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Stereoselective synthesis and functionalization of *N*-alkyl-β-lactams

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ABSTRACT

Novel polyfunctionalized *N*-alkyl-β-lactams were prepared with high stereoselectivity in an efficient manner by a palladium-catalyzed [2+2] carbonylative cycloaddition of allyl bromide with heteroarylidene *N*-alkyl-amines The type of alkyl group linked to the nitrogen atom influences the reaction stereoselectivity. Moreover, the C-3 and the C-4 positions of the azetidinone ring can be further stereoselectively functionalized inserting various groups through the generation of a stable azetidinyl carbanion and then captured by various electrophiles.

1. Introduction

The β-Lactam nucleus is the key to the biological activity of a large class of compounds characterized by the presence of this four-membered ring and differentiated by side chains, unsaturations, heteroatoms, and, in many cases, by the presence of five- or six-membered rings. The successful application of β-lactam antibiotics in the treatment of infectious diseases has been well documented for many years.[1] The potential use of some β-lactams as therapeutic agents for lowering plasma cholesterol levels,[2,3] as inhibitors of enzymes such as thrombin,[4] HLE (human leukocyte elastase) [5] and the protease, responsible for capsid assembly and viral maturation of HCMV (human cytomegalovirus),[6] has been documented as well. The β-lactam structure is also the essential scaffold of several antagonists directed to the vasopressin V1 receptor,[7] and 2-azetidinones have been reported to show apoptosis-inducing properties against human solid tumor cell lines.[8] Due to the large pharmacological potential and use of the β-lactam systems, intensive research has generated numerous methods for synthetizing this skeleton, and the topic has been deeply documented and reviewed several times.[9,10] Moreover, it is known that the biological activity performed by the β-lactam molecules depends not only on the type of substituents linked to the nitrogen N-1, the C-3 and the C-4 carbon atoms of the four-membered ring, but also on the stereochemistry of the β-lactam core. Among the numerous synthetic methodologies reported in the literature for preparing β-lactam compounds, some protocols proceed with high stereoselectivity, which depends either on the synthetic procedures or on the type of starting materials employed. For instance, complete *trans*-stereoselectivity has been observed in the carbonylative ring expansion of aziridines trimethylsilylsubstituted, using $Co_2(CO)_8$ as catalyst, to give β-lactams,[11] while the coupling of alkynes with nitrones catalyzed by Cu(I)/bis(aza-ferrocene) has been reported to produce β-lactams with excellent *cis*-diastereoselectivity.[12] The stereoselectivity is very often linked to the starting materials used for building the four-membered ring. As an example, the Staudinger reaction performed starting from prochiral imine chromium complexes showed complete *cis*-diastereoselection,[13] while high *trans*-diastereoselection was observed starting from *N*-phenylsulfenylimines.[14] Recently, modifiing slightly Torii's procedure,[15] our research group has reported the palladium-catalyzed [2+2] carbonylative cycloaddition of *N*-aryl imines of different structures to allyl halides to give α-vinyl β-lactams with good stereoselectivity for *trans*-isomers.[16] In this paper, we report the different results obtained performing the cyclocarbonylation of *N*-alkyl imines with allyl bromide demonstrating how the *N*-alkyl group can influence the stereoselection and investigating the mechanism.

2. Results and discussion

Novel *cis* and/or *trans* *N*-alkyl-4-aryl-3-vinyl-2-azetidinones were stereoselectively synthetized following a palladium-catalyzed [2+2] carbonylative cycloaddition procedure. Previously known (*E*)-arylidenalkyl amines **1**–**4**,[17] **5**–**7**,[18] **8**,[19] **10**,[20] **11**,[21] and unknown **9** underwent a [2+2] cycloaddition with allyl bromide under CO

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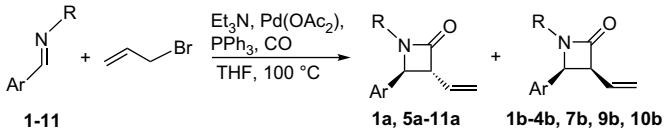
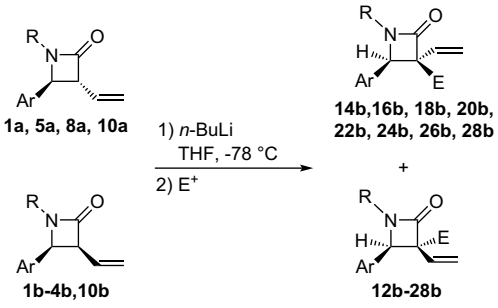
pressure (300–400 psi), in THF and $Pd(OAc)_2/PPh_3$ as the catalyst system, in the presence of triethylamine (Scheme 1), to afford the β-lactams **1a**, **5a**–**11a**, **1b**–**4b**, **7b**, **9b**, and **10b**.



Scheme 1.

The results herein reported show an interesting novelty as they highlight the strategic role played by the alkyl group, linked to the iminic nitrogen, in the β-lactam formation. For instance, the heteroarylidene *tert*-butylamines **2**–**4** afforded, by the Pd catalyzed [2+2] cycloaddition, the *cis* β-lactams **2b**–**4b** in good yields (Table 1, entries 2–4). The benzylidene *tert*-butylamine **1** produced both the diastereoisomers **1a** and **1b** but a good *cis*-diastereoselection was observed (*cis*/*trans*=90:10; Table 1, entry 1). Using the arylidene amines **5**–**11**, having at the iminic nitrogen sterically less hindered alkyl groups such as *n*-butyl (Table 1, entries 5–9), isopropyl (Table 1, entry 10), and ethyl substituents (Table 1, entry 11), a complete inversion of diastereoselectivity was noticed. For instance, the *trans*-isomer was the major product, while the *cis*-isomer was not observed or was isolated in traces. The steric hindrance of the R substituent at the lactamic nitrogen atom influences the ring formation, as showed by the results collected in Table 1. During the cyclization process, the bulky *tert*-butyl moiety drives the aryl and the vinyl groups to the same side with respect to the β-lactam ring, affording *cis*-structures. In the meantime, the *tert*-butyl moiety assumes a stable and fixed configuration lying in the opposite side with respect to the aryl and the vinyl substituents. NOESY NMR experiments performed on compounds **1b**–**4b** confirmed a high configurational stability of the nitrogen atom bearing the *tert*-butyl substituent. For instance, a strong NOESY interaction was noticed between the *tert*-butyl protons, bearing the β-lactam nitrogen, and the ones linked to the C-3 and the C-4 carbon atoms; while no interactions were observed between the *tert*-butyl and the aryl or the vinyl groups. Viceversa, in the remaining 2-azetidinones, a strong NOESY interaction was observed for the protons of the R group (*n*-Bu, *i*-Pr, and Et) either with the protons directly linked to the C-3 and the C-4 or with the protons of the aryl and the vinyl groups, indicating a fast interconversion at the nitrogen atom.

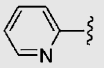
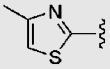
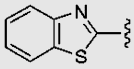
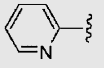
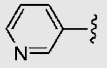
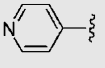
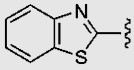
A strong energy difference also appears to persist in the carbanion generated by deprotonation of the C-3 carbon atom in the *N*-*tert*-butyl derivatives with respect to the remaining *N*-alkyl compounds. When **1b** was treated with *n*-BuLi at −78 °C in THF and quenched with an electrophile such as methyl iodide or allyl bromide, only *cis*-diastereomers **12b** and **13b** were isolated in high yields (Scheme 2 and Table 2, entries 1 and 3). The *cis*-configuration was unequivocally assigned by comparing the ^{1}H NMR chemical shift values of the vinyl moiety with those of similar structures.[22]



Scheme 2.

Analogous behaviour was showed by the functionalized products obtained from **2b**, **3b**, and **4b** after deprotonation and quenching with methyl iodide (Table 2, entries 6, 8, and 10), while in

Table 1
Synthesis of *N*-alkyl-β-lactams

Entry	Imine	R	Ar	Total yield[a] %	Product distribution[b]	
					trans	*cis*
1	**1**	*t*-Bu	Ph	85	**1a** (10)	**1b** (90)
2	**2**	*t*-Bu		78	—	**2b** (100)
3	**3**	*t*-Bu		75	—	**3b** (100)
4	**4**	*t*-Bu		75	—	**4b** (100)
5	**5**	*n*-Bu		81	**5a** (98)	**5b** (Traces)
6	**6**	*n*-Bu		79	**6a** (98)	**6b** (Traces)
7	**7**	*n*-Bu		81	**7a** (90)	**7b** (10)
8	**8**	*n*-Bu	Ph	90	**8a** (100)	—
9	**9**	*n*-Bu		78	**9a** (83)	**9b** (17)
10	**10**	*i*-Pr	Ph	95	**10a** (90)	**10b** (10)
11	**11**	Et	Ph	90	**11a** (100)	—

[a] Isolated yields.
[b] Diastereomeric ratios measured by GC and ^{1}H NMR spectroscopy.

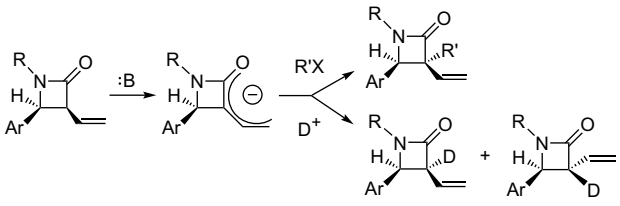
Table 2
Functionalization of *N*-alkyl-β-lactams

Entry	β-Lactam	R	E	Total yield[a] %	Product distribution[b]	
					trans	*cis*
1	**1b**	*t*-Bu	CH_3I	>99	—	**12b** (100)
2	**1a**	*t*-Bu	CH_3I	97	—	**12b** (100)
3	**1b**	*t*-Bu	CH_2=$CHCH_2Br$	95	—	**13b** (100)
4	**1a**	*t*-Bu	D_2O	>99	**14a** (22)	**14b** (78)
5	**1b**	*t*-Bu	D_2O	>99	**14a** (22)	**14b** (78)
6	**2b**	*t*-Bu	CH_3I	90	—	**15b** (100)
7	**2b**	*t*-Bu	CH_3OD	>99	**16a** (14)	**16b** (86)
8	**3b**	*t*-Bu	CH_3I	>99	—	**17b** (100)
9	**3b**	*t*-Bu	CH_3OD	92	**18a** (2)	**18b** (98)
10	**4b**	*t*-Bu	CH_3I	88	—	**19b** (100)
11	**4b**	*t*-Bu	CH_3OD	95	**20a** (15)	**20b** (85)
12	**5a**	*n*-Bu	CH_3I	>99	—	**21b** (100)
13	**5a**	*n*-Bu	CH_3OD	>99[c]	**22a** (45)	**22b** (55)
14	**8a**	*n*-Bu	CH_3I	88	—	**23b** (100)
15	**8a**	*n*-Bu	CH_3OD	97	**24a** (55)	**24b** (45)
16	**9a**	*n*-Bu	CH_3I	93	—	**25b** (100)
17	**9a**	*n*-Bu	CH_3OD	>99	**26a** (46)	**26b** (54)
18	**10a**	*i*-Pr	CH_3I	>99	—	**27b** (100)
19	**10a**	*i*-Pr	CH_3OD	>99	**28a** (30)	**28b** (70)
20	**10b**	*i*-Pr	CH_3I	93	—	**27b** (100)
21	**10b**	*i*-Pr	CH_3OD	>99	**28a** (30)	**28b** (70)

[a] Isolated yields.
[b] Diastereomeric ratios measured by GC and ^{1}H NMR spectroscopy.
[c] Total yield evaluated by GC.

the quenching with D^+ (D_2O or CH_3OD) also a small amount of the *trans*-isomers was formed (2–22%; Table 2, entries 5, 7, 9, and 11).

By deprotonation of the *trans*-isomer **1a** and quenching with CH_3I, the *cis*-diastereomer **12b** was still isolated as the only reaction product (Table 2, entry 2). Moreover, the same carbanion quenched with D^+ led to a *cis/trans* diastereomeric mixture (78:22; Table 2, entry 4). These results may be explained assuming that the alkyl halide binds the C-3 carbon from the face of the planar carbanion not hindered by the close aryl group linked at C-4 (Scheme 3), generating the *cis*-configurated β-lactam exclusively, even starting from the *trans*-isomer. A small group, instead, such as D^+ binds the C-3 indifferently from both sides of the planar carbanion leading to a *cis/trans* diastereomeric mixture (Scheme 3).



Scheme 3.

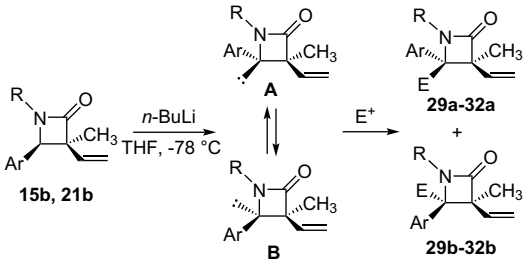
The treatment of *trans N*-*n*-butyl-β-lactams **5a**, **8a**, and **9a** with *n*-BuLi at −78 °C in THF led to the formation of a carbanion at C-3, which quenching with CH_3I still produced the functionalized *cis* β-lactams **21b**, **23b**, and **25b**, respectively (Table 2, entries 12, 14, and 16). Using, instead, the small electrophile D^+, 1:1 diastereomeric mixtures of *cis/trans* were observed (Table 2, entries 13, 15, and 17). The *N*-isopropyl-β-lactams *trans*-**10a** and *cis*-**10b** deprotonated with the same procedure described above, and quenched with D^+ produced both the same diastereomeric mixture showing *cis/trans* ratios of 70:30. The quenching, instead, of the same carbanions with CH_3I afforded the *cis*-diastereomer only. Once more, a bulky electrophile such as R′X prefers to bind the C-3 from the less hindered face of the carbanion generating *cis*-structures, exclusively. Viceversa, a small electrophile such as D^+ is not influenced by the steric hindrance of the aryl group at C-4 affording *cis/trans* diastereomeric mixtures in the proportion depending on the bulkiness of the alkyl group linked at the nitrogen atom. For instance, *t*-Bu, which is the more bulky, led preferentially to the *cis*-structure, *i*-Pr allowed an increasing amount of the *trans*-products, while *n*-Bu gave almost unitary diastereomeric ratios (Table 2).

Finally, the behavior of the carbanion generated by deprotonation of the C-4 carbon atom was investigated. When **15b** and **21b** were treated with *n*-BuLi at −78 °C in THF, and quenched with D^+, always mixtures of both diastereomers **29a**, **29b** and **31a**, **31b** were, respectively, isolated in almost 1:1 ratios (Table 3, entries 1 and 3). Viceversa, a fairly good diastereoselectivity was observed in the quenching with CH_3I leading to *trans/cis* ratios of 30:70 for **30a**, **30b** and 20:80 for **32a**, **32b**, respectively (Table 3, entries 2 and 4). These different results could be explained by the generation of a carbanion of tetrahedral structure where a more free interconversion at the β-lactamic nitrogen atom lead to a small difference of thermal stability between the structures **A** and **B** (Scheme 4). Moreover, the presence of two moieties linked at the close C-3 carbon atom could contribute to weaken the energy differences between the two structures. Then, smaller electrophiles were attacked indifferently by structures **A** and **B** having similar stability and leading to the two isomers with no diastereoselection. Bulky electrophiles, instead, even if attacked by the two carbanions **A** and **B** indifferently, preferred the less hindered *cis*-configuration for the final products, allowing a *cis*-diastereoselectivity.

Table 3
Functionalization of *N*-alkyl-3-methyl-β-lactams

Entry	β-Lactam	E	Total yield[a] %	Product distribution[b]	
				trans	*cis*
1	**15b**	D_2O	92[c]	**29a** (50)	**29b** (50)
2	**15b**	CH_3I	94	**30a** (31)	**30b** (69)
3	**21b**	D_2O	90[c]	**31a** (45)	**31b** (55)
4	**21b**	CH_3I	95	**32a** (20)	**32b** (80)

[a] Isolated yields.
[b] Diastereomeric ratios evaluated by GC and ^1H NMR spectroscopy.
[c] Total yield evaluated by GC.



Scheme 4.

3. Conclusion

We prepared in a diastereoselective way novel polyfunctionalized *N*-alkyl-β-lactams by palladium-catalyzed [2+2] carbonylative cycloaddition of *N*-alkyl imines to allyl bromide. The variety of these compounds can be further widened by functionalization reactions performed diastereoselectively. The steric hindrance of the *N*-alkyl group influences the ring formation and the subsequent functionalization affording *cis*- or *trans*-β-lactam depending on the C-3 and the C-4 carbon atom substituents. The stereoselection mechanism is also investigated and discussed. The continuous need to modify the structures of this class of pharmacologically relevant compounds, together with the ever-increasing requirement of obtaining molecules of fixed configuration, give a good relevance to this contribution. For instance, through the described methodology, it is possible to obtain compounds of desired configuration and variously substituted as the stereoselectivity can be controlled by the kind of the substituents and the nature of the reactants.

4. Experimental

4.1. General

n-Butyllithium (*n*-BuLi) was a commercial solution in hexanes (Aldrich) and was titrated with *N*-pivaloyl-*o*-toluidine prior to use.[23] THF, triethylamine, 4-formylmorpholine, 2-pyridinecarboxaldehyde, 3-pyridinecarboxaldehyde, 4-pyridinecarboxaldehyde, 4-methylthiazole, 2-aminothiazole, methanesulfonyl chloride, 2-aminopyridine, 3-aminopyridine, 2-aminothiophenol, glycolic acid, *n*- and *tert*-butylamine, ethylamine, isopropylamine, palladium(II) acetate, triphenylphosphine, and allyl bromide were of commercial grade (Aldrich) and used without further purification. Benzaldehyde of commercial grade (Aldrich) was purified by distillation prior to use. Petroleum ether refers to the 40–60 °C boiling fraction. The ^1H and the ^{13}C NMR spectra were recorded on a Bruker Avance 400 apparatus (400.13 and 100.62 MHz, for ^1H and ^{13}C, respectively) with $CDCl_3$ as solvent and TMS as internal standard (δ=7.24 for ^1H spectra; δ=77.0 for ^{13}C spectra). The IR spectra were recorded with an FT-IR spectrophotometer Digilab Scimitar Series

FTS 2000. GC–MS analyses were performed with an Agilent Technologies 6850 series II gas chromatograph (5% phenyl-polymethylsiloxane capillary column, 30 m, 0.25 mm i.d.), equipped with a 5973 Network massselective detector operating at 70 eV. The electrospray ionization (HR-ESI-MS) experiments were carried out in a hybrid QqTOF mass spectrometer (PE SCIEX-QSTAR) equipped with an ion spray ionization source. MS (+) spectra were acquired by direct infusion (5 μL/min) of a solution containing the appropriate sample (10 pmol/μL), dissolved in a solution 0.1% acetic acid, methanol/water 50:50 at the optimum ion voltage of 4800 V. The nitrogen gas flow was set at 30 psi (pounds per square inch) and the potentials of the orifice, the focusing ring and the skimmer were kept at 30, 50, and 25 V relative to ground, respectively. Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. TLC was performed on Merck silica gel plates with F_{254} indicator; viewing was by UV light (254 nm). Column chromatographies were performed on silica gel (63–200 mm) using petroleum ether/diethyl ether (Et_2O) mixtures as eluents. All reactions involving air-sensitive reagents were performed under nitrogen, in oven-dried glassware using syringe/septum cap techniques.

4.2. General procedure for the preparation of the *N*-alkylarylimines 1–8

The heteroarylimines **1**–**11** were prepared by dehydration reaction of 1 mmol of the appropriate amine with the corresponding aldehyde (1 mmol) in anhydrous Et_2O, in the presence of 7 g of molecular sieves (Aldrich, 4 Å, 1.6 mm pellets) for 7–16 h, following Taguchi's protocol.[24]

4.2.1. (1E)-N-(Benzothiazol-2-ylmethylene)butylamine ***9***

Yield 207 mg (95%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.96 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.42 (m, 2H, CH_3CH_2), 1.74 (m, 2H, $CH_3CH_2CH_2$), 3.73 (dt, J=1.2, 7.0 Hz, 2H, CH_2CH_2–N), 7.44 (t, J=7.9 Hz, 1H, ArH), 7.50 (t, J=7.9 Hz, 1H, ArH), 7.90 (d, J=7.9 Hz, 1H, ArH), 8.07 (d, J=7.9 Hz, 1H, ArH), 8.53 (s, 1H, N=*CH*); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.8, 20.4, 32.5, 61.1, 122.0, 124.0, 126.3, 126.4, 135.0, 153.4, 155.5, 167.4; FTIR (film): 2958, 2931, 2872, 1640, 1501, 1458, 1316, 760 cm^{-1}; GC–MS (70 eV) *m*/*z* 218 (5) [M$^+$], 189 (5), 175 (100), 162 (11), 148 (38), 135 (7), 108 (7); HRMS-ESI: calcd for $C_{12}H_{15}N_2S$: 219.0957 [M+H]$^+$; found: 219.0958.

4.3. General procedure for the preparation of the compounds 1a–11a, 1b–11b

A mixture of 1.0 mmol of **1**–**11**, 1.5 mmol of allyl bromide, 0.08 mmol of PPh_3, 0.02 mmol of $Pd(AcO)_2$, and 2 mmol of Et_3N were dissolved in 10 mL of solvent (THF) and placed in a 45 mL autoclave. The autoclave was purged, pressurized (400 psi CO), and then heated to 100 °C for 30–35 h. The reaction mixture was then cooled to room temperature and concentrated in vacuo. The crude mixture was chromatographed (silica gel, petroleum ether/Et_2O 1:1 for compounds **1a**, **1b**, **3b**, **4b**, **6a**, **6b**, **10a**, **10b**, **11a**, **11b**; petroleum ether/Et_2O 6:4 for **8a**, **9a**, **9b**; petroleum ether/Et_2O 2:8 for **2b**, **5a**, **5b**; only Et_2O for **7a**, **7b**) to afford pure products **1a**–**11a**, **1b**–**11b** (75–95%).

4.3.1. 1-tert-Butyl-4-phenyl-3-vinylazetidin-2-ones ***1a***, ***1b***

Overall yield 85%. Compound **1a**. Yield 19.5 mg (8.5%), yellow solid; mp 68.9–70.3 °C (petroleum ether); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.25 (s, 9H, $(CH_3)_3$), 3.45 (dd, J=2.0, 7.8 Hz, 1H, *CH*CH=CH_2), 4.33 (d, J=2.0 Hz, 1H, *CH*Ph), 5.23 (dd, J=17.2, 20.3 Hz, 2H, CH=CH_2), 5.87–5.96 (m, 1H, *CH*=CH_2), 7.30–7.37 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 28.1, 54.5, 60.6, 62.6, 118.7, 126.3, 128.2, 128.8, 131.3, 140.3, 168.1; FTIR ($CHCl_3$): 3065, 3031, 2974, 2932, 1747, 1457, 1367, 1226 cm^{-1}; GC–MS (70 eV) *m*/*z* 229 (<1) [M]$^+$, 146 (2), 130 (100), 129 (55), 115 (21), 84 (5), 79 (4), 57 (4); HRMS-ESI: calcd for $C_{15}H_{20}NO$: 230.1546 [M+H]$^+$; found: 230.1546. Compound **1b**. Yield 175 mg (76.5%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.30 (s, 9H, $(CH_3)_3$), 3.96 (dd, J=5.7, 5.8 Hz, 1H, *CH*CH=CH_2), 4.84 (d, J=5.7 Hz, 1H, *CH*Ar), 5.00–5.04 (m, 1H, *CH*=CH_2), 5.26–5.29 (m, 2H, CH=CH_2), 7.27–7.35 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ 28.1, 54.4, 57.2, 58.3, 119.8, 127.2, 128.0, 128.3, 130.0, 137.9, 168.2; FTIR ($CHCl_3$): 3065, 3009, 2976, 2931, 2873, 1734, 1367, 1265 cm^{-1}; GC–MS (70 eV) *m*/*z* 229 (<1) [M]$^+$, 146 (6), 130 (100), 129 (67), 115 (26), 77 (9), 84 (6), 57 (22); HRMS-ESI: calcd for $C_{15}H_{20}NO$: 230.1546 [M+H]$^+$; found: 230.1546.

4.3.2. 1-tert-Butyl-4-pyridin-2-yl-3-vinylazetidin-2-one ***2b***

Yield 179 mg (78%), yellow solid; mp 83.7–85.5 °C (petroleum ether); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.31 (s, 9H, $(CH_3)_3$), 4.06 (t, J=6.0 Hz, 1H, *CH*CH=CH_2), 4.98 (d, J=6.0 Hz, 1H, *CH*Ph), 4.99–5.03 (m, 1H, *CH*=CH_2), 5.28–5.30 (m, 2H, CH=CH_2), 7.20–7.23 (m, 1H, ArH), 7.39 (d, J=7.9 Hz, 1H, ArH), 7.70 (td, J=1.6, 7.9 Hz, 1H, ArH), 8.56 (d, J=4.6 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 28.1, 54.4, 56.9, 59.4, 120.3, 122.2, 122.7, 129.1, 136.0, 149.3, 158.1, 168.1; FTIR ($CHCl_3$): 3089, 3011, 2977, 2934, 1739, 1593, 1438, 1367 cm^{-1}; GC–MS (70 eV) *m*/*z* 230 (2) [M]$^+$, 174 (5), 147 (3), 130 (100), 78 (5), 57 (6); HRMS-ESI: calcd for $C_{14}H_{19}N_2O$: 231.1499 [M+H]$^+$; found: 231.1498.

4.3.3. 1-tert-Butyl-4-(4-methylthiazol-2-yl)-3-vinylazetidin-2-one ***3b***

Yield 187.5 mg (75%), yellow solid; mp 53.5–54.8 °C (petroleum ether); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.32 (s, 9H, $(CH_3)_3$), 2.40 (s, 3H, CH_3Ar), 4.04 (dd, J=6.2, 6.5 Hz, 1H, *CH*CH=CH_2), 5.09 (d, J=10.1 Hz, 1H, CH=CH_2), 5.16 (d, J=6.2 Hz, 1H, *CH*Ar), 5.31 (d, J=17.0 Hz, 1H, CH=CH_2), 5.39–5.43 (m, 1H, *CH*=CH_2), 6.85 (s, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 16.9, 28.0, 54.8, 56.0, 57.5, 113.9, 121.1, 128.4, 152.8, 167.7, 168.7. FTIR ($CHCl_3$): 3089, 2976, 2927, 1749, 1527, 1368, 1345 cm^{-1}; GC–MS (70 eV) *m*/*z* 250 (2) [M]$^+$, 194 (2), 167 (3), 150 (100), 127 (4), 99 (2), 71 (6), 57 (7); HRMS-ESI calcd for $C_{13}H_{19}N_2OS$: 251.1220 [M+H]$^+$; found: 251.1220.

4.3.4. 4-Benzothiazol-2-yl-1-tert-butyl-3-vinylazetidin-2-one ***4b***

Yield 214.5 mg (75%), yellow solid; mp 116.7–118.0 °C (petroleum ether); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.40 (s, 9H, $(CH_3)_3$), 4.18 (dd, J=6.0, 7.2 Hz, 1H, *CH*CH=CH_2), 5.09 (dd, J=0.9, 10.1 Hz, 1H, CH=CH_2), 5.31 (d, J=6.0 Hz, 1H, *CH*Ar), 5.37 (dd, J=0.9, 17.1 Hz, 1H, CH=CH_2), 5.48–5.52 (m, 1H, *CH*=CH_2), 7.40 (t, J=8.0 Hz, 1H, ArH), 7.48 (t, J=8.0 Hz, 1H, ArH), 7.89 (d, J=8.0 Hz, 1H, ArH), 8.00 (d, J=8.0 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 27.9, 54.9, 56.4, 57.7, 121.6, 121.7, 123.1, 125.4, 126.2, 128.0, 134.7, 153.0, 167.6, 170.9; FTIR ($CHCl_3$): 3070, 2980, 2936, 1747, 1370, 1348, 1229 cm^{-1}; GC–MS (70 eV) *m*/*z* 286 (2) [M]$^+$, 230 (3), 186 (100), 135 (4), 57 (8); HRMS-ESI: calcd for $C_{16}H_{19}N_2OS$: 287.1220 [M+H]$^+$; found: 287.1220.

4.3.5. 1-n-Butyl-4-pyridin-2-yl-3-vinylazetidin-2-ones ***5a***, ***5b***

Overall yield 81%. Compound **5a**. Yield 182 mg (79%), brown oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.84 (t, J=7.2 Hz, 3H, CH_3CH_2), 1.23–1.33 (m, 2H, CH_3CH_2), 1.39–1.47 (m, 2H, $CH_3CH_2CH_2$), 2.83–2.89 (m, 1H, CH_2CH_2–N), 3.45–3.52 (m, 1H, CH_2CH_2–N), 3.74 (dd, J=2.1, 7.6 Hz, 1H, *CH*CH=CH_2), 4.49 (d, J=2.1 Hz, 1H, *CH*Ar), 5.24 (d, J=10.3 Hz, 1H, CH=CH_2), 5.31 (d, J=17.1 Hz, 1H, CH=CH_2), 5.94–6.02 (m, 1H, *CH*=CH_2), 7.24 (dd, J=4.8, 7.7 Hz, 1H, ArH), 7.29 (d, J=7.7 Hz, 1H, ArH), 7.71 (t, J=7.7 Hz, 1H, ArH), 8.60 (d, J=4.8 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 19.8, 29.5, 40.6, 62.0, 62.2, 119.1, 120.8, 123.2, 131.1, 137.0, 149.9, 157.4, 168.0; FTIR ($CHCl_3$): 3009, 2964, 2930, 2875, 1748, 1577, 1431, 1400 cm^{-1}; GC–MS (70 eV) *m*/*z* 230 (20) [M]$^+$, 159 (10), 131 (93), 130 (100), 92 (10), 78

(13); HRMS-ESI: calcd for $C_{14}H_{19}N_2O$: 231.1499 $[M+H]^+$; found: 231.1499. Compound **5b**: traces; GC–MS (70 eV) *m*/*z* 230 (5) $[M]^+$, 159 (3), 131 (19), 130 (100), 92 (4), 78 (3).

*4.3.6. 1-n-Butyl-4-pyridin-3-yl-3-vinylazetidin-2-ones **6a**, **6b***

Overall yield 79%. Compound **6a**. Yield 177 mg (77%), brown oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.87 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.24–1.34 (m, 2H, CH_3CH_2), 1.41–1.48 (m, 2H, $CH_3CH_2CH_2$), 2.80–2.86 (m, 1H, CH_2CH_2–N), 3.43–3.45 (m, 1H, CH_2CH_2–N), 3.61 (dd, *J*=2.0, 7.7 Hz, 1H, *CH*CH=CH_2), 4.36 (d, *J*=2.0 Hz, 1H, *CH*Ar), 5.27 (d, *J*=10.8 Hz, 1H, CH=CH_2), 5.31 (d, *J*=17.4 Hz, 1H, CH=CH_2), 5.92–6.00 (m, 1H, *CH*=CH_2), 7.34 (dd, *J*=4.8, 7.8 Hz, 1H, ArH), 7.64 (d, *J*=7.8 Hz, 1H, ArH), 8.57 (s, 1H, ArH), 8.61 (d, *J*=4.8 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 20.0, 29.6, 40.5, 59.0, 63.4, 119.6, 124.0, 130.7, 133.3, 133.5, 148.4, 150.1, 167.6; FTIR ($CHCl_3$): 3010, 2963, 2932, 2875, 1748, 1579, 1432, 1400 cm^{-1}; GC–MS (70 eV) *m*/*z* 230 (<1) $[M]^+$, 163 (3), 131 (95), 130 (100), 104 (8), 92 (5), 78 (3); HRMS-ESI: calcd for $C_{14}H_{19}N_2O$: 231.1499 $[M+H]^+$; found: 231.1499. Compound **6b**: traces; GC–MS (70 eV) *m*/*z* 230 (<1) $[M]^+$, 163 (5), 131 (53), 130 (100), 104 (8), 92 (5), 78 (3).

*4.3.7. 1-n-Butyl-4-pyridin-4-yl-3-vinylazetidin-2-ones **7a**, **7b***

Overall yield 81%. Compound **7a**. Yield 168 mg (73%), brown oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.87 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.25–1.34 (m, 2H, CH_3CH_2), 1.40–1.49 (m, 2H, $CH_3CH_2CH_2$), 2.81–2.88 (m, 1H, CH_2CH_2–N), 3.44–3.52 (m, 1H, CH_2CH_2–N), 3.55 (dd, *J*=2.0, 7.8 Hz, 1H, *CH*CH=CH_2), 4.31 (d, *J*=2.0 Hz, 1H, *CH*Ar), 5.27 (d, *J*=9.3 Hz, 1H, CH=CH_2), 5.30 (d, *J*=16.1 Hz, 1H, CH=CH_2), 5.90–5.99 (m, 1H, *CH*=CH_2), 7.21 (d, *J*=5.4 Hz, 2H, ArH), 8.62 (d, *J*=5.4 Hz, 2H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 20.0, 29.6, 40.7, 60.1, 63.8, 119.7, 121.1, 130.5, 147.0, 150.5, 167.5; FTIR ($CHCl_3$): 3022, 3011, 2933, 2872, 1750, 1604, 1417 cm^{-1}; GC–MS (70 eV) *m*/*z* 230 (<1) $[M]^+$, 163 (1), 131 (68), 130 (100), 104 (9), 78 (5); HRMS-ESI: calcd for $C_{14}H_{19}N_2O$: 231.1499 $[M+H]^+$; found: 231.1499. Compound **7b**. Yield 18.4 mg (8%), oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.90 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.28–1.37 (m, 2H, CH_3CH_2), 1.43–1.55 (m, 2H, $CH_3CH_2CH_2$), 2.90–2.97 (m, 1H, CH_2CH_2–N), 3.53–3.62 (m, 1H, CH_2CH_2–N), 4.19 (dd, *J*=5.6, 6.3 Hz, 1H, *CH*CH=CH_2), 4.79 (d, *J*=5.6 Hz, 1H, *CH*Ar), 5.07 (d, *J*=9.6 Hz, 1H, CH=CH_2), 5.15–5.23 (m, 1H, CH=CH_2), 5.28–5.35 (m, 1H, *CH*=CH_2), 7.15 (d, *J*=5.4 Hz, 2H, ArH), 8.62 (d, *J*=5.4 Hz, 2H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 20.2, 29.6, 40.8, 58.0, 58.8, 121.1, 122.3, 128.4, 145.2, 150.0, 167.6; FTIR ($CHCl_3$): 3026, 3010, 2934, 2873, 1749, 1605, 1417 cm^{-1}; GC–MS (70 eV) *m*/*z* 230 (<1) $[M]^+$, 163 (2), 131 (57), 130 (100), 104 (10), 78 (4); HRMS-ESI: calcd for $C_{14}H_{19}N_2O$: 231.1499 $[M+H]^+$; found: 231.1499.

*4.3.8. 1-n-Butyl-4-phenyl-3-vinylazetidin-2-one **8a***

Yield 206 mg (90%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 0.88 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.25–1.35 (m, 2H, CH_3CH_2), 1.42–1.49 (m, 2H, $CH_3CH_2CH_2$), 2.79–2.86 (m, 1H, CH_2CH_2–N), 3.46–3.53 (m, 1H, CH_2CH_2–N), 3.59 (dd, *J*=1.5, 7.7 Hz, 1H, *CH*CH=CH_2), 4.33 (d, *J*=1.5 Hz, 1H, *CH*Ar), 5.24 (d, *J*=10.3 Hz, 1H, CH=CH_2), 5.30 (d, *J*=17.1 Hz, 1H, CH=CH_2), 5.93–6.02 (m, 1H, *CH*=CH_2), 7.30 (d, *J*=7.0 Hz, 2H, ArH), 7.33–7.41 (m, 3H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 20.1, 29.6, 40.2, 61.4, 63.8, 119.0, 126.3, 128.5, 129.0, 131.3, 137.6, 168.1; FTIR (film): 3032, 2958, 2931, 2873, 1757, 1457, 1397 cm^{-1}; GC–MS (70 eV) *m*/*z* 229 (<1) $[M]^+$, 162 (4), 130 (100), 129 (79), 115 (33), 104 (5), 91 (4), 77 (6); HRMS-ESI: calcd for $C_{15}H_{20}NO$: 230.1546 $[M+H]^+$; found: 230.1546.

*4.3.9. 4-Benzothiazol-2-yl-1-n-butyl-3-vinylazetidin-2-ones **9a**, **9b***

Overall yield 78%. Compound **9a**. Yield 186 mg (65%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.87 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.26–1.36 (m, 2H, CH_3CH_2), 1.49–1.56 (m, 2H, $CH_3CH_2CH_2$), 3.02–3.08 (m, 1H, CH_2CH_2–N), 3.55 (dt, *J*=7.7, 14.1 Hz, 1H, CH_2CH_2–N), 3.92 (dd, *J*=2.2, 7.4 Hz, 1H, *CH*CH=CH_2), 4.83 (d, *J*=2.2 Hz, 1H, *CH*Ar), 5.30 (d, *J*=10.2 Hz, 1H, CH=CH_2), 5.38 (d, *J*=17.1 Hz, 1H, CH=CH_2), 5.94–6.03 (m, 1H, *CH*=CH_2), 7.40 (t, *J*=8.1 Hz, 1H, ArH), 7.49 (t, *J*=8.1 Hz, 1H, ArH), 7.88 (d, *J*=8.1 Hz, 1H, ArH), 8.00 (d, *J*=8.1 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.4, 20.0, 29.4, 41.0, 58.9, 63.1, 119.9, 121.9, 123.2, 125.6, 126.4, 130.0, 134.7, 153.1, 167.2, 169.1; FTIR (film): 3064, 2958, 2931, 2872, 1766, 1437, 1391, 1313, 926 cm^{-1}; GC–MS (70 eV) *m*/*z* 286 (8) $[M]^+$, 259 (6), 219 (6), 186 (100), 175 (8), 148 (6); HRMS-ESI: calcd for $C_{16}H_{19}N_2OS$ 287.1220 $[M+H]^+$; found: 287.1220. Compound **9b**. Yield 37 mg (13%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.90 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.35 (sextet, *J*=7.3 Hz, 2H, CH_3CH_2), 1.58 (quintet, *J*=7.3 Hz, 2H, $CH_3CH_2CH_2$), 3.11–3.18 (m, 1H, CH_2CH_2–N), 3.64 (dt, *J*=7.8, 14.0 Hz, 1H, CH_2CH_2–N), 4.32 (dd, *J*=5.6, 7.0 Hz, 1H, *CH*CH=CH_2), 5.10 (d, *J*=10.2 Hz, 1H, CH=CH_2), 5.26 (d, *J*=5.6 Hz, 1H, *CH*Ar), 5.38 (d, *J*=16.0 Hz, 1H, CH=CH_2), 5.47–5.56 (m, 1H, *CH*=CH_2), 7.42 (t, *J*=8.0 Hz, 1H, ArH), 7.50 (t, *J*=8.0 Hz, 1H, ArH), 7.89 (d, *J*=8.0 Hz, 1H, ArH), 8.00 (d, *J*=8.0 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 20.2, 29.5, 41.3, 57.4, 59.4, 121.8, 123.2, 125.5, 126.3, 127.7, 128.5, 134.8, 153.3, 167.5, 168.1; FTIR ($CHCl_3$): 3066, 3011, 2963, 2934, 2875, 1753, 1514, 1437, 1314 cm^{-1}; GC–MS (70 eV) *m*/*z* 286 (5) $[M]^+$, 259 (3), 219 (3), 186 (100), 175 (5), 148 (3), 77 (2); HRMS-ESI: calcd for $C_{16}H_{19}N_2OS$: 287.1220 $[M+H]^+$; found: 287.1220.

*4.3.10. 1-Isopropyl-4-phenyl-3-vinylazetidin-2-ones **10a**, **10b***

Overall yield 95%. Compound **10a**. Yield 184 mg (85.5%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.03 (d, *J*=6.7 Hz, 3H, $(CH_3)_2CH$), 1.28 (d, *J*=6.7 Hz, 3H, $(CH_3)_2CH$), 3.56 (dd, *J*=2.1, 7.7 Hz, 1H, *CH*CH=CH_2), 3.77 (heptet, *J*=6.7 Hz, 1H, $(CH_3)_2CH$), 4.33 (d, *J*=2.1 Hz, 1H, *CH*Ar), 5.23 (d, *J*=10.4 Hz, 1H, CH=CH_2), 5.28 (d, *J*=17.1 Hz, 1H, CH=CH_2), 5.90–5.99 (m, 1H, *CH*=CH_2), 7.32–7.40 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 20.3, 21.2, 45.0, 60.3, 63.1, 119.0, 126.5, 128.4, 128.8, 131.1, 139.0, 167.9; FTIR (film): 3063, 3030, 2975, 2931, 1747, 1457, 1380, 1370 cm^{-1}; GC–MS (70 eV) *m*/*z* 215 (<1) $[M]^+$, 148 (2), 130 (100), 129 (67), 115 (27), 77 (6); HRMS-ESI: calcd for $C_{14}H_{18}NO$: 216.1389 $[M+H]^+$; found: 216.1390. Compound **10b**. Yield 20 mg (9.5%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.12 (d, *J*=6.7 Hz, 3H, $(CH_3)_2CH$), 1.32 (d, *J*=6.7 Hz, 3H, $(CH_3)_2CH$), 3.79 (heptet, *J*=6.7 Hz, 1H, $(CH_3)_2CH$), 4.03 (dd, *J*=5.3, 5.5 Hz, 1H, *CH*CH=CH_2), 4.82 (d, *J*=5.5 Hz, 1H, *CH*Ar), 5.02–5.05 (m, 1H, *CH*=CH_2), 5.25–5.31 (m, 2H, CH=CH_2), 7.26–7.39 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 20.3, 21.3, 45.3, 58.0, 120.0, 127.6, 128.1, 128.4, 129.5, 136.7, 168.2; FTIR (film): 3064, 3030, 2977, 2931, 1748, 1456, 1380, 1370 cm^{-1}; GC–MS (70 eV) *m*/*z* 215 (<1) $[M]^+$, 148 (2), 130 (100), 129 (67), 115 (27), 77 (6); HRMS-ESI: calcd for $C_{14}H_{18}NO$: 216.1389 $[M+H]^+$; found: 216.1389.

*4.3.11. 1-Ethyl-4-phenyl-3-vinylazetidin-2-one **11a***

Yield 181 mg (90%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.09 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 2.93–2.99 (m, 1H, CH_3CH_2–N), 3.48–3.57 (m, 1H, CH_3CH_2–N), 3.60 (dd, *J*=2.1, 6.9 Hz, 1H, *CH*CH=CH_2), 4.37 (d, *J*=2.1 Hz, 1H, *CH*Ar), 5.26 (d, *J*=10.4 Hz, 1H, CH=CH_2), 5.30 (d, *J*=17.1 Hz, 1H, CH=CH_2), 5.93–6.02 (m, 1H, *CH*=CH_2), 7.31–7.42 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 12.8, 35.4, 60.9, 63.7, 119.1, 126.3, 128.5, 129.0, 131.1, 137.7, 167.9; FTIR (film): 3032, 2978, 2934, 1756, 1457, 1397, 1360 cm^{-1}; GC–MS (70 eV) *m*/*z* 201 (<1) $[M]^+$, 130 (100), 129 (87), 115 (36), 91 (9), 77 (8); HRMS-ESI: calcd for $C_{13}H_{16}NO$: 202.1233 $[M+H]^+$; found: 202.1233.

4.4. General procedure for the functionalization of compounds 1a, 5a, 8a–10a, 1b–4b, 10b

To a stirred solution of 1 mmol of **1a**, **5a**, **8a**–**10a**, **1b**–**4b**, **10b** in THF (30 mL) at −78 °C, *n*-BuLi (2.5 M in hexanes, 0.5 mL, 1.2 mmol) was added dropwise under nitrogen. The resulting mixture was stirred at −78 °C for 20 min, and then the electrophile was added

(1.5 mmol). The reaction mixture was warmed up to room temperature and quenched with saturated aq NH_4Cl. The aqueous layer was extracted with Et_2O (3×20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford the pure functionalized β-lactams **14a**, **16a**, **18a**, **20a**, **22a**, **24a**, **26a**, **28a**, **12b**–**28b**; yields: 88–99%.

4.4.1. 1-tert-Butyl-3-methyl-4-phenyl-3-vinylazetidin-2-one *12b*

From β-lactam **1b**. Yield 241.6 mg (>99%), yellow solid; mp 49.3.5–50.1 °C (petroleum ether); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.23 (s, 9H, $(CH_3)_3$), 1.36 (s, 3H, CH_3CCH=CH_2), 4.31 (s, 1H, *CH*Ar), 4.87 (dd, J=1.6, 10.3 Hz, 1H, CH=CH_2), 5.08–5.15 (m, 1H, CH=CH_2), 5.24 (dd, J=1.6, 17.2 Hz, 1H, CH=CH_2), 7.18–7.28 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 20.9, 28.1, 54.1, 60.0, 66.8, 116.6, 127.5, 127.9, 128.2, 135.0, 138.2, 172.0; FTIR ($CHCl_3$): 3030, 3018, 2977, 2931, 2857, 1746, 1370, 1344 cm^{-1}; GC–MS (70 eV) m/z 243 (<1) $[M]^+$, 187 (5), 144 (70), 129 (100), 128 (28), 115 (7), 82 (5), 57 (9); HRMS-ESI: calcd for $C_{16}H_{22}NO$: 244.1703 $[M+H]^+$; found: 244.1703. From β-lactam **1a**. Yield 236 mg (97%).

4.4.2. 3-Allyl-1-tert-butyl-4-phenyl-3-vinylazetidin-2-one *13b*

Yield 255.5 mg (95%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.20 (s, 9H, $(CH_3)_3$), 2.46 (d, J=7.1 Hz, 2H, CCH_2CH=CH_2), 4.47 (s, 1H, *CH*Ar), 4.91 (dd, J=1.4, 10.8 Hz, 1H, CCH_2CH=CH_2), 5.00–5.18 (m, 3H, CH=CH_2), 5.32 (dd, J=1.4, 17.3 Hz, 1H, CH=CH_2), 5.76–5.87 (m, 1H, CH=CH_2), 7.15–7.32 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 28.2, 39.9, 54.2, 62.9, 63.0, 117.1, 118.7, 127.6, 127.7, 128.0, 133.2, 133.9, 137.9, 170.5; FTIR ($CHCl_3$): 3024, 3004, 2983, 2930, 1738, 1456, 1367, 1341 cm^{-1}; GC–MS (70 eV) m/z 269 (<1) $[M]^+$, 213 (2), 170 (19), 155 (9), 141 (13), 129 (100), 91 (10), 79 (9); HRMS-ESI: calcd for $C_{18}H_{24}NO$: 270.1859 $[M+H]^+$; found: 270.1860.

4.4.3. 1-tert-Butyl-3-deutero-4-phenyl-3-vinylazetidin-2-ones *14a*, *14b*

Overall yield 99%. Compound **14a**. Yield 50 mg (21.7%), yellow oil; The FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **1a**. In the ^{1}H NMR spectrum the signal at 3.45 ppm disappears, while the doublet at 4.33 ppm becomes a singlet; GC–MS (70 eV) m/z 230 (<1) $[M]^+$, 146 (1), 131 (100), 130 (45), 115 (18), 84 (3), 79 (3), 57 (5); HRMS-ESI: calcd for $C_{15}H_{19}DNO$: 231.1609 $[M+H]^+$; found: 231.1609. Compound **14b**. Yield 177 mg (77%), yellow oil; the FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **1b**. In the ^{1}H NMR spectrum the doublet at 3.96 ppm disappears, while the signal at 4.84 ppm becomes a singlet; GC–MS (70 eV) m/z 230 (<1) $[M]^+$, 146 (4), 131 (100), 129 (54), 115 (22), 77 (8), 84 (5), 57 (20); HRMS-ESI: calcd for $C_{15}H_{19}DNO$: 231.1609 $[M+H]^+$; found: 231.1609.

4.4.4. 1-tert-Butyl-3-methyl-4-pyridin-2-yl-3-vinylazetidin-2-one *15b*

Yield 220 mg (90%), yellow solid; mp 74.2–75.5 °C (petroleum ether); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.31 (s, 9H, $(CH_3)_3$), 1.53 (s, 3H, CH_3CCH=CH_2), 4.59 (s, 1H, *CH*Ar), 4.94 (dd, J=1.7, 10.2 Hz, 1H, CH=CH_2), 5.16–5.23 (m, 1H, CH=CH_2), 5.28 (dd, J=1.7, 17.4 Hz, 1H, CH=CH_2), 7.20 (dd, J=4.6, 7.7 Hz, 1H, ArH), 7.36 (d, J=7.7 Hz, 1H, ArH), 7.69 (t, J=7.7 Hz, 1H, ArH), 8.54 (d, J=4.6 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 20.9, 28.0, 54.1, 60.4, 67.6, 117.0, 122.1, 122.6, 134.4, 136.0, 149.1, 158.6, 171.9; FTIR ($CHCl_3$): 3019, 2972, 2931, 1736, 1593, 1437, 1368 cm^{-1}; GC–MS (70 eV) m/z 244 (2) $[M]^+$, 188 (22), 173 (3), 144 (100), 130 (25), 78 (7); HRMS-ESI: calcd for $C_{15}H_{21}N_2O$: 245.1655 $[M+H]^+$; found: 245.1656.

4.4.5. 1-tert-Butyl-3-deutero-4-pyridin-2-yl-3-vinylazetidin-2-ones *16a*, *16b*

Overall yield >99%. Compound **16a**. Yield 32 mg (13.8%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.25 (s, 9H, $(CH_3)_3$), 4.52 (s, 1H, *CH*Ar), 5.25 (d, J=10.4 Hz, 1H, CH=CH_2), 5.31 (d, J=17.5 Hz, 1H, CH=CH_2), 5.91–6.00 (m, 1H, CH=CH_2), 7.24 (dd, J=4.6, 7.7 Hz, 1H, ArH), 7.44 (d, J=7.7 Hz, 1H, ArH), 7.73 (t, J=7.7 Hz, 1H, ArH), 8.58 (d, J=4.6 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 28.1, 54.5, 61.2, 61.3, 119.0, 120.9, 123.1, 131.1, 136.9, 149.5, 159.8, 168.0; FTIR ($CHCl_3$): 3019, 2973, 2934, 1738, 1593, 1438, 1367 cm^{-1}; GC–MS (70 eV) m/z 231 (3) $[M]^+$, 174 (6), 158 (4), 131 (100), 78 (4); HRMS-ESI: calcd for $C_{14}H_{18}DN_2O$: 232.1561 $[M+H]^+$; found: 232.1562. Compound **16b**. Yield 196 mg (85%), yellow oil; the FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **2b**. In the ^{1}H NMR spectrum the double doublet at 4.06 ppm disappears, while the doublet at 4.98 ppm becomes a singlet; GC–MS (70 eV) m/z 231 (2) $[M]^+$, 174 (4), 147 (3), 131 (100), 78 (5), 57 (5); HRMS-ESI: calcd for $C_{14}H_{18}DN_2O$: 232.1561 $[M+H]^+$; found: 232.1562.

4.4.6. 1-tert-Butyl-3-methyl-4-(4-methylthiazol-2-yl)-3-vinylazetidin-2-one *17b*

Yield 262 mg (>99%), yellow solid; mp 79.2–80.5 °C (petroleum ether); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.35 (s, 9H, $(CH_3)_3$), 1.51 (s, 3H, CH_3CCH=CH_2), 2.43 (s, 3H, CH_3Ar), 4.77 (s, 1H, *CH*Ar), 5.05 (dd, J=2.9, 8.9 Hz, 2H, CH=CH_2), 5.36–5.39 (m, 1H, CH=CH_2), 6.87 (s, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 16.9, 20.6, 27.9, 54.5, 61.1, 64.0, 114.0, 117.9, 133.7, 152.6, 169.5, 171.7; FTIR ($CHCl_3$): 3025, 3015, 2983, 2934, 1735, 1461, 1369, 1343 cm^{-1}; GC–MS (70 eV) m/z 264 (4) $[M]^+$, 208 (8), 164 (100), 150 (11), 126 (7), 113 (11), 82 (23), 57 (16); HRMS-ESI: calcd for $C_{14}H_{21}N_2OS$: 265.1376 $[M+H]^+$; found: 265.1377.

4.4.7. 1-tert-Butyl-3-deutero-4-(4-methylthiazol-2-yl)-3-vinylazetidin-2-ones *18a*, *18b*

Overall yield 92%. Compound **18a**: traces; GC–MS (70 eV) m/z 251 (1) $[M]^+$, 194 (3), 167 (4), 151 (100), 127 (3), 71 (3), 57 (3). Compound **18b**. Yield 226 mg (90%), yellow solid; mp 53.5–54.8 °C (petroleum ether); the FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **3b**. In the ^{1}H NMR spectrum the double doublet at 4.04 ppm disappears, while the doublet at 5.16 ppm becomes a singlet; GC–MS (70 eV) m/z 251 (2) $[M]^+$, 194 (4), 167 (3), 151 (100), 127 (5), 71 (5), 57 (5); HRMS-ESI: calcd for $C_{13}H_{18}DN_2OS$: 252.1282 $[M+H]^+$; found: 252.1283.

4.4.8. 4-Benzothiazol-2-yl-1-tert-butyl-3-methyl-3-vinylazetidin-2-one *19b*

Yield 264 mg (88%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.39 (s, 9H, $(CH_3)_3$), 1.57 (s, 3H, CH_3CCH=CH_2), 4.88 (s, 1H, *CH*Ar), 5.03 (dd, J=2.1, 9.5 Hz, 1H, CH=CH_2), 5.37–5.45 (m, 2H, CH=CH_2), 7.41 (t, J=7.9 Hz, 1H, ArH), 7.49 (t, J=7.9 Hz, 1H, ArH), 7.88 (d, J=7.9 Hz, 1H, ArH), 8.00 (d, J=7.9 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 20.8, 27.9, 54.7, 61.5, 64.4, 118.3, 121.8, 123.0, 125.4, 126.2, 133.3, 134.8, 153.1, 171.4, 171.5; FTIR ($CHCl_3$): 3029, 3018, 2977, 2931, 1745, 1371, 1343 cm^{-1}; GC–MS (70 eV) m/z 300 (4) $[M]^+$, 244 (7), 200 (100), 186 (9), 135 (5), 82 (11); HRMS-ESI: calcd for $C_{17}H_{21}N_2OS$: 301.1376 $[M+H]^+$; found: 301.1377.

4.4.9. 4-Benzothiazol-2-yl-1-tert-butyl-3-deutero-3-vinylazetidin-2-ones *20a*, *20b*

Overall yield 95%. Compound **20a**. Yield 40 mg (14%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.35 (s, 9H, $(CH_3)_3$), 4.88 (s, 1H, *CH*Ar), 5.31 (d, J=10.1 Hz, 1H, CH=CH_2), 5.37 (d, J=17.1 Hz, 1H, CH=CH_2), 5.90–5.98 (m, 1H, CH=CH_2), 7.42 (t, J=7.8 Hz, 1H. ArH), 7.51 (t, J=7.8 Hz, 1H, ArH), 7.90 (d, J=7.8 Hz, 1H, ArH), 8.00 (d, J=7.8 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 28.0, 55.2, 58.2, 62.2, 119.8, 122.0, 123.3, 125.7, 126.4, 130.8, 134.8, 152.9, 167.5, 172.3; FTIR ($CHCl_3$): 3018, 2980, 2932, 1747, 1224 cm^{-1}; GC–MS (70 eV) m/z 287 (3) $[M]^+$, 230 (3), 187 (100), 135 (4), 57(8); HRMS-ESI: calcd for $C_{16}H_{18}DN_2OS$: 288.1282 $[M+H]^+$; found: 288.1283. Compound **20b**. The FTIR, ^{1}H and ^{13}C NMR data are the same of those

reported for **4b**. In the ^{1}H NMR spectrum the double doublet at 4.18 ppm disappears, while the doublet at 5.31 ppm becomes a singlet; GC–MS (70 eV) *m*/*z* 287 (2) $[M]^+$, 230 (3), 187 (100), 135 (4), 57(8); HRMS-ESI: calcd for $C_{16}H_{18}DN_2OS$: 288.1282 $[M+H]^+$; found: 288.1283.

4.4.10. 1-n-Butyl-3-methyl-4-pyridin-2-yl-3-vinylazetidin-2-one **21b**

Yield 242.6 mg (>99%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.91 (t, *J*=7.1 Hz, 3H, CH_3CH_2), 1.30–1.39 (m, 2H, CH_3CH_2), 1.47–1.54 (m, 2H, $CH_3CH_2CH_2$), 1.61 (s, 3H, $CH_3CCH{=}CH_2$), 2.92–2.99 (m, 1H, CH_2CH_2–N), 3.61–3.68 (m, 1H, CH_2CH_2–N), 4.60 (s, 1H, *CH*Ar), 4.92–4.95 (m, 1H, $CH{=}CH_2$), 5.23–5.27 (m, 2H, $CH{=}CH_2$), 7.17 (d, *J*=7.8 Hz, 1H, ArH), 7.23 (dd, *J*=4.6, 7.8 Hz, 1H, ArH), 7.70 (t, *J*=7.8 Hz, 1H, ArH), 8.59 (d, *J*=4.6 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 20.1, 20.7, 29.5, 40.2, 62.6, 68.0, 117.0, 121.5, 122.7, 134.2, 136.3, 149.6, 156.5, 171.4; FTIR ($CHCl_3$): 3010, 2963, 2932, 2875, 1748, 1579, 1432, 1400 cm^{-1}; GC–MS (70 eV) *m*/*z* 244 (22) $[M]^+$, 229 (5), 215 (4), 201 (3), 187 (5), 173 (15), 145 (68), 144 (100), 130 (43), 92 (19), 78 (14); HRMS-ESI: calcd for $C_{15}H_{21}N_2O$ 245.1655 $[M+H]^+$; found: 245.1656.

4.4.11. 1-n-Butyl-3-deutero-4-pyridin-2-yl-3-vinylazetidin-2-ones **22a, 22b**

Inseparable mixture of two *trans*- and *cis*-configurated diastereomers (dr=1:1 by ^{1}H NMR), the reaction was followed only via GC and ^{1}H NMR spectroscopy showing the formation of two compounds. From the ^{1}H NMR spectrum of the mixture we identified and assigned separate signals for **22a** and **22b**, respectively. Compound **22a**. The ^{1}H NMR data are the same of those reported for **5a** except the double doublet at 3.74 ppm that disappears, while the doublet at 4.49 ppm becomes a singlet. Compound **22b**. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.85 (t, *J*=7.2 Hz, 3H, CH_3CH_2), 1.22–1.32 (m, 2H, CH_3CH_2), 1.38–1.46 (m, 2H, $CH_3CH_2CH_2$), 2.90–2.98 (m, 1H, CH_2CH_2–N), 3.53–3.59 (m, 1H, CH_2CH_2–N), 4.88 (s, 1H, *CH*Ar), 4.92–4.95 (m, 1H, $CH{=}CH_2$), 5.26–5.29 (m, 2H, $CH{=}CH_2$), 7.22–7.28 (m, 2H, ArH), 7.61 (t, *J*=7.7 Hz, 1H, ArH), 8.60 (d, *J*=4.8 Hz, 1H, ArH). GC–MS performed on the mixture showed two peaks having the same fragmentation and $[M]^+$=231 (18).

4.4.12. 1-n-Butyl-3-methyl-4-phenyl-3-vinylazetidin-2-one **23b**

Yield 214 mg (88%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.90 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.27 (sextet, *J*=7.3 Hz, 2H, CH_3CH_2), 1.51 (quintet, *J*=7.3 Hz, 2H, $CH_3CH_2CH_2$), 1.60 (s, 3H, $CH_3CCH{=}CH_2$), 2.90–2.95 (m, 1H, CH_2CH_2–N), 3.50–3.55 (m, 1H, CH_2CH_2–N), 4.75 (s, 1H, *CH*Ar), 5.00–5.05 (m, 1H, $CH{=}CH_2$), 5.27–5.29 (m, 2H, $CH{=}CH_2$), 7.21 (d, *J*=7.2 Hz, 2H, ArH), 7.30–7.40 (m, 3H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.6, 20.2, 21.0, 29.7, 40.4, 58.9, 59.1, 120.1, 127.3, 128.1, 128.6, 129.4, 135.7, 168.3; FTIR (film): 3032, 2957, 2930, 2875, 1758, 1455, 1396 cm^{-1}; GC–MS (70 eV) *m*/*z* 243 (20) $[M]^+$, 228 (5), 144 (100), 91 (18), 77 (10); HRMS-ESI: calcd for $C_{16}H_{22}NO$: 244.1703 $[M+H]^+$; found: 244.1703.

4.4.13. 1-n-Butyl-3-deutero-4-phenyl-3-vinylazetidin-2-ones **24a, 24b**

Overall yield (97%). Compound **24a**. Yield 122 mg (53%), yellow oil; the FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **8a**. In the ^{1}H NMR spectrum the double doublet at 3.59 ppm disappears, while the doublet at 4.33 ppm becomes a singlet; GC–MS (70 eV) *m*/*z* 230 (<1) $[M]^+$, 162 (2), 131 (100), 130 (57), 104 (10), 78 (4); HRMS-ESI: calcd for $C_{15}H_{19}DNO$: 231.1609 $[M+H]^+$; found: 231.1609. Compound **24b**. Yield 99 mg (43%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.89 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.27–1.36 (m, 2H, CH_3CH_2), 1.47–1.54 (m, 2H, $CH_3CH_2CH_2$), 2.89–2.95 (m, 1H, CH_2CH_2–N), 3.53–3.60 (m, 1H, CH_2CH_2–N), 4.82 (s, 1H, *CH*Ar), 4.99–5.03 (m, 1H, $CH{=}CH_2$), 5.26–5.29 (m, 2H, $CH{=}CH_2$), 7.21 (d, *J*=7.2 Hz, 2H, ArH), 7.30–7.40 (m, 3H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.6, 20.2, 29.6, 40.4, 58.8, 59.0, 120.1, 127.4, 128.2, 128.6, 129.3, 135.6, 168.2; FTIR (film): 3032, 2958, 2931, 2873, 1757, 1457, 1397 cm^{-1}; GC–MS (70 eV) *m*/*z* 230 (<1) $[M]^+$, 163 (2), 132 (13), 131 (100), 139 (48), 104 (10), 78 (4); HRMS-ESI: calcd for $C_{15}H_{19}DNO$: 231.1609 $[M+H]^+$; found: 231.1609.

4.4.14. 4-Benzothiazol-2-yl-1-n-butyl-3-methyl-3-vinylazetidin-2-one **25b**

Yield 279 mg (93%); ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.89 (t, *J*=7.3 Hz, 3H, CH_3CH_2), 1.34 (sextet, *J*=7.3 Hz, 2H, CH_3CH_2), 1.55 (quintet, *J*=7.3 Hz, 2H, $CH_3CH_2CH_2$), 1.59 (s, 3H, $CH_3CCH{=}CH_2$), 3.09–3.15 (m, 1H, CH_2CH_2–N), 3.61–3.66 (m, 1H, CH_2CH_2–N), 4.95 (s, 1H, *CH*Ar), 5.12 (d, *J*=9.9 Hz, 1H, $CH{=}CH_2$), 5.40–5.55 (m, 2H, $CH{=}CH_2$), 7.39 (t, *J*=7.9 Hz, 1H, ArH), 7.50 (t, *J*=7.9 Hz, 1H, ArH), 7.90 (d, *J*=7.9 Hz, 1H, ArH), 8.00 (d, *J*=7.9 Hz, 1H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 13.5, 20.2, 20.5, 29.0, 41.1, 56.0, 57.0, 121.8, 123.2, 126.0, 126.3, 127.5, 128.5, 134.8, 153.2, 167.5, 168.2; FTIR (film): 3065, 2956, 2930, 2871, 1769, 1435, 1389, 1310 cm^{-1}; GC–MS (70 eV) *m*/*z* 300 (8) $[M]^+$, 259 (6), 219 (6), 201 (100), 175 (8), 148 (6); HRMS-ESI: calcd for $C_{17}H_{21}N_2OS$: 301.1376 $[M+H]^+$; found: 301.1377.

4.4.15. 4-Benzothiazol-2-yl-1-n-butyl-3-deutero-3-vinylazetidin-2-ones **26a, 26b**

Overall yield (>99%). Compound **26a**. Yield 129 mg (45%), yellow oil. The FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **9a**. In the ^{1}H NMR spectrum the double doublet at 3.92 ppm disappears, while the doublet at 4.83 ppm becomes a singlet; GC–MS (70 eV) *m*/*z* 287 (8) $[M]^+$, 259 (6), 219 (6), 187 (100), 175 (8), 148 (6); HRMS-ESI: calcd for $C_{16}H_{18}DN_2OS$ 288.1282 $[M+H]^+$; found: 288.1283. Compound **26b**. Yield 129 mg (45%), yellow oil; the FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **9b**. In the ^{1}H NMR spectrum the double doublet at 4.32 ppm disappears, while the doublet at 5.26 ppm becomes a singlet; GC–MS (70 eV) *m*/*z* 287 (5) $[M]^+$, 259 (3), 219 (3), 187 (100), 175 (5), 148 (3), 77 (2); HRMS-ESI: calcd for $C_{16}H_{18}DN_2OS$: 288.1282 $[M+H]^+$; found 288.1283.

4.4.16. 1-Isopropyl-3-methyl-4-phenyl-3-vinylazetidin-2-one **27b**

From β-lactam **10a**. Yield 228 mg (>99%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.13 (d, *J*=6.8 Hz, 3H, $(CH_3)_2CH$), 1.33 (d, *J*=6.8 Hz, 3H, $(CH_3)_2CH$), 1.49 (s, 3H, $CH_3CCH{=}CH_2$), 3.78 (heptet, *J*=6.8 Hz, 1H, $(CH_3)_2CH$), 4.39 (s, 1H, *CH*Ar), 4.98 (d, *J*=9.5 Hz, 1H, $CH{=}CH_2$), 5.20–5.30 (m, 2H, $CH{=}CH_2$), 7.22–7.35 (m, 5H, ArH); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 20.4, 20.6, 21.2, 45.0, 61.3, 66.5, 116.7, 127.6, 128.1, 128.3, 130.3, 134.9, 171.7; FTIR (film): 3062, 3030, 2975, 2933, 1747, 1457, 1380, 1370 cm^{-1}; GC–MS (70 eV) *m*/*z* 229 (<1) $[M]^+$, 214 (2), 186 (4), 144 (67), 129 (100), 104 (9), 82 (10); HRMS-ESI: calcd for $C_{15}H_{20}NO$: 230.1546 $[M+H]^+$; found: 230.1546. Compound **27b** (from β-lactam **10b**). Yield 213 mg (93%).

4.4.17. 3-Deutero-1-isopropyl-4-phenyl-3-vinylazetidin-2-ones **28a, 28b**

Overall yield >99%. Compound **28a** (from β-lactam **10a**). Yield 64 mg (29.7%). The FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **10a**. In the ^{1}H NMR spectrum the double doublet at 3.56 ppm disappears, while the doublet at 4.33 ppm becomes a singlet; GC–MS (70 eV) *m*/*z* 216 (<1) $[M]^+$, 148 (2), 131 (100), 129 (60), 115 (23), 77 (6); HRMS-ESI: calcd for $C_{14}H_{17}DNO$ 217.0121 $[M+H]^+$; found: 217.0121. Compound **28b** (from β-lactam **10a**). Yield 149 mg (69%); the FTIR, ^{1}H and ^{13}C NMR data are the same of those reported for **10b**. In the ^{1}H NMR spectrum the double doublet at 4.03 ppm disappears, while the doublet at 4.82 ppm becomes a singlet; GC–MS (70 eV) *m*/*z* 216 (<1) $[M]^+$, 148 (2), 131 (100), 130 (65), 115 (23), 77 (5); HRMS-ESI: calcd for $C_{14}H_{17}DNO$ 217.0121 $[M+H]^+$; found: 217.0122.

4.5. General procedure for the preparation of compounds 29a–32a, 29b–32b

To a stirred solution of 1 mmol of the 2-azetidinone **15b**, or **21b** in THF (30 mL) at −78 °C, *n*-BuLi (2.5 M in hexanes, 0.5 mL, 1.2 mmol) was added dropwise under nitrogen. The resulting mixture was stirred at −78 °C for 30 min, and then the electrophile was added (1.5 mmol). The reaction was warmed up to room temperature and quenched with saturated aq NH_4Cl. The aqueous layer was extracted with Et_2O (3×20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford the pure functionalized β-lactams **29a**–**32a** and **29b**–**32b**; yields: 90–95%.

4.5.1. 1-tert-Butyl-4-deutero-3-methyl-4-pyridin-2-yl-3-vinylazetidin-2-ones *29a*, *29b*

Inseparable mixture of two *trans*- and *cis*-configurated diastereomers (dr=1:1 by ^{1}H NMR), the reaction was followed only via GC and ^{1}H NMR spectroscopy showing the formation of two compounds. From the ^{1}H NMR spectrum of the mixture we identified and assigned separate signals for **29a** and **29b**, respectively. Compound **29a**. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.90 (s, 3H, CH_3CCH=CH_2), 1.32 (s, 9H, $(CH_3)_3$), 5.20 (d, J=10.1 Hz, 1H, CH=CH_2), 5.35 (d, J=17.1 Hz, 1H, CH=CH_2), 5.80–5.90 (m, 1H, CH=CH_2), 7.10–7.20 (m, 2H, ArH), 7.58 (t, J=7.5 Hz, 1H, ArH), 8.55 (d, J=4.5 Hz, 1H, ArH). Compound **29b**. The ^{1}H NMR data are the same of those reported for **15b** except the singlet at 4.59 ppm that disappears. GC–MS performed on the mixture showed two peaks having the same fragmentation and $[M]^+$=245 (<1).

4.5.2. 1-tert-Butyl-3,4-dimethyl-4-pyridin-2-yl-3-vinylazetidin-2-ones (*30a*+*30b*)

Overall yield 243 mg (94%), oil; inseparable mixture of two *trans*- and *cis*-configurated diastereomers (dr=1:2 by ^{1}H NMR). Compound **30a**. Yield 75 mg (29%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.73 (s, 3H, CH_3CCH=CH_2), 1.35 (s, 9H, $(CH_3)_3$), 1.86 (s, 3H, CH_3CAr), 5.25 (d, J=10.8 Hz, 1H, CH=CH_2), 5.39 (d, J=16.4 Hz, 1H, CH=CH_2), 5.83–5.89 (m, 1H, CH=CH_2), 7.19 (dd, J=4.7, 7.7 Hz, 1H, ArH), 7.51 (d, J=7.7 Hz, 1H, ArH), 7.67 (t, J=7.7 Hz, 1H, ArH), 8.60 (d, J=4.7 Hz, 1H, ArH); GC–MS (70 eV) m/z 258 (<1) $[M]^+$, 202 (10), 158 (100), 144 (20), 79 (7). Compound **30b**. Yield 168 mg (65%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 1.39 (s, 9H, $(CH_3)_3$), 1.45 (s, 3H, CH_3CCH=CH_2), 1.95 (s, 3H, CH_3CAr), 4.77 (d, J=10.6 Hz, 1H, CH=CH_2), 4.99–5.06 (m, 1H, CH=CH_2), 5.19 (d, J=17.5 Hz, 1H, CH=CH_2), 7.16 (dd, J=4.6, 7.8 Hz, 1H, ArH), 7.44 (d, J=7.8 Hz, 1H, ArH), 7.64 (t, J=7.8 Hz, 1H, ArH), 8.56 (d, J=4.6 Hz, 1H, ArH); GC–MS (70 eV) m/z 258 (<1) $[M]^+$, 202 (4), 158 (100), 144 (22), 79 (8). Compounds (**30a**+**30b**). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 17.4, 17.5, 21.2, 22.8, 28.7, 28.8, 54.9, 55.0, 63.2, 68.7, 70.5, 70.8, 115.5, 116.7, 121.6, 121.8, 122.5, 135.3, 135.5, 136.3, 148.5, 148.8, 162.2, 162.3, 171.5, 171.6; FTIR ($CHCl_3$): 3015, 2970, 2930, 1735, 1594, 1438, 1368 cm^{-1}; HRMS-ESI: calcd for $C_{16}H_{23}N_2O$: 259.1812 $[M+H]^+$; found: 259.1812.

4.5.3. 1-n-Butyl-4-deutero-3-methyl-4-pyridin-2-yl-3-vinylazetidin-2-ones *31a*, *31b*

Inseparable mixture of two *trans*- and *cis*-configurated diastereomers (dr=1:1 by ^{1}H NMR), the reaction was followed only via GC and ^{1}H NMR spectroscopy showing the formation of two compounds. From the ^{1}H NMR spectrum of the mixture we identified and assigned separate signals for **31**a and **31b**, respectively. Compound **31a**. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.79 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.25–1.40 (m, 2H, CH_3CH_2), 1.50–1.55 (m, 2H, $CH_3CH_2CH_2$), 1.56 (s, 3H, CH_3CCH=CH_2), 2.95–2.99 (m, 1H, CH_2CH_2–N), 3.56–3.65 (m, 1H, CH_2CH_2–N), 5.25 (d, J=10.0 Hz, 1H, CH=CH_2), 5.31 (d, J=17.1 Hz, 1H, CH=CH_2), 6.05–6.10 (m, 1H, CH=CH_2), 7.17 (d, J=7.7 Hz, 1H, ArH), 7.25 (dd, J=4.7, 7.7 Hz, 1H, ArH), 7.65 (t, J=7.7 Hz, 1H, ArH), 8.60 (d, J=4.7 Hz, 1H, ArH). Compound **31b**. The ^{1}H NMR data are the same of those reported for **21b** except the singlet at 4.60 ppm that disappears. GC–MS performed on the mixture showed two peaks having the same fragmentation and $[M]^+$=245 (18).

4.5.4. 1-n-Butyl-3,4-dimethyl-4-pyridin-2-yl-3-vinylazetidin-2-ones (*32a*+*32b*)

Overall yield 245 mg (95%), oil; inseparable mixture of two *trans*- and *cis*-configurated diastereomers (dr=1:4 by ^{1}H NMR). Compound **32a**. Yield 49 mg (19%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.79 (s, 3H, CH_3CCH=CH_2), 0.94 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.22–1.30 (m, 2H, CH_3CH_2), 1.61–1.68 (m, 2H, $CH_3CH_2CH_2$), 1.71 (s, 3H, CH_3CAr), 2.92–2.99 (m, 1H, CH_2CH_2–N), 3.24–3.30 (m, 1H, CH_2CH_2–N), 5.26 (d, J=9.5 Hz, 1H, CH=CH_2), 5.43 (d, J=17.3 Hz, 1H, CH=CH_2), 5.90–5.96 (m, 1H, CH=CH_2), 7.15–7.27 (m, 2H, ArH), 7.70 (t, J=8.0 Hz, 1H, ArH), 8.62 (d, J=4.5 Hz, 1H, ArH). Compound **32b**. Yield 196 mg (76%), yellow oil; ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 0.94 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.20–1.28 (m, 2H, CH_3CH_2), 1.46 (s, 3H, CH_3CCH=CH_2), 1.60–1.67 (m, 2H, $CH_3CH_2CH_2$), 1.80 (s, 3H, CH_3CAr), 3.08–3.12 (m, 1H, CH_2CH_2–N), 3.44–3.49 (m, 1H, CH_2CH_2–N), 4.77 (dd, J=3.0, 8.8 Hz, 1H, CH=CH_2), 5.08–5.14 (m, 2H, CH=CH_2), 7.15–7.24 (m, 2H, ArH), 7.66 (t, J=7.9 Hz, 1H, ArH), 8.59 (d, J=4.0 Hz, 1H, ArH). Compounds (**32a**+**32b**): ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 12.4, 13.7, 16.8, 17.9, 19.8, 20.0, 20.6, 21.3, 31.2, 31.6, 39.2, 39.4, 40.6, 45.5, 64.4, 69.4, 115.5, 116.6, 117.0, 120.6, 121.0, 121.5, 121.9, 122.7, 135.9, 136.1, 149.1, 149.4, 161.0, 161.1, 171.5, 171.8; FTIR ($CHCl_3$): 3010, 2961, 2931, 2873, 1747, 1579, 1432, 1400 cm^{-1}; GC–MS (70 eV) m/z 258 (3) $[M]^+$, 243 (2), 215 (1), 187 (5), 159 (33), 158 (100), 144 (21), 106 (9), 78 (7); HRMS-ESI: calcd for $C_{16}H_{23}N_2O$: 259.1812 $[M+H]^+$; found: 259.1812.

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