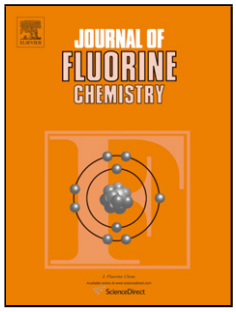


Title: 5-*Exo-dig* Aminocylization/Hydroxyfluorination of Propargylic Carbamates

Authors: Antonio Arcadi, Marco Chiarini, Luana Del Vecchio, Fabio Marinelli

PII: S0022-1139(18)30092-7
DOI: https://doi.org/10.1016/j.jfluchem.2018.04.002
Reference: FLUOR 9148

To appear in: *FLUOR*

Received date: 28-2-2018
Accepted date: 3-4-2018

Please cite this article as: Arcadi A, Chiarini M, Del Vecchio L, Marinelli F, 5-*Exo-dig* Aminocylization/Hydroxyfluorination of Propargylic Carbamates, *Journal of Fluorine Chemistry* (2010), https://doi.org/10.1016/j.jfluchem.2018.04.002

5-*Exo-dig* Aminocylization/Hydroxyfluorination of Propargylic Carbamates

Antonio Arcadi [a,*], *Marco Chiarini* [b], *Luana Del Vecchio* [a], *and Fabio Marinelli* [a,*]

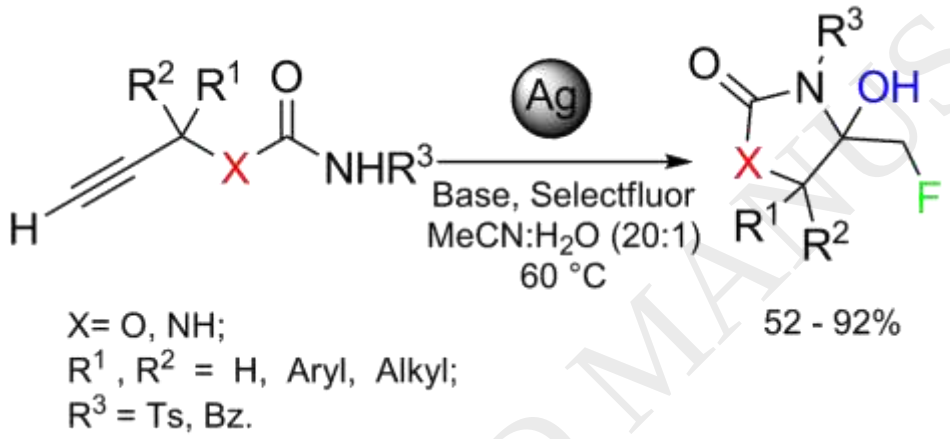
[a] *Dipartimento di Scienze Fisiche e Chimiche Università degli Studi di L'Aquila; Via Vetoio, 67100 Coppito (AQ), Italy*

[b] *Facoltà di Bioscienze e Tecnologie Agro-Alimentari e Ambientali, Università degli Studi di Teramo; Via R. Balzarini 1, 64100 Teramo (TE), Italy*

Antonio Arcadi e-mail: antonio.arcadi@univaq.it

Fabio Marinelli e-mail: fabio.marinelli@univaq.it

GRAPHICAL ABSTRACT



Highlights:

- Annulation/hydroxyfluorination of propargylic carbamates was investigated.
- An efficient approach to the synthesis of 4-fluoromethyl-4-hydroxy-oxazolidinones is reported.
- Diastereomeric enriched fluorohydroxy-oxazolidinones were isolated.
- Steroidal propargylic carbamates led to the formation of α-fluoroketone derivatives by a ring opening reaction of flurohydroxyoxazolidinones.

Keywords

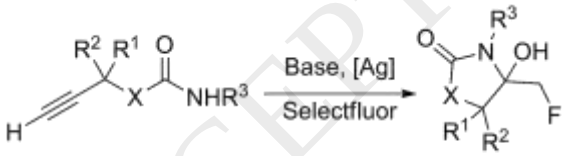
Propargylic carbamates; Sequential reactions; Annulation; Hydroxyfluorination; 4-Fluoromethyl-4-hydroxy-oxazolidinones.

Abstract

The unprecedented annulation/hydroxyfluorination of propargylic carbamates to give 4-fluoromethyl-4-hydroxy-oxazolidinones was investigated. The reaction was effectively promoted by $NaHCO_3$ and/or silver catalysis. The peculiar behavior of propargylic carbamates bearing a chiral steroidal moiety is described. Extensions and limitations of the procedure with respect to urea derivatives, homopropargyl compounds, internal alkynes and one-pot transformations of propargylic alcohols with isocyanates are reported.

1. Introduction

The key role of fluorinated substances in a wide range of applications [1,2] in academia and industry is spurring on the development of efficient introduction methods of fluorine into organic compounds [3-28]. Usually, fluorinated substituents can accomplish significant modulation of molecular properties of pharmaceuticals and bioactive substances such as solubility, bioavailability, metabolic stability and binding affinity to target proteins [29]. Many synthetic strategies have been developed for the fluorination [3-28], among them the combination of cyclization and fluorination reaction in a single operation provides a powerful tool to assemble fluorinated heterocycles from unsaturated compounds bearing a close heteroatom nucleophile. Various metal-catalyzed intramolecular aminofluorination [30-34] and oxyfluorination reactions [35-44] of alkenes [45-47] or their metal-free alternative [48,49] have been developed. The cycloisomerization/fluorination sequence of alkynes is emerging as an attractive, and step- economic, tool to access fluorinated heterocyclic derivatives [50-58]. As part of our ongoing interest in the development of efficient methodologies for the selective preparation of fluorinated compounds [59,60], we envisaged to investigate the sequential annulation/hydroxyfluorination reaction of propargylic carbamates/ureas (Scheme 1).



X= O, NH; R^1, R^2 = H, Aryl, Alkyl; R^3 = Ts, Bz.

Scheme 1. Annulation/hydroxyfluorination of propargylic carbamates/ureas

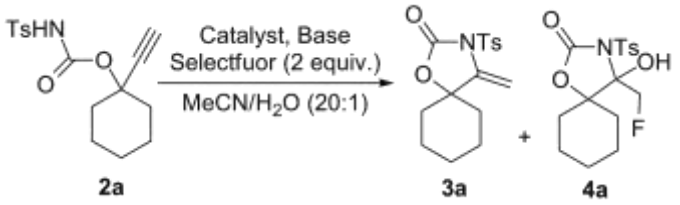
Cycloisomerization reactions of these derivatives represent a viable alternative to the synthesis of products of great interest in both the pharmaceutical [61,62] and agricultural [63] industries because of their significant biological activities as inhibitors, sigma receptors, and antibiotics [64-69]. In fact, the introduction of the fluoromethyl group (CH_2F) is of pivotal importance in many biologically active compounds and has become a powerful tool with regard to isostere-based drug design [70-71]. However, methods for the synthesis of

monofluoromethyl substituted molecules are quite limited [72,73], and to the best of our knowledge sequential cycloisomerization/hydroxyfluorination reaction of propargylic carbamates/ureas is unprecedented. On the basis of these evidences, we have investigated the synthesis of fluorometyl-hydroxy-oxazolidinone/imidazolinone derivatives.

2. Results and discussion

Firstly, we explored the effectiveness of the $NaHCO_3$-promoted and silver-catalyzed sequential cyclization/hydroxyfluorination of the readily available propargylic tosylcarbamates **2** [74]. Silver catalysts have been reported to effectively activate the carbon-carbon triple bond [75] by acting as a π-Lewis acid and to be crucial for the fluorination process [76-80]. Moreover, very recently a silver-catalyzed hydroxyfluorination of styrenes with Selectfluor and H_2O afforded vicinal fluorohydrins with exclusive anti-Markovnikov-type regioselectivity [76]. The reaction of the spiro 1-ethynylcyclohexyltosilcarbamate **2a** with an excess of Selectfluor (2 equiv.) in the presence of a stoichiometric amount of $NaHCO_3$ in a mixture of CH_2CN/H_2O (20:1) at 60 °C achieved the isolation of the desired **4a** in 57% yield (Table 1, entry 1), unsurprisingly along with 14% of the cycloisomerization product 4-methylene-3-tosyl-1-oxa-3-azaspiro[4,5]decan-2-one **3a** as a side-product. In fact, studies on the base promoted cyclization of *O*-propargylic carbamates **2** to give enamine type derivatives **3** were previously reported [81-83] as well as the hydroxyfluorination of the 2-methylene-1-tosylpyrrolidine derivatives under metal free conditions [57]. The fluoro hemiaminal type compound **4a** was isolated in higher yield in the presence of a catalytic amount of $AgNO_3$ (0.1 equiv.) both performing the reaction at 60 °C or at room temperature for a more prolonged time (Table 1, entries 2, 3). By contrast with previously reported results AuCl resulted a less efficient catalyst (Table 1, entries 4, 5) [84,85]. However, the reaction took also place to give **4a** in high yield in the absence of $NaHCO_3$ (Table 1, entry 6). Conversely, the fluorination reaction failed to occur, without the base, when the catalyst was $NaAuCl_4 \cdot 2H_2O$ (5 mol%) and the reaction was carried out at room temperature (Table 1, entry 7). In this latter case only a partial conversion of **2a** (recovered in 36 % yield) to **3a** was observed. The starting tosylcarbamate **2a** was recovered under base and metal free conditions allowing to rule out the possibility of formation of product **4a** by a direct electrophilic fluorination of the starting carbamate **2a** [86-89].

Table 1. Optimization of the sequential annulation/hydroxyfluorination of the 1-ethylcyclohexyl tosylcarbamate **2a**



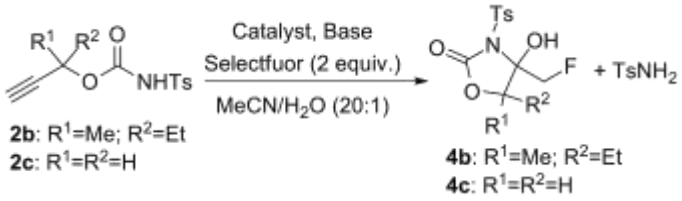
2a **3a** **4a**

Entry	Base	Catalyst	Temperature (°C) time(h)	**4a** % yield [a]
1	$NaHCO_3$	/	60/6	57 (14) [b]
2	$NaHCO_3$	$AgNO_3$	60/2	87
3	$NaHCO_3$	$AgNO_3$	rt/24	94 (4) [b]
4	$NaHCO_3$	AuCl	60/2	60
5	$NaHCO_3$	AuCl	rt/24	60
6	/	$AgNO_3$	60/6	82 (4) [b]
7	/	$NaAuCl_4 \cdot 2H_2O$	rt/24	- (38) [b]
8	/	/	60/6	/

[a] Isolated yields; [b] Figures in bracket refer to the isolated yield of **3a**.

The requirement to combine $NaHCO_3$ with the silver catalyst was essential in dependence on the features of the starting tosylcarbamate **2**. Indeed, by investigating the effect of substituents at the propargylic position of the carbamates **2** (Table 2), we found that the hydrolysis of **2b** and **2c** to give tosylamide was predominant over the sequential cyclyzation/hydroxyfluorination in the absence of the silver catalyst (**4b** was recovered only in low yield and **4c** found only in traces, Table 2, entry 1, 2), whereas **4b-c** were isolated in good yields when **2b-c** where reacted with Selectfluor in the presence of both $NaHCO_3$ and $AgNO_3$ at 60 °C for 2h or at room temperature for 24h (Table 2, entries 3-5). The prevalence of the hydrolysis of **2c** was also observed by omitting $NaHCO_3$ (Table 2, entry 6).

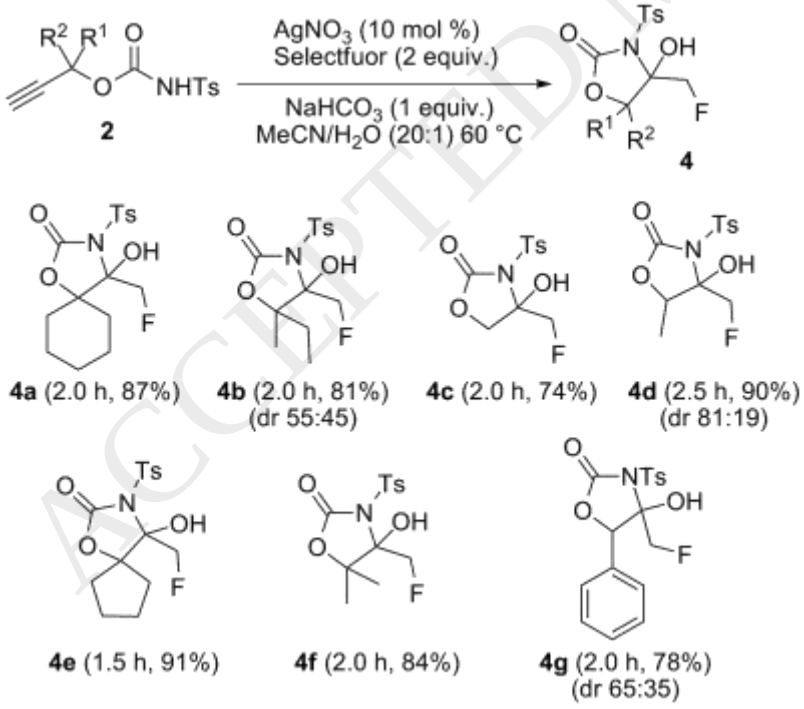
Table 2. Optimization of the sequential annulation/hydroxyfluorination**.**



Entry	tosylcabamate	Base [a]	Catalyst [b]	Temperature (°C) time(h)	**4** % yield [c]
1	**2b**	$NaHCO_3$	/	60/7	29 (40) [d]
2	**2c**	$NaHCO_3$	/	60/24	- (56) [d,e]
3	**2b**	$NaHCO_3$	$AgNO_3$	60/2	81
4	**2c**	$NaHCO_3$	$AgNO_3$	60/2	74
5	**2c**	$NaHCO_3$	$AgNO_3$	rt/24	83
6	**2c**	/	$AgNO_3$	60/21	33 (56) [d]

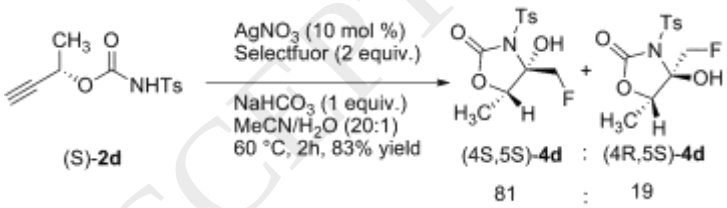
[a] 1.0 equivalent, if present; [b] 0.1 equivalent, if present; [c] Isolated yields; [d] Figures in bracket refer to the isolated yield of $TsNH_2$; [e] **2c** was recovered in 23% yield.

Secondly, the scope of the silver-catalyzed reaction of a variety of tosyl propargylic carbamates was explored (Scheme 2).



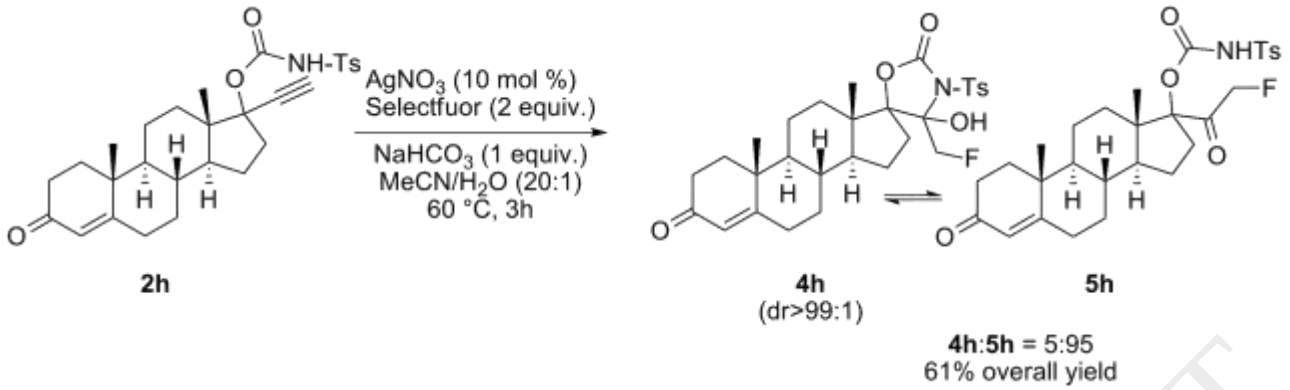
Scheme 2. Substrate scope of the sequential silver-catalyzed annulation/hydroxyfluorination of propargylic tosyl carbamates **2**.

Notably, the Ag-catalyzed cyclization of carbamates **2** showed very high regio- and chemoselectivity leading only to five-membered cyclic products derived from N-cyclization. In fact, in no case the silver-catalyzed intramolecular *O- 5-exo-dig* annulation was observed [90]. The exclusive formation of the Markovnikov-type hydroxyfluorination products **4** rules out their formation by means of silver-catalyzed radical hydroxyfluorination process [76]. The *N*-tosyl 4-fluoromethyl-4-hydroxy-oxazolidinones **4** were isolated usually in god to high yields. The tosylcarbamates bearing a monosubstituent (R^1 = substituent, R^2 = H) or different substituent ($R^1 \neq R^2$) at the propargylic position, gave the corresponding fluoro derivatives as diasteromeric mixtures. The diastereomeric composition, for all fluorinated compounds, was determined by integration of ^{19}F NMR signals. Moreover, to shed a light on the relative configuration of the diastereomers, we prepared the (*S*)-but-3-yn-2-yl tosylcarbamate (*S*)-**2d** from the commercial available (*S*)-(-)-3-butyn-2-ol (Scheme 3). In consideration that the subsequent reaction leading to the corresponding oxazolidinone should leave the stereocenter at carbon 5 unchanged, we take advantage of the *NOESY* experiment to easily differentiate between the two diastereoisomers. In fact (4*S*,5*S*)-**4d** should show a strong *NOE* cross peak between the proton bound at carbon 5 and the methylene CH_2F, whereas the (4*R*,5*S*)-**4d** should show the opposite pattern with a strong *NOE* interaction between the methyl at carbon 5 and the methylene CH_2F. Data from *NOESY* showed that the major isomer was (4*S*,5*S*)-**4d** and the minor one was (4*R*,5*S*)-**4d** (see Supporting Information).



Scheme 3. Sterochemical outcome of the sequential silver-catalyzed catalyzed annulation/hydroxyfluorination of (*S*)-but-3-yn-2-yl tosylcarbamate **2d**.

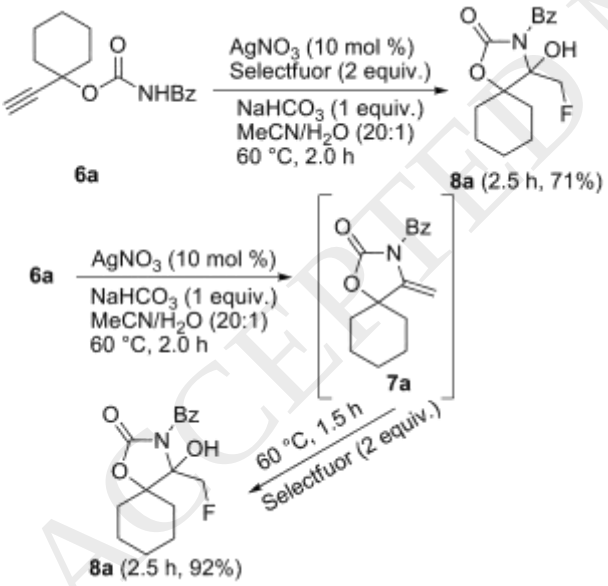
Surprisingly, although the steroidal sterically bulky chiral counterpart in **2h** was a good reaction component, delivering the product as a single diastereoisomer (> 99:1 dr), equilibrium of the hemiaminal type derivative **4h** with the α-fluoroketone **5h** was observed (**4h**:**5h** = 5:95; 61% overall yield) (Scheme 4).



Scheme 4. 4-Fluorometyl-4-hydroxy-oxazolidinone **4h** *vs.* α-fluoroketone **5h**.

The formation of the α-fluoroketone is clearly shown by the appearance of a characteristic ketone doublet at ca. 200 ppm with ^{2}J coupling F-C of ca. 15 Hz (for **5h** 203.4 ppm and $^{2}J_{F\text{-}C}$ = 14.8 Hz). Moreover, nearly all ^{13}C NMR signals are different for **4h** and **5h**.

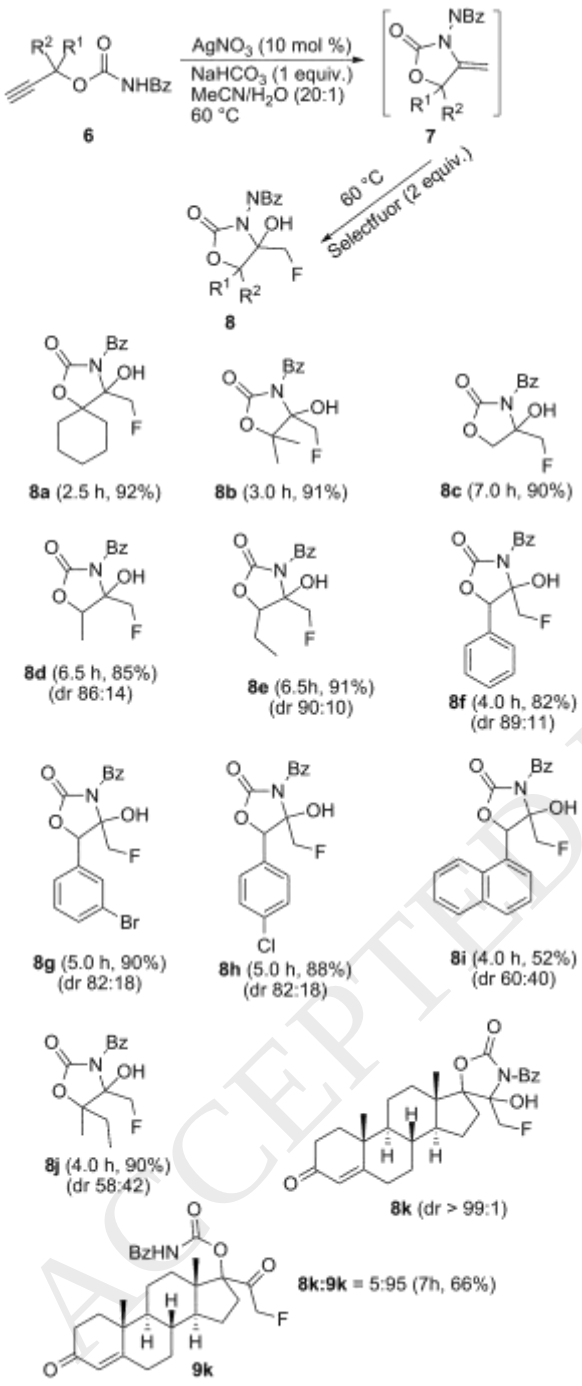
When the procedure was extended to the benzoylcarbamates **6a,** the formation of the 4-fluoromethyl-4-hydroxy-oxazolidinone **8a** was accomplished in satisfactory yield. A better result was observed by combining the silver catalyzed annulation with the hydroxyfluorination step in the same reaction flask (Scheme 5).



Scheme 5. Domino *vs.* combined silver-catalyzed annulation/hydroxyfluorination of the benzoyl carbamate **6a**.

Usually the combined procedure allowed the isolation of the 3-benzoyl-4-(fluoromethyl)-4-hydroxy-oxazolidin-2-ones **8** in higher yield than the domino process. The reaction conditions resulted

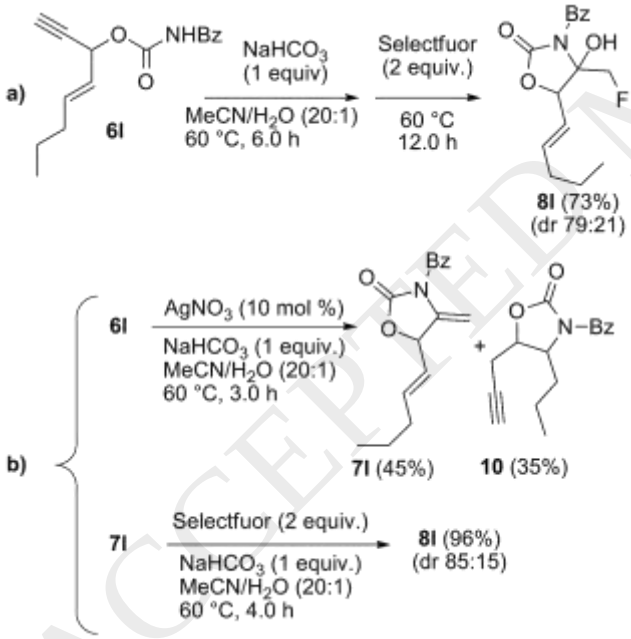
compatible with a number of functional groups including alkyl, aryl, conjugated ketone, chloro and bromo substituents (Scheme 6).



Scheme 6. Combined silver-catalyzed annulation/hydroxyfluorination of the benzoyl carbamates **6**.

The reaction of annulation/hydroxyfluorination was substantially insensitive to change of substrate, in fact yields and diastereomeric ratio were comparable. Monosubstituted propargylic

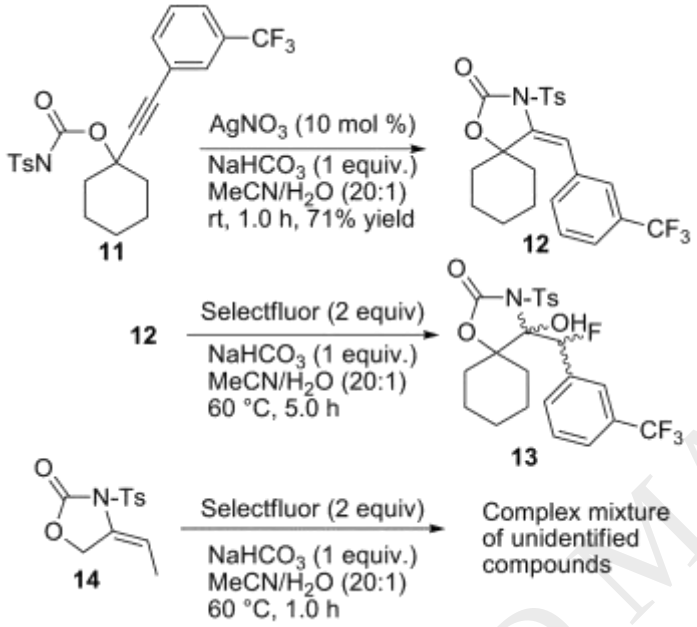
benzoylcarbamates **6d-j** delivered the corresponding diastereo enriched products **8d-j** in 82-91 % yields with up to 90:10 dr ratio. Even if the steroidal derivative **8k** was isolated as single diastereomer, the α-fluoroketone **9k** resulted the major component of the products mixture (**8k**/**9k** = 5:95; 66% overall yield). As well as for the tosyl derivative **4h**, the formation of α-fluoroketone **9k** involving an easy ring opening of the hemiaminal type steroidal scaffold was revealed by the appearance of the characteristic ketone doublet at 203.6 ppm with $^{2}J_{F\text{-}C}$ = 15.1 Hz. Interestingly, the hydroxyfluorination of terminal C-C double bond tolerates the presence of an internal one. Then, the (*E*)-3-benzoyl-λ^2-azanyl)-4-methylene-5-(pent-1-en-1-yl)oxazolidin-2-one **7l** led only to the formation of (*E*)-3-benzoyl-λ^2-azanyl)-4-(fluoromethy)-4-hydroxy-5-(pent-1-en-yl)oxazolidin-2-one **8l** in almost quantitative yield (Scheme 7). In this latter case, it was remarkable the advantage of the combined silver-free one-flask procedure that allowed the chemoselective formation of **8l** from **6l** in prolonged reaction (Scheme 7, a). The competitive *5-exo-trig* annulation of **6l** giving the trans-3-benzoyl-4-propyl-5-prop-2-yn-1-yl-1,3-oxazolidin-2-one **10** was promoted by silver catalysis (Scheme 7, b) and can be avoided in the absence of catalyst (Scheme 7, a).



Scheme 7. Silver catalyzed domino annulation/hydroxyfluorination and combined base promoted annulation/hydroxyfluorination of the benzoyl carbamate **6l.**

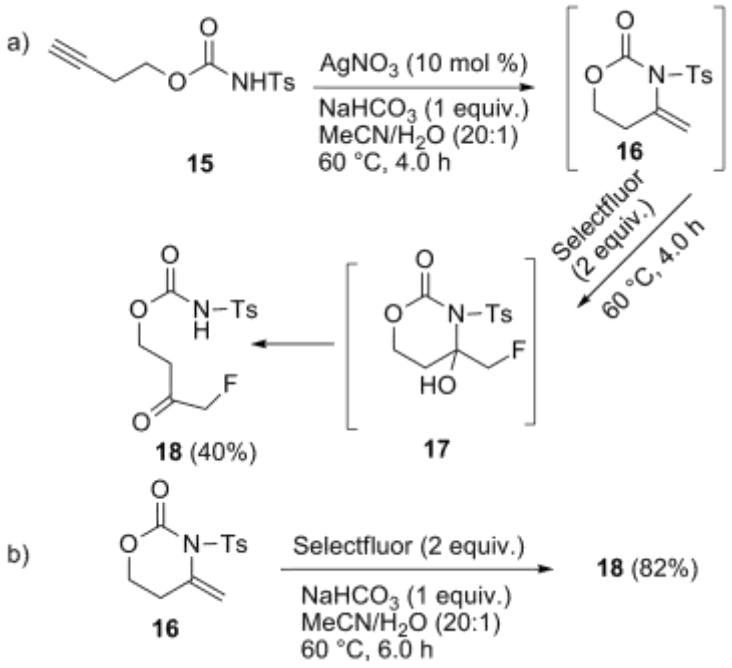
Although the microwave assisted formation of α-fluorohydrins from internal alkenes with Selectfluor has been reported [91], the use of carbamates with a tethered internal alkyne which can easily cycloisomerize to 4-arylidene/alkylideneoxazolidin-2-ones resulted unsuitable substrates for the

present process because of the lack of regio- and stereoselectivity of hydoxyfluorination step. Indeed, while we isolated in good yield the (*E*)-3-tosyl-4-(3-trifluoromethyl)benzylidene)-1-oxa-3-azaspiro[*4.5*]decan-2-one **12**, in the following fluorination step only partial conversion (35 %) of **12** into all the hydroxyfluoro stereoisomers **13** occurred (Scheme 8). Even worse a complex mixture of fluoroderivatives was observed when the (*E*)-4-ethylidene-3-tosyloxazolidin-2-one **14** underwent fluorination with Selectfluor under our reaction conditions (Scheme 8).



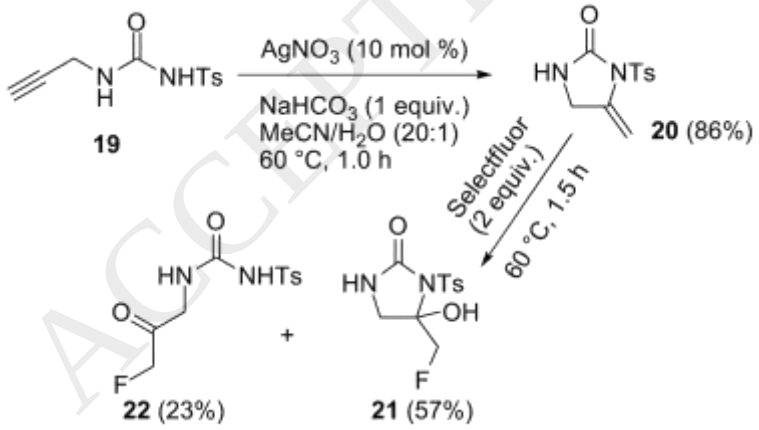
Scheme 8. Unselective hydroxyfluorination reactions.

Moreover, we tried the synthesis of a six-membered cyclic 4-(fluoromethyl)-4-hydroxy-3-tosyl-1,3-oxazin-2-one **17** (Scheme 9). The *6-endo-dig* cyclization of the but-3-yn-1-yl tosylcarbamate **15** to the intermediate tosylenamide **16** resulted more difficult compared to *5-exo-dig* process. However, we failed to isolate compound **17** because of its fast interconversion into the α-fluoroketone **18**. As seen for the synthesis of **8l**, also **18** was obtained in higher yield, under silver free conditions, from the cyclic enamide derivative **16** (Scheme 9, b).



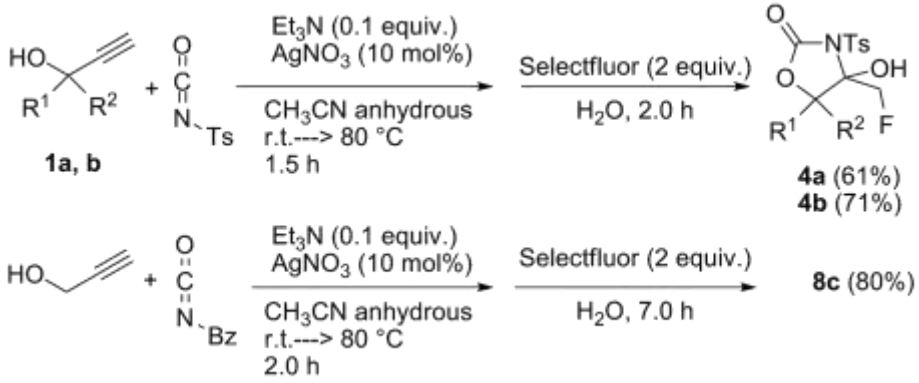
Scheme 9. Hydroxyfluorination reaction of the but-3-yn-1-yl tosylcarbamate **15** and the 4-methylene-3-tosyl-1,3-oxazinan-2-one **16**.

Analogously the application of the procedure to the tosylurea derivative **19** showed that its cyclization afford the imidazolidinone **20** as major product which in turn underwent hydroxyfluorination to give the corresponding 5-(fluoromethyl)-5-hydroxy-1-tosylimidazolin-2-one **21** together with the *N*-((3-fluoro-2-oxopropyl)carbamoyl)-4-methylbenzenesulfonamide **22** in 80 % overall yield (Scheme 10).



Scheme 10. Hydroxyfluorination of 5-methylene-1-tosylimidazolidin-2-one **20**.

Finally, the target 4-fluoromethyl-4-hydroxy-oxazolidinones **4** and **8** could be directly obtained from propargylic alcohols in a one-flask process (Scheme 11).



Scheme 11. One flask synthesis of 4-fluoromethyl-4-hydroxy-oxazolidinones **4** and **8** from propargylic alcohols.

3. Conclusions

In conclusion, the aminocylization/hydroxyfluorination of propargylic carbamates can allow an efficient approach to the synthesis of the corresponding 4-fluoromethyl-4-hydroxy-oxazolidinones under mild conditions with tolerance for a variety of functional groups. These Markovnikov-type derivatives can be also obtained directly by reacting propargylic alcohols with isocyanates in the same flask. The effectiveness of the base promoted and silver-catalyzed sequential aminocyclization/hydroxyfluorination of the readily available propargylic tosyl- and benzoylcarbamates was thoroughly investigated. Propargylic tosyl- and benzoylcarbamates bearing different substituents at the propargylic position gave the corresponding diastereomeric enriched fluorohydroxy-oxazolidinones. Chiral steroidal propargylic carbamates led to the formation of the corresponding flurohydroxyoxazolidinone derivative as a single diastereomer which was prone to interconvert into the α-fluoroketone derivative by a ring opening reaction.

4. Experimental section

4.1. Materials and methods

All reactions were carried out with magnetic stirring and were monitored by TLC on silica gel 60Å (Fluorochem). IR spectra were recorded in KBr pellets or neat in NaCl on a Perkin-Elmer Spectrum Two FT-IR spectrometer. ^{1}H NMR spectra were recorded at 400 MHz on a Bruker Avance III spectrometer. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in $CDCl_3$ or in Dimethyl sulfoxide-d_6 (δ = 2.49 ppm) as an internal standard. ^{13}C NMR spectra were taken on the

same machine at 100.6 MHz and were calibrated with $CDCl_3$ (δ = 77.00 ppm) or Dimethyl sulfoxide-d6 (δ = 30.50 ppm). ^{19}F NMR spectra were recorded at 376 MHz and CF_3COOH (δ = -76.55) was employed as external standard for the ^{19}F NMR measurement. Mass measurement was performed using a MALDI-TOF spectrometer AB SCIEX TOF/TOF 5800 System. Unless otherwise stated, all starting materials, catalysts, and solvents were commercially available and were used as purchased. Reaction products were purified by flash chromatography on silica gel (60-200 μm) by elution with n-hexane/EtOAc mixtures. All tosylcarbamates **2a** [92], **2b** [93], **2c** [94], **2d** [81], **2f** [81], and **2g** [95] and benzoylcarbamates **6a** [96], **6c** [81], except **2e**, **6b**, **6d-l** and **11**, were previously described and prepared according to the literature. Compounds **3a** [96], **15** [97], **16** [98], **19** [99] and **20** [99] are known products and were identified by comparison of the reported physical and spectral data.

4.2. Synthesis of starting materials

*4.2.1 General procedure for preparation of Tosylcarbamates (**2**)*

To a dry 50 mL 1-necked round-bottomed flask containing the propargylic alcohol (2 mmol) dissolved in 5 mL of THF was added TsNCO (2.2 mmol) dropwise via syringe at room temperature. After complete addition, the reaction was allowed to stir at 60 °C for 2.0 hour. The solvent was then stripped off and the crude was purified by flash chromatography to give the desired tosylcarbamate **2**.

(8R,9S,10R,13S,14S,17R)-17-ethynyl-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl tosylcarbamate 2h. White solid (95% yield, 0.968 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 75/25). IR (KBr): 3271, 2116, 1753, 1659, 1352, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.93-7.91 (m, 2H, Tos), 7.34.7.32 (m, 2H, Tos), 5.74 (s, 1H, C_{sp2}-H), 2.68-2.61 (m, 1H), 2.56 (s, 1H, C_{sp}-H), 2.48-2.26 (m, 4H), 2.44 (s, 3H, CH_3, Tos), 2.11-2.00 (m, 2H), 1.84 -1.31 (m, 10H), 1.19 (s, 3H, Me), 1.09-0.90 (m, 3H), 0.84 (s, 3H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 199.6 (C=O), 170.9 (Cq), 148.9 (C=O), 144.8 (Cq), 135.8 (Cq), 129.5 (2CH), 128.0 (2CH), 123.9 (CH), 86.8 (Cq), 81.7 (C_{sp}q), 76.3 (C_{sp}-H), 53.1 (CH), 48.3 (CH), 47.6 (Cq), 38.5 (Cq), 37.1 (CH_2), 35.8 (CH), 35.6 (CH_2), 33.8 (CH_2), 32.7 (CH_2), 32.6 (CH_2), 31.3 (CH_2), 23.3 (CH_2), 21.6 (CH_2), 20.5 (Me, Tos), 17.3 (Me), 13.2 (Me) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{29}H_{36}NO_5S$: $[M+H]^+$ 510.2314, Found: 510.2310.

*4.3. Typical procedure for the sequential silver-catalyzed annulation / hydoxyfluronination of tosylcarbamates (**2**): synthesis of 4-(fluoromethyl)-4-hydroxy-3-tosyl-1-oxa-3-azaspiro[4.5]decan-2-one **4a**.*

To a solution of 1-ethynylcyclohexyl tosylcarbamate **2a** (130 mg, 0.40 mmol, 1 equiv.) in MeCN/H_2O (20:1) (2.10 mL), were added $NaHCO_3$ (35 mg, 0.40 mmol, 1 equiv.), $AgNO_3$ (7 mg, 0.1 equiv.) and Selectfluor (286 mg, 0.80 mmol, 2 equiv.). After complete addition, the reaction was allowed to stir at 60 °C for 2 hours and monitored by TLC. Upon completion, the solvent was then stripped off and the crude was purified by flash chromatography (*n*-Hexane/EtOAc: 80/20) to give 4-(fluoromethyl)-4-hydroxy-3-tosyl-1-oxa-3-azaspiro[4.5]decan-2-one **4a** (124 mg, 87% yield). White solid IR (KBr): 3469, 1781, 1750, 1365, 1172, 663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99-7.96 (m, 2H, Tos), 7.35-7.33 (m, 2H, Tos), 4.85 (dd, J_{H-F} =46.3 Hz, J_{H-H} =0.5 Hz, 2H, CH_2F), 4.30 (br, 1H, OH), 2.44 (s, 3H, CH_3, Tos), 1.97-1.15 (m, 10H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.2 (C=O), 145.9 (Cq, Tos), 134.5 (Cq, Tos), 129.7 (2CH, Tos), 129.0 (2CH, Tos), 92.3 (d, *J*= 21.5 Hz, Cq), 87.0 (d, *J*= 1.1 Hz, Cq), 81.8 (d, *J*= 180.7 Hz, CH_2F), 30.5 (d, *J*= 3.9 Hz, CH_2), 30.4 (CH_2), 24.6 (CH_2), 21.8 (CH_3, Tos), 21.7 (CH_2), 21.4 (CH_2) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -222.0 (t, *J*=46.3 Hz, 1F) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{16}H_{21}FNO_5S$: $[M+H]^+$ 358.1124, Found: 358.1122.

5-Ethyl-4-(fluromethyl)-4-hydroxy-5-methyl-3-tosyloxazolidin-2-one 4b. Yellow solid (110 mg, 81% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3407, 1768, 1371, 1284, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ =7.99-7.97 (m, 2H, Tos, major+minor), 7.36-7.34 (m, 2H, Tos, major+minor), 4.87 (dd, J_{H-F} = 46.1 Hz, J_{H-H} = 10.6 Hz, 1H, CH_2F, major), 4.86 (d, J_{H-F} = 46.4 Hz, 2H, CH_2F, minor), 4.83 (dd, J_{H-F} = 46.6 Hz, J_{H-H} = 10.6 Hz, 1H, CH_2F, major), 4.32 (br, 1H, OH, minor), 4.27 (br, 1H, OH, major), 2.44 (s, 5.5H, Ts-CH_3, Tos, major+minor), 1.95-1.68 (m, 2H, $\underline{C}H_2$, major+minor), 1.47 (d, J_{H-F} = 1.9 Hz, 3H, CH_3, major), 1.37 (s, 3H, CH_3, minor), 1.02 (t, *J* =7.4, 3H, $CH_2\underline{C}H_3$, minor), 0.95 (t, *J* =7.5, 3H, $CH_2\underline{C}H_3$, major) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.31 (C=O, major), 150.27 (C=O, minor), 145.94 (Cq, Tos, major), 145.92 (Cq, Tos, minor), 134.58 (Cq, Tos, minor), 134.55 (Cq, Tos, major), 129.68 (2CH, Tos, minor), 129.67 (2CH, Tos, major),129.01 (2CH, Tos, major), 128.97 (2CH, Tos, minor), 92.6 (d, *J*= 21.6 Hz, Cq, minor), 92.4 (d, *J*= 21.4 Hz, Cq, major), 88.4 (d, *J*= 1.0 Hz, Cq, minor), 87.8 (d, *J*= 1.1 Hz, Cq, major), 82.2 (d, *J*= 181.4 Hz, CH_2F, major), 81.9 (d, *J*= 180.4 Hz, CH_2F, minor), 28.4 ($\underline{C}H_2$, major), 27.3 (d, *J*= 3.5 Hz, $\underline{C}H_2$, minor), 21.8 (Ts-CH_3, major+minor), 19.0 (d, *J*= 4.2 Hz, CH_3, major), 18.7 (CH_3, minor), 7.9 ($CH_2\underline{C}H_3$, minor), 7.8

($CH_2\underline{C}H_3$, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.1 (td, *J*=46.3 Hz, *J*=1.9 Hz, 55%), -222,0 (t, *J*=46.3 Hz, 45%) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{14}H_{19}FNO_5S$: $[M+H]^+$ 332.0968, Found: 332.0967.

4-(Fluoromethyl)-4-hydroxy-3-tosyloxazolidin-2-one 4c. Oil (115 mg, 74% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (neat): 3345, 1774, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.98-7.95 (m, 2H, Tos), 7.38-7.35 (m, 2H, Tos), 5.05 (dd, J_{H-F} = 46.5 Hz, J_{H-H} = 10.0 Hz, 1H, CH_2F), 4.58 (dd, J_{H-F} = 46.2 Hz, J_{H-H} = 10.0 Hz, 1H, CH_2F), 4.55 (br, 1H, OH), 4.45 (dd, J_{H-H} = 9.7 Hz, J_{H-F} = 2.1 Hz, 1H, CH_2), 4.25 (dd, J_{H-H} = 9.7 Hz, J_{H-F} = 2.6 Hz, 1H, CH_2), 2.45 (s, 3H, Tos) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 151.2 (C=O), 146.2 (Cq, Tos), 134.2 (Cq, Tos), 129.7 (2CH, Tos), 128.9 (2CH, Tos), 89.2 (d, *J*= 22.3 Hz, Cq), 82.1 (d, *J*= 180.3 Hz, CH_2F), 71.7 (d, *J*= 2.3 Hz, CH_2), 21.8 (CH_3, Tos) ppm ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -223.6 (td, *J*=46.3 Hz, *J*=2.3 Hz, 1F, CH_2F) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{11}H_{13}FNO_5S$: $[M+H]^+$ 290.0498, Found: 290.0500.

4-(Fluoromethyl)-4-hydroxy-5-methyl-3-tosyloxazolidin-2-one 4d. Yellow solid (147 mg, 90% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3351, 1750, 1371, 1172, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.98-7.95 (m, 2H, Tos, major+minor), 7.37-7.34 (m, 2H, major+minor), 5.00 (dd, J_{H-F} = 46.5 Hz, J_{H-H} = 10.1 Hz, 1H, CH_2F, major), 4.91 (ddd, J_{H-F} = 46.2 Hz, J_{H-H} = 10.5 Hz, J_{H-H} = 0.6 Hz, 1H, CH_2F, minor), 4.73 (dd, J_{H-F} = 46.2 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F, minor), 4.66 (qd, J_{H-H} = 6.5 Hz, J_{H-F} = 2.0 Hz, 1H, CH, major), 4.53 (dd, J_{H-F} = 46.5 Hz, J_{H-H} = 10.1 Hz, 1H, CH_2F, major), 4.53 (qd, J_{H-H} = 6.5 Hz, J_{H-F} = 1.9 Hz, 1H, CH, minor), 4.20 (br, 1H, OH, major+minor), 2.44 (s, 3H, CH_3, Tos, major), 2,43 (s, 3H, CH_3, Tos, minor), 1.50 (dd, J_{H-H} = 6.7 Hz, J_{H-F} = 1.8 Hz, 3H, CH_3, minor), 1.41 (d, J_{H-H} = 6.5 Hz, 3H, CH_3, major) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.9 (C=O, major), 150.5 (C=O, minor), 146.1 (Cq, Tos, minor), 146.0 (Cq, Tos, major), 134.34 (Cq, Tos, major), 134.28 (Cq, Tos, minor), 129.72 (2CH, Tos, minor), 129.70 (2CH, Tos, major), 128.98 (2CH, Tos, minor), 128.96 (2CH, Tos, major), 91.0 (d, *J*= 21.7 Hz, Cq, minor), 89.8 (d, *J*= 21.0 Hz, Cq, major), 82.1 (d, *J*= 180.6 Hz, CH_2F, major), 80.9 (d, *J*= 0.8 Hz, CH, minor), 80.6 (d, *J*= 181.0 Hz, CH_2F, minor), 77.2 (d, *J*= 2.2 Hz, CH, major), 21.76 (CH_3, Tos, minor), 21.75 (CH_3, Tos, major), 14.1 (d, *J*= 4.0 Hz, CH_3, minor), 13.5 (d, *J*= 0.9 Hz, CH_3, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -222.1 (td, *J*=46.2 Hz, *J*=1.9 Hz, 19%), -223,9 (td, *J*=46.5 Hz, *J*=2.0 Hz, 81%) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{12}H_{15}FNO_5S$: $[M+H]^+$ 304.0655, Found: 304.0657.

4-(Fluoromethyl)-4-hydroxy-3-tosyl-1-oxa-3-azaspiro[4.4]nonan-2-one 4e. White solid (154 mg, 91% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3326, 1743, 1172, 1346, 1172, 676 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99-7.97 (m, 2H, Tos), 7.36-7.34 (m, 2H, Tos), 4.91 (dd, J_{H-F} =46.3 Hz, J_{H-H} =10.5 Hz, 1H, CH_2F), 4.76 (dd, J_{H-F} =46.3 Hz, J_{H-H} =10.5 Hz, 1H, CH_2F), 4.35 (br, 1H, OH), 2.45 (s, 3H, CH_3), 2.19-1.72 (m, 8H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.3 (C=O), 145.9 (Cq, Tos), 134.6 (Cq, Tos), 129.7 (2CH, Tos), 128.9 (2CH, Tos), 96.8 (d, *J*= 1.1 Hz, Cq), 91.2 (d, *J*= 21.5 Hz, Cq), 82.2 (d, *J*= 181.5 Hz, CH_2F), 33.1 (CH_2), 33.0 (d, *J*= 3.5 Hz, CH_2), 23.0 (CH_2), 21.8 (CH_3, Tos), 21.7 (CH_2) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.76 (t, *J*=46.3 Hz, 1F) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{15}H_{19}FNO_5S$: $[M+H]^+$ 344.0968, Found: 344.0972.

4-(Fluoromethyl)-4-hydroxy-5,5-dimethyl-3-tosyloxazolidin-2-one 4f. White solid (125 mg, 84% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3475, 1781 1284, 1172, 670 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00-7.96 (m, 2H, Tos), 7.37-7.33 (m, 2H, Tos), 4.87 (dd, J_{H-F} =46.3 Hz, J_{H-H} = 0.9 Hz, 2H, CH_2F), 4.26 (br, 1H, OH), 2.44 (s, 3H, CH_3, Tos), 1.53 (d, *J* = 1.7 Hz, 3H, CH_3), 1.43 (s, 3H, CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.3 (C=O), 146.0 (Cq, Tos), 134.5(Cq, Tos), 129.7 (2CH, Tos), 129.0 (2CH, Tos), 92.0 (d, *J*= 21.8 Hz, Cq), 86.0 (Cq), 82.2 (d, *J*= 180.4 Hz, CH_2F), 22.8 (CH_3), 22.3 (d, *J*= 3.8 Hz, CH_3), 21.7 (CH_3, Tos) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -222.36 (t, *J*=46.1 Hz, 1F) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{13}H_{17}FNO_5S$: $[M+H]^+$ 318.0811, Found: 318.0813.

4-(Fluoromethyl)-4-hydroxy-5-phenyl-3-tosyloxazolidin-2-one 4g. Oil (105 mg, 78% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (neat): 3438, 1371, 1787, 1172, 676 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02-7.99 (m, 2H, major +minor), 7.43-7.31 (m, 7H, major+minor), 5.56 (d, *J*= 2.0 Hz, 1H, CH-Ph, major), 5.45 (s, 1H, CH-Ph, minor), 5.18 (dd, J_{H-F} = 46.5 Hz, *J*= 10.2 Hz, 1H, CH_2F, major), 4.61 (ddd, J_{H-F} = 46.3 Hz, *J*= 10.2 Hz, *J*= 0.9 Hz, 1H, CH_2F, minor), 4.57 (dd, J_{H-F}= 46.4 Hz, *J*= 10.2 Hz, 1H, CH_2F, major), 4.06 (dd, J_{H-F}= 45.7 Hz, *J*= 10.2 Hz, 1H, CH_2F, minor), 3.74 (br, 1H, OH, major +minor), 2.46 (s, 3H, Tos-Me, major +minor) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 151.2 (C=O), 150.5 (C=O), 146.2 (Cq), 146.0 (Cq), 134.5 (Cq), 134.3 (Cq), 131.0 (Cq), 130.5 (Cq), 130.0 (2CH), 129.7 (CH), 129.7 (2CH), 129.6 (CH), 129.2 (d, *J*= 0.7 Hz, 2CH), 129.1 (d, *J*= 0.6 Hz, 2CH), 128.8 (2CH), 128.7 (2CH), 127.5 (d, *J*= 0.3 Hz, 2CH), 126.4 (d, *J*= 1.8 Hz, 2CH), 92.1 (d, *J*= 21.0 Hz, Cq), 90.2 (d, *J*= 20.6 Hz, Cq), 85.4 (CH), 81.43 (d, *J*= 180.6 Hz,

CH_2F), 81.40 (d, *J*= 2.2 Hz, CH), 80.2 (d, *J*= 181.0 Hz, CH_2F), 22.8 (CH_3) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -222.9 (t, *J*=45.9 Hz, 35 %), -223.4 (t, *J*=46.7 Hz 65 %) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{17}H_{17}FNO_5S$: $[M+H]^+$ 366.0811, Found: 366.0815.

(8*R*,9*S*,10*R*,13*S*,14*S*)-4'-(fluoromethyl)-4'-hydroxy-10,13-dimethyl-3'-tosyl-1,6,7,8,9,10,11,12,13,14,15,16-dodecahydrospiro[cyclopenta*[a]*phenanthrene-17,5'-oxazolidine]-2',3(2*H*)-dione 4h (minor) and (8*R*,9*S*,10*R*,13*S*,14*S*)-17(2-fluoroacetyl)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta*[a]*phenanthrene-17-yl tosylcarbamate 5h (major). White solid (83 mg, 61% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3438, 3252, 1743, 1656, 1458, 1166, 806, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.92-7.90 (m, 2H, Tos, **5h**), 7.72-7.70 (m, 2H, Tos, **4h**), 7.55-7.53 (m, 2H, Tos, **4h**), 7.37-7.35 (m, 2H, Tos, **5h**), 5.76 (s, 1H, **4h**), 5.74 (s, 1H, **5h**), 4.76 (dd, J_{H-F} = 46.7 Hz, J_{H-H} = 16.6 Hz, 1H, CH_2F, **4h**), 4.66 (dd, J_{H-F} = 47.2 Hz, J_{H-H} = 15.7 Hz, 1H, CH_2F, **5h**), 4.47 (dd, J_{H-F} = 46.6 Hz, J_{H-H} = 15.7 Hz, 1H, CH_2F, **5h**), 2.75-2.62 (m, 1H, CH_2, **4h**+**5h**), 2.46 (s, 3H, CH_3, Tos, **4h**+**5h**), 2.42-2.26 (m, 4H, CH_2, **4h**+**5h**), 2.00-1.95 (m, 1H, CH_2, **4h**+**5h**), 1.85-1.56 (m, 7H, CH_2, **4h**+**5h**), 1.46-1.26 (m, 3H, CH+CH_2, **4h**+**5h**), 1.20 (s, 3H, CH_3, **4h**), 1.17 (s, 3H, CH_3, **5h**), 1.11-0.81 (m, 3H, CH+CH_2, **4h**+**5h**) 0.98 (s, 3H, CH_3, **5h**), 0.92 (s, 3H, CH_3, **4h**) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 203.4 (d, *J*= 14.8 Hz, C=O, **5h**), 199.8 (C=O, **4h**), 199.7 (C=O, **5h**), 170.93 (Cq, **4h**), 170.87 (Cq, **5h**), 150.8 (C=O, **5h**), 149.8 (Cq, **4h**), 146.1 (Cq, Tos, **4h**), 145.4 (Cq, Tos, **5h**), 135.5 (Cq, Tos, **5h**), 132.4 (Cq, Tos, **4h**), 130.9 (2CH, Tos, **4h**), 129.7 (2CH, Tos, **5h**), 128.8 (2CH, Tos, **4h**), 128.1 (2CH, Tos, **5h**), 124.01 (CH, **5h**), 123.98 (CH, **4h**), 97.2 (Cq, **5h**), 89.3 (Cq, **4h**), 84.2 (d, *J*= 184.6 Hz, CH_2, **5h**), 82.8 (d, *J*= 185.6 Hz, CH_2, **4h**), 53.1 (CH, **4h**), 52.7 (CH, **5h**), 48.9 (CH, **4h**), 48.2 (Cq, **5h**), 47.1 (CH, **5h**), 46.9 (Cq, **4h**), 38.6 (Cq, **4h**), 38.4 (Cq, **5h**), 35.7 (CH_2, **4h**), 35.6 (CH_2, **5h**), 35.5 (CH, **4h**+**5h**), 33.9 (CH_2, **4h**), 33.8 (CH_2, **5h**), 33.4 (CH_2, **4h**+**5h**), 33.2 (CH_2, **4h**), 33.1 (CH_2, **5h**), 32.6 (CH_2, **5h**), 31.4 (CH_2, **4h**), 31.3 (CH_2, **5h**), 24.3 (CH_2, **5h**), 23.6 (CH_2, **4h**), 21.8 (CH_3, Tos, **4h**), 21.7 (CH_3, Tos, **5h**), 17.4 (CH_3, **4h**), 17.3 (CH_3, **5h**), 14.8 (CH_3, **5h**), 14.1 (CH_3, **4h**) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.90 (t, *J*=46.7 Hz, **4h**, 5%), -231.72 (t, *J*=46.9 Hz, **5h**, 95%) ppm; HRMS m/z (ESI) positive ion, calculated for **4h** $C_{22}H_{33}FNO_4$: $[M+H]^+$ 394.2394, Found: 394.2387; HRMS m/z (ESI) positive ion, calculated for **5h** $C_{29}H_{36}FKNO_6S$: $[M+K]^+$ 584.1884, Found: 584.1876.

*4.4. General procedure for preparation of Benzoylcarbamates (**6**).*

To a dry 50 mL 1-necked round-bottomed flask containing the propargylic alcohol (2 mmol) dissolved in 5 mL of DCE was added BzNCO (2.2 mmol) dropwise via syringe at room temperature. After complete addition, the reaction was allowed to stir at room temperature for 1 hour. The solvent was then stripped off and the crude was purified by flash chromatography to give the desired benzoylcarbamate **6**.

2-Methylbut-3-yn-2-ylbenzoylcarbamate 6b. White solid (88% yield, 0.407 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 75/25). IR (KBr): 3288, 3199, 2120, 1766, 1527, 1218, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (s, 1H, NH), 7.86-7.84 (m, 2H, Bz), 7.59-7.55 (m, 1H, Bz), 7.48-7.45 (m, 2H, Bz), 2.59 (s, 1H, C_{sp}-H), 1.76 (s, 6H, $2CH_3$) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 165.1 (C=O, Bz), 149.1 (C=O), 133.1 (Cq, Bz), 132.9 (CH), 128.8 (2CH), 127.7 (2CH), 83.8 (C_{sp}q), 74.0 (Cq), 73.3 (C_{sp}-H), 28.8 ($2CH_3$) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{13}H_{13}KNO_3$: $[M+K]^+$ 270.0533, Found: 270.0528.

But-3-yn-2-ylbenzoylcarbamate 6d. White solid (95% yield, 0. 412 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 75/25). IR (KBr): 3270, 3188, 2129, 1775, 1678, 1519, 1209, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (s, 1H, NH), 7.90-7.87 (m, 2H, Bz), 7.60-7.56 (m, 1H, Bz), 7.50-7.45 (m, 2H, Bz), 5.52 (qd, *J* = 6.7 Hz, *J* = 2.2 Hz, 1H), 2.51 (d, *J* = 2.2 Hz, 1H, C_{sp}-H), 1.55 (d, *J* = 6.7 Hz, 3H, CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 165.0 (C=O, Bz), 149.8 (C=O), 133.1 (CH), 132.8 (Cq, Bz), 128.8 (2CH), 127.8 (2CH), 81.3 (C_{sp}q), 74.0 (C_{sp}-H), 62.1 (CH), 21.3 (CH_3) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{12}H_{11}KNO_3$: $[M+K]^+$ 256.0376, Found: 256.0380.

Pent-1-yn-3-ylbenzoylcarbamate 6e. Oil (90% yield, 0.416 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 75/25). IR (neat): 3270, 3226, 2120, 1757, 1687, 1527, 1209, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49 (s, 1H, NH), 7.89-7.86 (m, 2H, Bz), 7.60-7.56 (m, 1H, Bz), 7.50-7.46 (m, 2H, Bz), 5.40 (td, *J* = 6.5 Hz, *J* = 2.2 Hz, 1H), 2.51 (d, *J* = 2.2 Hz, 1H, C_{sp}-H), 1.85 (m, 2H, CH_2), 1.04 (d, *J* = 7.4 Hz, 3H, CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.9 (C=O, Bz), 150.0 (C=O), 133.1 (CH), 132.8 (Cq, Bz), 128.8 (2CH), 127.8 (2CH), 80.2 (C_{sp}q), 74.6 (C_{sp}-H), 67.0 (CH), 27.9 (CH_2), 9.1 (CH_3) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{13}H_{13}KNO_3$: $[M+K]^+$ 270.0533, Found: 270.0535.

1-Phenylprop-2-yn-1-ylbenzoylcarbamate 6f. Yellow solid (83% yield, 0.463 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 85/15). IR (KBr): 3296, 2129, 1775, 1695, 1492, 890 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (s, 1H, NH), 7.83-7.80 (m, 2H), 7.58-7.54 (m, 3H), 7.47-7.42 (m, 2H), 7.38-7.35 (m, 3H), 6.51 (d, *J* = 2.3 Hz, 1H), 2.72 (d, *J* = 2.3 Hz, 1H, C_{sp}-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.8 (C=O, Bz), 149.7 (C=O), 135.6 (Cq), 133.1 (CH, Bz), 132.7 (Cq, Bz), 129.4 (CH), 128.81 (2CH, Bz), 128.77 (2CH), 128.0 (2CH), 127.7 (2CH, Bz), 79.4 (C_{sp}q), 76.6 (C_{sp}-H), 67.2 (CH) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{17}H_{13}KNO_3$: $[M+K]^+$ 318.0533, Found: 318.0531.

1-(3-bromophenyl)prop-2-yn-ylbenzoylcarbamate 6g. White solid (83% yield, 0.296 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3327, 3220, 2111, 1776, 1753, 1524, 1189, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (s, 1H, NH), 7.85-7.82 (m, 2H), 7.71 (t, *J* = 1.8 Hz, 1H), 7.57 (tt, *J* = 7.4 Hz, *J* = 1.3 Hz, 1H), 7.51-7.44 (m, 4H), 7.24 (t, *J* = 7.9 Hz, 1H), 6.47 (d, *J* = 2.3 Hz, 1H), 2.74 (d, *J* = 2.3 Hz, 1H, C_{sp}-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.7 (C=O, Bz), 149.5 (C=O), 137.8 (Cq), 133.2 (CH, Bz), 132.6 (Cq, Bz), 132.5 (CH), 130.9 (CH), 130.3 (CH), 128.9 (2CH, Bz), 127.7 (2CH, Bz), 126.6 (CH), 122.7 (CBr), 78.8 (C_{sp}q), 77.1 (C_{sp}-H), 66.3 (CH) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{17}H_{12}BrKNO_3$: $[M+K]^+$ 395.9638, Found: 395.9636.

1-(4-Chlorophenyl)prop-2-yn-ylbenzoylcarbamate 6h. Yellow solid (82% yield, 0.278 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3305, 3243, 2120, 1750, 1492, 1200, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (s, 1H, NH), 7.85-7.82 (m, 2H), 7.59-7.55 (m, 1H), 7.50-7.43 (m, 4H), 7.34-7.31 (m, 2H), 6.48 (d, *J* = 2.3 Hz, 1H), 2.73 (d, *J* = 2.3 Hz, 1H, C_{sp}-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.8 (C=O, Bz), 149.7 (C=O), 135.5 (Cq), 134.2 (CCl), 133.2 (CH, Bz), 132.6 (Cq, Bz), 129.4 (2CH), 129.0 (2CH), 128.9 (2CH, Bz), 127.8 (2CH, Bz), 79.0 (C_{sp}q), 76.9 (C_{sp}-H), 66.4 (CH) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{17}H_{12}ClKNO_3$: $[M+K]^+$ 352.0143, Found: 352.0140.

1-(Naphthalen-1-yl)prop-2-yn-yl benzoylcarbamate 6i. Yellow solid (94% yield, 0.403 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3285, 2125, 1757, 1510, 1189, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (br, 1H, NH), 7.90-7.88 (m, 3H), 7.77-7.75 (m, 2H), 7.60-7.40 (m, 7H), 7.18 (d, *J* = 2.3 Hz, 1H), 2.79 (d, *J* = 2.3 Hz, 1H, C_{sp}-H) ppm; ^{13}C NMR (100.6

MHz, $CDCl_3$): δ = 164.7 (C=O, Bz), 149.6 (C=O), 134.0 (Cq), 133.1 (CH, Bz), 132.7 (Cq, Bz), 130.8 (Cq), 130.5 (CH), 130.4 (Cq), 128.9 (CH), 128.8 (2CH, Bz), 127.6 (2CH, Bz), 127.1 (CH), 127.0 (CH), 126.2 (CH), 125.2 (CH), 123.5 (CH), 79.3 (C_{sp}q), 77.2 (C_{sp}-H), 65.6 (CH) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{21}H_{15}KNO_3$: $[M+K]^+$ 368.0689, Found: 368.0686.

3-Methylpent-1-yn benzoylcarbamate 6j. White solid (86% yield, 0.422 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3296, 3196, 2111, 1766, 1536, 1230, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.31 (br, 1H, NH), 7.86-7.83 (m, 2H), 7.59-7.55 (m, 1H), 7.49-7.45 (m, 2H), 2.60 (s, 1H, C_{sp}-H), 2.16-2.03 (m, 1H, CH_2), 1.97-1.87 (m, 1H, CH_2), 1.77 (s, 3H, Me), 1.08 (t, *J* = 7.4 Hz, 3H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 165.0 (C=O, Bz), 149.2 (C=O), 133.1 (Cq), 132.9 (CH), 128.8 (2CH, Bz), 127.7 (2CH, Bz), 82.8 (C_{sp}q), 78.0 (Cq), 74.2 (C_{sp}-H), 34.4 ($\underline{CH_2}CH_3$), 26.0 ($CH_2\underline{CH_3}$), 8.5 (CH_3) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{14}H_{15}KNO_3$: $[M+K]^+$ 284.0689, Found: 284.0691.

(8R,9S,10R,13S,14S,17R)-17-ethynyl-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl benzoylcarbamate 6k. White solid (52% yield, 0.477 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3283, 3261, 2111, 1793, 1660, 1492, 1182, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.45 (s, 1H, NH), 7.87-7.85 (m, 2H, Bz), 7.60-7.56 (m, 1H, Bz), 7.50-7.46 (m, 2H, Bz), 5.73 (s, 1H, C_{sp2}-H), 2.84-2.76 (m, 1H), 2.68 (s, 1H, C_{sp}-H), 2.47-2.17 (m, 5H), 2.08-2.02 (m, 1H), 1.89-1.36 (m, 10H), 1.20 (s, 3H, Me), 1.16-0.90 (m, 2H), 1.00 (s, 3H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 199.5 (C=O), 170.9 (Cq), 164.9 (C=O), 150.2 (C=O), 133.1 (Cq), 132.9 (CH), 128.8 (2CH), 127.8 (2CH), 123.9 (CH), 86.4 (Cq), 82.3 (Cq), 76.2 (C_{sp}-H), 53.2 (CH), 48.4 (CH), 47.7 (Cq), 38.6 (Cq), 37.3 (CH_2), 35.9 (CH), 35.6 (CH_2), 33.9 (CH_2), 32.8 (CH_2), 32.7 (CH_2), 31.5 (CH_2), 23.5 (CH_2), 20.6 (CH_2), 17.4 (Me), 13.5 (Me) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{29}H_{33}KNO_4$: $[M+K]^+$ 498.2047, Found: 498.2044.

(*E*)-Oct-4-en-1-yn-3-ylbenzoylcarbamate 6l. Yellow solid (76% yield, 0.412 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 95/5). IR (KBr): 3294, 3243, 2120, 1771, 1687, 1534, 1194, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.35 (br, 1H, NH), 7.87-7.84 (m, 2H), 7.60-7.56 (m, 1H), 7.49-7.45 (m, 2H), 6.12-6.04 (m, 1H), 5.93-5.90 (m, 1H), 5.59 (ddt *J* = 15.3 Hz, *J* = 6.7 Hz, *J* = 1.5 Hz, 1H), 2.62 (d, *J* = 2.2 Hz, 1H, C_{sp}-H), 2.05 (q, *J* = 6.7 Hz, 2H), 1.41 (td, *J* = 14.8 Hz, *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.8 (C=O, Bz), 149.7 (C=O),

138.1 (CH), 133.1 (CH, Bz), 132.9 (Cq, Bz), 128.9 (2CH, Bz), 127.7 (2CH, Bz), 123.9 (CH), 79.1 (C_{sp}q), 75.8 (C_{sp}-H), 66.1 (CH), 34.0 (CH_2), 21.8 (CH_2), 13.6 (Me) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{16}H_{17}KNO_3$: $[M+K]^+$ 310.0845, Found: 310.0850.

(*E*)-3-(benzoyl-λ²-azanyl)-4-methylene-5-(pent-1-en-1-yl)oxazolidin-2-one 7l. Yellow solid (45% yield, 0.048 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 95/5). IR (KBr): 1780, 1706, 1347, 1194, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.66 (m, 2H), 7.59-7.54 (m, 1H), 7.46-7.41 (m, 2H), 6.02 (dtd, *J* = 15.1 Hz, *J* = 6.8 Hz, *J* = 0.6 Hz, 1H), 5.64 (dd, *J* = 2.4 Hz, *J* = 2.3 Hz, 1H), 5.54 (ddt, *J* = 15.1 Hz, *J* = 8.1 Hz, *J* = 1.5 Hz, 1H), 5.41 (dt, *J* = 8.1 Hz, *J* = 2.2 Hz, 1H), 4.62 (t, *J* = 2.2 Hz, 1H), 2.13 (qt, *J* = 7.4 Hz, *J* = 1.4 Hz, 2H), 1.48 (sextet, *J* = 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H, Me) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 169.0 (C=O, Bz), 152.8 (C=O), 140.1 (Cq), 139.9 (CH), 133.4 (Cq, Bz), 132.9 (CH, Bz), 129.1 (2CH), 128.2 (2CH), 124.7 (CH), 94.0 ($C_{sp2}H_2$), 79.8 (CH), 34.1 (CH_2), 21.8 (CH_2), 13.6 (Me) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{16}H_{17}KNO_3$: $[M+K]^+$ 310.0845, Found: 310.0845.

*4.5. Typical procedure for the combined silver-catalyzed annulation /hydoxyfluronination of benzoylcarbamates (**6**): synthesis of 3-Bezoyl-4-(fluoromethyl)-4-hydroxy-1-oxa-3-azaspiro[4.5]decan-2-one **8a**.*

To a solution of 1-ethynylcyclohexyl benzoylcarbamate **6a** (104 mg, 0.38 mmol, 1 equiv.) in MeCN/H_2O (20:1) (2.10 mL), ere added $NaHCO_3$ (32 mg, 0.38 mmol, 1 equiv.) and $AgNO_3$ (6 mg, 0.038 mmol, 0.1 equiv.). After complete addition, the reaction was allowed to stir at 60 °C and monitored by TLC. Then, Selectfluor (269 mg, 0.76 mmol, 2 equiv.) was added to the reaction mixture which was allowed to stir at 60 °C. Upon completion, the solvent was then stripped off and the crude was purified by flash chromatography (*n*-Hexane/EtOAc: 80/10) to give the 3-bezoyl-4-(fluoromethyl)-4-hydroxy-1-oxa-3-azaspiro[4.5]decan-2-one **8a** (108 mg, 92% yield). White solid. IR (KBr): 3500, 1787, 1681, 1265, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71-7.69 (m, 2H, Bz), 7.62-7.57 (m, 1H, Bz), 7.47-7.43 (m, 2H, Bz), 4.85 (dd, J_{H-F} = 46.4 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F), 4.71 (dd, J_{H-F} = 46.4 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F), 4.47 (br, 1H, OH), 2.23-2.08 (m, 2H, CH_2), 1.78-1.56 (m, 8H, CH_2) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.1 (C=O, Bz), 151.7 (C=O), 133.6 (CH), 132.6 (Cq), 129.5 (2CH), 128.2 (2CH), 90.2 (d, *J*= 19.0 Hz, Cq), 86.3 (d, *J*= 1.3 Hz, Cq), 79.9 (d, *J*= 182.9 Hz, CH_2F), 31.3 (d, *J*= 4.7 Hz, CH_2), 29.2 (CH_2), 24.8 (CH_2), 21.6 (d, *J*= 1.0 Hz, CH_2), 21.5 (CH_2) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.9 (t, *J*=46.4 Hz) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{16}H_{18}FKNO_4$: $[M+K]^+$ 346.0857, Found: 346.0856.

3-Benzoyl-4-(fluoromethyl)-4-hydroxy-5,5-dimethyloxazolidin-2-one 8b. White solid (105 mg, 91% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 85/15). IR (KBr): 3500, 1775, 1695, 1306, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72-7.69 (m, 2H), 7.62-7.55 (m, 1H), 7.47-7.43 (m, 2H), 4.87 (dd, J_{H-F} = 46.3 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F), 4.70 (dd, J_{H-F} = 46.3 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F), 4.56 (br, 1H, OH), 1.63 (d, J_{H-F} = 2.9 Hz, 3H, CH_3), 1.56 (s, 3H, CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 172.9 (C=O, Bz), 151.7 (C=O), 133.6 (CH), 132.5 (Cq), 129.5 (2CH), 128.2 (2CH), 90.0 (d, *J*= 19.3 Hz, Cq), 85. 2 (d, *J*= 1.0 Hz, Cq), 80.2 (d, *J*= 182.6 Hz, CH_2F), 23.1 (d, *J*= 5.0 Hz, CH_3), 21.5 (CH_3) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -222.2 (tq, *J*=46.3 Hz, *J*=2.9 Hz) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{13}H_{14}FNO_4$: $[M+H]^+$ 268.0985, Found: 268.0989.

3-Benzoyl-4-(fluoromethyl)-4-hydroxyoxazolidin-2-one 8c. White solid (95mg, 90% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3500, 1775, 1695, 1306, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73-7.70 (m, 2H), 7.64-7.60 (m, 1H), 7.50-7.45 (m, 2H), 4.91 (dd, J_{H-F} = 46.5 Hz, J_{H-H} = 10.2 Hz, 1H, CH_2F), 4.71 (br, 1H, OH), 4.56 (dd, J_{H-H} = 9.6 Hz, J_{H-F} = 2.8 Hz, 1H, CH_2), 4.44 (dd, J_{H-F} = 46.5 Hz, J_{H-H} = 10.2 Hz, 1H, CH_2F), 4.35 (dd, J_{H-H} = 9.6 Hz, J_{H-F} = 2.8 Hz, 1H, CH_2) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 172.7 (C=O, Bz), 152.2 (C=O), 133.8 (CH), 132.1 (Cq), 129.7 (2CH), 128.2 (2CH), 88.2 (d, *J*= 20.1 Hz, Cq), 79.2 (d, *J*= 181.8 Hz, CH_2F), 70.2 (CH_2) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.4 (tt, *J*=46.5 Hz, *J*=2.8 Hz) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{11}H_{11}FNO_4$: $[M+H]^+$ 240.0672, Found: 240.0675.

3-Benzoyl-4-(fluoromethyl)-4-hydroxy-5-methyloxazolidin-2-one 8d. White solid (110 mg, 85% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3429, 1784, 1678, 1262, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74-7.72 (m, 2H, major), 7.70-7.68 (m, 2H, minor), 7.64-7.58 (m, 1H, major+minor), 7.48-7.44 (m, 2H, major+minor), 4.97 (dd, J_{H-F} = 46.4 Hz, J_{H-H} = 10.4 Hz, 1H, CH_2F, minor), 4.85 (dd, J_{H-F} = 47.2 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F, major), 4.69 (dd, J_{H-F} = 46.2 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F, minor), 4.36 (dd, J_{H-F} = 46.1 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F, major), 4.81 (qd, J_{H-H} = 6.6 Hz, J_{H-F} = 2.5 Hz, 1H, CH-Me, major+minor), 4.55 (br, 1H, OH, major+minor), 1.61 (dd, J_{H-H} = 6.8 Hz, J_{H-F} = 2.4 Hz, 3H, CH_3, minor), 1.51 (d, J_{H-H} = 6.6 Hz, 3H, CH_3, major) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.2 (C=O, Bz, major), 172.8 (C=O, Bz, minor), 152.1 (C=O, major), 151.6 (C=O, minor), 133.8 (CH, Bz, major), 133.5 (CH, Bz, minor), 132.5 (Cq, Bz, minor), 132.2 (Cq, Bz, major), 129.8 (2CH, Bz, major), 129.4 (2CH, Bz, minor), 128.24 (2CH,

Bz, major), 128.16 (2CH, Bz, minor), 89.3 (d, *J*= 19.8 Hz, Cq, minor), 88.6 (d, *J*= 18.6 Hz, Cq, major), 79.2 (d, *J*= 181.9 Hz, CH_2F, minor), 76.6 (d, *J*= 182.6 Hz, CH_2 F, major), 75.6 (d, *J*= 1.3 Hz, CH, major+minor), 14.8 (d, *J*= 4.8 Hz, CH_3, minor), 12.3 (CH_3, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.9 (ddd, *J*=47.2 Hz, *J*=46.2 Hz, *J*=2.4 Hz, 86%), -222.3 (td, *J*=46.2 Hz, *J*=2.4 Hz, 14%) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{12}H_{12}FKNO_4$: $[M+K]^+$ 292.0387, Found: 292.0391.

3-Benzoyl-5-ethyl-4-(fluoromethyl)-4-hydroxyoxazolidin-2-one 8e. White solid (91% yield, 0.113 g) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3456, 1784, 1669, 1253, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73-7.71 (m, 2H, major), 7.69-7.67 (m, 2H, minor), 7.62-7.58 (m, 1H, major+minor), 7.47-7.43 (m, 2H, major+minor), 4.91 (ddd, J_{H-F} = 46.4 Hz, J_{H-H} = 10.4 Hz, J_{H-H} = 0.6 Hz, 1H, CH_2F, minor), 4.85 (dd, J_{H-F} = 47.3 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F, major), 4.67 (dd, J_{H-F} = 46.1 Hz, J_{H-H} = 10.4 Hz, 1H, CH_2F, minor), 4.61 (br, 1H, OH, major+minor), 4.56 (ddd, J_{H-H} = 9.0 Hz, J_{H-H} = 4.7 Hz, J_{H-F} = 2.6 Hz, 1H, CH-Et, major+minor), 4.36 (dd, J_{H-F} = 46.2 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F, major), 2.04-1.79 (m, 2H, CH_2-Me, major+minor), 1.16 (td, *J* = 7.4 Hz, *J* = 0.4 Hz, 3H, CH_3, minor), 1.14 (t, *J* = 7.5 Hz, 3H, CH_3, major) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.1 (C=O, Bz, major), 172.6 (C=O, Bz, minor), 152.1 (C=O, major), 151.7 (C=O, minor), 133.8 (CH, Bz, major), 133.4 (CH, Bz, minor), 132.6 (Cq, Bz, minor), 132.3 (Cq, Bz, major), 129.7 (2CH, Bz, major), 129.3 (2CH, Bz, minor), 128.2 (2CH, Bz, major), 128.1 (2CH, Bz, minor), 89.3 (d, *J*= 19.9 Hz, Cq, minor), 88.7 (d, *J*= 18.6 Hz, Cq, major), 85.2 (d, *J*= 1.3 Hz, CH-Et, minor), 80.6 (d, *J*= 1.2 Hz, CH-Et, major), 79.1 (d, *J*= 181.5 Hz, CH_2F, minor), 79.0 (d, *J*= 181.5 Hz, CH_2F, major), 22.4 (d, *J*= 4.3 Hz, CH_2Me, minor), 20.7 (CH_2Me, major), 10.3 (CH_3, minor), 10.0 (CH_3, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.6 (td, *J*=46.7 Hz, *J*=2.4 Hz, 90%), -222.0 (t, *J*=46.4 Hz, 10%) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{13}H_{14}FKNO_4$: $[M+K]^+$ 306.0544, Found: 306.0545.

3-Benzoyl-5-ethyl-4-(fluoromethyl)-4-hydroxy-5-phenyloxazolidin-2-one 8f. Yellow solid (105 mg, 82% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 85/15). IR (KBr): 3491, 1802, 1678, 1244, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79-7.77 (m, 2H, major), 7.72-7.70 (m, 2H, minor), 7.65-7.58 (m, 1H, major+minor), 7.50-7.42 (m, 7H, major+minor), 5.68 (d, *J*= 1.8 Hz, 1H, CH-Ph, major), 5.56 (s, 1H, CH-Ph, minor), 4.89 (dd, J_{H-F} = 47.3 Hz, *J*= 10.5 Hz, 1H, CH_2F, major), 4.85 (br, 1H, OH, minor), 4.65 (ddd, J_{H-F} = 46.3 Hz, *J*= 10.0 Hz, *J*= 0.7 Hz, 1H, CH_2F, minor), 4.46 (br, 1H, OH, major), 4.42 (dd, J_{H-F}= 46.2 Hz, *J*= 10.5 Hz, 1H, CH_2F, major), 4.12 (dd, J_{H-F}= 45.5 Hz, *J*= 10.0

Hz, 1H, CH_2F, minor) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.0 (C=O, Bz, major), 172.4 (C=O, Bz, minor), 152.2 (C=O, major), 151.6 (C=O, minor), 134.0 (CH, Bz, major), 133.3 (CH, Bz, minor), 132.5 (Cq, Bz, minor), 132.1 (Cq, Bz, major), 130.13 (Cq, Ph, major), 130.07 (Cq, Ph, minor), 129.84 (2CH, Bz, major), 129.82 (CH, Ph, major), 129.6 (CH, Ph, minor), 129.2 (2CH, Bz, minor), 128.7 (2CH, Ph, minor), 128.4 (2CH, Ph, major), 128.3 (2CH, Bz, major), 128.2 (2CH, Bz, minor), 127.9 (2CH, Ph, major), 126.4 (d, *J*= 1.6 Hz, 2CH, Ph, minor), 90.3 (d, *J*= 19.7 Hz, Cq, COH, minor), 89.1 (d, *J*= 18.2 Hz, Cq, COH, major), 84.5 (d, *J*= 0.8 Hz, CH-Ph, minor), 80.2 (d, *J*= 1.6 Hz, CH-Ph, major), 79.1 (d, *J*= 181.1 Hz, CH_2F, minor), 78.3 (d, *J*= 183.0 Hz, CH_2F, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.2 (ddd, *J*=47.3 Hz, *J*=46.2 Hz, *J*=2.4 Hz, 89 %), -223.7 (t, *J*=45.8 Hz 11 %) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{17}H_{14}FKNO_4$: $[M+K]^+$ 354.0544, Found: 354.0548.

3-benzoyl-5-(3-bromophenyl)-4-(fluoromethyl)-4-hydroxyoxazolidin-2-one 8g. Yellow solid (95 mg, 90% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3434, 1785, 1683, 1245, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.80-7.77 (m, 2H, major), 7.72-7.70 (m, 2H, minor), 7.67-7.57 (m, 3H, major+minor), 7.51-7.47 (m, 2H, major+minor), 7.41-7.37 (m, 1H, major+minor), 7.36-7.30 (m, 1H, major+minor), 5.63 (d, *J*= 2.0 Hz, 1H, CH-Ph, major), 5.53 (s, 1H, CH-Ph, minor), 4.91 (dd, J_{H-F} = 47.2 Hz, *J*= 10.6 Hz, 1H, CH_2F, major), 4.82 (br, 1H, OH, minor), 4.70 (ddd, J_{H-F} = 46.3 Hz, *J*= 10.2 Hz, *J*= 0.8 Hz, 1H, CH_2F, minor), 4.52 (t, J_{H-F} = 1.4 Hz, 1H, OH, major), 4.43 (dd, J_{H-F}= 46.2 Hz, *J*= 10.6 Hz, 1H, CH_2F, major), 4.15 (dd, J_{H-F}= 45.6 Hz, *J*= 10.1 Hz, 1H, CH_2F, minor) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.0 (C=O, Bz, major), 172.4 (C=O, Bz, minor), 151.9 (C=O, major), 151.1 (C=O, minor), 134.1 (CH, Bz, major), 133.4 (CH, Bz, minor), 132.9 (CH, Ph, major), 132.8 (CH, Ph, minor), 132.52 (Cq, major), 132.48 (Cq, minor), 132.4 (Cq, minor), 132.0 (Cq, major), 131.0 (CH, Ph, major), 130.3 (CH, Ph, minor), 129.93 (CH, Ph, major), 129.89 (2CH, Bz, major), 129.5 (CH, Ph, minor), 129.1 (2CH, Bz, minor), 128.4 (2CH, Bz, major), 128.2 (2CH, Bz, minor), 126.5 (CH, Ph, major), 125.1 (d, *J*= 1.6 Hz, CH, Ph, minor), 122.9 (Cq, CBr, minor), 122.6 (Cq, CBr, major), 90.3 (d, *J*= 19.8 Hz, Cq, COH, minor), 89.1 (d, *J*= 18.3 Hz, Cq, COH, major), 83.5 (CH-Ph, minor), 79.3 (d, *J*= 1.9 Hz, CH-Ph, major), 79.0 (d, *J*= 181.4 Hz, CH_2F, minor), 78.4 (dd, *J*= 182.3 Hz, *J*= 1.4 Hz, CH_2F, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.1 (dddd, *J*=47.3 Hz, *J*=46.2 Hz, *J*=2.2 Hz, *J*=1.4 Hz, 82 %), -223.7 (t, *J*=46.0 Hz 18 %) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{17}H_{13}BrFKNO_4$: $[M+K]^+$ 431.9649, Found: 431.9651.

3-Benzoyl-5-(4-chlorophenyl)-4-(fluoromethyl)-4-hydroxyoxazolidin-2-one 8h. Oil (105 mg, 88% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3447, 1802, 1687, 1156, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81-7.77 (m, 2H, major), 7.72-7.69 (m, 2H, minor), 7.67-7.66 (m, 1H, major+minor), 7.51-7.38 (m, 6H, major+minor), 5.65 (d, *J*= 2.3 Hz, 1H, CH-Ph, major), 5.54 (s, 1H, CH-Ph, minor), 4.90 (dd, J_{H-F} = 47.2 Hz, *J*= 10.6 Hz, 1H, CH_2F, major), 4.81 (br, 1H, OH, minor), 4.69 (ddd, J_{H-F} = 46.3 Hz, *J*= 10.1 Hz, *J*= 0.7 Hz, 1H, CH_2F, minor), 4.50 (br, 1H, OH, major), 4.40 (dd, J_{H-F}= 46.3 Hz, *J*= 10.6 Hz, 1H, CH_2F, major), 4.12 (dd, J_{H-F}= 45.6 Hz, *J*= 10.1 Hz, 1H, CH_2F, minor) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.0 (C=O, Bz, major), 172.4 (C=O, Bz, minor), 152.0 (C=O, major), 151.2 (C=O, minor), 136.0 (C-Cl, major), 135.7 (C-Cl, minor), 134.1 (CH, Bz, major), 133.3 (CH, Bz, minor), 132.4 (Cq, Bz, minor), 132.0 (Cq, Bz, major), 130.18 (Cq, Ph, major), 130.14 (Cq, Ph, minor), 129.9 (2CH, Bz, major), 129.4 (2CH, Ph, major), 129.14 (2CH, Bz, minor), 129.05 (2CH, Ph, minor), 128.7 (2CH, Ph, major), 128.4 (2CH, Bz, major), 128.2 (2CH, Bz, minor), 127.9 (d, *J*= 1.8 Hz, 2CH, Ph, minor), 90. 2(d, *J*= 19.7 Hz, Cq, COH, minor), 89.0 (d, *J*= 18.2 Hz, Cq, COH, major), 83.8 (d, *J*= 0.8 Hz, CH-Ph, minor), 79.6 (d, *J*= 1.8 Hz, CH-Ph, major), 79.0 (d, *J*= 181.3 Hz, CH_2F, minor), 78.3 (d, *J*= 183.3 Hz, CH_2F, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.1 (ddd, *J*=47.2 Hz, *J*=46.3 Hz, *J*=2.3 Hz, 82 %), -223.7 (t, *J*=45.9 Hz 18 %) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{17}H_{13}ClFKNO_4$: $[M+K]^+$ 388.0154, Found: 388.0150.

3-Benzoyl-4-(fluoromethyl)-4-hydroxy-5-(naphthalen-1-yl)oxazolidin-2-one 8i. White solid (60 mg, 52% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3457, 1792, 1674, 1330, 726 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12-7.39 (m, 12H, major+minor), 6.61 (d, *J*= 2.0 Hz, 1H, CH-Ant, major), 6.38 (s, 1H, CH-Ant, minor), 5.21 (br, 1H, OH, minor), 4.95 (dd, J_{H-F} = 47.4 Hz, *J*= 10.7 Hz, 1H, CH_2F, major), 4.59 (ddd, J_{H-F} = 46.5 Hz, *J*= 10.1 Hz, *J*= 0.7 Hz, 1H, CH_2F, minor), 4.51 (br, 1H, OH, major), 4.50 (dd, J_{H-F}= 46.0 Hz, *J*= 10.7 Hz, 1H, CH_2F, major), 3.96 (dd, J_{H-F}= 45.4 Hz, *J*= 10.2 Hz, 1H, CH_2F, minor) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 172.8 (C=O, Bz, major), 172.7 (C=O, Bz, minor), 152.5 (C=O, major), 151.8 (C=O, minor), 133.9 (CH, Bz, major), 133.6 (Cq, Ant, major), 133.5 (Cq, Ant, minor), 133.3 (CH, Bz, minor), 132.7 (Cq, Bz, minor), 132.3 (Cq, Bz, major), 131.2 (Cq, Ant, major), 131.1 (Cq, Ant, minor), 130.71 (Cq, Ant, major), 130.70 (Cq, Ant, minor), 130.24 (CH, Ant, major), 130.15 (CH, Ant, minor), 129.92 (CH, Ant, major), 129.85 (CH, Ant, minor), 129.84 (2CH, Bz, major), 129.4 (CH, Ant, major), 129.2 (2CH, Bz, minor), 129.1 (CH, Ant, minor), 128.3 (2CH, Bz, major), 128.2 (2CH, Bz, minor), 127.20 (CH, Ant, minor), 127.15 (CH, Ant,

major), 126.1 (CH, Ant, minor), 125.9 (CH, Ant, major), 125.3 (CH, Ant, minor), 125.1 (CH, Ant, major), 122.8 (CH, Ant, minor), 121.8 (d, *J*= 1.4 Hz, CH, Ant, minor), 90.5 (d, *J*= 18.8 Hz, Cq, COH, minor), 89.6 (d, *J*= 18.5 Hz, Cq, COH, major), 81.7 (CH-Ant, minor), 76.7 (d, *J*= 1.5 Hz, CH-Ant, major), 79.1 (d, *J*= 182.1 Hz, CH_2F, minor), 78.1 (d, *J*= 182.2 Hz, CH_2F, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -219.7 (t, *J*=46.0 Hz 40 %), -220.8 (ddd, *J*=47.5 Hz, *J*=45.7 Hz, *J*=2.1 Hz, 60 %)ppm; HRMS m/z (ESI) positive ion, calculated for $C_{21}H_{16}FKNO_4$: $[M+K]^+$ 404.0700, Found: 404.0698.

3-Benzoyl-5-ethyl-4-(fluoromethyl)-4-hydroxy-5-methyloxazolidin-2-one 8j. White solid (88 mg, 90% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3482, 1757, 1695, 1306, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.72-7.68 (m, 2H, major+minor), 7.62-7.57 (m, 1H, major+minor), 7.47-7.43 (m, 2H, major+minor), 4.89 (dd, J_{H-F} = 46.4 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F, minor), 4.88 (dd, J_{H-F} = 46.5 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F, major), 4.74 (dd, J_{H-F} = 46.2 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F, minor), 4.68 (dd, J_{H-F} = 46.2 Hz, J_{H-H} = 10.5 Hz, 1H, CH_2F, major), 4.57 (br, 1H, OH, major+minor), 2.11-2.01 (m, 1H, CH_2-Me, major+minor), 1.93-1.82 (m, 1H, CH_2-Me, major+minor), 1.59 (d, *J* = 3.1 Hz, 3H, CH_3, Et, major), 1.53 (s, 3H, CH_3, Et, minor), 1.14 (t, *J* = 7.4 Hz, 3H, Me, minor), 1.09 (t, *J* = 7.5 Hz, 3H, Me, major) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.0 (C=O, Bz, major), 172.9 (C=O, Bz, minor), 152.72 (C=O, major), 151.68 (C=O, minor), 133.56 (CH, Bz, major), 133.52 (CH, Bz, minor), 132.59 (Cq, Bz, minor), 132.57 (Cq, Bz, major), 129.51 (2CH, Bz, major), 129.47 (2CH, Bz, minor), 128.22 (2CH, Bz, major), 128.20 (2CH, Bz, minor), 90.5 (d, *J*= 19.6 Hz, Cq, COH, minor), 90.4 (d, *J*= 18.7 Hz, Cq, COH,major), 87.6 (d, *J*= 1.0 Hz, Cq, CMeEt, minor), 87.1 (d, *J*= 1.2 Hz, Cq, CMeEt, major), 80.3 (d, *J*= 183.6 Hz, CH_2F, major), 80.2 (d, *J*= 182.1 Hz, CH_2 F, minor), 27.9 (d, *J*= 4.5 Hz, CH_2Me, minor), 27.4 (CH_2Me, major), 19.6 (d, *J*= 5.4 Hz, CH_3, Me, major), 17.5 (CH_3, Me, minor), 8.1 (CH_3, Et, major), 7.9 (d, *J*= 1.3 Hz, CH_3, Et, minor) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -220.4 (tq, *J*=46.4 Hz, *J*=3.0 Hz, 58%), -222.4 (tt, *J*=46.3 Hz, *J*=2.2 Hz, 42%) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{13}H_{14}FKNO_4$: $[M+K]^+$ 320.0700, Found: 320.0702.

(8*R*,9*S*,13*S*,14*S*)-3'-benzoyl-4'-(fluoromethyl)-4'-hydoxy-10,13-dimethyl-1,6,7,8,9,10,11,12,13,14,15,16-dodecahydrospiro[cyclopenta*[a]*phenanthrene-17,5'-oxazolidine]-2',3(2*H*)-dione 8k and (8*R*,9*S*,10*R*,13*S*,14*S*)-17-(2-fluoroacetyl)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecadydro-1*H*-cyclopenta*[a]*phenanthren-17-yl benzoylcarbamate 9k (8k:9k = 5:95). White solid (69 mg, 66% yield) after purification by flash

chromatography (*n*-Hexane/EtOAc: 70/30). IR (KBr): 3420, 3323, 1775, 1678, 1510, 1209, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (br, 1H, NH, major), 7.87-7.84 (m, 2H, Bz, major+minor), 7.65-7.60 (m, 1H, Bz, major+minor), 7.53-7.49 (m, 2H, Bz, major), 7.47-7.43 (m, 2H, Bz, minor), 5.87 (s, 1H, minor), 5.72 (d, *J* = 1.0 Hz, 1H, major), 5.13 (dd, J_{H-F} = 47.2 Hz, J_{H-H} = 15.6 Hz, 1H, CH_2F major), 4.93 (dd, J_{H-F} = 46.8 Hz, J_{H-H} = 15.6 Hz, 1H, CH_2F major), 4.90 (dd, J_{H-F} = 46.1 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F minor), 4.77 (dd, J_{H-F} = 47.1 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F minor), 2.90-2.81 (m, 1H, CH_2, major+minor), 2.45-2.26 (m, 4H, CH_2, major+minor), 2.00-1.78 (m, 5H, major+minor), 1.72-1.60 (m, 4H, major+minor), 1.52-1.40 (m, 3H, major+minor), 1.19 (s, 3H, CH_3, major), 1.15 (s, 3H, CH_3, major), 1.26-1.04 (m, 1H, major+minor) 0.93-086 (m, 1H major+minor) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 203.6 (d, *J*= 15.1 Hz, C=O, major), 199.5 (C=O, minor), 199.3 (C=O, major), 170.8 (Cq, minor), 170.5 (Cq, major), 164.5 (C=O, Bz, major+minor), 152.2 (C=O, major), 133.4 (CH, Bz, major), 133.0 (CH, Bz, minor), 132.7 (Cq, Bz, minor), 132.5 (Cq, Bz, major), 129.0 (2CH, Bz, major), 128.9 (2CH, Bz, minor), 128.1 (2CH, Bz, minor), 127.8 (2CH, Bz, major), 124.1 (CH, major), 123.9 (CH, minor), 97.1 (d, *J*= 0.9 Hz, Cq, major), 84.8 (d, *J*= 184.8 Hz, CH_2, major), 81.5 (d, *J*= 185.3 Hz, CH_2, minor), 52.82 (CH, minor), 52.76 (CH, major), 49.0 (Cq, minor), 48.3 (Cq, major), 47.6 (CH, minor), 47.3 (CH, major), 38.6 (Cq, minor), 38.4 (Cq, major), 36.3 (CH, minor), 35.7 (CH_2, minor), 35.62 (CH, major), 35.59 (CH_2, major), 33.9 (CH_2, minor), 33.8 (CH_2, major), 33.6 (CH_2, major+minor), 33.20 (CH_2, minor), 33.18 (d, *J*= 1.1 Hz, CH_2, major), 32.7 (CH_2, minor), 32.6 (CH_2, major), 31.5 (CH_2, minor), 31.4 (CH_2, major), 24.5 (CH_2, major), 23.4 (CH_2, minor), 20.9 (CH_2, minor), 20.6 (CH_2, major), 17.5 (CH_3, minor), 17.4 (CH_3, major), 16.3 (CH_3, minor), 15.0 (CH_3, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -223.8 (t, *J*=46.9 Hz, 5%), -231.3 (t, *J*=47.0 Hz, 95%) ppm; HRMS m/z (ESI) positive ion, calculated for major $C_{29}H_{34}FKNO_5$: $[M+K]^+$ 534.2058, Found: 534.2055;

(*E*)-3-Benzoyl-4-(fluoromethyl)-4-hydoxy-5-(pent-1-en-1-yl)oxazolidin-2-one 8l. White solid (45 mg, 96% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 80/20). IR (KBr): 3452, 1790, 1673, 1417, 1170, 723 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76-7.73 (m, 2H, major), 7.70-7.68 (m, 2H, minor), 7.63-7.59 (m, 1H, major+minor), 7.48-7.43 (m, 2H, major+minor), 6.08-6.01 (m, 1H, major+minor), 5.74-5.67 (m, 1H, major+minor), 4.98 (dd, J_{H-H} = 8.8 Hz, J_{H-F} = 2.3 Hz, 1H, CH_2F, major), 4.94 (dd, J_{H-F} = 46.0 Hz, J_{H-H} = 10.1 Hz, 1H, CH_2F, minor), 4.84 (dd, J_{H-F} = 47.3 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F, major), 4.66 (br, 1H, OH, minor), 4.57 (dd, J_{H-F} = 45.4 Hz, J_{H-H} = 10.1 Hz, 1H, CH_2F, minor), 4.48(br, 1H, OH, major), 4.30 (dd, J_{H-F} = 46.0 Hz, J_{H-H} = 10.3 Hz, 1H, CH_2F, major), 2.19-213

(m, 2H, CH_2, major+minor), 1.53-1.44 (m, 2H, CH_2, major+minor), 0.95 (t, *J* = 7.4 Hz, 3H, Me, minor), 0.94 (t, *J* = 7.4 Hz, 3H, Me, major) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 173.1 (C=O, Bz, major), 172.8 (C=O, Bz, minor), 152.1 (C=O, major), 151.7 (C=O, minor), 142.2 (CH, major), 141.5 (CH, minor), 133.9 (CH, Bz, major), 133.4 (CH, Bz, minor), 133.2 (Cq, Bz, minor), 132.3 (Cq, Bz, major), 129.8 (2CH, Bz, major), 129.4 (2CH, Bz, minor), 128.3 (2CH, Bz, major), 128.1 (2CH, Bz, minor), 120.9 (d, *J* = 4.4 Hz, CH, minor), 119.4 (CH, major), 89.4 (d, *J*= 19.4 Hz, Cq, COH, minor), 89.0 (d, *J*= 18.3 Hz, Cq, COH, major), 85.2 (d, *J*= 1.2 Hz, CH, minor), 80.5 (d, *J*= 1.4 Hz, CH, major), 79.3 (d, *J*= 181.5 Hz, CH_2F, minor), 78.1 (d, *J*= 181.6 Hz, CH_2 F, major), 34.4 (CH_2, major), 34.3 (CH_2, minor), 21.8 (CH_2, minor), 21.7 (CH_2, major), 13.57 (CH_3, minor), 13.55 (CH_3, major) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -221.5 (ddd, *J*=46.8 Hz, *J*=46.6 Hz, *J*=2.9 Hz, 85%), -222.0 (td, *J*=46.1 Hz, *J*=3.4 Hz, 15%) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{16}H_{18}FKNO_4$: $[M+K]^+$ 346.0857, Found: 346.0856.

***trans*-3-benzoyl-4-propyl-5-prop-2-yn-1-yl-1,3-oxazolidin-2-one 10.** Oil (38 mg, 35% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 95/5). IR (KBr): 3285, 2125, 1790, 1687, 1375 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68-7.65 (m, 2H, Bz), 7.56-7.52 (m, 1H, Bz), 7.44-7.52 (m, 2H, Bz), 4.57 (dt, *J* = 7.5 Hz, *J* = 5.4 Hz, 1H, CH), 4.35 (dt, *J* = 5.9 Hz, *J* = 2.9 Hz, 1H, CH), 2.96 (ddd, *J* = 17.2 Hz, *J* = 6.3 Hz, *J* = 2.7 Hz, 1H, CH_2), 2.67 (dt, *J* = 17.2 Hz, *J* = 2.7 Hz, 1H, CH_2), 2.13 (t, *J* = 2.7 Hz, 1H, C_{sp}-H), 1.85-1.70 (m, 2H, CH_2), 1.63-1.46 (m, 2H, CH_2), 1.01 (t, *J* = 7.3 Hz, 3H, CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 170.1 (C=O, Bz), 152.7(C=O, Bz), 133.2 (Cq, Bz), 132.5 (CH, Bz), 129.1 (2CH, Bz), 127.9 (2CH, Bz), 78.2 (CH), 77.7 (C_{sp}-q), 72.6 (C_{sp}-H), 57.8 (CH), 36.6 (CH_2), 21.6 (CH_2), 17.9 (CH_2), 13.7 (CH_3) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{16}H_{17}KNO_3$: $[M+K]^+$ 310.0846, Found: 310.0843.

1-((3-(Trifluoromethyl)phenyl)ethynyl)cyclohexyl) tosyl-λ²-azanecarboxylate 11. White solid (419 mg, 79% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 85/15). IR (KBr): 3355, 3261, 2358, 1753, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ =7.82-7.79 (m, 2H), 7.68-7.67 (m, 1H), 7.60-7.54 (m, 2H), 7.44.7.40 (m, 1H), 7.29-7.27 (m, 2H), 5.13 (br, 1H, NH), 2.41 (s, 3H, Ts-CH_3), 2.03-2.00 (m, 2H, CH_2), 1.78-1.56 (m, 8H, CH_2), 1.34-1.27 (m, 2H, CH_2) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 150.5 (C=O), 143.5 (Cq, Tos), 139.2 (Cq, Tos), 134.8 (q, *J* = 1.2 Hz, CH), 130.9 (q, *J* = 32.3 Hz, C-CF_3), 129.7 (2CH, Tos), 128.8 (2CH, Tos), 128.7 (Cq), 128.5 (q, *J* = 3.8 Hz, CH), 126.4 (CH), 124.8

(q, *J* = 3.8 Hz, CH), 123.7 (q, *J* = 272.2 Hz, CF_3), 94.5 (Cq), 82.9 (Cq), 69.2 (Cq), 39.9 ($2CH_2$), 25.2 (CH_2), 23.4 ($2CH_2$), 21.5 (Ts-CH_3) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{23}H_{22}KF_3NO_4S$: $[M+K]^+$ 504.0859, Found: 504.0860.

(*E*)-3-tosyl-4-(3-(trifluoromethyl)benzilidene)-1-oxa-3-azaspiro[4.5]decan-2-one 12. White solid (113 mg, 71% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 85/15). IR (KBr): 3229, 1790, 1333, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ =7.64-7.37 (m, 6H), 7.24-7.22 (m, 2H), 6.05 (s, 1H, =CH), 2.41 (s, 3H, Ts-CH_3), 1.76-1.50 (m, 8H, CH_2), 0.92-0.82 (m, 2H, CH_2) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 152.3 (C=O), 145.9 (Cq, Tos), 138.6 (Cq), 136.5 (Cq), 134.5 (Cq, Tos), 131.8 (CH), 130.7 (q, *J* = 32.4 Hz, C-CF_3), 129.5 (2CH, Tos), 128.8 (q, *J* = 1.2 Hz, CH), 128.7 (2CH, Tos), 125.2 (q, *J* = 3.8 Hz, CH), 124.1 (q, *J* = 3.8 Hz, CH), 124.0 (q, *J* = 272.5 Hz, CF_3), 111.5 (CH), 87.6 (Cq), 35.6 ($2CH_2$), 24.6 ($2CH_2$), 21.72 (Ts-CH_3), 21.67 (CH_2) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{23}H_{22}KF_3NO_4S$: $[M+K]^+$ 504.0859, Found: 504.0857.

4-(fluoro(3-(trifluoromethyl)phenyl)methyl)-4-hydroxy-3-tosyl-1-oxa-3-azaspiro[4.5]decan-2-one 13. Reaction gave a complex mixture of inseparable compounds that has been analyzed both with high-resolution mass spectrometry and ^{13}C, ^{19}F, ^1H -NMR. Data gave us evidence of the presence in the mixture of compound **13**. The mixture, analyzed with MALDI-TOF HR-Mass spectrometry, gave, for compound **13**, two peak corresponding at $[M+Na]^+$ and at $[M+K]^+$ with the same isotopic profile of the calculated one for the same molecular formula (see Supporting Information). Moreover, we found, in ^{13}C-NMR, characteristic doublet of CHF at 91.6 ppm with $J_{C\text{-}F}$ = 187.6 Hz and characteristic doublets in^{19}F-NMR at -187.8 ppm and in ^1H- NMR at 5.73 sharing the same coupling constant of $J_{H\text{-}F}$ = 43.0 Hz.

4-fluoro-3-oxobutyl tosylcarbamate 18. White solid (46 mg, 82% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 60/40). IR (KBr): 3359, 3261, 1739, 1310, 672 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.89-7.87 (m, 2H, Tos), 7.34-7.32 (m, 2H, Tos), 5.28 (br, 2H, NH), 4.79 (d, $J_{H\text{-}F}$ = 47.3 Hz, 2H, CH_2F), 4.37 (d, *J* = 6.0 Hz, 2H, CH_2), 2.84 (d, *J* = 6.0 Hz, 2H, CH_2), 2.44 (s, 3H, Me, Tos) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 204.0 (d, *J* = 19.9 Hz, C=O), 150.5 (C=O), 145.2 (Cq, Tos), 135.4 (Cq, Tos), 129.7 (2CH, Tos), 128.3 (2CH, Tos), 85.0 (d, *J* = 184.5 Hz, CH_2F), 60.5 (CH_2), 37.1

(CH_2), 21.7 (CH_3, Tos) ppm; ^{19}F NMR (376.4 MHz, $CDCl_3$): δ = -229.0 (t, *J*=47.3 Hz) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{12}H_{15}FNO_5S$: $[M+H]^+$ 304.0655, Found: 304.0651.

5-(fluoromethyl)-5-hydroxy-1-tosylimidazolidin-2-one 21 + *N*-((3-fluoro-2-oxopropyl)carbamoyl)-4-methylbenzenesulfonamide 22. White solid (69 mg, 82% yield) after purification by flash chromatography (*n*-Hexane/EtOAc: 40/60). IR (KBr): 3359, 3322, 1748, 1669, 1352, 667 cm^{-1}; ^1H NMR (400 MHz, DMSO): δ = 7.87-7.85 (m, 2H, Tos, **21**), 7.71-7.69 (m, 2H, Tos, **22**), 7.58 (br, 2H, NH, **22**), 7.40-7.38 (m, 2H, Tos, **21**), 7.36-7.34 (m, 2H, Tos, **22**), 7.27 (br, 2H, NH, **21**), 5.04 (d, J_{H-F} = 46.6 Hz, 2H, CH_2F, **22**), 4.92 (dd, J_{H-F} = 46.7 Hz, J_{H-H} = 9.3 Hz, 1H, CH_2F, **21**), 4.53 (dd, J_{H-F} = 46.3 Hz, J_{H-H} = 9.3 Hz, 1H, CH_2F, **21**), 3.95 (d, *J* = 5.2 Hz, 2H, CH_2, **22**), 3.56 (dd, J_{H-H} = 10.6 Hz, J_{H-F} = 2.1 Hz, 1H, CH_2, **21**), 3.35 (br, 1H, OH, **21**), 3.19 (dd, J_{H-H} = 10.6 Hz, J_{H-F} = 2.1 Hz, 1H, CH_2, **21**), 3.38 (s, 3H, CH_3, Tos, **21**), 2.36 (s, 3H, CH_3, Tos, **22**) ppm; ^{13}C NMR (100.6 MHz, DMSO): δ = 202.1 (d, *J* = 16.4 Hz, C=O, **22**), 153.8 (NC=O, **21**), 151.5 (NC=O, **22**), 144.0 (Cq, Tos, **21**), 143.8 (Cq, Tos, **22**), 137.2 (Cq, Tos, **22**), 137.0 (Cq, Tos, **21**), 129.5 (2CH, Tos, **22**), 129.1 (2CH, Tos, **21**), 128.3 (2CH, Tos, **21**), 127.2 (2CH, Tos, **22**), 89.4 (d, *J* = 21.8 Hz, COH, **21**), 84.2 (d, *J* = 178.4 Hz, CH_2F, **22**), 83.4 (d, *J* = 172.9 Hz, CH_2F, **21**), 48.8 (d, *J* = 2.3 Hz, CH_2, **21**), 45.9 (CH_2, **22**), 21.1 (CH_3, Tos, **21**), 21.0 (CH_3, Tos, **22**) ppm; ^{19}F NMR (376.4 MHz, DMSO): δ = -223.5 (d, *J*=46.5 Hz, 78%, **21**), -234.3 (d, *J*=46.6 Hz, 22%, **22**) ppm; HRMS m/z (ESI) positive ion, calculated for $C_{11}H_{14}FN_2O_4S$: $[M+H]^+$ 289.0658, Found: 289.0660.

*4.6. Typical one-flask preparation of fluorohydrins 4/6 directly from propargylic alcohols. One-flask preparation 4-(Fluoromethyl)-4-hydroxy-3-tosyl-1-oxa-3-azaspiro[4.4]nonan-2-one **4b**.*

To a solution of 1-ethynylcyclopentan-1-ol (170 mg, 1,54 mmol, 1 equiv.) in 4 mL of dry CH_3CN were added, under N_2, Et_3N (16 mg, 0.154 mmol, 0.1 equiv.), $AgNO_3$ (26 mg, 0.1 equiv.) and TsNCO (304 mg, 1.54 mmol, 1 equiv.) dropwise via syringe at room temperature. After complete addition, the reaction was allowed to stir at 80 °C for 2 hours. Then, Selectfluor (1091 mg, 0.31 mmol, 2 equiv.) was added to the reaction mixture which was allowed to stir at 80 °C for additional 2 hours. Upon completion, the solvent was then stripped off and the crude was purified by flash chromatography (*n*-Hexane/EtOAc: 80/20) to give 4-(Fluoromethyl)-4-hydroxy-3-tosyl-1-oxa-3-azaspiro[4.4]nonan-2-one **4b** (370 mg, 71% yield).

Acknowledgements

We gratefully acknowledge the University of L'Aquila for financial support.

Supporting Information.

^{1}H and ^{13}C NMR spectra; NOESY of **4d** and **10**; HRMS of **13**.

References

[1] P. Kirsch, Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications, Wiley-VCH, Weinheim, 2013.

[2] T. Hiyama, Organofluorine Compounds: Chemistry and Applications (Ed.: H. Yamamoto), Springer, Berlin, 2000.

[3] J.L. Howard, Y. Sagatov, L. Repusseau, C. Schotten, D.L. Browne, Controlling reactivity through liquid assisted grinding: the curious case of mechanochemical fluorination, Green Chem. 19 (2017) 2798-2802.

[4] M.K. Narayanam, G. Ma, P.A. Champagne, K.N. Houk, J.M. Murphy, Synthesis of [^{18}F]Fluoroarenes by Nucleophilic Radiofluorination of N-Arylsydnones, Angew. Chem. Int. Ed. 56 (2017) 13006-13010.

[5] X. Ma, M. Diane, G. Ralph, C. Chen, M.R. Biscoe, Stereospecific Electrophilic Fluorination of Alkylcarbastannatrane Reagents, Angew. Chem. Int. Ed. 56 (2017) 12663-12667.

[6] Z. Zhao, L. Racicot, G.K. Murphy, Fluorinative Rearrangements of Substituted Phenylallenes Mediated by (Difluoroiodo)toluene: Synthesis of α-(Difluoromethyl)styrenes, Angew. Chem. Int. Ed. 56 (2017) 11620-11623.

[7] Y. Zhang, W. Yan, Y. Wang, Z. Weng, Copper-Catalyzed Synthesis of Indol-3-yl α-(Difluoromethyl)-α-(trifluoromethyl)carbinols: Construction of Difluoromethylated sp^3 Carbon Centers, Org. Lett. 19 (2017) 5478-5481.

[8] A.L. Trifonov, V.V. Levin, M.I. Struchkova, A.D. Dilman, Difluoromethylation of Carboxylic Acids via the Addition of Difluorinated Phosphorus Ylide to Acyl Chlorides, Org. Lett. 19 (2017) 5304-5307.

[9] Y. Gao, Z. Hu, J. Dong, J. Liu, X. Xu, Chemoselective Double Annulation of Two Different Isocyanides: Rapid Access to Trifluoromethylated Indole-Fused Heterocycles, Org. Lett. 19 (2017) 5292-5295.

[10] Q. Zhao, T. Poisson, X. Pannecouke, J.-P. Bouillon, T. Besset, Pd-Catalyzed Diastereoselective Trifluoromethylthiolation of Functionalized Acrylamides, Org. Lett. 19 (2017) 5106-5109.

[11] L. Yang, S. Li, L. Cai, Y. Ding, L. Fu, Z. Cai, H. Ji, G. Li, Palladium-Catalyzed C–H Trifluoroethoxylation of N-Sulfonylbenzamides, Org. Lett. 19 (2017) 2746-2749.

[12] A.C. Sather, S.L. Buchwald, The Evolution of Pd^0/Pd^{II}-Catalyzed Aromatic Fluorination, Acc. Chem. Res. 49 (2016) 2146-2157.

[13] N.O. Ilchenko, M.A. Cortés, K.J. Szabó, Palladium-Catalyzed Iodofluorination of Alkenes Using Fluoro-Iodoxole Reagent, ACS Catal. 6 (2016) 447-450.

[14] B.J. Groendyke, D.I. AbuSalim, S.P. Cook, Iron-Catalyzed, Fluoroamide-Directed C-H Fluorination, J. Am. Chem. Soc. 138 (2016) 12771-12774.

[15] J. Mirý, C. del Pozo, F.D. Toste, S. Fustero, Enantioselective Palladium-Catalyzed Oxidative β,β-Fluoroarylation of α,β-Unsaturated Carbonyl Derivatives, Angew. Chem. Int. Ed. 55 (2016) 9045-9049.

[16] I. Saidalimu, M. Guo, E. Tokunaga, N. Shibata, Direct Fluoro-aminosulfenylation of Active Methylenes by Dialkylaminosulfur Trifluorides under Catalyst-Free Conditions, Asian J. Org. Chem. 5 (2016) 1208-1212.

[17] H. Sun, Y. Zhang, P. Chen, Y.-D. Wu, X. Zhang, Y. Huang, Ligand-Assisted Palladium(II)/(IV) Oxidation for sp^3 C-H Fluorination, Adv. Synth. Catal. 358 (2016) 1946-1957.

[18] Q. Wang, Y. Jiang, R. Sun, X.-Y. Tang, M. Shi, Gold-Catalyzed Fluorination–Hydration: Synthesis of α-Fluorobenzofuranones from 2-Alkynylphenol Derivatives, Chem. Eur. J. 22 (2016) 14739-14745.

[19] X. Zeng, S. Liu, Z. Shi, G. Liu, B. Xu, Synthesis of α-Fluoroketones by Insertion of HF into a Gold Carbene, Angew. Chem. Int. Ed. 55 (2016) 10032-10036.

[20] J. Zhang, H. Zhang, D. Shi, H. Jin, Y. Liu, Facile and Diverse Synthesis of Benzo[b]fluorenone Derivatives through a Copper/Selectfluor-Catalyzed Tandem Annulation of 1,6-Enynes, Eur. J. Org. Chem. (2016) 5545-5558.

[21] D. Heeran, G. Sandford, Fluorination of pyrrole derivatives by Selectfluor, Tetrahedron 72 (2016) 2456-2463.

[22] K. Sato, G. Sandford, K. Shimizu, S. Akiyama, M.J. Lancashire, D.S. Yufit, A. Tarui, M. Omote, I. Kumadaki, S. Harusawa, A. Ando, Synthesis of fluorinated isoxazoles using Selectfluor: preparation and characterization of 4-fluoroisoxazole, 4,4,5-trifluoroisoxazoline and 4,4-difluoro-5-hydroxyisoxazoline systems from one-pot and multi-step processes, Tetrahedron 72 (2016) 1690-1698.

[23] P.R. Savoie, J.T. Welch, Preparation and Utility of Organic Pentafluorosulfanyl-Containing Compounds, Chem. Rev. 115 (2015) 1130-1190.

[24] X. Yang, T. Wu, R.J. Phipps, F.D. Toste, Advances in Catalytic Enantioselective Fluorination, Mono-, Di-, and Trifluoromethylation, and Trifluoromethylthiolation Reactions, Chem. Rev. 115 (2015) 826-870.

[25] T. Liang, C.N. Neumann, T. Ritter, Introduction of Fluorine and Fluorine-Containing Functional Groups, Angew. Chem. Int. Ed. 52 (2013) 8214-8264.

[26] M.F. Kuehnel, D. Lentz, T. Braun, Synthesis of Fluorinated Building Blocks by Transition-Metal-Mediated Hydrodefluorination Reactions, Angew. Chem. Int. Ed. 52 (2013) 3328-3348.

[27] C. Hollingworth, V. Gouverneur, Transition metal catalysis and nucleophilic fluorination, Chem. Commun. 48 (2012) 2929-2942.

[28] G. Liu, Transition metal-catalyzed fluorination of multi carbon–carbon bonds: new strategies for fluorinated heterocycles, Org. Biomol. Chem. 10 (2012) 6243-6248.

[29] J. Wang, M. Sánchez-Roselló, J.L. Aceña, C. del Pozo, A.E. Sorochinsky, S. Fustero, V.A. Soloshonok, H. Liu, Fluorine in Pharmaceutical Industry: Fluorine-Containing Drugs Introduced to the Market in the Last Decade (2001–2011), Chem. Rev. 114 (2014) 2432-2506.

[30] W. Yuan, K.J. Szabó, Catalytic Intramolecular Aminofluorination, Oxyfluorination, and Carbofluorination with a Stable and Versatile Hypervalent Fluoroiodine Reagent, Angew. Chem. Int. Ed. 54 (2015) 8533-8537.

[31] Z. Li, L. Song, C. Li, Silver-Catalyzed Radical Aminofluorination of Unactivated Alkenes in Aqueous Media, J. Am. Chem. Soc. 135 (2013) 4640-4643.

[32] T. Wu, J. Cheng, P. Chen, G. Liu, Regioselective palladium-catalyzed intramolecular oxidative aminofluorination of unactivated alkenes, Chem. Commun. 49 (2013) 8707-8709.

[33] T. Xu, X. Mu, H. Peng, G. Liu, Silver-Catalyzed Intramolecular Aminofluorination of Activated Allenes, Angew. Chem. Int. Ed. 50 (2011) 8176-8179.

[34] T. Wu, G. Yin, G. Liu, Palladium-Catalyzed Intramolecular Aminofluorination of Unactivated Alkenes, J. Am. Chem. Soc. 131 (2009) 16354-16355.

[35] J. Zhao, M. Jiang, J.-T. Liu, Synthesis of Fluoromethyl-Substituted Isoxazolines via Transition Metal-Free Oxyfluorination of Alkenyl Oximes, Adv. Synth. Catal. 359 (2017) 1626-1630.

[36] N.O. Ilchenko, M. Hedberg, K. Szabó, Fluorinative ring-opening of cyclopropanes by hypervalent iodine reagents. An efficient method for 1,3-oxyfluorination and 1,3-difluorination, J. Chem. Sci. 8 (2017) 1056-1061.

[37] H. Wu, B. Yang, L. Zhu, R. Lu, G. Li, H. Lu, High-Valent Palladium-Promoted Formal Wagner–Meerwein Rearrangement, Org. Lett. 18 (2016) 5804-5807.

[38] J.-F. Zhao, X.-H. Duan, H. Yang, L.-N. Guo, Transition-Metal-Free Oxyfluorination of Olefinic Amides for the Synthesis of Fluorinated Heterocycles, J. Org. Chem. 80 (2015) 11149-11155.

[39] D. Parmar, M. Rueping, Mild and metal-free oxy- and amino-fluorination for the synthesis of fluorinated heterocycles, Chem. Commun. 50 (2014) 13928-13931.

[40] L.F. Lourie, Y.A. Serguchev, M.V. Ponomarenko, E.B. Rusanov, M.V. Vovk, N.V. Ignat'ev, Electrophilic fluorocyclization of unsaturated alcohols in ionic liquids, Tetrahedron 69 (2013) 833-838.

[41] Z. Yuan, H. Peng, G. Liu, Palladium-Catalyzed Intramolecular Fluorooxylation of Styrenes, Chin. J. Chem. 31 (2013) 908-914.

[42] B. Lü, C. Fu, S. Ma, Study on the selectivity in the electrophilic monofluorination of 2,3-allenoates with Selectfluor: an efficient synthesis of 4-fluoro-2(5H)-furanones and 3-fluoro-4-oxo-2(E)-alkenoates, Org. Biomol. Chem. 8 (2010) 274-281.

[43] S.C. Wilkinson, O. Lozano, M. Schuler, M.C. Pacheco, R. Salmon, V. Gouverneur, Electrophilic Fluorocyclization of Allyl Silanes, Angew. Chem. Int. Ed. 48 (2009) 7083-7086.

[44] C. Zhou, Z. Ma, Z. Gu, C. Fu, S. Ma, An Efficient Approach for Monofluorination via Aqueous Fluorolactonization Reaction of 2,3-Allenoic Acids with Selectfluor, J. Org. Chem. 73 (2008) 772-774.

[45] X. Yang, L. He, G.C. Tsui, Hydroxytrifluoromethylation of Alkenes Using Fluoroform-Derived $CuCF_3$, Org Lett. 19 (2017) 2446-2449.

[46] J.R. Wolstenhulme, J. Rosenqvist, O. Lozano, J. Ilupeju, N. Wurz, K.M. Engle, G.W. Pidgeon, P.R. Moore, G. Sandford, V. Gouverneur, Asymmetric Electrophilic Fluorocyclization with Carbon Nucleophiles, Angew. Chem. Int. Ed. 52 (2013) 9796-9800.

[47] Y. Liu, J. Zhu, J. Qian, Z. Xu, Gold-Catalyzed Simultaneous Formation of C–C, C═O, and C–F bonds in the Presence of Selectfluor: A Synthesis of Fluoroindenes from Allene Esters, J. Org. Chem. 77 (2012) 5411-5417.

[48] H. Egami, J. Asada, K. Sato, D. Hashizume, Y. Kawato, Y. Hamashima, Asymmetric Fluorolactonization with a Bifunctional Hydroxyl Carboxylate Catalyst, J. Am. Chem. Soc. 137 (2015) 10132-10135.

[49] S. Suzuki, T. Kamo, K. Fukushi, T. Hiramatsu, E. Tokunaga, T. Dohi, Y. Kita, N. Shibata, Iodoarene-catalyzed fluorination and aminofluorination by an Ar-I/HF·pyridine/mCPBA system, Chem. Sci. 5 (2014) 2754-2760.

[50] N. Asari, Y. Takemoto, Y. Shinomoto, T. Yagyu, A. Yoshimura, V.V. Zhadankin, A. Saito, Catalytic Cycloisomerization–Fluorination Sequence of N-Propargyl Amides by Iodoarene/HF Pyridine/Selectfluor Systems, Asian J. Org. Chem. 5 (2016) 1314-1317.

[51] Y. Jeong, B.-I. Kim, J.K. Lee, J.-S. Ryu, Direct Synthesis of 4-Fluoroisoxazoles through Gold-Catalyzed Cascade Cyclization–Fluorination of 2-Alkynone O-Methyl Oximes, J. Org. Chem. 79 (2014) 6444-6455.

[52] L. Yang, X. Ma, F. Song, J. You, Silver-catalyzed one-pot cyclization/fluorination of 2-alkynylanilines: highly efficient synthesis of structurally diverse fluorinated indole derivatives, Chem. Commun. 50 (2014) 3024-3026.

[53] D. Malhotra, L. Liu, W. Wang, M. Durham, G.B. Hammond, B. Xu, Gold catalyzed synthesis of fluorinated tetrahydrofurans and lactones, J. Fluorine Chem. 167 (2014) 179-183.

[54] S. Li, Z. Li, Y. Yuan, Y. Li, L. Zhang, Y. Wu, Gold(I)-Catalyzed Aminohalogenation of Fluorinated N′-Aryl-N-Propargyl Amidines for the Synthesis of Imidazole Derivatives under Mild Conditions, Chem. Eur. J. 19 (2013) 1496-1501.

[55] J. Qian, Y. Liu, J. Zhu, B. Jiang, Z. Xu, A Novel Synthesis of Fluorinated Pyrazoles via Gold(I)-Catalyzed Tandem Aminofluorination of Alkynes in the Presence of Selectfluor, Org. Lett. 13 (2011) 4220-4223.

[56] A. Simonneau, P. Garcia, J.-P. Goddard, V. Mouriès-Mansuy, M. Malacria, L. Fensterbank, Combination of gold catalysis and Selectfluor for the synthesis of fluorinated nitrogen heterocycles, Beilstein J. Org. Chem. 7 (2011) 1379-1386.

[57] T. de Haro, C. Nevado, Gold-Catalyzed Synthesis of α-Fluoro Acetals and α-Fluoro Ketones from Alkynes, Adv. Synth. Catal. 352 (2010) 2767-2772.

[58] M. Schuler, F. Silva, C. Bobbio, A. Tessier, V. Gouverneur, Gold(I)-Catalyzed Alkoxyhalogenation of β-Hydroxy-α,α-Difluoroynones, Angew. Chem. Int. Ed. 47 (2008) 7927-7930.

[59] A. Arcadi, E. Pietropaolo, A. Alvino, V. Michelet, Aminofluorination of 2-alkynylanilines: a Au-catalyzed entry to fluorinated indoles, Beilstein J. Org. Chem. 10 (2014) 449-458.

[60] A. Arcadi, E. Pietropaolo, A. Alvino, V. Michelet, One-Pot Gold-Catalyzed Aminofluorination of Unprotected 2-Alkynylanilines, Org Lett. 15 (2013) 2766-2769.

[61] A.R. Renslo, G.W. Luehr, M.F. Gordeev, Recent developments in the identification of novel oxazolidinone antibacterial agents, Bioorg. Med. Chem. 14 (2006) 4227-4240.

[62] T.A. Mukhtar, G.D. Wright, Streptogramins, Oxazolidinones, and Other Inhibitors of Bacterial Protein Synthesis, Chem. Rev. 105 (2005) 529-542.

[63] A. Arnoldi, E. Betto, G. Farina, A. Formigoni, R. Galli, A. Griffin, Synthesis of some 3-phenyl-1-substituted(or 1,1- disubstituted)prop-2-yn-1-ols and their in-vivo activity against some phytopathogenic fungi, Pestic. Sci. 13 (1982) 670-678.

[64] S. Yan, M.J. Miller, T.A. Wencewicz, U. Möllmann, Syntheses and antibacterial activity studies of new oxazolidinones from nitroso Diels–Alder chemistry, Bioorg. Med. Chem. Lett. 20 (2010)1302-1305.

[65] T.A. Mukhtar, G.D. Wright, Streptogramins, Oxazolidinones, and Other Inhibitors of Bacterial Protein Synthesis, Chem. Rev. 105 (2005) 529-542.

[66] H. Kakeya, M. Morishita, H. Koshino, T.-i. Morita, K. Kobayashi, H. Osada, Cytoxazone: A Novel Cytokine Modulator Containing a 2-Oxazolidinone Ring Produced by *Streptomyces* sp., J. Org. Chem. 64 (1999) 1052-1053.

[67] H. Prücher, R. Gottschlich, A. Haase, M. Stohrer, C. Seyfried, (5S)-3-aryl-5-(1-piperidinylmethyl)-2-oxazolidinones, a new class of potential neuroleptics with a high affinity for sigma receptors, Bioorg. Med. Chem. Lett. 2 (1992) 165-170.

[68] S.H. Rosenberg, H.D. Kleinert, H.H. Stein, D.L. Martin, M.A. Chekal, J. Cohen, D.A. Egan, K.A. Tricarico, W.R. Baker, Design of a well-absorbed renin inhibitor, J. Med. Chem. 34 (1991) 469-471.

[69] K.S. Gates, R.B. Silverman, 5-(Aminomethyl)-3-aryl-2-oxazolidinones. A novel class of mechanism-based inactivators of monoamine oxidase B, J. Am. Chem. Soc. 112 (1990) 9364-9372.

[70] J.-P. Bégué, D. Bonnet-Delpon, Bioorganic and Medicinal Chemistry of Fluorine, Wiley, Hoboken, 2008.

[71] M.R. Karagas, Jr.G.L. Cushing, E.R. Greeberg, L.A. Mott, S.K. Spencer, D.W. Nierenberg, Non-melanoma skin cancers and glucocorticoid therapy, Br. J. Cancer, 85 (2001) 683-686.

[72] J. Zhao, M. Jiang, J.-T. Liu, Synthesis of Fluoromethyl-Substituted Isoxazolines via Transition Metal-Free Oxyfluorination of Alkenyl Oximes, Adv. Synth. Catal. 359 (2017) 1626-1630 and references therein.

[73] Y.-C. Han, Y.-D. Zhang, Q. Jia, J. Cui, C. Zhang, Hypervalent-Iodine-Mediated Ring-Contraction Monofluorination Affording Monofluorinated Five-Membered Ring-Fused Oxazolines, Org. Lett. 19 (2017) 5300-5303.

[74] K. Ohe, T. Ishihara, N. Chatani, Y. Kawasaki, S. Murai, A facile preparation of 4-alkylidene-3-tosyloxazolidin-2-ones from propargylic alcohols and p-toluenesulfonyl isocyanate using a cuprous iodide/triethylamine catalyst, J. Org. Chem. 56 (1991) 2267-2268.

[75] K. Sekine, T. Mawatari, T. Yamada, Synthesis of Oxazolidin-2-ones by Tandem Cyclization of Propargylic Alcohols and Phenyl Isocyanate Promoted by Silver Catalysts as π-Lewis Acids, Synlett 26 (2015) 2447-2450 and references therein.

[76] Y. Li, X. Jiang, C. Zhao, X. Fu, X. Xu, P. Tang, Silver-Catalyzed Anti-Markovnikov Hydroxyfluorination of Styrenes, ACS Catal. 7 (2017) 1606-1609.

[77] C. Wang, J. Cai, M. Zhang, X. Zhao, Ag-Assisted Fluorination of Unprotected 4,6-Disubstituted 2-Aminopyrimidines with Selectfluor, J. Org. Chem. 82 (2017) 1260-1265.

[78] J. Huang, L. Li, H. Chen, T. Xiao, Y. He, L. Zhou, Silver-catalyzed geminal aminofluorination of diazoketones with anilines and N-fluorobenzenesulphonimide, Org. Chem. Front. 4 (2017) 529- 533.

[79] H. Chen, L. Zhu, C. Li, Silver-catalyzed radical carbofluorination of unactivated alkenes with acetic acid in aqueous solution, Org. Chem. Front. 4 (2017) 565-568.

[80] Y.-L. Zhu, A.-F. Wang, J.-Y Du, B.-R. Leng, S.-J Tu, D.-C. Wang, P. Wei, W.-J. Hao, B. Jiang, Ag-Catalyzed difluorohydration of β-alkynyl ketones for diastereoselective synthesis of 1,5-dicarbonyl compounds, Chem. Commun. 53 (2017) 6397-6400.

[81] R. Ramesh, Y. Chandrasekaran, R. Megha, S. Chandrasekaran, Base catalyzed cyclization of N-aryl and N-alkyl-O-propargyl carbamates to 4-alkylidene-2-oxazolidinones, Tetrahedron 63 (2007) 9153-9162.

[82] Y. Tamaru, M. Kimura, S. Tanaka, S. Kure, Z. Yoshida, Convenient Synthesis of 4-Methylene-2-oxazolidinones and 4-Methylenetetrahydro-1,3-oxazin-2-ones via Transition-Metal Catalyzed Intramolecular Addition of Nitrogen Atom to Acetylenic Triple Bond, Bull. Chem. Soc. Jpn. 67 (1994) 2838-2849.

[83] M. Kimura, S. Kure, Z. Yoshida, S. Tanaka, K. Fugami, Y. Tamaru, Convenient synthesis of densely functionalized N-substituted 4-methylene-2-oxazolidinone, Tetrahedron Lett. 31 (1990) 4887-4890.

[84] K. Chen, S. Zhu, NHC–AuCl/Selectfluor: An Efficient Catalytic System for π-Bond Activation, Sylett 28 (2017) 640-653.

[85] S. Ritter, Y. Horino, J. Lex, H.-G. Schmalz, Gold-Catalyzed Cyclization of O-Propargyl Carbamates under Mild -Conditions: A Convenient Access to 4-Alkylidene-2-oxazolidinones, Synlett 17 (2006) 3309-3313.

[86] B. Tréguier, S.P. Roche, Double Annulative Cascade of Tryptophan-Containing Peptides Triggered by Selectfluor, Org. Lett. 16 (2014) 278-281.

[87] T.M. Nguyen, H.A. Duong, J.-A. Richard, C.W. Johannes, F. Pincheng, D. Kwong Jia Ye, E.L. Shuying, Cascade fluorofunctionalisation of 2,3-unsubstituted indoles by means of electrophilic fluorination, Chem. Commun. 49 (2013) 10602-10604.

[88] L.F. Lourie, Y.A. Serguchev, M.V. Ponomarenko, E.B. Rusanov, M.V. Vovk, N.V. Ignat'ev, Electrophilic fluorocyclization of unsaturated alcohols in ionic liquids, Tetrahedron 69 (2013) 833-838.

[89] Y.H. Lim, Q. Ong, H.A. Duong, T.M. Nguyen, C.W. Johannes, Direct Conversion of Indoles to 3,3-Difluoro-2-oxindoles via Electrophilic Fluorination, Org. Lett. 14 (2012) 5676-5679.

[90] G. Bianchi, M. Chiarini, F. Marinelli, L. Rossi, A. Arcadi, Product Selectivity Control in the Heteroannulation of o-(1-Alkynyl)benzamides, Adv. Synth. Catal. 352 (2010) 136-142.

[91] J. Zhou, X. Jiang, C. Jin, Z. Guo, B. Su, W. Su, One-Pot L-Proline-Mediated Stereoselective α-C(sp2)–H Fluorination of α,β-Unsaturated Aldehydes through Methoxyfluorination–Elimination, Eur. J. Org. Chem. 2017, 3631-3634.

[92] J.K. Howard, M. Müller, A. Berry, A. Nelson, An Enantio- and Diastereoselective Chemoenzymatic Synthesis of α-Fluoro β-Hydroxy Carboxylic Esters, Angew. Chem. Int. Ed. 55 (2016) 6767-6770.

[93] A. Arcadi, Regio and Stereoselective Synthesis of (E)-4-Arylidene/alkenylidene-3-tosyloxazolidin-2-ones through Palladium-Catalyzed Reactions of Aryl Iodides/Vinyl Triflates with Propargyl Tosylcarbamates, Synlett, 8 (1997) 941-943.

[94] Y. Yin, W. Ma, Z. Chai, G. Zhao, Et_2Zn-catalyzed intramolecular hydroamination of alkynyl sulfonamides and the related tandem cyclization/addition reaction, *J. Org. Chem. 72 (***2007**) 5731-5736.

[95] A. Lei, X. Lu, Palladium(II)-Catalyzed Tandem Intramolecular Aminopalladation of Alkynes and Conjugate Addition. Synthesis of Oxazolidinones, Imidazolidinones, and Lactams, Org. Lett. 2 (2000) 2699-2702.

[96] S.K. Alamsetti, A.K.Å., Persson, J.-E. Bäckvall, Palladium-Catalyzed Intramolecular Hydroamination of Propargylic Carbamates and Carbamothioates, Org. Lett. 16 (2014) 1434-1437.

[97] R. Isaksson, I. Kumpina, M. Larhed, J. Wannberg, Tetrahedron Lett. 2016, 57, 1476-1478, Tetrahedron Lett. 57 (2016) 1476-1478.

[98] S.K. Alamsetti, A.K.Å., Persson, T. Jiang, J.-E. Bäckvall, Scalable Synthesis of Oxazolones from Propargylic Alcohols through Multistep Palladium(II) Catalysis: β-Selective Oxidative Heck Coupling of Cyclic Sulfonyl Enamides and Aryl Boroxines, Angew. Chem. Int. Ed. 52 (2013) 13745-13750.

[99] G. Verniest, A. Padwa, Gold- and Silver-Mediated Cycloisomerizations of N-Propargylamides, Org. Lett. 10 (2008) 4379-4382.