 (2H, d, J_{HH} = 7.5 Hz), 7.61 (2H, d, J_{HH} = 7.5 Hz), 7.50–7.38 (5H, m), 5.91 (1H, s), 4.97 (1H, dt, J_{HF} = 43.7 Hz, J_{HH} = 4.5 Hz), 4.67–4.63 (1H, m), 2.36–2.27 (1H, m), 2.20–2.04 (3H, m). ¹⁹F (CDCl₃, 377 MHz) δ: -185.1. ¹³C (CDCl₃, 100 MHz) δ: 167.5 (d, J_{CF} = 19.8 Hz), 141.4, 140.3, 140.2, 128.9 (2C), 127.7 (2C), 127.6, 127.1 (2C), 126.6 (2C), 85.7 (d, J_{CF} = 176.0 Hz), 57.2, 27.3 (d, J_{CF} = 4.0 Hz), 26.3 (d, J_{CF} = 21.0 Hz). m/z [EI (+ve)] 269.0 [M]⁺, HRMS found [M]⁺ 269.1214, C₁₇H₁₆FNO requires 269.1216. IR (thin film) ν_{max} = 3239, 2949, 2356, 1676, 1486 cm⁻¹.

Crystallographic data collection and refinement details

X-ray diffraction data of crystals of 11a were collected at 150 K on an Oxford Diffraction Gemini CCD diffractometer equipped with an Oxford Cryosystems Cryostream low-temperature device and using graphite monochromated Cu Ka radiation $(\lambda = 1.54184 \text{ Å})$. Data reduction was carried out and an analytical numeric absorption correction was applied [based on expressions derived in R. C. Clark and J. S. Reid, Acta Crystallogr., Sect. A: Fundam. Crystallogr., 1995, 51, 887-897] using the CrysAlisPro [Oxford Diffraction Limited., Version 1.171.33.55, Oxfordshire, UK]. The structures were all solved by direct methods using the program SHELXS97 [SHELX, G. M. Sheldrick, Acta Crystallogr., Sect. A: Fundam. Crystallogr., 2008, 64, 112-122] and refined using full-matrix leastsquares refinement on F^2 using SHELXL97 [SHELX, G. M. Sheldrick, Acta Crystallogr., Sect. A: Fundam. Crystallogr., 2008, 64, 112-122] within the WinGX program suite [L. J. Farrugia, J. Appl. Crystallogr., 1999, 32, 837-838]. The Flack x parameter [H. D. Flack, Acta Crystallogr., Sect. A: Fundam. Crystallogr., 1983, 39, 876.] was determined for 11a.

Acknowledgements

We would like to thank the EPSRC and AstraZeneca for postgraduate support (T.C.). The authors also thank Dr Ian Sword, the EPSRC (grant EP/H005692/1) and AstraZeneca for funding.

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