EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201402535

Ring-Closing Metathesis of Vinyl Fluorides towards α-Fluorinated α,β-Unsaturated Lactams and Lactones

Michael Marhold,[a] Christian Stillig,[a] Roland Fröhlich,[a] and Günter Haufe*[a]

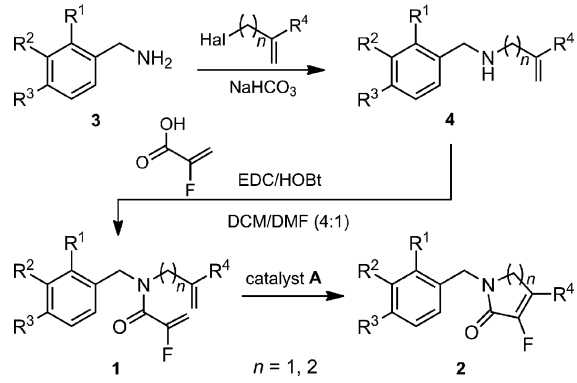
Keywords: Homogeneous catalysis / Cyclization / Metathesis / Fluorine / Lactams / Lactones / Nitrogen heterocycles

Ring-closing olefin metathesis reactions (RCM) using Grubbs II or Hoveyda's catalysts have been applied to a series of *N*-alkenyl-*N*-benzyl-α-fluoroacrylamides. α-Fluoro-α,β-unsaturated γ- or δ-lactams incorporating a fluorinated double bond were obtained in moderate to good yields, depending on the nature of substituents on the benzyl ring. The corresponding seven- and eight-membered lactams were not formed under similar conditions. When the *N*-benzyl group was replaced by an *N*-tosyl group, the corresponding ε-lactam was also formed in 38 % yield. When *N*-(2-fluoroallyl) derivatives were used instead of fluoroacryloyl derivatives, six-, seven-, and eight-membered N-heterocycles were obtained in low yields. This method was also used to synthesize fluorinated α,β-unsaturated analogues of pyrrolizidine and indolizidine alkaloids from prolinol, and also to synthesize *N*-benzyl-3-fluoroquinolone in three steps from commercially available 2-vinylaniline in 44 % overall yield. Also 3-fluorocoumarin and 3-fluorochromene were prepared from *o*-vinylphenol, and 3-fluoro-benzoxepine was available from *o*-allylphenol.

Introduction

Since the development of well-defined active catalysts by Schrock and Grubbs in the 1990s, olefin metathesis took a giant leap forward to become one of the most important tools for C–C bond formation.[1] This reaction has been applied successfully to a wide variety of substrates,[2] which shows its huge versatility and benefit. The importance of this new tool for synthetic chemistry was acknowledged by the Nobel Prize committee in 2005, when Chauvin, Grubbs, and Schrock were rewarded for the discovery and mechanistic investigations of the method.[3]

The reaction is widely adaptable for fluorine-free compounds, and there are also many examples of the synthesis of unsaturated carbocycles and heterocycles bearing fluorine substituents away from the double bonds.[4] In contrast, to date, there are only few reports of metathesis reactions involving a fluorinated double bond. A couple of years ago, we reported preliminary results on the ring-closing metathesis (RCM) reactions of *N*-benzyl-protected *N*-alkenyl-*N*-fluoroacrylamides **1** to give α,β-unsaturated *N*-benzyllactams **2** bearing a fluorine in the α position (Scheme 1).[5] Independently, and almost simultaneously, Brown et al.[6] and Rutjes et al.[7] published similar examples of ring-closing metathesis with vinyl fluorides.



Scheme 1. Synthesis of substituted *N*-benzyl α,β-unsaturated α-fluoro γ- and δ-lactams **2** starting from benzylamines **3** via secondary amines **4** and acrylamides **1**. EDC = *N*-1-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide hydrochloride; HOBt = 1-hydroxy-1*H*-benzotriazole.

In this study, we have extended the scope of this reaction and, we have used Grubbs II catalyst (**A**) and Hoveyda's catalyst (**B**) (Figure 1) to synthesize fluorinated analogues of natural N- and O-heterocyclic compounds.

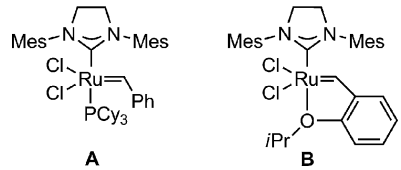


Figure 1. Grubbs II (**A**) and Hoveyda's (**B**) catalysts.

[a] Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster,
Corrensstr. 40, 48149 Münster, Germany
E-mail: haufe@uni-muenster.de
http://www.uni-muenster.de/Chemie.oc/haufe/haufe.html

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402535.

Results and Discussion

Unsaturated Fluorinated *N*-Benzyl Lactams by RCM of *N*-Alkenyl-*N*-benzyl-2-fluoroacrylamides

First, we prepared substituted *N*-alkenyl-*N*-benzyl-*N*-(2-fluoroacryl)amides **1** as RCM precursors from the corresponding benzylamines (i.e., **3**) and ω-haloalkenes via **4**. Then, various substituted *N*-benzyl-substituted α,β-unsaturated α-fluoro-γ-lactams **2** were synthesized using 2–4 mol-% of the highly active[8] Grubbs II catalyst (**A**), as shown in Figure 1, Scheme 1, and Table 1.

Table 1. Synthesized fluorinated α,β-unsaturated *N*-benzyl γ- and δ-lactams **2**.

Entry	R^1	R^2	R^3	R^4	*n*	Products	Yield of **1** [%]	Yield of **2** [%]
1	H	H	H	H	1	**a**	70[a]	79[a]
2	H	H	H	H	2	**b**	48[a]	86[a]
3	H	H	H	H	3	**c**	52[a]	0[a,b]
4	H	H	H	H	4	**d**	52[a]	0[a,c]
5	H	H	H	CH_3	1	**e**	41[a]	46[a]
6	H	H	Cl	H	1	**f**	30	73
7	H	Cl	H	H	1	**g**	40	65
8	Cl	H	H	H	1	**h**	43	76
9	H	H	F	H	1	**i**	66	70
10	H	H	F	H	2	**j**	57[a]	76[a]
11	H	F	H	H	1	**k**	40	77
12	H	H	CF_3	H	1	**l**	44	44
13	H	H	NO_2	H	1	**m**	46	33
14	H	CF_3	H	H	1	**n**	55	77
15	H	H	*t*Bu	H	1	**o**	93[d]	86
16	H	H	OMe	H	2	**p**	73[a]	81[a]
17	H	H	OMe	H	3	**q**	80	0
18	OMe	H	OMe	H	1	**r**	42	34
19	H	OMe	OMe	H	0	**s**	78	0

[a] Ref.[5] [b] The "homodimer" incorporating non-fluorinated double bonds was isolated (40%). [c] The "homodimer" incorporating non-fluorinated double bonds was identified by HRMS, but was not isolated. [d] Crude product.

RCM reactions leading to γ- and δ-lactams generally gave yields ranging from 65 to 77%. Attempted cyclization reactions to form seven- or eight-membered lactams (Table 1, entries 3, 4, and 17) failed. Electron-donating substituents like *tert*-butyl (Table 1, entry 15) or *para*-methoxy (Table 1, entry 16) groups increased the yield to 81 or 86%, while substrates with electron-deficient substituents like trifluoromethyl (Table 1, entry 12) or nitro (Table 1, entry 13) groups in the *para* position gave significantly lower yields of 44 or 33%, respectively. Surprisingly, the RCM reaction of a *meta*-trifluoromethyl-substituted precursor (Table 1, entry 14) performed well to give a 77% yield, while a substrate with methoxy substituents in both the *ortho* and *para* positions (Table 1, entry 18) gave a dramatically reduced yield of 34%, and compound **1s**, with methoxy groups in the *meta* and *para* positions (Table 1, entry 19), did not give any RCM product.

The results also show that six-membered rings were formed in slightly higher yields (Table 1, entries 2, 10, and 16) than their five-membered analogues (Table 1, entries 1 and 9), and that cyclization to seven- and eight-membered rings did not work at all, even with *p*-methoxy precursor **1q** (Table 1, entries 3, 4, and 17). Similar non-fluorinated medium-sized rings have been obtained in reasonable yields.[9]

The structures of compounds **2i** and **2p** were proved by X-ray diffraction (Figure 2).

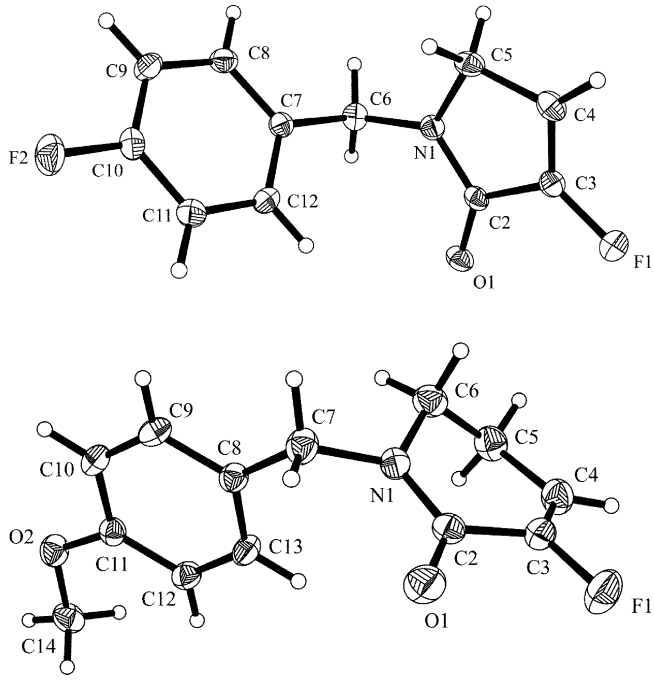
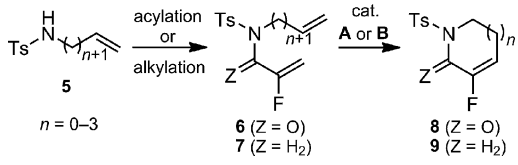


Figure 2. X-ray crystal structures of compounds **2i** and **2p**.

In 2003, Osipov and Dixneuf synthesized a wide variety of non-fluorinated lactams and other N-heterocycles with different substituents on nitrogen using RCM.[10] Hoveyda et al. assembled five- to eight-membered *N*-tosyl heterocycles in good to excellent yields using one of his catalysts.[11] With their work as a basis, we went on to investigate the synthesis of fluorinated analogues of five- to eight-membered *N*-tosyl heterocycles using RCM. The synthetic pathway is shown in Scheme 2, the yields are given in Table 2 and the X-ray structure of compound **7c** is shown in Figure 3. Similar compounds have recently been made by ring-closing metathesis by Rutjes et al.[7]



Scheme 2. RCM of monofluorinated *N*-tosyl-substituted aza-α,ω-diene systems.

Starting from *N*-alkenyl-*N*-tosylamides **5**, the corresponding *N*-alkenyl-*N*-(2-fluoroacryl)-*N*-tosylamides (i.e., **6a**–**6d**) or *N*-alkenyl-*N*-(2-fluoroallyl)-*N*-tosylamides (i.e., **7a**–**7d**) were synthesized (Table 2). These compounds were then used for RCM reactions. For acrylamides **6**, Grubbs II catalyst (**A**) was useful. It gave γ- and δ-lactams **8a** and **8b**

Table 2. Synthesis from **6** or **7** of fluorinated α,β-unsaturated *N*-tosyl γ- and δ-lactams **8**, and fluorinated *N*-tosyl heterocycles **9**.

Entry	Z	*n*	Products	Yield of **6/7** [%]	Catalyst (mol-%)	Yield of **8/9** [%]	Homodimer [%]
1	O	0	**a**	68	**A** (4)	58	0
2	O	1	**b**	85	**A** (2)	78	0
3	O	2	**c**	59	**A** (2)	38[a]	39
4	O	3	**d**	83	**A** (2)	0	6 (GC)
5	H_2	0	**a**	92	**B** (4)	0	0
6	H_2	1	**b**	70	**B** (4)	23	0
7	H_2	2	**c**	74	**B** (4)	32	0
8	H_2	3	**d**	74	**B** (4)	18 (GC)	5 (GC)

[a] In addition, ring-contracted product **8b** (23%) was isolated.

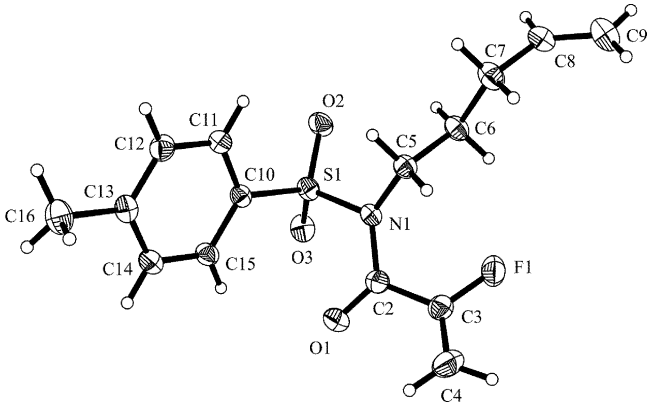


Figure 3. X-ray structure of compound **6c**.[13]

in moderate or good yields, but the yield of ε-lactam **8c** was low. In the latter case, besides **8c**, the δ-lactam (i.e., **8b**), formed by isomerization of the double bond in the starting material, was isolated in 23% yield.[12] Moreover, 39% of the non-fluorinated "homodimer" was also formed by cross metathesis. From **6d**, only a minor amount of the "homodimer" was formed; no lactams could be identified.

Hoveyda's catalyst (**B**) was shown to be useful for the formation of fluorinated dihydropyridine sulfonamides **9**, for which the Grubbs II catalyst (**A**) failed in our hands. However, *N*-tosylpyrroline **9a** was not formed at all, and the yields of compounds **9b**–**9d** were very low (Table 2, entries 5–8). An 80% yield of **9c** was obtained with the Grubbs II catalyst.[7c]

The X-ray structures of fluorinated γ-lactam **8a** and fluorinated dihydropyridine derivative **9b** are shown in Figure 4.

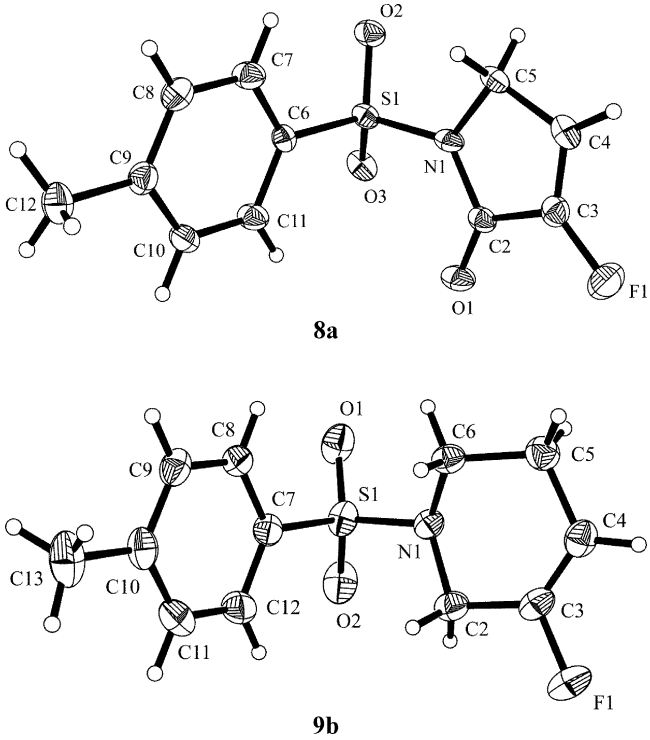


Figure 4. X-ray crystal structures of compounds **8a** and **9b**.[13]

Synthesis of Fluorinated Analogues of Bicyclic Alkaloids

Natural products very frequently feature N-heterocycles. Alkaloids like pyrrolizidines and indolizidines are particularly interesting due to their biological activity (Figure 5).[14,15]

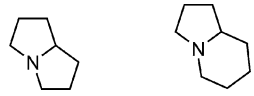
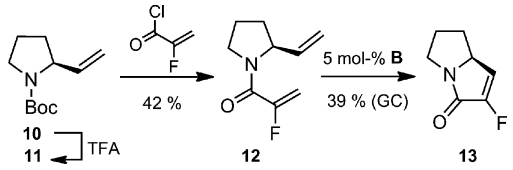


Figure 5. Basic skeletons of pyrrolizidine and indolizidine alkaloids.

Non-fluorinated bicyclic nitrogen-containing systems have been synthesized by RCM before,[16] and this area was reviewed a couple of years ago.[17] Subjecting vinyl fluorides to RCM would allow the formation of fluorinated alkaloid scaffolds.

Based on a route towards pyrrolizidines published by Nakagawa,[18] (*S*)-2-fluoro-5,6,7,7a-tetrahydropyrrolizin-3-one (**13**), a fluorinated analogue of pyrrolactam A, was synthesized from Boc-protected (*S*)-2-vinylpyrrolidine **10** (Scheme 3; Boc = *tert*-butoxycarbonyl), which is available from (*S*)-prolinol in three known steps.[18]

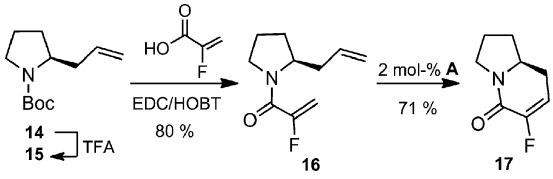
Boc-deprotection with trifluoroacetic acid to form **11** (43% yield), followed by attachment of the fluoroacryloyl moiety, gave metathesis precursor **12** in 42% yield. Ring-closing metathesis using Hoveyda's catalyst (5 mol-%) led to a compound tentatively assigned as the desired product, (*S*)-2-fluoro-5,6,7,7a-tetrahydropyrrolizin-3-one (**13**), in 39% yield (based on GC–MS and accurate mass data). Un-



Scheme 3. Formation of (*S*)-6-fluoro-2,3-dihydro-1*H*-pyrrolizin-5(7a*H*)-one (**15**) using RCM as key step. TFA = trifluoroacetic acid.

fortunately, due to its instability during chromatography on silica gel, it was not possible to isolate a pure sample.

Indolizidines are one of the most common substructures found in alkaloids. More than 15000 compounds contain this skeleton.[15] Non-fluorinated indolizidines, such as a derivative of (–)-coniceine, have already been prepared using RCM.[19] Considering these results, we planned a synthesis of fluorinated derivative **17**. Starting from Boc-protected (*S*)-2-allylpyrrolidine (**14**),[19] nitrogen deprotection and subsequent attachment of the 2-fluoroacrylic moiety at the nitrogen of **15** led to metathesis precursor **16**. The RCM reaction was carried out with Grubbs II catalyst (**A**; 2 mol-%) to give target compound (*S*)-6-fluoro-2,3,8,8a-tetrahydroindolizin-5(1*H*)-one (**17**) in 71% yield (Scheme 4, Figure 6).



Scheme 4. Synthesis of (*S*)-6-fluoro-2,3,8,8a-tetrahydroindolizin-5(1*H*)-one (**17**).

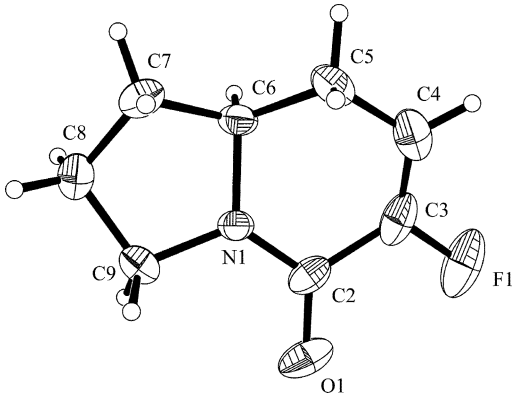
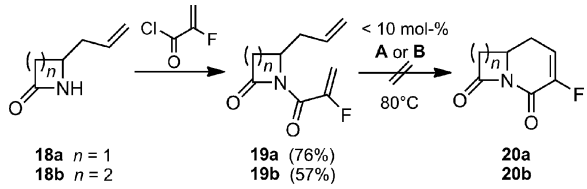


Figure 6. X-ray crystal structure of compound **17**.[13]

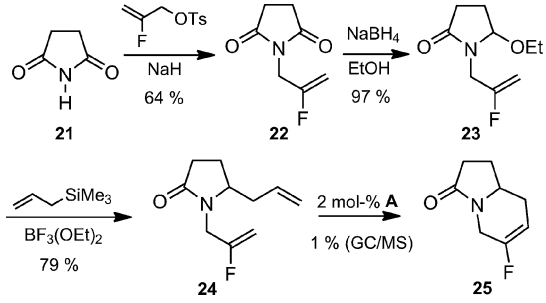
The successful preparation of pyrrolizidine analogue **13** and indolizidine derivative **17** led us to attempt the synthesis of α-fluorinated α,β-unsaturated azabicyclic imides, i.e., 1-azabicyclo[4.2.0]oct-3-ene and 1-azabicyclo-[4.3.0]non-3-ene derivatives.

Therefore, 4-allylazetidin-2-one (**18a**)[20] and 5-allylpyrrolidinone (**18b**)[21] were prepared following known procedures. Treatment with 2-fluoroacrylic acid chloride gave metathesis precursors **19a** and **19b**. Unfortunately all attempts to cyclize **19a** and **19b** to give imides **20a** and **20b** failed (Scheme 5). The corresponding fluorine-free β-lactams were obtained in good yields 15 years ago.[20] Attempts to facilitate the RCM of **19b** by addition of titanium isopropoxide[22] were unsuccessful.



Scheme 5. Attempts to synthesize 3-fluoro-1-azabicycloalk-3-enediones (**23a** and **23b**) by RCM.

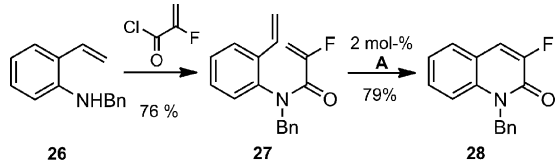
In our preliminary communication, we tried to synthesize the regioisomer (i.e., **25**) of (*S*)-6-fluoro-2,3,8,8a-tetrahydroindolizin-5(1*H*)-one (**17**) with the carbonyl functionality in the 9-position instead of the 2-position, but got a yield of the target product of only 1% (by GC) (Scheme 6).[5] All our subsequent attempts to improve this cyclization, even under harsh conditions (110 °C), have failed. A low yield was also observed in the synthesis of the non-fluorinated analogue of **25** using Schrock's catalyst.[16c]



Scheme 6. Formation of 6-fluoro-1,2,8,8a-tetrahydro-indolizin-3(5*H*)-one (**25**) by RCM of compound **24**.[5]

Synthesis of 3-Fluoroquinolone

Fluoroquinolones are appealing targets for synthesis by RCM. *N*-Benzyl-3-fluoroquinolone (**28**) was previously synthesized by Schlosser et al. in an eight-step sequence.[23] We approached the synthesis of **28** using a three-step sequence starting from commercially available 2-vinylaniline, which was first benzylated by reductive amination of benzaldehyde according to Schellenberg[24] to give **26**.[25] Subsequent acylation with α-fluoroacrylic acid chloride gave *N*-benzyl-*N*-(2-vinylphenyl)fluoroacrylamide (**27**). This compound was then subjected to RCM to give *N*-benzyl-3-fluoroquinolone (**28**) in 79% yield (Scheme 7). The structure was confirmed by X-ray analysis, as shown in Figure 7.



Scheme 7. Synthesis of *N*-benzyl-3-fluoroquinolone (**28**).

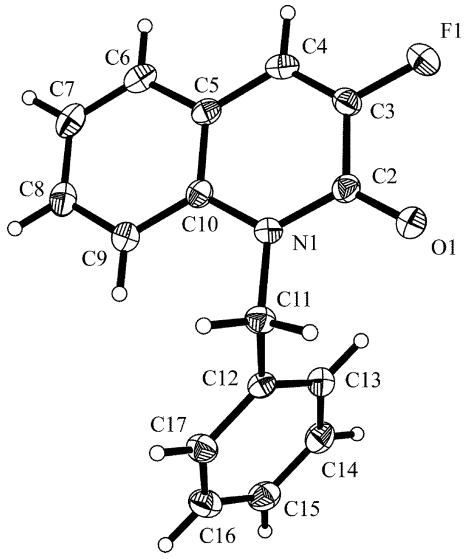
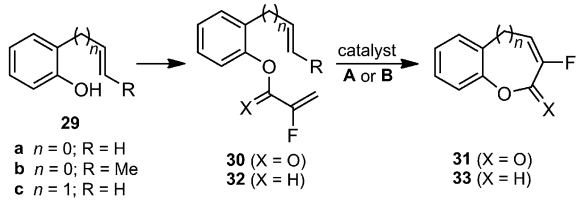


Figure 7. X-ray crystal structure of *N*-benzyl-3-fluoroquinolone (**28**).[13]

Synthesis of Fluorinated O-Heterocycles

Several RCM-mediated syntheses of non-fluorinated O-heterocycles are known in the literature.[26] Inspired by these results, we explored the scope of the formation of fluorinated analogues of coumarin, chromene, and 1-dihydrobenzoxepine derivatives (Scheme 8).



Scheme 8. Formation of O-heterocycles **32** or **34** by RCM.

Starting from 2-(alken-1-yl)phenols **29**, RCM precursors **30** and **32** that would lead to six- and seven-membered O-heterocycles **31** or **33** were prepared. These precursors were used for RCM with differing degrees of success. A poor result was obtained for the conversion of *o*-vinylphenol derivative **30a** into coumarin derivative **31a** using Grubbs II catalyst (**A**), as described in our earlier paper[5] (Table 3, entry 1). Starting from **30b**, in which the vinyl group is replaced by a prop-1-en-1-yl group, the yield of **31a** was significantly higher (Table 3, entry 2). This method minimized "homodimerization", which was the main process in the reaction of **30a**.[5] However, attempted cyclization of allylphenol derivative **30c** failed to form seven-membered ring **31c** (Table 3, entry 3). In this case, a "homodimeric" product was isolated in 57% yield; isomerization of the double bond of **30c** followed by formation of **31a** was not observed.[12]

Table 3. Synthesized O-heterocycles **31** and **33**.

Entry	X	*n*	R	Catalyst (mol-%)	Product	Yield [%]
1	O	0	H	**A** (2)	**31a**	16[a]
2	O	1	H	**A** (2)	**31c**	0[b]
3	O	0	Me	**A** (2)	**31a**	79
4	H_2	0	H	**B** (2)	**33a**	31
5	H_2	1	H	**B** (5)	**33b**	85[c]

[a] In addition, "homodimeric" product (40%) was observed.[5] [b] "homodimeric" product (57%) was isolated.[27] [c] Contains impurities.

The corresponding benzo-condensed cyclic ethers were formed with variable levels of success. First, RCM precursors **32** were prepared from **29** with 2-fluoroallyl tosylate.[28] 2-Fluorochromene (**33a**) was obtained in 31% yield from **32a** using Hoveyda's catalyst (**B**), and fluorinated benzoxepine derivative **33b** was isolated in 85% yield from **32b** under the same conditions. Earlier attempts by Brown to prepare **33b** by RCM with Grubbs II catalyst (**A**) were not entirely successful. The molecule was formed under harsh conditions, but it could not be isolated or completely characterized.[6]

Conclusions

In conclusion, this study shows that Grubbs's 2nd generation catalyst (**A**) and Hoveyda's catalyst (**B**) do catalyse ring-closing metathesis reactions of azadiene systems bearing a fluorine atom on one of the double bonds. Terminal *N*-alkenyl-*N*-benzyl-*N*-(α-fluoroacryl)amides (**1**) are cyclized to give α-fluoro-α,β-unsaturated γ- and δ-lactams **2** in moderate to good yields, but seven- or eight-membered lactams were not formed. The cyclization of the analogous toluenesulfonamides using catalyst **A** (2 mol-%) was also successful for γ- and δ-lactams. A 38% yield of the ε-lactam was even obtained, but the eight-membered lactam was not formed under the same conditions. Starting from the corresponding *N*-(2-fluoroallyl)amines instead of the amides in the presence of catalyst **B** (4 mol-%), the expected 3-fluoro-3-pyrrolines were not formed. Even the corresponding six-, seven-, and eight-membered heterocycles were difficult to access, and were only formed in low yields. Grubbs II catalyst A failed completely to catalyse the latter cyclizations. Furthermore, a pyrrolizidine derivative, an analogue of pyrrolactam A, containing an α-fluoro-α,β-unsaturated γ-lactam, was formed in a low yield. On the other hand, a fluorinated indolizidine derivative, i.e., an analogue of conicein, was formed from prolinol in five steps in a good overall yield. We do not yet have an explanation as to why the RCM of the fluorinated analogue of indolizidine alkaloid **17** worked, while the reaction was unsuccessful with similar systems. We continue to work with other catalysts. Finally,

3-fluorocoumarin was prepared using Grubbs II catalyst (**A**), and 3-fluorochromene and 3-fluoro-benzoxepine were synthesized using Hoveyda's catalyst (**B**).

Experimental Section

General Methods: ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded with Bruker DPX300, ARX300, and AV400, and Varian INOVA (500 MHz) and Unity plus (600 MHz) spectrometers. Spectra were recorded in solution in $CDCl_3$, CD_3CN, or [D$_6$]DMSO, and tetramethylsilane was used as an internal standard. $CFCl_3$ was used as the internal standard for ^{19}F NMR spectra. Chemical shifts are expressed as δ [ppm] values relative to the internal standard. Mass spectrometry was carried out with Waters-Micromass GCT or Quattro LCZ, Bruker Daltronics MicroTof, and Thermo-Fisher Scientific LTQ Orbitrap LTQ XL mass spectrometers. Merck silica gel 60 (230–400 mesh) was used for column chromatography. Analytical and preparative HPLC was carried out with a Knauer RP-HPLC instrument with K-1800 pumps and an S-2500 UV detector. Elemental analyses were carried out at the Organisch-Chemisches Institut, University of Münster using Foss Heraeus CHN-O-Rapid and Elementar-Analysesystem VarioEL III analysers. Unless otherwise specified, starting materials were purchased from commercial suppliers and used without further purification. Solvents were purified by distillation and, if necessary, dried according to standard procedures. Starting materials were synthesized according to published protocols as reported in the Supporting Information.

General Procedures

Synthesis of Substituted *N*-Allyl-*N*-benzyl-α-fluoroacrylamides

A. Coupling of Amines with α-Fluoroacrylic Acid Chloride (General Procedure 1): The amine was dissolved in dry dichloromethane (10 mL) and dry DMF (2.5 mL), and the solution was stirred for 1 h. α-Fluoroacrylic acid chloride (108 mg, 1.0 mmol) was then added, and the solution was stirred at room temperature for 20 h. Diethyl ether (25 mL) was added, and the mixture was washed with hydrochloric acid (5%), saturated $NaHCO_3$ solution, and brine (25 mL). The organic layer was dried with magnesium sulfate, and the solvent was removed in vacuo. The crude product was purified by column chromatography, eluting with dichloromethane.

B. Coupling of Amines with α-Fluoroacrylic Acid (General Procedure 2): *N*-Ethyl-*N*′-(3-dimethylaminopropylcarbodiimide) hydrochloride (EDC; 198 mg, 1.0 mmol) and 1-hydroxy-1*H*-benzotriazole hydrate (HOBt; 135 mg, 1.0 mmol) were dissolved in dry dichloromethane (10 mL) and dry DMF (2.5 mL), and the mixture was stirred for 1 h. α-Fluoroacrylic acid (90 mg, 1.0 mmol) and the amine (1.0 mmol) were then added, and the was stirred at room temperature for 20 h. Diethyl ether (25 mL) was added, and the solution was washed with hydrochloric acid (5%), saturated $NaHCO_3$ solution, and brine (25 mL). The organic layer was dried with magnesium sulfate, and the solvent was removed in vacuo. The crude product was purified by column chromatography, eluting with an appropriate solvent.

Synthesis of *N*-Alkenyl-*N*-(2-fluoroallylic)-*N*-tosyl Amides (General Procedure 3): The amine (4.0 mmol) was dissolved in dry DMF (20 mL), and 2-fluoroallyl tosylate (0.92 g, 4.0 mmol) and potassium carbonate (1.19 g, 4.0 mmol) were added at room temp. The mixture was then heated at reflux for 48 h. The mixture was allowed to cool to room temperature, then diethyl ether (20 mL) and water (20 mL) were added. The aqueous phase was separated and extracted with diethyl ether (10 mL). The combined organic phase was washed with water and brine (10 mL each), and dried with magnesium sulfate. The solvent was removed in vacuo, and the crude product was purified by column chromatography.

Olefin Metathesis (General Procedure 4): The α,ω-diene (0.7 mmol) was dissolved in dry toluene (1.25 mL) under an argon atmosphere in a Schlenk flask, and then Grubbs II catalyst (**A**; 11.89 mg, 0.014 mmol, 2 mol-%) or Hoveyda's catalyst (**B**; 8.78 mg, 0.014 mmol, 2 mol-%) was added. The reaction mixture was stirred at 80 °C for 16 h. The solvent was removed in vacuo, and the crude product was purified by column chromatography, eluting with an appropriate solvent.

Typical Examples – Metathesis Precursors

***N*-Allyl-*N*-(4-fluorobenzyl)-2-fluoroacrylamide (1i):** According to General Procedure 1, *N*-(4-fluorobenzyl)prop-2-en-1-yl-amine (**4i**; 3.3 g, 20 mmol) was treated with α-fluoroacrylic acid chloride (2.17 g, 22 mmol) to give **1i** (3.12 g, 66%) as a colourless oil after column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.89 (d, $^3J_{H,H}$ = 5.7 Hz, 2 H), 4.55 (s, 2 H), 5.13 (dd, $^2J_{H,H}$ = 3.5, $^3J_{H,F}$ = 16.9 Hz, 1 H), 5.18 (m, 2 H), 5.34 (dd, $^2J_{H,H}$ = 3.5, $^3J_{H,F}$ = 47.4 Hz, 1 H), 5.77 (m, 1 H), 6.96–7.28 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 47.7, 49.8, 99.7 ($^2J_{C,F}$ = 15.0 Hz), 115.6 ($^3J_{C,F}$ = 22.1 Hz), 118.5, 130.4, 132.1, 132.6, 158.3 (d, $^1J_{C,F}$ = 272.7 Hz), 161.7 (d, $^1J_{C,F}$ = 245.6 Hz), 162.4 (d, $^2J_{C,F}$ = 30.9 Hz) ppm. ^{19}F NMR ($CDCl_3$, 282 MHz): δ = –105.2 (m) –115.5 (m) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 237.2 (20) $[M]^+$, 196.2 (100) $[M-C_3H_5]^+$, 125.2 (35) $[C_6H_4FCH_2NH_2]^+$, 109.2 (55) $[C_6H_4FCH_2]^+$, 95.2 (15) $[C_6H_4F]^+$, 83.1 (25) $[C_4H_5NO]^+$, 73.1 (75) $[C_3H_2FO]^+$, 45.1 (20) $[CH_2CF]^+$.

***N*-(But-3-enyl)-*N*-(4-fluorobenzyl)-2-fluoroacrylamide (1j):** According to General Procedure 2, α-fluoroacrylic acid (360 mg, 4.0 mmol) was treated with *N*-but-3-enyl-*N*-(4-fluorobenzyl)amine (**4j**; 716 mg, 4.0 mmol) in the presence of EDC (791 mg, 4.0 mmol) and HOBt (541 mg, 4.0 mmol) to give **1j** (575 mg, 57%) as a colourless oil after column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (dt, $^3J_{H,H}$ = 7.5, $^3J_{H,H}$ = 7.2 Hz, 2 H), 3.36 (dt, $^3J_{H,H}$ = 7.2, $^2J_{H,H}$ = 2.1 Hz, 2 H), 4.58 (s, 2 H), 5.05 (m, 2 H), 5.12 (dd, $^2J_{H,H}$ = 3.0, $^3J_{H,F}$ = 17.1 Hz, 1 H), 5.32 (dd, $^2J_{H,H}$ = 3.0, $^3J_{H,F}$ = 47.7 Hz, 1 H), 5.72 (m, 1 H), 7.02 (dd, $^3J_{H,H}$ = $^3J_{H,F}$ = 8.7 Hz, 2 H), 7.23 (dd, $^3J_{H,H}$ = $^3J_{H,F}$ = 7.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.9, 46.9, 48.2, 99.5 (d, $^2J_{C,F}$ = 20.0 Hz), 115.5 ($^2J_{C,F}$ = 21.5 Hz, 2 C), 117.2, 129.4 (2 C), 132.2, 134.3, 157.8 (d, $^1J_{C,F}$ = 270.6 Hz), 162.2 (d, $^1J_{C,F}$ = 244.0 Hz), 162.4 (d, $^2J_{C,F}$ = 29.8 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –104.4 (d, $^3J_{F,H}$ = 35.5 Hz), –105.9 (d, $^3J_{F,H}$ = 35 Hz), –114.9 (m), –121.2 (dd, $^3J_{F,H}$ = 47.9, $^3J_{F,H}$ = 15.2 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 251 (2) $[M]^+$, 210 (14) $[M-C_3H_5]^+$, 196 (2) $[M-C_4H_7]^+$, 142 (2) $[M-FC_6H_5CH_2]^+$, 110 (10) $[FC_7H_8]^+$, 109 (100) $[FC_6H_5CH_2]^+$, 83 (11) $[FC_5H_5]^+$, 73 (10) $[CH_2CFCO]^+$, 45 (5) $[CH_2CF]^+$. $C_{14}H_{15}F_2NO$ (251.27): calcd. C 66.92, H 6.02, N 5.57; found C 66.69, H 6.14, N 5.57.

***N*-Allyl-*N*-(2-fluoroacryl)-4-tosylamide (6a):** According to General Procedure 3, *N*-allyl-4-tosylamide (**5a**; 386 mg, 1.8 mmol) was treated with α-fluoroacrylic acid chloride (198 mg, 1.8 mmol) and triethylamine (185 mg, 257 μL, 1.8 mmol). Purification by column chromatography (cyclohexane/ethyl acetate, 5:1) gave target compound **6a** (346 mg, 68%) as a white solid, m.p. 62 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.44 (s, 3 H), 4.45 (ddd, $^4J_{H,H}$ = 1.6, $^2J_{H,H}$ = 3.1, $^3J_{H,H}$ = 5.7 Hz, 2 H), 5.17–5.29 (m, 3 H), 5.42 (dd, $^2J_{H,H}$ = 3.6, $^3J_{H,F}$ = 45.2 Hz, 1 H), 5.82 (ddt, $^3J_{H,H}$ = 5.6, $^3J_{H,H}$ = 10.6, $^3J_{H,H}$ = 16.6 Hz, 1 H), 7.33 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H), 7.88 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6, 49.1, 102.3 (d, $^2J_{C,F}$ = 15.2 Hz), 118.7, 128.6 (2 C), 129.5 (2 C), 132.4,

135.7, 145.1, 156.1 (d, $^1J_{C,F}$ = 271.1 Hz), 162.0 ($^2J_{C,F}$ = 33.3 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –108.8 (dd, $^3J_{H,F}$ = 15.4, $^3J_{H,F}$ = 43.7 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 283 (0.2) $[M]^+$, 219 (12), 156 (1) $[CH_3C_6H_5SO_2H]^+$, 155 (13) $[CH_3C_6H_5SO_2]^+$, 128 (6) $[M - CH_3C_6H_5SO_2]^+$, 112 (83) $[C_6H_7NF]^+$, 91 (100) $[C_7H_7]^+$, 73 (53) $[C_3H_2OF]^+$, 65 (45) $[C_5H_5]^+$, 41 (384) $[C_3H_5]^+$.

(*S*)-1-(2-Allylpyrrolidin-1-yl)-2-fluoroprop-2-en-1-one (16): According to General Procedure 2, EDC (1.27 g, 6.40 mmol) and HOBt (0.86 g, 6.40 mmol) were dissolved in dry dichloromethane (64 mL) and DMF (16 mL). After 1 h, amine (*S*)-**15** (0.71 g, 6.40 mmol) and fluoroacrylic acid (0.58 g, 6.40 mmol) were added, and the mixture was stirred overnight. Purification by column chromatography gave compound **16** (936 mg, 80%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72–1.96 (m, 4 H, 5-H/6-H), 2.16–2.44 (m, 2 H, 3-H), 3.62 (m, 2 H, 7-H), 4.23 (m, 1 H, 4-H), 5.08 (m, 2 H, 1-H), 5.11 (m, 1 H, 10-H$_{cis}$), 5.44 (dd, $^2J_{H,H}$ = 2.2, $^3J_{H,F}$ = 47.0 Hz, 1 H, 10-H$_{trans}$), 5.75 (m, 1 H, 2-H) (broad signals because of dynamic effects of the fluoroacrylate group) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.6 (t, C-6), 28.5 (t, C-5), 36.9 (t, C-3), 48.2 (d, C-7), 57.8 (s, C-4), 99.5 (dt, $^2J_{C,F}$ = 15.8 Hz, C-10), 117.5 (t, C-1), 134.3 (s, C-2), 158.2 (d, $^1J_{C,F}$ = 273.3 Hz, C-9), 160.2 (s, C-8) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –109.5 (dd, $^3J_{F,H}$ = 16.4, $^3J_{F,H}$ = 46.9 Hz) ppm. Because of the hindered rotation of the fluoroacrylamide group, a second set of minor signals is present in ^{13}C and ^{19}F NMR spectra (see Supporting Information). MS (GC–MS, 70 eV): *m*/*z* (%) = 183 (0) $[M]^+$, 142 (95) $[M - CH_2CHCH_2]^+$, 106 (3), 73 (100) $[COCFCH_2]^+$, 70 (48) $[142 - COCFCH_2]^+$, 68 (6), 55 (4), 45 (41) $[CFCH_2]^+$, 41 (38) $[CH_2CHCH_2]^+$.

***N*-Benzyl-2-fluoro-*N*-(2-vinylphenyl)acrylamide (27):** According to General Procedure 1, amine **26** (469 mg, 2.24 mmol) was treated with fluoroacrylic acid chloride (243 mg, 2.24 mmol) in the presence of Et_3N (226 mg, 2.24 mmol) in dichloromethane (15 mL) to give compound **27** (482 mg, 76%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.33 (d, $^2J_{H,H}$ = 13.8 Hz, 1 H), 4.90 (dd, $^2J_{H,H}$ = 3.0, $^3J_{H,F}$ = 15.9 Hz, 1 H), 5.30 (dd, $^2J_{H,H}$ = 3.0, $^3J_{H,F}$ = 47.3 Hz, 2 H), 5.71 (d, $^3J_{H,H}$ = 17.5 Hz, 2 H), 6.62 (dd, $^3J_{H,H}$ = 11.0, $^3J_{H,H}$ = 17.5 Hz, 1 H), 6.72 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H), 7.09–7.30 (m, 7 H), 7.56 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.7, 100.7 (dt, $^2J_{C,F}$ = 15.4 Hz), 117.0, 126.3, 127.7, 128.2, 128.3, 128.4, 129.0, 129.6, 131.6 (2 C), 135.2, 135.9, 138.7, 157.2 (d, $^1J_{C,F}$ = 272.3 Hz), 161.7 (d, $^2J_{C,F}$ = 28.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –106.65 (dd, $^3J_{H,F}$ = 45.7, $^3J_{H,F}$ = 15.9 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 281/282 (4/0.5) $[M]^+$, 261 (1) $[M - HF]^+$, 235 (1) $[261 - C_2H_2]^+$, 208 (4) $[M - C_2H_2CFCO]^+$, 190 (26) $[M - C_6H_5CH_2]^+$, 178 (2) $[M - C_6H_4CHCH_2]^+$, 118 (3) $[C_8H_7NH]^+$, 103 (2) $[C_8H_7]^+$, 91 (100) $[C_6H_5CH_2]^+$, 77 (5) $[C_6H_5]^+$, 73 (8) $[CH_2CFCO]^+$, 65 (9) $[C_5H_5]^+$.

2-Prop-1-enylphenyl-α-fluoroacrylate (30b): The synthesis was carried out according to General Procedure 1, starting from (*E*/*Z*)-2-prop-1-enylphenol (**29b**; 2.68 g, 20.0 mmol) and α-fluoroacrylic acid chloride (2.10 g, 23.0 mmol). The crude product was purified by chromatography (toluene/ethyl acetate, 4:1) to give an (*E*/*Z*)-mixture of **30b** (3.20 g, 78%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.75 (dd, $^3J_{H,H}$ = 1.6, $^4J_{H,H}$ = 1.6 Hz, 3 H, 1-H$_{trans}$), 1.87 (dd, $^3J_{H,H}$ = 6.6 Hz, 3 H, 1-H$_{cis}$), 5.03 (dm, $^3J_{H,H}$ = 8.7 Hz, 1 H, 2-H$_{trans}$), 5.08 (m, 1 H, 2-H$_{cis}$), 5.49 (dd, $^2J_{H,H}$ = 3.3, $^3J_{H,F}$ = 12.9 Hz, 1 H, 12-H$_{cis}$), 5.88 (dd, $^2J_{H,H}$ = 3.3, $^3J_{H,F}$ = 42.9 Hz, 1 H, 12-H$_{trans}$), 5.88 (m, 1 H, 3-H), 7.05–7.51 (m, 4 H, 5-H–8-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4/18.8, 104.0/104.2 (t, $^2J_{C,F}$ = 15.3 Hz), 121.8/122.1, 123.7/126.1, 123.9/126.6, 126.7/128.0, 127.7/129.0, 129.6/130.6, 146.7/147.7, 152.8 (d, $^1J_{C,F}$ = 262.0 Hz), 158.3/158.8 (d, $^2J_{C,F}$ = 36.2 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ = –116.8 (dd, $^3J_{F,H}$ = 8.3, $^3J_{F,H}$ = 41.7 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 206 (46) $[M]^+$, 186 (8) $[M - HF]^+$, 133 (100) $[M - CH_2CFCO]^+$, 131 (62), 115 (17), 105 (74), 91 (3) $[C_6H_5CH_2]^+$, 89 (10) $[CH_2CFCO_2]^+$, 77 (31) $[C_6H_5]^+$, 73 (58) $[CH_2CFCO]^+$, 65 (3) $[C_5H_5]^+$, 45 (3) $[CH_2CF]^+$. HRMS (ESI): calcd. for $C_{12}H_{11}FO_2$ 206.0743; found 206.0734.

Typical Examples – Metathesis Products.

3-Fluoro-1-(4-fluorobenzyl)-1*H*-pyrrol-2(5*H*)-one (2i): The synthesis was carried out according to General Procedure 4, starting from *N*-allyl-*N*-(4-fluorobenzyl)-2-fluoroacrylamide (**1i**; 237 mg, 1.0 mmol) with either Grubbs II catalyst (**A**; 18 mg, 0.021 mmol, 2 mol-%) or Hoveyda catalyst (**B**; 12 mg, 0.020 mmol, 2 mol-%). Compound **2i** was obtained (144 mg, 70% with Grubbs II catalyst; 146 mg, 71% with Hoveyda's catalyst) as colourless crystals, m.p. 77 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.78 (dd, $^3J_{H,H}$ = 2.2, $^2J_{H,F}$ = 5.8 Hz, 2 H), 4.69 (s, 2 H), 6.29 (dt, $^3J_{H,H}$ = 2.2, $^3J_{H,F}$ = 0.8 Hz, 1 H), 7.34–7.64 (m, 4 H, 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.2 (d, $^3J_{C,F}$ = 5.7 Hz), 46.1, 112.8 (d, $^2J_{C,F}$ = 6.5 Hz), 115.7 (d, $^2J_{C,F}$ = 21.6 Hz), 129.8 (d, $^3J_{C,F}$ = 8.2 Hz), 132.1 (d, $^4J_{C,F}$ = 3.2 Hz), 152.7 (d, $^1J_{C,F}$ = 276.3 Hz), 162.4 (d, $^1J_{C,F}$ = 246.7 Hz), 162.8 (d, $^2J_{C,F}$ = 31.2 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –114.5 (m), –136.6 (d, $^3J_{H,F}$ = 0.8 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 209.2 (65) $[M]^+$, 208.2 (55) $[M - H]^+$, 109.2 (100) $[C_6H_4FCH_2]^+$ 86.1 (25) $[C_4H_3FO]^+$, 58.1 (10) $[C_3H_3F]^+$, 45.1 (15) $[CH_2CF]^+$. $C_{11}H_9ClFNO$ (225.65): calcd. C 63.16, H 4.34, N 6.70; found C 63.14, H 4.05, N 6.50.

3-Fluoro-1-(4-fluorobenzyl)-5,6-dihydropyridin-2(1*H*)-one (2j): The synthesis was carried out according to General Procedure 4, starting from *N*-(but-3-enyl)-*N*-(4-fluorobenzyl)-α-fluoroacrylamide (**1j**; 175.7 mg, 0.7 mmol) and catalyst **A** (2 mol-%). Compound **2j** was obtained (119 mg, 76%) as a brownish solid, m.p. 69 °C (diethyl ether). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (m, 2 H), 3.32 (t, $^3J_{H,H}$ = 7.2 Hz, 2 H), 4.57 (s, 2 H), 5.98 (dt, $^3J_{H,H}$ = 4.5, $^3J_{H,F}$ = 15.0 Hz, 1 H), 6.99 (m, 2 H), 7.26 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1 (dt, $^3J_{C,F}$ = 6.4 Hz), 44.5, 49.0, 112.8 (dd, $^2J_{C,F}$ = 15.2 Hz), 115.4 (2 dd, $^2J_{C,F}$ = 21.4 Hz), 129.7 (2 dd, $^3J_{C,F}$ = 7.6 Hz), 132.4 (d, $^4J_{C,F}$ = 4.1 Hz), 149.6 (d, $^1J_{C,F}$ = 253.3 Hz), 159.7 (d, $^2J_{C,F}$ = 31.6 Hz), 162.2 (d, $^1J_{C,F}$ = 244.4 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –114.9 (m), –127.5 (m) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 223 (41) $[M]^+$, 222 (5) $[M - H]^+$, 123 (13) $[FC_6H_5CH_2N]^+$, 110 (10) $[FC_7H_8]^+$, 109 (100) $[FC_6H_5CH_2]^+$, 95 (15) $[FC_6H_6]^+$, 83 (33) $[FC_5H_5]^+$, 57 (24) $[FC_3H_2]^+$, 51 (21) $[C_4H_3]^+$.

3-Fluoro-*N*-tosyl-1*H*-pyrrol-2(5*H*)-one (8a): The synthesis was carried out according to General Procedure 4, but with 2 mol-% Grubbs II catalyst (15 mg, 0.024 mmol), starting from *N*-allyl-*N*-(2-fluoroacryl)-*N*-tosylamide (**6a**; 346 mg, 1.2 mmol). The metathesis product was separated by column chromatography (Et_2O), and purified by crystallization (CH_2Cl_2) to give **8a** (180 mg, 58%) as white crystals, m.p. 151 °C (CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.44 (s, 3 H), 4.35 (dd, $^3J_{H,H}$ = 2.4, $^4J_{H,F}$ = 6.0 Hz, 2 H) 6.51 (dt, $^3J_{H,F}$ = 0.9, $^3J_{H,H}$ = 2.4 Hz, 1 H) 7.35 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H), 7.95 (d, $^3J_{H,H}$ = 8.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6, 45.3, 117.2 (d, $^2J_{C,F}$ = 7.5 Hz), 128.0 (2 C), 129.9 (2 C), 134.6, 145.7, 150.7 (d, $^1J_{C,F}$ = 277.8 Hz), 160.1 (d, $^2J_{C,F}$ = 30.5 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –135.2 (d, $^3J_{H,F}$ = 8.3 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 255 (0) $[M]^+$, 191 (100), 155 (9) $[CH_3C_6H_5SO_2]^+$, 100 (8) $[M - CH_3C_6H_5SO_2]^+$, 91 (96) $[C_7H_7]^+$, 65 (45) $[C_5H_5]^+$, 41 (5) $[C_3H_5]^+$. HRMS (ESI): calcd. for $C_{11}H_{10}FNO_3SNa$ $[M + Na]^+$ 278.0263; found 278.0258. $C_{11}H_{10}FNO_3S$ (255.27): calcd. C 51.76, H 3.95, N 5.49; found C 51.86, H 3.93, N 5.37.

(*S*)-6-Fluoro-2,3,8,8a-tetrahydroindolizin-5(1*H*)-one (17): According to General Procedure 4, (*S*)-**16** (117 mg, 0.64 mmol) was dissolved in dry toluene (1.2 mL) and treated with Grubbs II catalyst (**A**; 11.0 mg) to give (*S*)-**17** (71 mg, 71%) as white crystals. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.65 (m, 1 H), 1.86 (m, 1 H), 2.07 (m, 1 H), 2.25 (m, 1 H), 2.31 (m, 1 H), 2.46 (m, 1 H), 3.49 (m, 1 H), 3.66 (m, 1 H), 3.82 (m, 1 H), 5.94 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6, 27.6 (dt, $^3J_{C,F}$ = 5.9 Hz), 33.0, 44.3, 56.9, 111.4 (dd, $^2J_{C,F}$ = 14.8 Hz), 151.5 (d, $^1J_{C,F}$ = 255.7 Hz), 157.9 (d, $^2J_{C,F}$ = 28.6 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –130.5 (t, $^3J_{F,H}$ = 9.2 Hz) ppm. MS (ESI): *m*/*z* (%) = 178 $[M + Na]^+$.

1-Benzyl-3-fluoroquinolin-2(1*H*)-one (28): The synthesis was carried out according to General Procedure 4 (16 h at 80 °C), starting from **27** (482 mg, 1.71 mmol). Chromatographic purification gave compound **28** (342 mg, 79%) as a brownish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.58 (s, 2 H), 7.18–7.45 (m, 9 H), 7.51 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.3, 115.1, 118.5 (d, $^2J_{C,F}$ = 17.4 Hz), 123.1, 126.6, 127.4, 128.4, 128.5, 128.8, 129.5, 135.6, 136.4, 150.4 (d, $^1J_{C,F}$ = 252.0 Hz), 156.6 (d, $^2J_{C,F}$ = 25.6 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –128.20 (d, $^3J_{F,H}$ = 10.6 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 253/254 (28/3) $[M]^+$, 252 (9) $[M - H]^+$, 176 (3) $[M - C_6H_5 + H]^+$, 162 (1) $[M - C_7H_6]^+$, 146 (19) $[M - C_7H_8N]^+$, 91 (100) $[C_7H_7]^+$, 77 (2) $[C_6H_5]^+$, 65 (13).

3-Fluorocoumarin (31a): According to General Procedure 4, 2-prop-1-enylphenyl α-fluoroacrylate (**30b**; 206 mg, 1.0 mmol) was treated with Grubbs II catalyst (**A**; 17 mg, 0.02 mmol, 2 mol-%). Purification by chromatography with diethyl ether, followed by recrystallization from toluene gave compound **31a** (130 mg, 79%), m.p. 147 °C (toluene). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.65 (m, 5 H, 2-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 116.7, 118.0 (d, $^3J_{C,F}$ = 3.7 Hz), 121.1 (dd, $^2J_{C,F}$ = 16.4 Hz), 125.2, 127.7 (dd, $^4J_{C,F}$ = 6.2 Hz), 130.7, 146.5 (d, $^1J_{C,F}$ = 259.1 Hz), 147.66, 154.2 (d, $^2J_{C,F}$ = 32.9 Hz) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –129.9 (d, $^3J_{F,H}$ = 8.2 Hz) ppm. MS (GC–MS, 70 eV): *m*/*z* (%) = 164 (82) $[M]^+$, 136 (55) $[M - CO]^+$, 108 (100), 107 (75), 81 (25), 63 (35).

Supporting Information (see footnote on the first page of this article): Experimental details, spectroscopic data and copies of the NMR and MS data of important new intermediates and final products.

Acknowledgments

This project was supported by the Deutsche Forschungsgemeinschaft (DFG) (SFB 424, project A11).

[1] a) R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413–4450; b) A. J. Phillips, A. D. Abell, *Aldrichim. Acta* **1999**, *32*, 75–88; c) A. Fürstner, *Angew. Chem. Int. Ed.* **2000**, *39*, 3012–3043; *Angew. Chem.* **2000**, *112*, 3140–3172; d) T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18–29; e) R. R. Schrock, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2003**, *42*, 4592–4633; *Angew. Chem.* **2003**, *115*, 4740–4782; f) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127–2188; g) A. Deiters, S. F. Martin, *Chem. Rev.* **2004**, *104*, 2189–2238; h) R. H. Grubbs, *Tetrahedron* **2004**, *60*, 7117–7140; i) C. Samojłowicz, K. Grela, *Chem. Rev.* **2009**, *109*, 3708–3742; j) G. C. Vougioukalakis, R. H. Grubbs, *Chem. Rev.* **2010**, *110*, 1746–1787.

[2] a) A. K. Chatterjee, J. P. Morgan, M. Scholl, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 3783–3784; b) M. H. D. Postema, D. Calimente, L. Liu, T. L. Behrmann, *J. Org. Chem.* **2000**, *65*, 6061–6068; c) J. S. Clark, J. G. Kettle, *Tetrahedron Lett.* **1997**, *38*, 127–130; d) C. F. Sturino, J. C. Y. Wong, *Tetrahedron Lett.* **1998**, *39*, 9623–9626; e) J. D. Rainier, J. M. Cox, S. P. Allwein, *Tetrahedron Lett.* **2001**, *42*, 179–181; f) K. F. W. Hekking, F. L. van Delft, F. P. J. T. Rutjes, *Tetrahedron* **2003**, *59*, 6751–6758; g) K. F. W. Hekking, M. H. A. Moelands, F. L. van Delft, F. P. J. T. Rutjes, *J. Org. Chem.* **2006**, *71*, 6444–6450; h) M. Arisawa, Y. Terada, M. Nakagawa, A. Nishida, *Angew. Chem. Int. Ed.* **2002**, *41*, 4732–4734; *Angew. Chem.* **2002**, *114*, 4926–4928; i) S. S. Kindeman, J. H. van Maarseveen, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *Org. Lett.* **2001**, *3*, 2045–2048; j) Q. Yao, A. Rodriguez Motta, *Tetrahedron Lett.* **2004**, *45*, 2447–2451; k) P. R. Hanson, D. S. Stojanova, *Tetrahedron Lett.* **1999**, *40*, 3297–3300; l) M. S. M. Timmer, H. Ovaa, D. V. Philippov, G. A. van der Marel, J. H. van Boom, *Tetrahedron Lett.* **2000**, *41*, 8635–8638; m) D. S. Stojanova, P. R. Hanson, *Org. Lett.* **2000**, *2*, 1769–1772; n) S. E. Denmark, S.-M. Yang, *Org. Lett.* **2001**, *3*, 1749–1752; o) A. J. Ashe III, X. Fang, *Org. Lett.* **2000**, *2*, 2089–2091.

[3] a) Y. Chauvin, *Angew. Chem. Int. Ed.* **2006**, *45*, 3740–3747; *Angew. Chem.* **2006**, *118*, 3824–3831; b) R. R. Schrock, *Angew. Chem. Int. Ed.* **2006**, *45*, 3748–3759; *Angew. Chem.* **2006**, *118*, 3832–3844; c) R. H. Grubbs, *Angew. Chem. Int. Ed.* **2006**, *45*, 3760–3765; *Angew. Chem.* **2006**, *118*, 3845–3850.

[4] a) S. Fustero, A. Navarro, B. Pina, J. G. Soler, A. Bartolomé, A. Asensio, A. Simón, P. Bravo, G. Fronza, A. Volonterio, M. Zanda, *Org. Lett.* **2001**, *3*, 2621–2624; b) S. Fustero, A. Bartolomé, J. F. Sanz-Carvera, M. Sánchez-Roselló, J. G. Soler, C. R. de Arellano, A. S. Fuentes, *Org. Lett.* **2003**, *5*, 2523–2526; c) S. Fustero, M. Sánchez-Roselló, D. Jiménez, J. F. Sanz-Carvera, C. del Pozo, J. L. Aceña, *J. Org. Chem.* **2006**, *71*, 2706–2714; d) V. De Matteis, F. L. van Delft, H. Jacobi, S. Lindell, J. Tiebes, F. P. J. T. Rutjes, *J. Org. Chem.* **2006**, *71*, 7527–7532; e) S. Gille, A. Ferry, T. Billard, B. R. Langlois, *J. Org. Chem.* **2003**, *68*, 8932–8935; f) S. Fustero, M. Sánchez-Roselló, V. Rodrigo, C. del Pozo, J. F. Sanz-Carvera, A. Simon, *Org. Lett.* **2006**, *8*, 4129–4132.

[5] M. Marhold, A. Buer, H. Hiemstra, J. H. van Maarseveen, G. Haufe, *Tetrahedron Lett.* **2004**, *45*, 57–60.

[6] S. S. Salim, R. K. Bellingham, V. Satcharoen, R. C. D. Brown, *Org. Lett.* **2003**, *5*, 3403–3406.

[7] a) V. De Matteis, F. L. van Delft, R. de Gelder, J. Tiebes, F. P. J. T. Rutjes, *Tetrahedron Lett.* **2004**, *45*, 959–963; b) V. De Matteis, F. L. van Delft, J. Tiebes, F. P. J. T. Rutjes, *Eur. J. Org. Chem.* **2006**, 1166–1176; c) V. De Matteis, O. Dufay, D. C. J. Waalboer, F. L. van Delft, J. Tiebes, F. P. J. T. Rutjes, *Eur. J. Org. Chem.* **2007**, 2667–2675; d) V. De Matteis, F. L. van Delft, J. Tiebes, F. P. J. T. Rutjes, *Synlett* **2008**, 351–354; e) V. De Matteis, Ph. D. Thesis, Nijmegen, **2008**.

[8] B. F. Straub, *Angew. Chem. Int. Ed.* **2005**, *44*, 5974–5977; *Angew. Chem.* **2005**, *117*, 6129–6132.

[9] M. E. Maier, *Angew. Chem. Int. Ed.* **2000**, *39*, 2073–2077; *Angew. Chem.* **2000**, *112*, 2153–2157.

[10] S. N. Osipov, P. Dixneuf, *Russ. J. Org. Chem.* **2003**, *39*, 1211–1220.

[11] A. H. Hoveyda, D. G. Gillingham, J. J. Van Veldhuizen, O. Kataoke, S. B. Garber, J. S. Kingsbury, J. P. A. Harrity, *Org. Biomol. Chem.* **2004**, *2*, 8–23.

[12] Several examples of double-bond isomerizations in RCM reactions have been observed earlier. See this review: B. Schmidt, *Eur. J. Org. Chem.* **2004**, 1865–1880.

[13] Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre: CCDC-984782 (for **2i**), -984783 (for **2p**), -984784 (for **6c**), -984785 (for **8a**), -984786 (for **9b**), -984787 (for **17**) and -984787 (for **28**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, Fax: +44-1223-336033 or deposit@ccdc.cam.ac.uk.

[14] a) L. G. Miller, *Arch. Int. Med.* **1998**, *158*, 2200–2211; b) J. R. Liddell, *Nat. Prod. Rep.* **2002**, *19*, 773–781; c) S. G. Pyne, N. Y. Tang, *Curr. Org. Chem.* **2005**, *9*, 1393–1418; d) J. A. Vanecko,

F. G. West, *Heterocycles* **2007**, *74*, 125–143; e) M. S. Majik, S. G. Tilve, *Synthesis* **2012**, *44*, 125–143.
[15] a) I. W. Southon, G. A. Cordell, J. Buckingham, *Dictionary of Alkaloids*, Chapman & Hall, London **1989**, p. 890; b) J. P. Michael, *Nat. Prod. Rep.* **2008**, *25*, 139–165, and cited earlier reviews in this series.
[16] a) S. F. Martin, H.-J. Chen, A. K. Courtney, Y. Liao, M. Pätzel, M. N. Ramser, A. S. Wagman, *Tetrahedron* **1996**, *52*, 7251–7264; b) L. Manzoni, M. Colombo, C. Scolastico, *Tetrahedron Lett.* **2004**, *45*, 2623–2625; c) E. S. Sattely, G. A. Cortez, D. C. Moebius, R. R. Schrock, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 8526–8533.
[17] J. B. Brenneman, S. F. Martin, *Curr. Org. Chem.* **2005**, *9*, 1535–1549.
[18] M. Arisawa, E. Takezawa, A. Nishida, M. Mori, M. Nakagawa, *Synlett* **1997**, 1179–1180.
[19] S. H. Park, H. J. Kang, S. Ko, S. Park, S. Chang, *Tetrahedron: Asymmetry* **2001**, *12*, 2621–2624.
[20] C. A. Tarling, A. B. Holmes, R. E. Markwell, N. Pearson, *J. Chem. Soc. Perkin Trans. 1* **1999**, 1695–1701.
[21] a) J. C. Hubert, J. B. P. A. Wijnberg, W. N. Speckamp, *Tetrahedron* **1975**, *31*, 1437–1441; b) J. B. P. A. Wijnberg, H. E. Schoemaker, W. N. Speckamp, *Tetrahedron* **1978**, *34*, 179–187.
[22] A. Fürstner, K. Langemann, *J. Am. Chem. Soc.* **1997**, *119*, 9130–9136.
[23] G. Shi, S. Takagishi, M. Schlosser, *Tetrahedron* **1994**, *50*, 1129–1134.
[24] K. A. Schellenberg, *J. Org. Chem.* **1963**, *28*, 3259–3261.
[25] S. R. Wisniewski, C. L. Guenther, O. A. Argintaru, G. A. Molander, *J. Org. Chem.* **2014**, *79*, 365–378.
[26] T.-W. Tsai, E.-C. Wang, K.-S. Huang, S.-R. Li, Y.-F. Wang, Y.-L. Lin, Y.-H. Chen, *Heterocycles* **2004**, *63*, 1771–1781.
[27] M. Marhold, *Ph. D. Thesis*, University of Münster, Germany, **2004**.
[28] a) K.-W. Laue, G. Haufe, *Synthesis* **1998**, 1453–1456; b) D. M. Shendage, R. Fröhlich, K. Bergander, G. Haufe, *Eur. J. Org. Chem.* **2005**, 719–727.

Received: May 4, 2014
Published Online: August 5, 2014

