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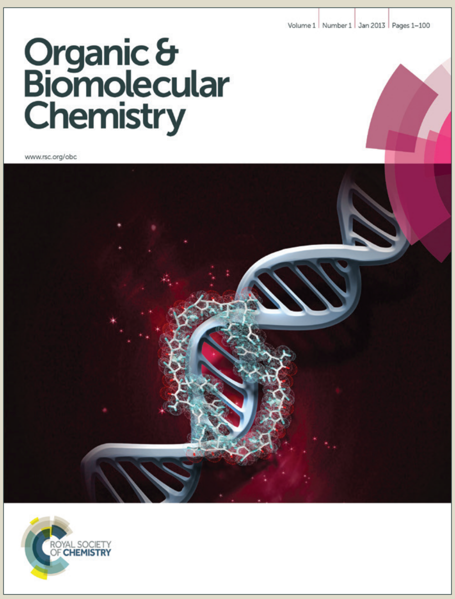

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Short, Efficient Synthesis of Fluorinated δ-Lactams.

Thomas J. Cogswell,[a] Craig S. Donald,[b] De-Liang Long,[a,§] Rodolfo Marquez[a†]*

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DOI: 10.1039/b000000x [DO NOT ALTER/DELETE THIS TEXT]

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

Introduction

Fluorination has been used to increase the potency and 'drug-like' 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 medical chemistry and natural systems. For instance, aripiprazole **1**, is used currently for the treatment of schizophrenia and bipolar disorders (Figure 1).[3]

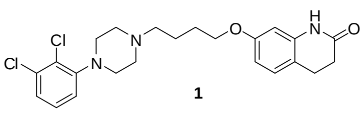


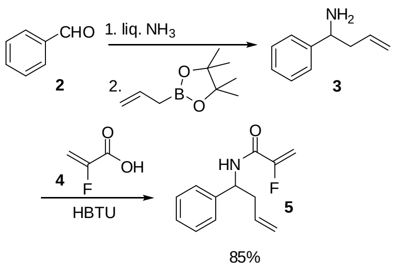
Fig. 1 Aripiprazole **1**.

Thus, it is not suprising, that considerable time and efforts have been directed towards the synthesis of fluorinated δ-lactams.[4,5,6] 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, efficient route to the synthesis of fluorinated δ-lactams starting from 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.

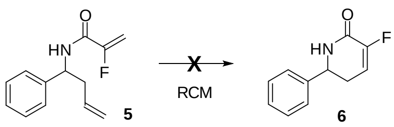
Results and Discussion

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% over the 2 steps (Scheme 1).



Scheme 1. Formation of dialkene **5** from benzaldehyde **2**.

Amide **5** was then treated with a range of metathesis catalysts in the attempt to induce ring closure (Scheme 2), however only a complex mixture of cross metathesis products resulted, with none of the desired cyclised product **6** being detected.



Scheme 2. Attempted RCM reaction with dialkene **5**.

The lack of cyclisation could be attributed to interaction of the ruthenium catalyst with the amide group which prevents the ring closing metathesis from taking place, in a situation similar to that reported by Vilar and co-workers.[8]

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

Thus, reaction of *p*-methoxybenzylamine with benzaldehyde yielded the corrosponding 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** then proceeded to generate the desired amide **8a** in good yield.

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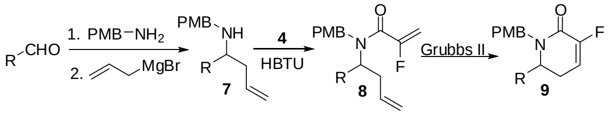
Gratifyingly, PMB protection of the amide unit allowed the ring closing metathesis reaction to proceed smoothly to yield the unsaturated lactam **9a** in quantitative yield (Table 1).



R	Yield		Yield		Yield	
Ph	95%	**7a**	63%	**8a**	quant	**9a**
4-MeOPh	80%	**7b**	66%	**8b**	quant	**9b**
4-CF_3Ph	66%	**7c**	45%	**8c**	quant	**9c**
1-Naphthyl	99%	**7d**	31%	**8d**	quant	**9d**
4-BrPh	97%	**7e**	54%	**8e**	99%	**9e**
i-Butyl	76%	**7f**	74%	**8f**	85%	**9f**
cyclohexyl	74%	**7g**	70%	**8g**	89%	**9g**
2-furyl	83%	**7h**	28%	**8h**	64%	**9h**
N-Ts 2-pyrrole	85%	**7i**	50%	**8i**	77%	**9i**
2-pyridyl	73%	**7j**	68%	**8j**	---	**9j**

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

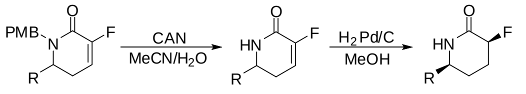
With the benzaldehyde example working efficiently, the scope of the methodology was explored (Table 1). Electron donating and electron withdrawing substituents on the aromatic ring were both tested with good results in all cases through the four step sequence. The electron withdrawing analogue being 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 any of the desired fluorinated δ-lactam **9j** under any of the conditions attempted. This was rationalised in the same manner to the previous example (Scheme 2), where the presence of an unprotected nitrogen atom was thought to bind to the Ru catalyst.

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.



R	Yield		Yield	
Ph	94%	**10a**	98%	**11a**
4-MeOPh	40%	**10b**	83%	**11b**
4-CF_3Ph	47%	**10c**	quant	**11c**
Naph	61%	**10d**	quant	**11d**
4-BrPh	72%	**10e**	quant	**11a**
i-Butyl	97%	**10f**	quant	**11f**
cyclohexyl	79%	**10g**	quant	**11g**

Table 2. Synthesis of δ-lactams **11a-g**.

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 (Figure 2).[10]

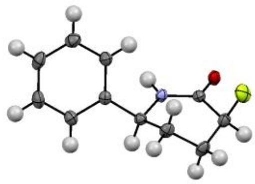
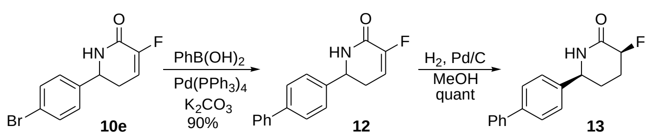


Table 2. Crystal structure of fluorinated δ-lactam, **11a**.

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).



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.

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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.

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 40-60 °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 (υmax) are reported in wavenumbers (cm^{-1}). Proton magnetic resonance spectra (^1H NMR), fluorine magnetic resonance spectra (^{19}F) and carbon magnetic resonance spectra (^{13}C NMR) were recorded at 400 MHz, 377 MHz and 100 MHz or at 500 MHz, 470 MHz and 125 MHz respectively. ^{13}C 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) 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 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 spectrometery operating at a resolution of 15000 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 (λmax254nm) and/or by staining with either anisaldehyde, potassium permanganate, iodine or cerium ammonium molybdate followed by heating.

1-Phenylbut-3-en-1-ylamine, 3.[12] Benzaldehyde (0.21 g, 2.0 mmol) was dissolved in methanol (4 mL) and the resulting solution was cooled to -78 °C. NH_3 (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 x 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 (3x 20 mL). The combined CH_2Cl_2 phases were then dried (Na_2SO_4), 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 ($CDCl_3$, 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), 1.6 (2H, br s). ^{13}C ($CDCl_3$, 125 MHz) δ: 145.8, 135.4, 128.4, 127.9, 126.4, 117.7, 55.4, 44.2.

2-Fluoroacrylic Acid, 4.[13] Commercially available 2-fluoroacrylic acid methyl ester (0.87 mL, 9.6 mmol) was dissolved in EtOH/H_2O (8.7:1.3, 10mL). Aq. NaOH (2M) 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 (6M) 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 ($CDCl_3$, 400 MHz) δ: 11.5 (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). ^{19}F ($CDCl_3$, 470 MHz) δ: -118.3. ^{13}C ($CDCl_3$, 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 ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -121.3. ^{13}C ($CDCl_3$, 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, $C_{13}H_{15}FNO$ requires 220.1138. IR (thin film) υmax = 3338, 1651, 1529, 1190 cm^{-1}.

1-(Toluene-4'-sulfonyl)-1*H*-pyrrol-2-carboxaldehyde.[14] 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 H_2O (20 mL), and extracted with CH_2Cl_2 (2 x 25 mL). The combined organics were then dried (Na_2SO_4) and the solvent was removed *in vacuo*. The resulting crude residue was purified by flash column chromatography (0-10% EtOAc in petroleum

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ether) to yield the tosylated pyrrole as a white solid (2.47 g, 9.9 mmol, 94%).

^{1}H ($CDCl_3$, 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). ^{13}C ($CDCl_3$, 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. Na_2SO_4 (2 g) was dried under vacuum in a round bottom flask for 10 min. 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 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 x 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, 7a.[15] Following General Procedure A, benzaldehyde (0.95 mL, 9.4 mmol) 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.

^{1}H ($CDCl_3$, 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). ^{13}C ($CDCl_3$, 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, 7b.[16] Following General Procedure A, 4-methoxybenzaldehyde (0.84 mL, 7.3 mmol) 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 **7b** (1.67 g, 5.6 mmol, 77% yield) as a pale yellow oil.

^{1}H ($CDCl_3$, 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). ^{13}C ($CDCl_3$, 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) 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.

^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -62.3. ^{13}C ($CDCl_3$, 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, $C_{19}H_{21}F_3NO$ requires 336.1575. IR (thin film) υmax = 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) 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.

^{1}H ($CDCl_3$, 400 MHz) δ: 8.10 (1H, appd, J_{HH} = 7.41 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). ^{13}C ($CDCl_3$, 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, $C_{22}H_{24}NO$ requires 318.1858. IR (thin film) υmax = 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) 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.

^{1}H ($CDCl_3$, 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). ^{13}C ($CDCl_3$,

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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, $C_{18}H_{21}{}^{79}BrNO$ requires 346.0807. IR (thin film) υmax = 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) 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 ($CDCl_3$, 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_H = 6.6 Hz). ^{13}C ($CDCl_3$, 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, $C_{16}H_{26}NO$ requires 248.2014. IR (thin film) υmax = 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) 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 ($CDCl_3$, 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). ^{13}C ($CDCl_3$, 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, $C_{18}H_{28}NO$ requires 274.2168. IR (thin film) υmax = 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) 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 ($CDCl_3$, 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). ^{13}C ($CDCl_3$, 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, $C_{16}H_{20}NO_2$ requires 258.1494. IR (thin film) υmax = 2930, 2850, 1511, 1441, 1246, 1035 cm^{-1}.

4'-Methoxy-*N*-[1-(1''-(toluene-4'''-sulfonyl)-1*H*-pyrrol-2''-yl)-3-butenyl]benzylamine, 7i. Following General Procedure A, 1-(toluene-4'-sulfonyl)-1H-pyrrol-2-carboxaldehyde (1 g, 4.02 mmol) 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 ($CDCl_3$, 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). ^{13}C ($CDCl_3$, 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, $C_{23}H_{26}N_2O_3SNa$ requires 433.1556. IR (thin film) υmax = 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) 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 ($CDCl_3$, 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). ^{13}C ($CDCl_3$, 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, $C_{17}H_{21}N_2O$ requires 269.1654. IR (thin film) υmax = 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.

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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.

^{1}H ($CDCl_3$, 400 MHz) δ: 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -102.4, -114.2. ^{13}C ($CDCl_3$, 125 MHz) δ: 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, $C_{21}H_{22}FNO_2$ requires 339.1635. IR (thin film) υmax = 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.

^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -102.1, -104.2. ^{13}C ($CDCl_3$, 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, $C_{22}H_{24}FNO_3$ requires 369.1740. IR (thin film) υmax = 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.

^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -62.3, -102.5, -104.4. ^{13}C ($CDCl_3$, 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, $C_{22}H_{21}F_4NO_2$ requires 407.1508. IR (thin film) υmax = 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.

^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -103.7, -103.8. ^{13}C ($CDCl_3$, 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, $C_{25}H_{24}FNO_2$ requires 389.1791. IR (thin film) υmax = 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.

^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -102.3, -104.2. ^{13}C ($CDCl_3$, 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, $C_{21}H_{21}{}^{79}BrFNO_2$ requires 417.0740. IR (thin film) υmax = 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.

^{1}H ($CDCl_3$, 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

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(3H, d, J_{HH} = 6.4 Hz,), 0.74 (3H, d, J_{HH} = 6.0 Hz). ^{19}F ($CDCl_3$, 377 MHz) δ: -102.4 (dd, J_{FH} = 47.5, 16.2 Hz), -103.6 (dd, J_{FH} = 46.5, 15.1 Hz). ^{13}C ($CDCl_3$, 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, $C_{19}H_{27}FNO_2$ requires 320.2026. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 400 MHz) δ: 7.32 (2H, d, J_{HHH} = 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -102.7. ^{13}C ($CDCl_3$, 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, $C_{21}H_{29}FNO_2$ requires 346.2182. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -103.5, -105.3. ^{13}C ($CDCl_3$, 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, $C_{19}H_{20}FNO_3$ requires 329.1428. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -103.9. ^{13}C ($CDCl_3$, 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, $C_{26}H_{27}FN_2O_2S$ requires 482.1676. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -102.5, -105.1. ^{13}C ($CDCl_3$, 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, $C_{20}H_{22}FN_2O_2$ requires 341.1665. IR (thin film) υmax = 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.

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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -126.8. ^{13}C ($CDCl_3$, 125 MHz) δ: 159.8 (d, J_{CF} = 30 Hz), 159.2, 149.4 (d, J_{CF} = 251 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, $C_{19}H_{18}FNO_2$ requires 311.1322. IR (thin film) υmax = 2933, 2837, 1651, 1512, 1247, 1176, 1031 cm^{-1}.

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3-Fluoro-1-(4'-methoxybenzyl)-6-(4''-methoxyphenyl)-5,6-dihydro-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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -126.7. ^{13}C ($CDCl_3$, 125 MHz) δ: 159.7 (d, J_{CF} = 30 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, $C_{20}H_{20}FNO_3$ requires 341.1427. IR (thin film) *υ*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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -62.3, -126.1. ^{13}C ($CDCl_3$, 125 MHz) δ: 159.6 (d, J_{CF} = 30 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, $C_{20}H_{17}F_4NO_2$ requires 379.1195. IR (thin film) *υ*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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -127.5. ^{13}C ($CDCl_3$, 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, $C_{23}H_{20}FNO_2$ requires 361.1478. IR (thin film) *υ*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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -126.3. ^{13}C ($CDCl_3$, 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, $C_{19}H_{18}{}^{79}BrFNO_2$ requires 390.0505. IR (thin film) *υ*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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -127.6. ^{13}C ($CDCl_3$, 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, $C_{17}H_{22}FNO_2$ requires 291.1635. IR (thin film) *υ*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.
^{1}H ($CDCl_3$, 400 MHz) δ: 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -128.2. ^{13}C ($CDCl_3$, 125 MHz) δ: 159.2, 159.0 (d, J_{CF} = 31.1 Hz), 149.5 (d, J_{CF} = 253.2 Hz, *C*F), 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

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$[M+H]^+$ 318.1871, $C_{19}H_{25}FNO_2$ requires 318.1869. IR (thin film) υmax = 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. ^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -126.3. ^{13}C ($CDCl_3$, 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, $C_{17}H_{16}FNO_3$ requires 301.1114. IR (thin film) υmax = 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. ^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -127.9. ^{13}C ($CDCl_3$, 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, $C_{24}H_{23}FN_2O_4SNa$ requires 477.1255. IR (thin film) υmax = 2955, 1630, 1515, 1447, 1276, 1205 cm^{-1}.

General procedure D: removal of *p*-methoxybenzyl protecting group. The cyclic amide (1 eq) was dissolved in a $MeCN/H_2O$ (8:2, 4 mL) mixture and ceric ammonium nitrate was added portion wise. The resulting solution was stirred at rom temperature until completion indicated by TLC analysis (7 h). The reaction was quenched with aq. sat. $NaHCO_3$ (10 mL) and extracted with diethyl ether (3 x 10 mL). The orgaincs were combined, dried (Na_2SO_4) and evaporated *in vacuo*. The crude material was purified 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. ^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -129.9. ^{13}C ($CDCl_3$, 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, $C_{11}H_{10}FNO$ requires 191.0746. IR (thin film) υmax = 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. ^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -130.0. ^{13}C ($CDCl_3$, 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, $C_{12}H_{13}FNO_2$ requires 222.09230. IR (thin film) υmax = 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. ^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -62.4, -129.1. ^{13}C ($CDCl_3$, 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, $C_{12}H_9F_4NO$ requires 259.0620. IR (thin film) υmax = 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. ^{1}H ($CDCl_3$, 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_H = 4.6 Hz), 5.74 (1H, br s),

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5.56 (1H, t, J_{HH} = 8.5 Hz), 2.81-2.76 (2H, m). ^{19}F ($CDCl_3$, 470 MHz) δ: -129.6. ^{13}C ($CDCl_3$, 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, $C_{15}H_{12}FNO$ requires 241.0903. IR (thin film) υmax = 1715, 1797, 1320, 1180 cm^{-1}.

3-Fluoro-6-(4'-bromophenyl)-5,6-dihydro-1*H*-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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -129.6. ^{13}C ($CDCl_3$, 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) υmax = 1705, 1685, 1205, 1010 cm^{-1}.

3-Fluoro-6-isobutyl-5,6-dihydro-1*H*-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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -130.1. ^{13}C ($CDCl_3$, 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, $C_9H_{15}FNO$ requires 172.1138. IR (thin film) υmax = 3219, 2934, 2906, 1696, 1669, 1264, 1206 cm^{-1}.

3-Fluoro-6-cyclohexane-5,6-dihydro-1*H*-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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -130.5. ^{13}C ($CDCl_3$, 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, $C_{11}H_{17}FNO$ requires 198.1294. IR (thin film) υmax = 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 (Na_2SO_4) and the solvent 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -180.3. ^{13}C ($CDCl_3$, 125 MHz) δ: 167.5 (d, J_{CF} = 20 Hz), 141.4, 129.0 (2C), 128.4, 126 1 (2C), 85.7 (d, J_{CF} = 175 Hz), 57.3, 27.3 (d, J_{CF} = 3.75 Hz), 26.2 (d, J_{CF} = 20 Hz). *m/z* [EI (+ve)] 193.1 $[M]^+$. HRMS found $[M]^+$ 193.0904, $C_{11}H_{12}FNO$ requires 193.0903. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 400 MHz) δ: 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -184.8. ^{13}C ($CDCl_3$, 125 MHz) δ: 167.2 (d, J_{CF} = 22 Hz), 159.6, 133.4, 127.3 (2C), 114.4 (2C), 85.7 (d, J_{CF} = 176 Hz), 57.0, 55.4, 27.4 (d, J_{CF} = 4.6 Hz), 26.4 (d, J_{CF} = 21 Hz). *m/z* [EI (+ve)] 223.1 $[M]^+$. HRMS found $[M]^+$ 223.0999, $C_{12}H_{14}FNO_2$ requires 223.1009. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -62.4, -185.0. ^{13}C ($CDCl_3$, 125 MHz) δ: 167.4 (d, J_{CF} = 22 Hz), 145.4, 130.9, 130.6, 126.6 (2C), 126.1 (2C), 85.5 (d, J_{CF} = 176 Hz), 57.0, 27.2 (d, J_{CF} = 4.2 Hz), 26.1 (d, J_{CF} = 21 Hz).

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m/z [EI (+ve)] 261.1 $[M]^+$. HRMS found $[M]^+$ 261.0773, $C_{12}H_{11}F_4NO$ requires 261.0777. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -186.1. ^{13}C ($CDCl_3$, 100MHz) 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, $C_{15}H_{15}FNO$ requires 244.1138. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -185.0. ^{13}C ($CDCl_3$, 125 MHz) δ: 167.4 (d, J_{CF} = 20 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} = 3.75 Hz), 22.6, 22.3. *m/z* [CI (+ve)] 174.1 $[M+H]^+$, HRMS found $[M+H]^+$ 174.1300, $C_9H_{17}FNO$ requires 174.1294. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 500 MHz) δ: 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). ^{19}F ($CDCl_3$, 470 MHz) δ: -184.6. ^{13}C ($CDCl_3$, 125 MHz) δ: 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, $C_{11}H_{18}FNO$ requires 199.1372. IR (thin film) υmax = 2926, 2870, 1664, 1410 cm^{-1}.

3-Fluoro-6-(4'-phenylphenyl)-5,6-dihydro-1*H*-pyridin-2-one, 12. Dihydropyridone **10e** (98 mg, 0.36 mmol) was dissolved in a mixture of toluene (12 mL) and H_2O (2 mL). K_2CO_3 (0.11 g, 0.79 mmol), $PhB(OH)_2$ (88 mg, 0.72 mmol) and $Pd(PPh_3)_4$ (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 H_2O (1 x 10 mL) and brine (1 x 10 mL) and then dried (Na_2SO_4) 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.
^{1}H NMR ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -129.8. ^{13}C ($CDCl_3$, 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, $C_{17}H_{14}FNO$ requires 267.1059. IR (thin film) υmax = 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.
^{1}H ($CDCl_3$, 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). ^{19}F ($CDCl_3$, 377 MHz) δ: -185.1. ^{13}C ($CDCl_3$, 100MHz) 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, $C_{17}H_{16}FNO$ requires 269.1216. IR (thin film) υmax = 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 Kα radiation (λ = 1.54184 Å) radiation. Data reduction was carried out and an analytical numeric absorption correction applied [based on expressions derived in Clark, R. C. & Reid, J. S. *Acta Cryst.* 1995, *A51*, 887-897] using CrysAlisPro [Oxford Diffraction Limited., Version 1.171.33.55, Oxfordshire, UK]. The structures were all solved by direct methods using the program SHELXS97 [SHELX, Sheldrick, G. M. *Acta Cryst.* 2008, *A64*, 112-122] and refined using full-matrix least-squares refinement on F^2 using SHELXL97 [SHELX Sheldrick, G. M. *Acta Cryst.* 2008, *A64*, 112-122] within the WinGX program suite [Farrugia, L. J. *J. Appl. Cryst.* 1999, *32*, 837-838]. The Flack *x* parameter [Flack, H. D. *Acta Cryst.* 1983, *A39*, 876.] was determined for 11a.
Full refinement details are given in the SI and the CIF files. Crystallographic data (excluding structure factors) have been

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deposited with the Cambridge Crystallographic Data Centre (CCDC1006297), and copies of these data can be obtained free of charge via www. ccdc.cam.ac.uk/data_request/cif.

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