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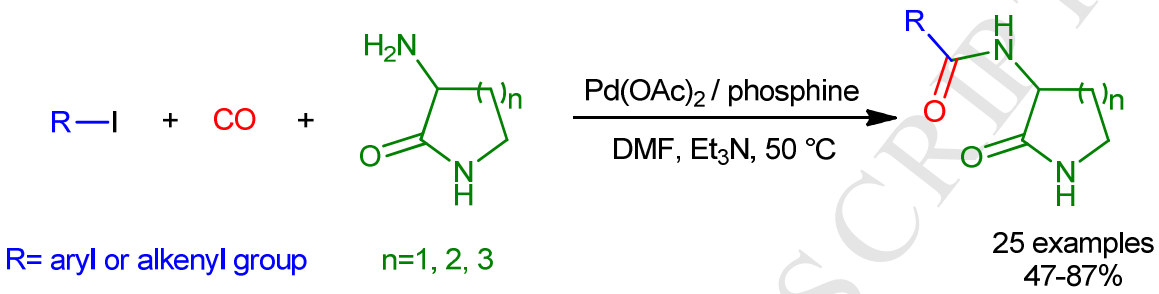
Graphical abstract



Novel synthesis of 3-carboxamidolactam derivatives via palladium-catalysed aminocarbonylation.

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Abstract: Aminocarbonylation of alkenyl and (hetero)aryl iodides using medium-sized 3-aminolactams as *N*-nucleophiles was carried out in the presence of *in situ* palladium(0) catalysts. While the iodoalkenes were converted to the corresponding carboxamide under mild reaction condition (1 bar of CO, 50 °C) by using $Pd(OAc)_2$ / PPh_3 catalysts, the iodobenzene shown decreased reactivity (39% conversion after 2 days) under the similar reaction conditions in the presence of 3-aminoazepan-2-one. The reactivity of iodobenzene and other iodo(hetero)aromatic substrates was increased with 3-aminoazepan-2-one under high (40 bar) carbon monoxide pressure, but the chemoselectivity was shifted towards the 2-ketocarboxamides formed via double carbon monoxide insertion (except 2-iodopyridine). Changing triphenylphosphine to Xantphos, the expected carboxamides were chemoselectively formed in all cases when iodo(hetero)aryl substrates were used in the presence of all of the three 3-aminolactams under mild reaction conditions. The products synthesized in the reactions mentioned above were isolated in moderate to high yields.

Key-words: palladium, 3-aminolactam, carbonylation, carbon monoxide, carboxamide

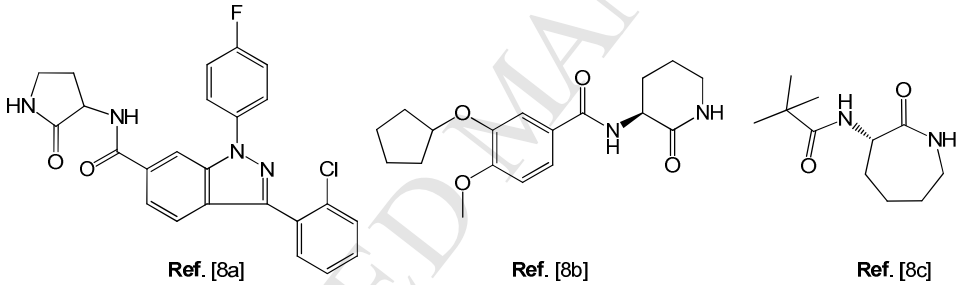
1. Introduction

Aminocarbonylation, *i.e*. the palladium-catalysed carbonylation of alkenyl or aryl halides (preferentially iodides) or their synthetic surrogates, sulfonates (preferentially triflates) in the presence of N-nucleophiles was discovered by Heck *et al* ('Heck carbonylation')[1] and widely applied in synthesis.[2] This homogeneous catalytic procedure proved to be highly efficient for the synthesis of carboxamides possessing even more complicated skeletons of biological importance.[3] The double insertion of CO leading to 2-ketocarboxamides was also investigated.[4]

The mechanistic details of the reaction were also investigated but most studies are focused on the oxidative addition step only.[5] To the best of our knowledge, sporadic results are published on a reaction mechanism involving carbon monoxide activation and insertion. [6] Recently, computational chemistry studies were also started to shed some light onto mechanistic details. [7]

Concerning N-nucleophiles, a wide variety of primary and secondary amines, among them functionalised ones such as amino acid esters, N-heterocycles, *etc*. have already been used. Aminolactams are challenging nucleophiles for aminocarbonylation since the series of N-acylated aminolactams with biological importance could be available in this way.[8]

Fig. 1. 3-(Acylamino)lactam-based compounds of biological importance



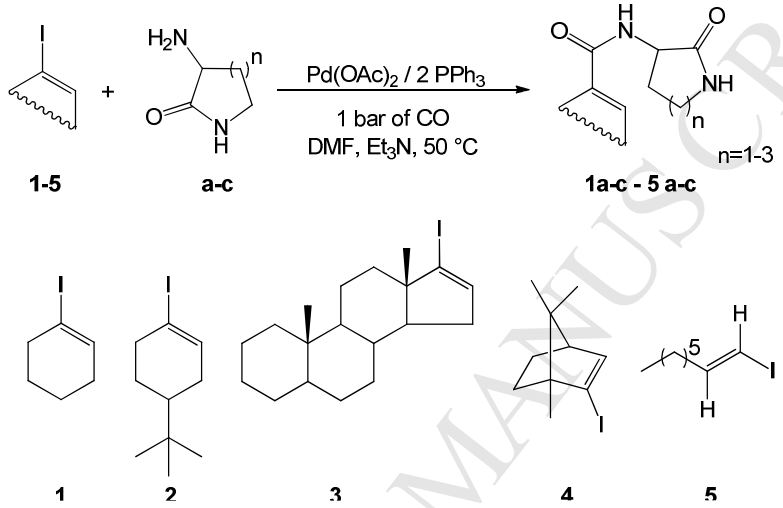
Ref. [8a] **Ref**. [8b] **Ref**. [8c]

In this paper, the use of aminolactams as building block in aminocarbonylation reaction will be described. In other words, the highly efficient acylation of the amino functionality of a lactam ring via palladium-catalysed reaction can be carried out.

2. Results and discussion

*2.1. Aminocarbonylation of iodoalkenes (**1-5**) in the presence of 3-amino lactam (**a-c**) N-nucleophiles*

1-Iodocyclohexene (**1**), 4-*tert*-butyl-1-iodocyclohexene (**2**), 17-iodoandrost-16-ene (**3**), 2-iodobornene (**4**), and *trans*-1-iodo-1-octene (**5**) were aminocarbonylated using 3-aminoazepan-2-one (**a**, n=3), 3-aminopiperidin-2-one (**b**, n=2) and 3-aminopyrrolidin-2-one (**c**, n=1) under carbon monoxide atmosphere (*Scheme 1*). A coordinatively unsaturated, low-ligated palladium(0) catalyst, prepared *in situ* from palladium(II) acetate and two molar equivalents of triphenylphosphine, was used.[9] According to the generally accepted mechanism[10], the palladium(0) catalyst is indispensable to oxidatively add the starting iodoalkene substrate.



Scheme 1. Aminocarbonylation of iodoalkenes (**1**-**5**) in the presence of 3-aminolactams (**a**-**c**)

The substrates have shown excellent reactivity leading to practically complete conversion within less than 2 hours (*Table 1, entries 1, 2; 12, 13*) under standard conditions (1 bar CO, 50 ^{o}C). The reaction was completely chemoselective, *i.e.*, carboxamides were formed exclusively due to single CO insertion. All three aminolactams (**a**-**c**) proved to be excellent N-nucleophile.

A slight decrease of the reaction temperature (to 40 ^{o}C) resulted in longer reaction times needed to get full conversion (*entry 3 and 6*). Increasing CO pressure did not affect the chemoselectivity, and no double CO insertion was observed (*entry 5*). The high conversion and selectivity enabled facile isolation of the target compounds in good to excellent yields.

It is worth noting that the widely used solvent DMF can be substituted for green solvents such as GVL (γ-valerolactone) (*entry 7*) and methyl 4-methoxybutyrate[11] (*entry 8*) without substantial loss of activity.

Table 1. Aminocarbonylation of **1-5** in the presence of 3-aminolactams [a)]

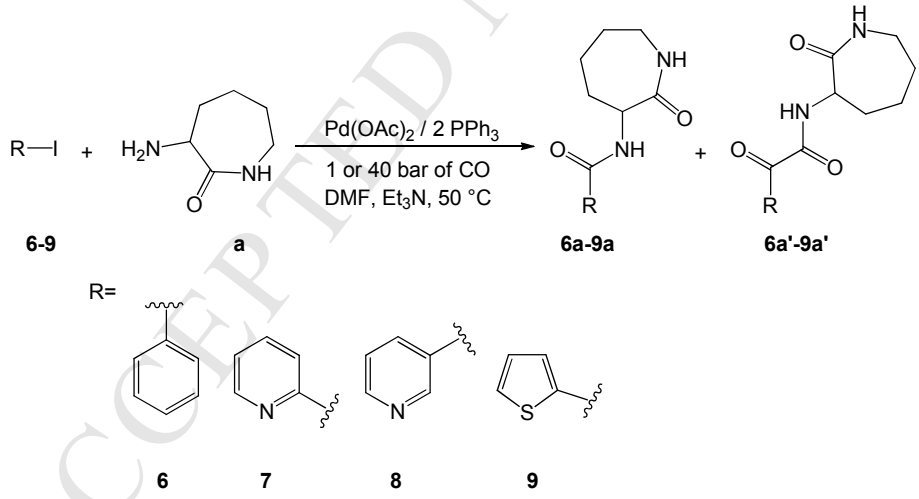
Entry	Substrate	Amine	R. time [h]	Conv. [b)] [%]	Isolated yield [c)] [%]
1	**1**	**a**	1	90	n. i. [h)]
2	**1**	**a**	2	>98	87 (**1a**)
3 [d)]	**1**	**a**	5	>98	79 (**1a**)
4	**2**	**a**	1	>98	74 (**2a**)
5 [e)]	**2**	**a**	2	88	n. i. [h)]
6 [d)]	**2**	**a**	5	>98	72 (**2a**)
7 [f)]	**2**	**a**	1	>98	70 (**2a**)
8 [g)]	**2**	**a**	4	>98	61 (**2a**)
9	**3**	**a**	1	>98	81 (**3a**)
10	**4**	**a**	1	>98	87 (**4a**)
11	**5**	**a**	1	>98	76 (**5a**)
12	**1**	**b**	1	90	n. i. [h)]
13	**1**	**b**	2	>98	75 (**1b**)
14	**2**	**b**	1	40	n. i. [h)]
15	**2**	**b**	2	>98	73 (**2b**)
16	**3**	**b**	3	>98	67 (**3b**)
17	**4**	**b**	1	>98	75 (**4b**)
18	**5**	**b**	1	>98	72 (**5b**)
19	**1**	**c**	1	>98	51 (**1c**)
20	**3**	**c**	4	>98	54 (**3c**)
21	**5**	**c**	1	>98	52 (**5c**)

a) Reaction conditions: 0.5 mmol of substrate (**1-5**), 0.55 mmol of 3-aminolactams (**a-c**), 0.0125 mmol of $Pd(OAc)_2$, 0.025 mmol of PPh_3, 0.25 mL (1.625 mmol) of Et_3N, 5 mL of DMF, 1 bar of CO, 50 ^oC.
b) Determined by GC-MS.
c) Yields of the isolated target compound (based on the substrates (**1-5**))
d) The reaction was carried out in THF at 40 ^oC.
e) The reaction was carried out at 40 bar of CO.
f) The reaction was carried out in GVL.
g) The reaction was carried out in methyl 4-methoxybutyrate.
h) Not isolated.

*2.2. Aminocarbonylation of iodoarenes (**6-9**) using 3-amino-ε-caprolactam (**a**) in the presence of $Pd(OAc)_2$ / 2 PPh_3 catalysts*

The parent 'in situ' catalytic system formed from $Pd(OAc)_2$ and 2 PPh_3 was tested in the aminocarbonylation of various iodoarenes (**6-9**) with 3-amino-ε-caprolactam (**a**) as N-nucleophile. The aminocarbonylation of iodoaromatics needed longer reaction times than the iodalkenes (*2.1.*). Furthermore, in contrast to the iodoalkene substrates, a mixture of two products were obtained in all cases (*Scheme 2*). The single and double CO insertion led to the formation of carboxamides (**6a**-**9a**) and 2-ketocarboxamides (**6a'**-**9a'**), respectively.

In general, the formation of carboxamides is favored at atmospheric pressure using substrate **6** *(entries 1-3.)*. Due to the low conversion (42%) after 48 hours the reaction had to be carried out under high carbon monoxide pressure (40 bar) to reach complete conversion (*entry 6., Fig. 2.*). Using iodobenzene (**6**) and other iodoheteroaromatic substrates (**8-9**), the 2-ketocarboxamides (**6a', 8a', 9a'**) were preferentially formed at elevated carbon monoxide pressure (*entries 6., 10., 12.*). 2-Iodopyridine (**7**) as model compound has shown a completely different behavior regarding chemoselectivity: the corresponding 2-ketocarboxamide (**7a'**) was formed as minor product even at high pressure (*entry 8.*). This observation is in accordance with the results obtained in our previous systematic investigations with nitrogen-containing iodoheteroaromatics.[12] Comparing the reactivity of the heteroaryl iodides, the 2-iodopyridine (**7**) showed much more reactivity (75% conversion after 6 hours) than the 3-iodopyridine (**8**) and the 2-iodothiophene (**9**) substrates in the presence of 3-amino-ε-caprolactam at 40 bar of carbon monoxide pressure (*Fig. 3.*).



Scheme 2. Aminocarbonylation of iodoarenes (**6-9**) with 3-amino-ε-caprolactam (**a**) in the presence of $Pd(OAc)_2$ / 2 PPh_3 catalysts

Table 2. Aminocarbonylation of iodoarenes (**6-9**) with 3-amino-ε-caprolactam (**a**) in the presence of $Pd(OAc)_2$ / 2 PPh_3 catalysts [a)]

Entry	Substrate	R. time [h]	p(CO) [bar]	Conv. [b)] [%]	Ratio of the carbonylated products [b)]	
					carboxamide (**6a-9a**)	2-ketocarboxamide (**6a'-9a'**)
1	**6**	2	1	<1	66 (**6a**)	34 (**6a'**)
2	**6**	20	1	10	78 (**6a**)	22 (**6a'**)
3	**6**	48	1	42	73 (**6a**)	27 (**6a'**)
4	**6**	2	40	4	23 (**6a**)	77 (**6a'**)
5	**6**	20	40	43	27 (**6a**)	73 (**6a'**)
6	**6**	48	40	95	24 (**6a**)	76 (**6a'**), 47 [c)]
7	**7**	6	40	75	95 (**7a**)	5 (**7a'**)
8	**7**	24	40	>98	93 (**7a**), 81 [c)]	7 (**7a'**)
9	**8**	48	40	84	25 (**8a**)	75 (**8a'**), 38 [c)]
10	**8**	96	40	>98	22 (**8a**)	78 (**8a'**)
11	**9**	48	40	73	12 (**9a**)	88 (**9a'**)
12	**9**	96	40	>98	12 (**9a**)	88 (**9a'**), 44 [c)]

a) Reaction conditions: 0.5 mmol of substrate (**6-9**), 0.55 mmol of 3-amino- ε-caprolactam (**a**), 0.0125 mmol of $Pd(OAc)_2$, 0.025 mmol of PPh_3, 0.25 mL (1.625 mmol) of Et_3N, 5 mL of DMF, 1 or 40 bar of CO, 50 °C.
b) Determined by GC-MS.
c) Yields of the isolated target compounds (%), (based on the substrates (**6-9**)).

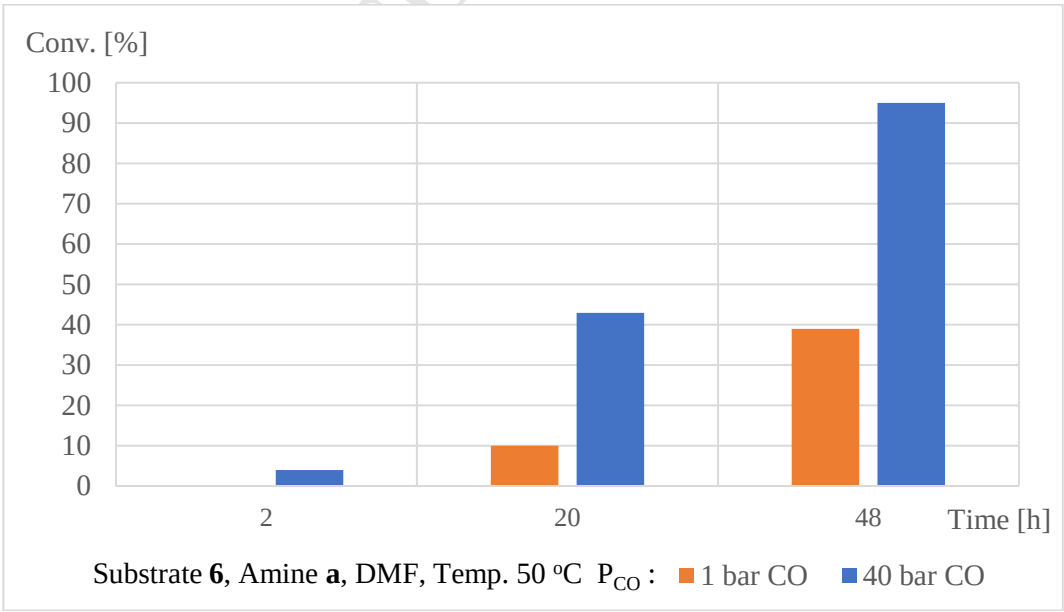


Fig. 2. Conversion as a function of time of the aminocarbonylation of **6** in the presence of amine **a**.

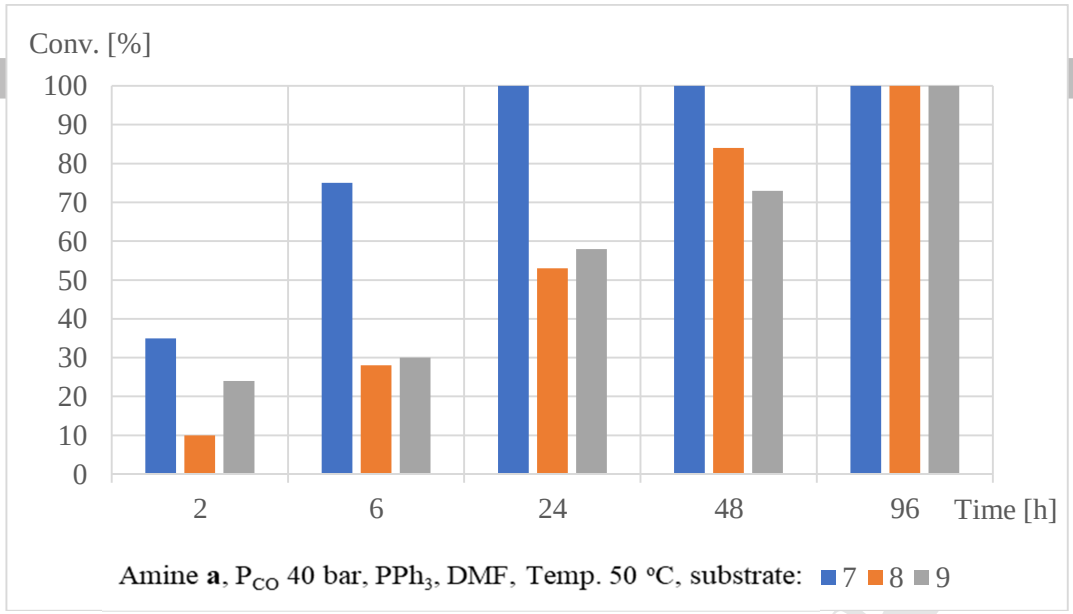
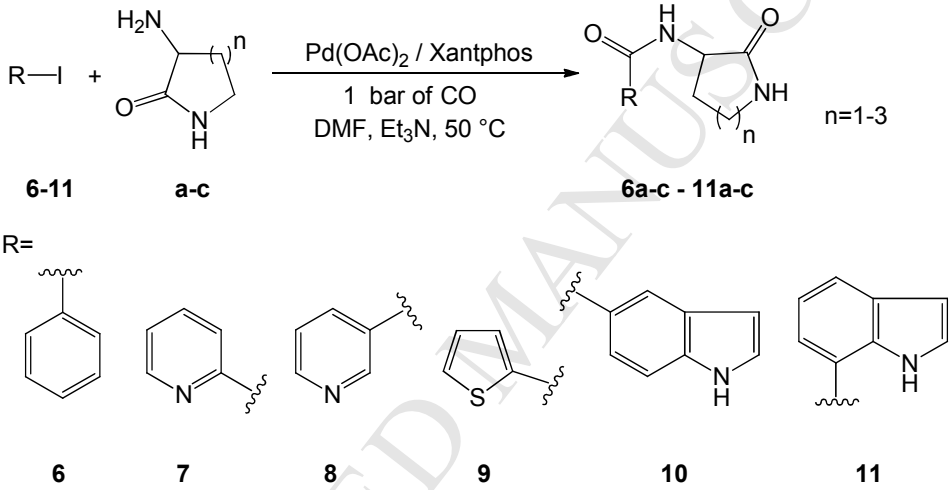


Fig. 3. Conversion as a function of time of the aminocarbonylation of **7**, **8** and **9** in the presence of amine **a**

2.3 *Aminocarbonylation of iodoarenes (**6-11**) in the presence of 3-aminolactam (**a-c**) N-nucleophiles using Xantphos*

Using the observations above obtained with the parent Pd-PPh_3 catalytic system, a large bite-angle ligand, Xantphos was selected to achieve higher yields and selectivities in the aminocarbonylation of iodoarenes (*Scheme 3*). In fact, an active catalyst even at atmospheric pressure both in DMF (*Table 3, entries 1-3*) and THF (*entries 7-10*) was obtained for the aminocarbonylation of **6** with **a** (n=3) as nucleophile. The Xantphos-containing system provided not only higher activity but also prefect selectivity toward carboxamide at low pressure. As expected, a carboxamide / 2-ketocarboxamide mixture was obtained at 40 bar CO pressure (*entries 4-6*). Under standard mild conditions (1 bar CO, 50 ^{o}C) high selectivity toward carboxamide products was observed with the other iodoarenes (**7**-**11**) as well (*entries 11-15*).

The other two nucleophiles (**b** (n=2) and **c** (n=1)) has shown similar activities with the series of substrates (*entries 16-25*).



Scheme 3. Aminocarbonylation of iodoarenes (**6-11**) in the presence of 3-aminolactam (**a-c**) N-nucleophiles using Xantphos

Table 3. Aminocarbonylation of iodoarenes (**6-11**) in the presence of 3-aminolactams (**a-c**) N-nucleophiles using Xantphos

Entry	Substrate	Amine	R. time [h]	Conv. [b] [%]	% of Carboxamide [b]
1	**6**	**a**	1	63	100 (**6a**)
2	**6**	**a**	4	88	100 (**6a**)
3	**6**	**a**	24	>98	100 (**6a**), 77 [c]
4 [d]	**6**	**a**	6	13	20 [e] (**6a**)
5 [d]	**6**	**a**	24	30	40 [e] (**6a**)
6 [d]	**6**	**a**	48	88	36 [e] (**6a**)
7 [f]	**6**	**a**	24	52	100 (**6a**)
8 [f]	**6**	**a**	48	95	100 (**6a**)
9 [g]	**6**	**a**	24	71	100 (**6a**)
10 [g]	**6**	**a**	48	>98	100 (**6a**)
11	**7**	**a**	1	>98	100 (**7a**), 88 [c]
12	**8**	**a**	22	>98	100 (**8a**), 54 [c]
13	**9**	**a**	22	>98	100 (**9a**), 68 [c]
14	**10**	**a**	22	>98	100 (**10a**), 69 [c]
15	**11**	**a**	22	>98	100 (**11a**), 74 [c]
16	**6**	**b**	6	95	100 (**6b**)
17	**6**	**b**	8	>98	100 (**6b**), 56 [c]
18	**7**	**b**	1	94	100 (**7b**)
19	**7**	**b**	2	>98	100 (**7b**), 76 [c]
20	**8**	**b**	12	84	100 (**8b**)
21	**8**	**b**	24	>98	100 (**8b**), 36 [c]
22	**9**	**b**	12	81	100 (**9b**)
23	**9**	**b**	24	>98	100 (**9b**), 45 [c]
24	**10**	**b**	24	>98	100 (**10b**), 71 [c]
25	**6**	**c**	2	>98	100 (**6c**), 47 [c]

a) Reaction conditions: 0.5 mmol of substrate (**6-11**), 0.55 mmol of 3-aminolactams (**a-c**), 0.0125 mmol of $Pd(OAc)_2$, 0.0125 mmol of Xantphos, 0.25 mL (1.625 mmol) of Et_3N, 5 mL of DMF, 1 bar of CO, 50 ^oC.
b) Determined by GC-MS.
c) Yields of the isolated target compounds (%), (based on the substrates (**6-11**)).
d) The reaction was carried out at 40 bar of CO.
e) The corresponding 2-ketocarboxamide (**6a'**) was also formed in the reaction. The ratio of the products was determined by GC-MS.
f) The reaction was carried out in THF at 40 ^oC.
g) The reaction was carried out in THF at 50 ^oC.

Comparing the Pd-PPh_3 and Pd-Xantphos systems, the higher activity of the latter is obvious (*Fig. 4*). In case of the Xantphos system, the higher CO pressure resulted in lower activity (*Fig. 5*). That is, carbon monoxide has an inhibition effect on catalytic activity.

The DMF proved to be more suitable solvent than THF (*Fig 6*). In general, approximately one day is needed to accomplish aminocarbonylation with nucleophile **a** under given conditions. However, 2-iodopyridine (**7**), the substrate providing carboxamide only, can be fully converted within 1 h (*Fig. 7*). A similar phenomenon, *i.e.* the high reactivity of **7** was observed using nucleophile **b** (*Fig. 8*).

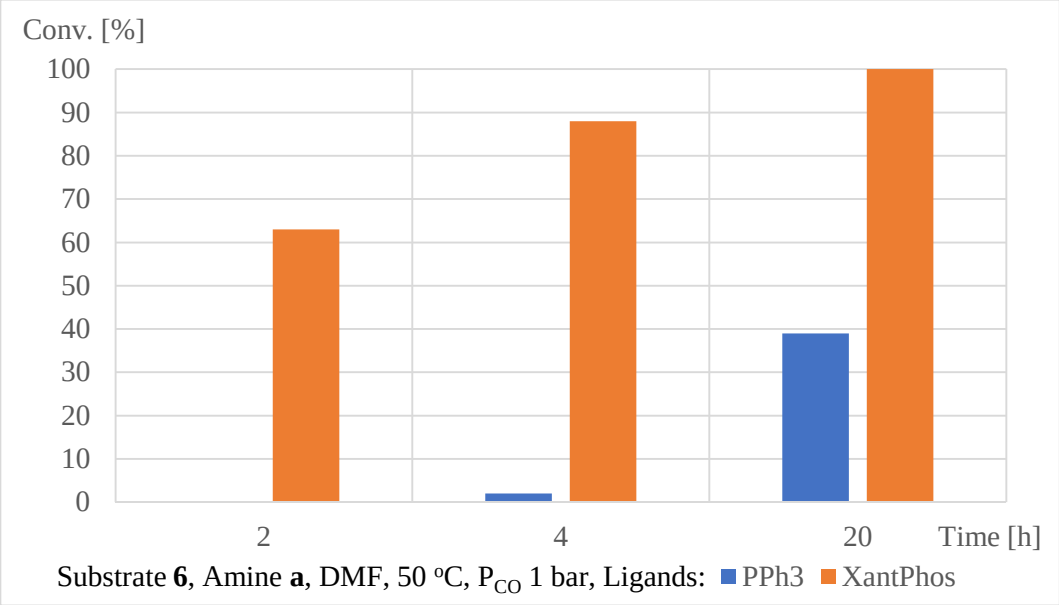


Fig. 4. Conversion as a function of time of the aminocarbonylation of **6** in the presence of amine **a**.

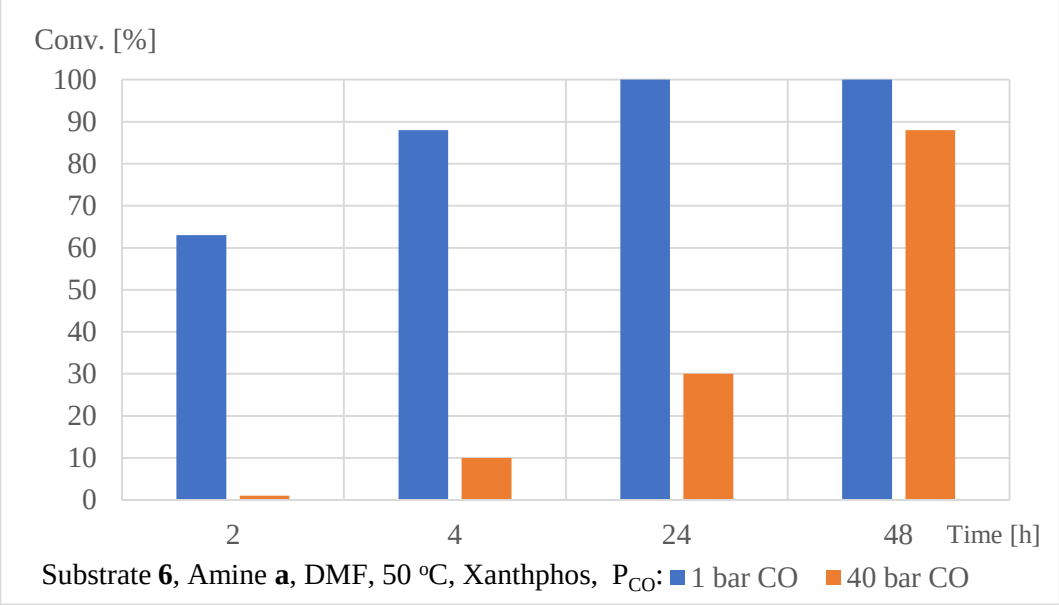


Fig. 5. Conversion as a function of time of the aminocarbonylation of **6** in the presence of amine **a**.

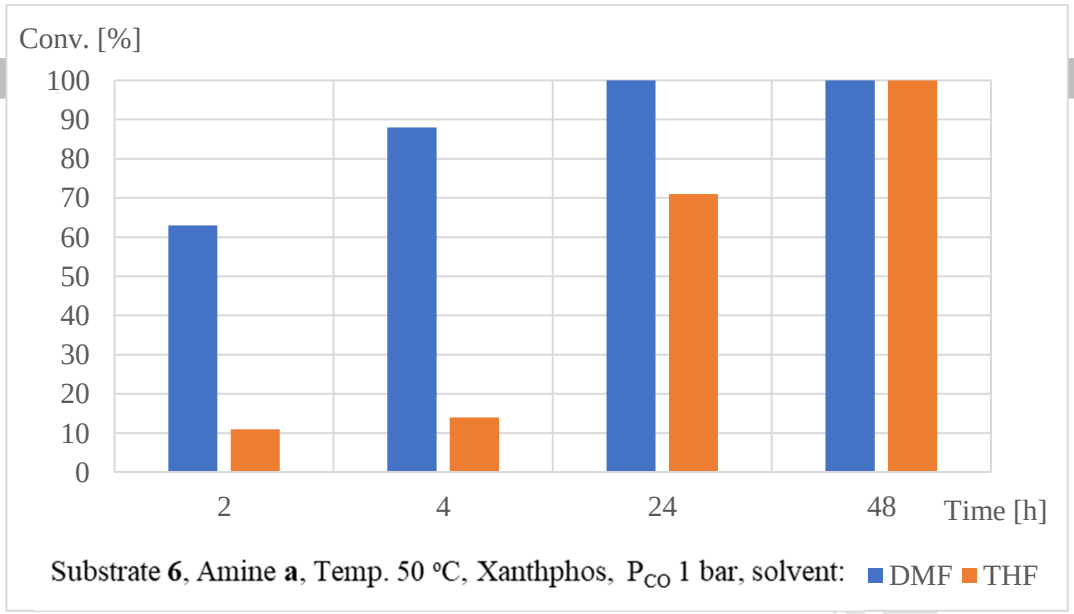


Fig. 6. Conversion as a function of time of the aminocarbonylation of **6** in the presence of amine **a**.

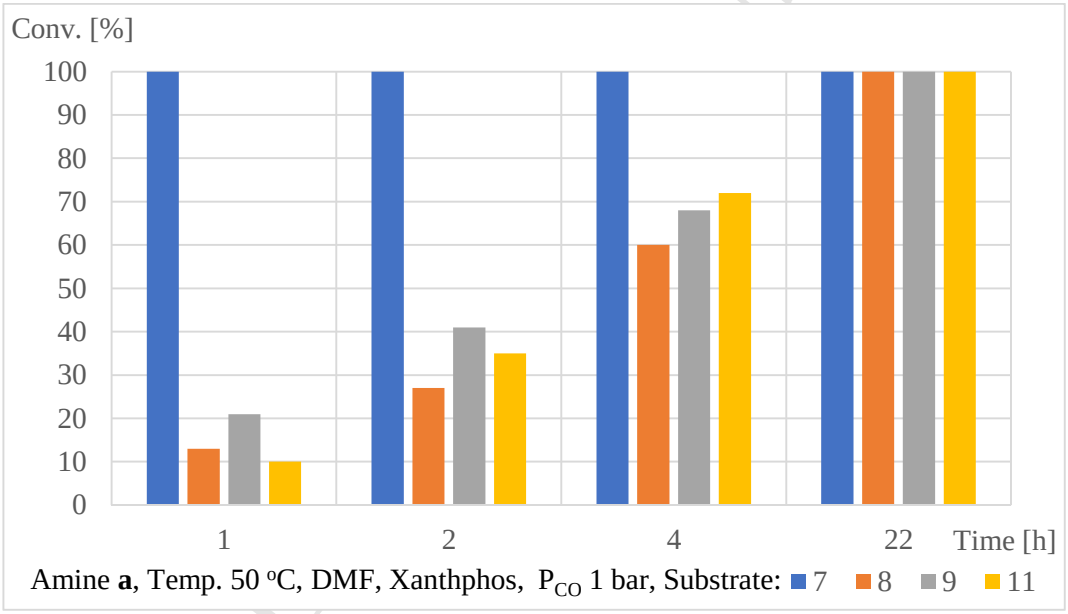


Fig. 7. Conversion as a function of time of the aminocarbonylation of **7, 8, 9** and **11** in the presence of amine **a**.

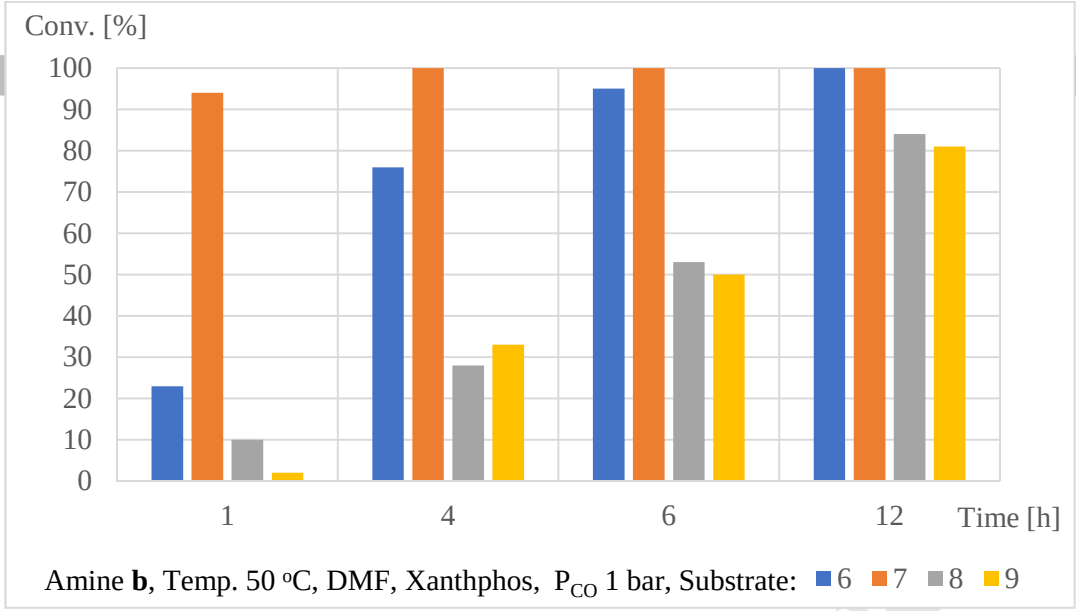


Fig. 8. Conversion in a function of time of the aminocarbonylation of **6, 7, 8,** and **9** in the presence of amine **b**.

2.4. Conclusions

In summary, medium-sized 3-aminolactam derivatives (3-amino-azepan-2-one, 3-amino-piperidin-2-one, 3-amino-pyrrolidin-2-one) can be used as *N*-nuclophiles in palladium-catalysed aminocarbonylation. Compounds with iodoalkene functionalities, among them compounds possessing biologically important skeletons, undergo facile aminocarbonylation toward carboxamides as exclusive products in the presence of $Pd(OAc)_2$ / PPh_3 catalysts at atmospheric carbon monoxide pressure. In contrast, the iodo(hetero)arenes have shown much lower reactivity than the above mentioned iodoalkenes using the similar catalysts and reaction conditions. Increasing the carbon monoxide pressure (40 bar) the chemoselectivity was shifted towards the corresponding 2-ketocarboxamides (except 2-iodopyridine) due to double CO insertion. However, the aminocarbonylation of the iodo(hetero)aryl substrates with 3-aminolactam nucleophiles was carried out under atmospheric carbon monoxide pressure by using Xantphos instead of the monodentate PPh_3 providing selectively the expected carboxamide derivatives.

As described above, the yields of the target compounds are of synthetic importance especially in case of 7- and 6-membered lactams (*Fig. 9a* and *Fig. 9b*, respectively). The yields are acceptable even with 5-membered lactam (**c**) (*Fig. 9c*). It has to be added that the isolation procedures were not optimized, *i.e.* the yields depicted in *Fig. 9a-c* were obtained under these conditions.

In this way, a new synthetic method for the synthesis of various 3-(acylamino)-lactams has been described. The mild reaction conditions, the high selectivity and the moderate to high isolated yields, as well as the presence of the medium-sized lactam rings make this reaction of both synthetic and pharmacological importance.

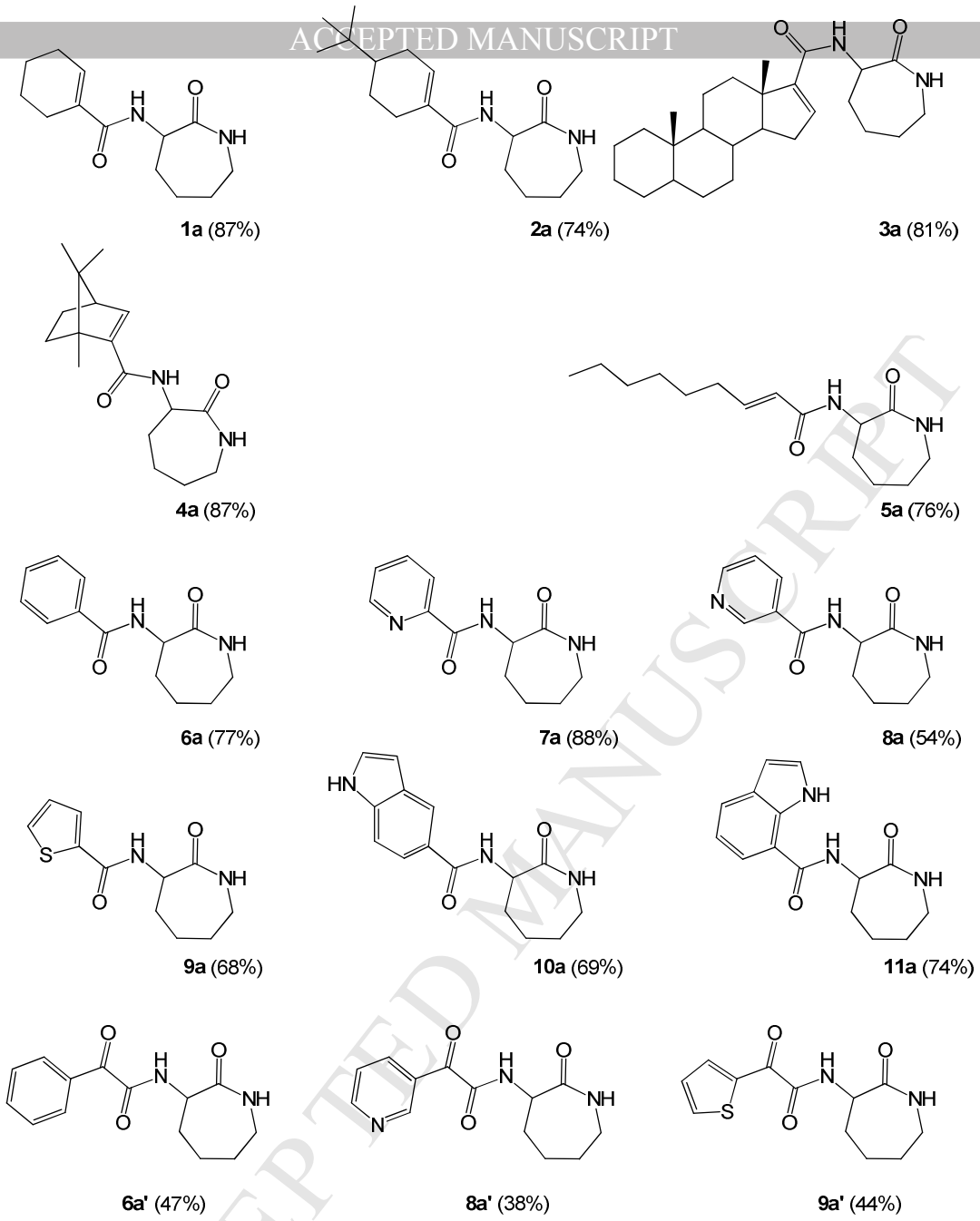


Fig. 9a. Products formed in the aminocarbonylation of **1-11** using **a** as nucleophile (isolated yields in brackets).

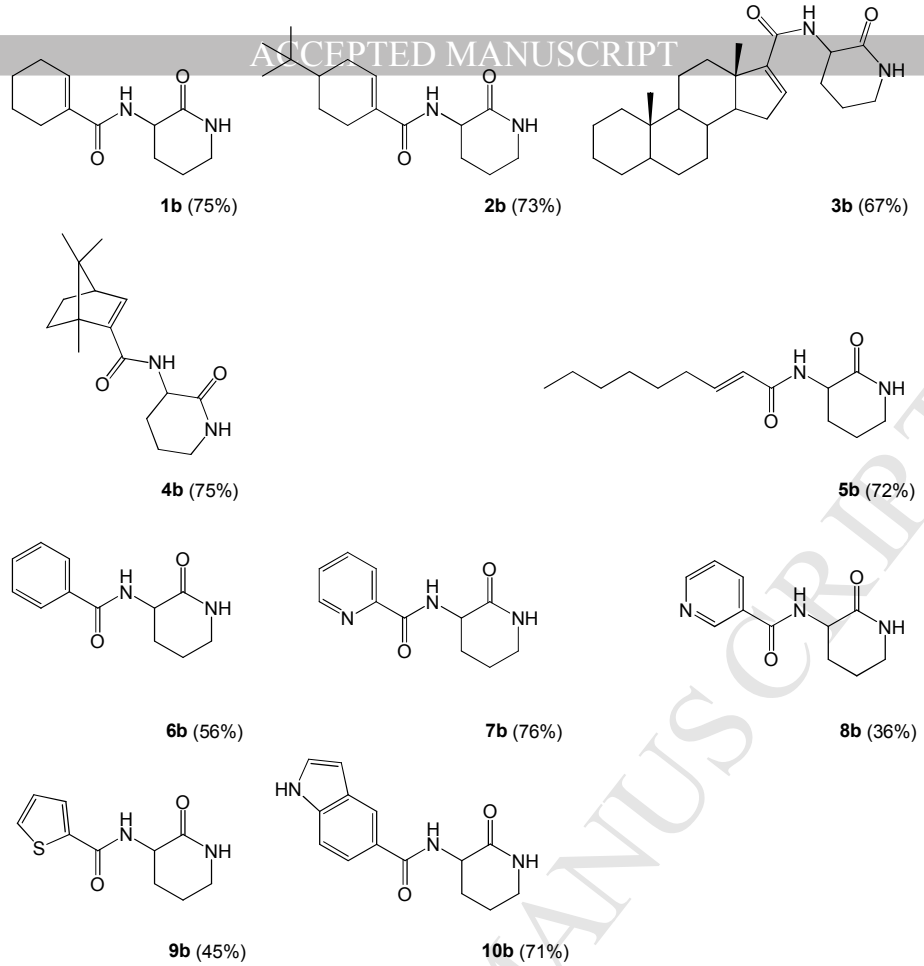


Fig. 9b. Products formed in the aminocarbonylation of **1**-**10** using **b** as nucleophile (isolated yields in brackets).

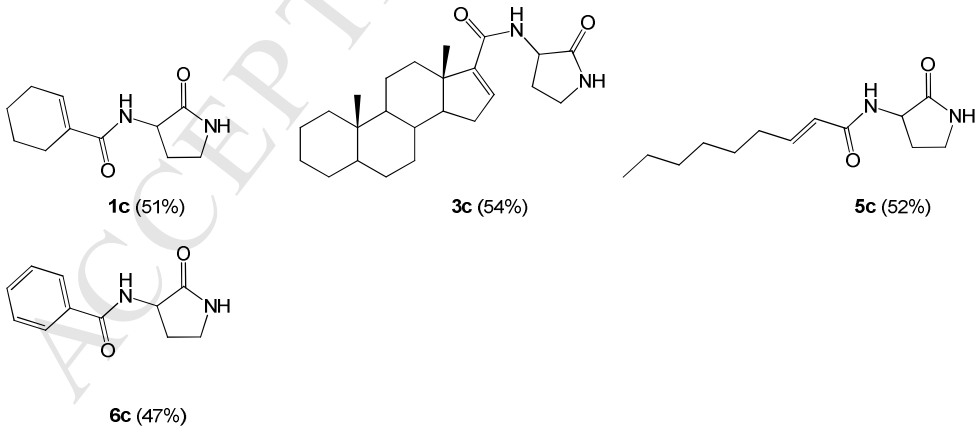


Fig. 9c. Products formed in the aminocarbonylation of **1**, **3**, **5** and **6** using **c** as nucleophile (isolated yields in brackets).

3. Experimental

3.1. General procedures

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Avance III 500 spectrometer at 500 and 125.7 MHz, respectively. Chemical shifts δ are reported in ppm relative to $CHCl_3$ (7.26 and 77.00 ppm for ^{1}H and ^{13}C, respectively). Elemental analyses were measured on a 1108 Carlo Erba apparatus. The FT-IR spectra were taken in KBr pellets using an IMPACT 400 spectrometer (Nicolet) applying a DTGS detector in the region of 400-4000 cm^{-1}, the resolution was 4 cm^{-1}. The amount of the samples was *ca*. 0.5 mg. Mass spectrometry data have been obtained using a GC-MS system consisting of a Perkin Elmer AutoSystem XL gas-chromatograph. Melting points are uncorrected and were measured with a Büchi apparatus. TLC plates (silica gel or aluminium oxide on TLC Al foils with fluorescence indicator 254 nm) were purchased from Sigma-Aldrich. The eluents used in thin-layer chromatography are specified below.

trans-1-Iodo-1-octene (**5**), iodo(hetero)aromatic substrates (**6-11**) and 3-aminolactams (**a-c**) were purchased from Sigma-Aldrich and were used without further purification. 1-Iodocyclohexene[13] (**1**), 4-tert-butyl-1-iodocyclohexene[13] (**2**), 17-androst-16-ene[14] (**3**), 2-iodobornene[15] (**4**) were synthesized by the modified Barton-procedure[16].

The characterization of the carboxamides **1a**[8c], **6a**[17], **7a**[18], **8a**[17], **9a**[19] **6b**[17], **8b**[17], which were synthesized by the conventional (acylation) reactions was already published. The compounds isolated in this work gave practically identical spectra. However, due to some further analytical details (for instance detailed description of NMR spectra) the full characterization is given below for all compounds.

*3.2. Aminocarbonylation of iodoalkenes (**1-5**) and iodo(hetero)arenes (**6-11**) in the presence of nucleophiles **a-c** under atmospheric pressure of carbon monoxide.*

In a typical experiment $Pd(OAc)_2$ (2.81 mg, 0.0125 mmol), triphenylphosphine (6.55 mg, 0.025 mmol) or Xantphos (7.23 mg, 0.0125 mmol), iodoalkene (**1-5**) or iodo(hetero)arene (**6-11**) substrates (0.5 mmol), and 3-aminolactams (3-amino-azepan-2-one (**a**), 3-amino-piperidin-2-one (**b**), 3-amino-pyrrolidin-2-one (**c**)) (0.55 mmol) and triethylamine (0.25 mL) were dissolved in DMF (5 mL) under argon in a 100 mL three-necked flask equipped with reflux condenser connected to a balloon filled with argon. The atmosphere was changed to carbon monoxide. The reaction was conducted for the given reaction time upon stirring at 50 °C and analyzed by Gc and GC-MS. The cooled reaction mixture was then distilled to dryness under reduced pressure. The residue was dissolved in chloroform (15 mL) and washed twice with water (15 mL). The organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure to a solid material. All compounds (except **10a**, **10b**) were subjected to column chromatography (Silicagel 60 (Sigma), 0.063-0.200 mm) or Aluminum oxide (Sigma), activated, neutral, Brockmann activity I), $CHCl_3$/MeOH or $CHCl_3$/EtOH eluent mixtures (the exact ratios are specified in *Characterization* (3.4) for each compound). In the case of **10a** and **10b** chloroform (10 mL) was added to the residue and the insoluble material (product) was filtered and dried.

*3.3. Aminocarbonylation of iodoalkenes (**1-5**) and iodo(hetero)arenes (**6-11**) in the presence of nucleophiles **a-c** under atmospheric pressure of carbon monoxide.*

In a typical experiment $Pd(OAc)_2$, triphenylphosphine or Xantphos, iodoalkene (**1-5**) or iodo(hetero)arene (**6-11**) and 3-aminolactam nucleophile (**a-c**) and triethylamine were used in the same amount as above and were dissolved in 5 mL of DMF under argon in a 100 mL autoclave. The atmosphere was changed to carbon dioxide and the autoclave was pressurized to the given pressure with carbon monoxide. (Caution: High pressure carbon monoxide should only be used with adequate ventilation (hood) using CO sensors as well.) The reaction was conducted for the given reaction time upon stirring at 50 °C. After the given reaction time the reaction mixture was cooled to room temperature and the autoclave was carefully depressurized in a well-ventilated hood. The product mixture was analyzed by GC and GC-MS. The work-up of the reaction mixture was identical to that discussed for the atmospheric experiments.

3.4. Characterization of the products

3.4.1. *N*-(2'-Oxoazepan-3'-yl)cyclohex-1-enecarboxamide (**1a**)

Yield: 103 mg (87%), White powder, m.p. 177-178 °C; [Anal. Calcd. for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53; N, 11.85. Found: C, 66.00; H, 8.42; N, 11.75.]; R_f (2% MeOH/$CHCl_3$) 0.35. δ_H (500 MHz, $CDCl_3$) 7.17 (1H, d, *J* 4.2 Hz, CO*NH*), 6.74-6.69 (1H, m, *CH*=C), 6.16 (1H, br s, CO*NH*-CH_2), 4.59 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.39-3.23 (2H, m, CH_2NH), 2.26 (1H, br d, 13.0 Hz, lactam CH_2), 2.36-2.23 (2H, m, CH_2CH=C), 2.22-2-17 (2H, m, CH_2CH=C), 2.26 (1H, br d, *J* 14.4 Hz, lactam *CH*), 2.08-1.98 (1H, m, lactam *CH*), 1.95-1.82 (2H, m, lactam *CH* x2), 1.74-1.68 (2H, m, cyhex *CH* x2), 1.66-1.58 (2H, m, cyhex *CH* x2), 1.56-1.37 (2H, br m, lactam *CH* x2). δ_C NMR (125.7 MHz) 175.9, 1.67.5, 134.0, 132.9, 52.2, 42.2, 31.7, 29.0, 27.0, 25.4, 24.1, 22.1, 21.6. IR (KBr, ν (cm^{-1})): 3403, 3212 (NH), 1676 (lactam CON), 1656 (CON), 1626 (C=C), 1504 (NH); MS m/z (rel. int.): 236 (66, M^+), 191 (5), 164 (6), 137 (4), 127 (89), 109 (100), 81 (76), 53 (28).

3.4.2. 4-(*tert*-Butyl)-*N*-(2'-oxoazepan-3'-yl)cyclohex-1-enecarboxamide (**2a**)

Yield: 108 mg (74%), White solid material, m.p. 216-217 °C; [Anal. Calcd. for $C_{17}H_{28}N_2O_2$: C, 69.83; H, 9.65; N, 9.58. Found: C, 69.81; H, 9.80; N, 9.43.]; R_f (2% MeOH/$CHCl_3$) 0.47. δ_H (500 MHz, $CDCl_3$) 7.16 (1H, br s, CO*NH*), 6.76-6.72 (1H, m, *CH*=C), 6.60 (1H, br s, CO*NH*-CH_2), 4.58 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.37-3.22 (2H, m, CH_2NH), 2.28-1.80 (8H, br m, overlapping of 4 x lactam *CH* and 4 x cyhex *CH*), 1.54-1.36 (2H, br m, lactam *CH* x2), 1.33-1.23 (1H, m, cyhex *CH*), 1.22-1.12 (1H, m, cyhex *CH*). δ_C NMR (125.7 MHz) 176.0, 167.2, 134.5, 132.7, 52.1, 43.4, 42.2, 32.1, 31.7, 31.6, 28.9, 28.0, 27.1, 25.6, 23.6. IR (KBr, ν (cm^{-1})): 3378, 3246 (NH), 1680 (lactam CON), 1658 (CON), 1631 (C=C), 1510 (NH);

MS m/z (rel. int.): 292 (68, M^+), 277 (9), 264 (3), 235 (15), 207 (5), 182 (10), 165 (56), 127 (100), 107 (41), 84 (29), 57 (44), 51 (20).

3.4.3. *N*-(2'-Oxoazepan-3'-yl)androst-16-ene-17-carboxamide (**3a**), (ca. 1/1 mixture of two epimers)

Yield: 167 mg (81%), White solid material, m.p. 203-204 °C; [Anal. Calcd. for $C_{26}H_{40}N_2O_2$: C, 75.68; H, 9.77; N, 6.79. Found: C, 75.74; H, 9.64; N, 6.55.]; R_f (3% MeOH/$CHCl_3$) 0.59. δ_H (500 MHz, $CDCl_3$) 7.15/7.13 (1H, d, *J* 6.1 Hz, CO*NH*), 6.47/6.43 (1H, dd, *J* 3.0 Hz, 1.6 Hz, *16 CH*=C), 6.23 (1H, br s, CO*NH*-CH_2), 4.59 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.43-3.19 (2H, m, *CH_2*NH), 2.30-2.11 (3H, m, overlapping of lactam *CH* and 2 x skeleton *CH*), 2.09-0-73 (25H, br m, 20 x skeleton protons and 5 x lactam protons), 1.01/0.98 (3H, s, 18-*CH_3*), 0.84 (3H, s, 19-*CH_3*). δ_C NMR (125.7 MHz) 175.8, 165.1/164.9, 150.4/150.2, 136.8/136.6, 56.9/56.8, 55.2, 52.1/52.0, 47.3, 46.5/46.4, 42.2, 38.5, 36.5, 35.1/34.9, 33.8, 32.0, 31.8/31.7, 31.6/31.5, 29.1, 29.0, 28.9, 28.0, 26.8, 22.2, 20.7, 16.6/16.5, 12.2. IR (KBr, ν (cm^{-1})): 3301, 3208 (NH), 1677 (lactam CON), 1650 (CON), 1630 (C=C), 1525 (NH); MS m/z (rel. int.): 412 (81, M^+), 397 (100), 342 (2), 302 (7), 284 (37), 267 (45), 255 (43), 207 (3), 161 (12), 127 (60), 91 (28), 68 (25), 55 (25).

3.4.4. 1,7,7-Trimethyl-*N*-(2'-oxoazepan-3'-yl)bicyclo[2.2.1]hept-2-ene-2-carboxamide (**4a**), (ca. 1/1 mixture of two epimers)

Yield: 126 mg (87%), White solid material, m.p. 154-155 °C; [Anal. Calcd. for $C_{17}H_{26}N_2O_2$: C, 70.31; H, 9.02; N, 9.65. Found: C, 70.20; H, 9.21; N, 9.57.]; R_f (3% MeOH/$CHCl_3$) 0.47. δ_H (500 MHz, $CDCl_3$) 7.10 (1H, br s, CO*NH*), 6.54/6.51 (1H, d, *J* 3.3 Hz, 3-*CH*=C), 6.29 (1H, br s, CO*NH*-CH_2), 4.59 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.39-3.21 (2H, m, *CH_2*NH), 2.42 (1H, dd, *J* 4.1 Hz, 3.2 Hz, 4-*CH*), 2.17/2.14 (br d, *J* 13.8 Hz, lactam *CH*), 2.07-1.98 (1H, m, lactam *CH*), 1.96-1.80 (3H, br m, overlapping of 2 x lactam CH and 5-CH_a*H_b*), 1.63 (1H, ddd, *J* 12.1 Hz, 9.1 Hz, 3.5 Hz, 6-CH_a*H_b*), 1.58-1.36 (2H, br m, lactam *CH* x2), 1.31-1.21 (4H, s and m, overlapping of 8-CH_3 and 6-*CH_a*H_b), 1.07-0.98 (1H m, 5-*CH_a*H_b), 0.83/0.82 (3H, s, 9-CH_3), 0.80 (3H, s, 10-CH_3). δ_C NMR (125.7 MHz) 175.9/175.8, 166.1/165.8, 145.0/144.7, 139.4/139.3, 56.8/56.6, 54.4/54.3, 52.0/51.9, 51.9/51.8, 42.2, 31.9/31.8, 31.4/31.3, 29.0, 28.0/27.9, 24.9/24.8, 19.4, 19.2/19.1, 11.9/11.7. IR (KBr, ν (cm^{-1})): 3300, 3212 (NH), 1670 (lactam CON), 1644 (CON), 1630 (C=C), 1525 (NH); MS m/z (rel. int.): 290 (28, M^+), 262 (7), 235 (2), 199 (1), 162 (100), 147 (49), 135 (37), 129 (22), 119 (42), 101 (18), 91 (35), 84 (15), 77 (16), 55 (25).

3.4.5. (E)-*N*-(2-Oxoazepan-3-yl)non-2-enamide (**5a**)

Yield: 101 mg (76%), White powder, m.p. 165-166 °C; [Anal. Calcd. for $C_{15}H_{26}N_2O_2$: C, 67.63; H, 9.84; N, 10.52. Found: C, 67.76; H, 9.89; N, 10.38.]; R_f (3% MeOH/$CHCl_3$) 0.75. δ_H (500 MHz, $CDCl_3$) 6.92 (1H, d, *J* 5.6 Hz, CO*NH*), 6.85 (1H, dt, *J* 15.2 Hz, 7.1 Hz, *=CH*), 6.74 (1H, br s, CO*NH*-CH_2), 5.87 (1H, dt, *J*

15.3 Hz, 1.3 Hz, =*CH*), 4.62 (1H, ddd, 11.3, 5.4, 1.4 Hz, *CH*NH), 3.39-3.22 (2H, m, CH_2NH), 2.25-2.11 (3H, br m, overlapping of lactam CH and chain CH_2), 2.07-1.98 (1H, m, lactam *CH*), 1.95-1.82 (2H, m, lactam *CH* x2), 1.57-1.37 (4H, br m, overlapping of 2 x lactam *CH* and chain CH_2), 1.36-1.23 (6H, m, 3 x chain CH_2), 0.91 (3H, t, *J* 6.9 Hz, CH_3). δ_C NMR (125.7 MHz)175.8, 165.1, 145.0, 123.5, 52.1, 42.2, 32.0, 31.7, 31.6, 28.9, 28.8, 28.2, 27.9, 22.6, 14.1. IR (KBr, ν (cm^{-1})): 3316, 3218 (NH), 1671 (lactam CON), 1663 (CON), 1624 (C=C), 1529 (NH); MS m/z (rel. int.): 266 (27, M^+), 238 (2), 209 (9), 181 (39), 156 (16), 139 (38), 127 (100), 110 (26), 99 (22), 83 (38), 69 (42), 55 (92).

3.4.6. *N*-(2'-Oxoazepan-3'-yl)benzamide (**6a**)

Yield: 90 mg (77%), White powder, m.p. 208-209 °C; [Anal. Calcd. for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.34; H, 6.90; N, 11.83.]; R_f (3% MeOH/$CHCl_3$) 0.43. δ_H (500 MHz, $CDCl_3$) 7.87 (2H, d, *J* 7.1 Hz, CH_{ortho}(Ph)), 7.70 (1H, d, *J* 4.9 Hz, CO*NH*), 7.52 (1H, t, *J* 7.4Hz, CH_{para}(Ph)), 7.46 (2H, t, *J* 7.4 Hz, CH_{meta}(Ph)), 6.74 (1H, br s, CO*NH*-CH_2), 4.75 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.42-3.26 (2H, m, CH_2NH), 2.26 (1H, br d, *J* 12.7 Hz, lactam *CH*), 2.11-2.00 (1H, m, lactam *CH*), 1.98-1.87 (2H, m, lactam *CH* x2), 1.66-1.53 (1H, m, lactam *CH*), 1.51-1.40 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 175.9, 166.3, 134.2, 131.6, 128.5, 127.1, 52.6, 42.2, 31.6, 28.9, 28.0. IR (KBr, ν (cm^{-1})): 3254, 3204 (NH), 1661 (lactam CON), 1649 (CON), 1540 (NH); MS m/z (rel. int.): 232 (18, M^+), 204 (1), 175 (8), 135 (3), 127 (28), 105 (100), 77 (68), 51 (17).

3.4.7. 2-Oxo-*N*-(2'-oxoazepan-3'-yl)-2-phenylacetamide (**6a'**)

Yield: 61 mg (47%), White solid material, m.p. 199-200 °C; [Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.52; H, 6.05; N, 10.64.]; R_f (3% MeOH/$CHCl_3$) 0.60. δ_H (500 MHz, $CDCl_3$) 8.32 (2H, d, *J* 7.4 Hz, CH_{ortho}(Ph)), 8.28 (1H, d, *J* 5.8 Hz, CO*NH*), 7.64 (1H, t, *J* 7.4Hz, CH_{para}(Ph)), 7.50 (2H, t, *J* 7.4 Hz, CH_{meta}(Ph)), 7.22 (1H, br s, CO*NH*-CH_2), 4.68 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.39-3.33 (2H, m, CH_2NH), 2.22 (1H, br d, 12.9 Hz, lactam *CH*), 2.15-2.06 (1H, m, lactam *CH*), 1.98-1.88 (2H, m, lactam *CH* x2), 1.72-1.61 (1H, m, lactam *CH*), 1.54-1.30 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 187.5, 174.8, 161.4, 134.3, 133.4, 131.0, 128.5, 52.4, 42.2, 31.1, 28.8, 28.0. IR (KBr, ν (cm^{-1})): 3368, 3212 (NH), 1690 (lactam CON), 1656 (CON), 1503 (NH); MS m/z (rel. int.): 217 (3, M^+-43), 189 (1), 155 (100), 127 (4), 105 (35), 77 (40), 51 (13).

3.4.8. *N*-(2'-Oxoazepan-3'-yl)picolinamide (**7a**)

Yield: 103 mg (88%), White powder, m.p. 187-188 °C; [Anal. Calcd. for $C_{12}H_{15}N_3O_2$: C, 61.79; H, 6.48; N, 18.01. Found: C, 61.60; H, 6.52; N, 18.11.]; R_f (1% MeOH/$CHCl_3$; aluminium oxide) 0.56. δ_H (500 MHz, $CDCl_3$) 9.18 (1H, d, *J* 4.7 Hz, CO*NH*),8.64 (1H, d, *J* 4.6 Hz, Py CH), 8.18 (1H, d, *J* 7.7 Hz, Py CH),

7.86 (1H, dt, *J* 7.6, 1.2 Hz, Py *CH*), 7.44 (1H, dd, *J* 7.8 Hz, 4.9 Hz, Py *CH*), 6.40 (1H, br s, CO*NH*-CH_2), 4.76 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.46-3.26 (2H, m, *CH_2*NH), 2.23 (1H, br d, *J* 13.8 Hz, lactam *CH*), 2.14-2.02 (1H, m, lactam *CH*), 1.99-1.87 (2H, m, lactam *CH* x2), 1.73-1.60 (1H, m, lactam *CH*), 1.55-1.41 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 175.4, 163.7, 150.0, 148.5, 137.1, 126.1, 122.0, 52.3, 42.2, 31.7, 29.0, 28.1. IR (KBr, ν (cm^{-1})): 3341, 3251 (NH), 1670 (lactam CON), 1658 (CON), 1513 (NH); MS m/z (rel. int.): 233 (28, M^+), 205 (10), 188 (13), 161 (4), 147 (31), 127 (38), 106 (32), 99 (38), 78 (100), 51 (24).

3.4.9. *N*-(2'-Oxoazepan-3'-yl)nicotinamide (**8a**)

Yield: 63 mg (54%), White powder, m.p. 225-226 °C; [Anal. Calcd. for $C_{12}H_{15}N_3O_2$: C, 61.79; H, 6.48; N, 18.01. Found: C, 61.59; H, 6.40; N, 17.79.]; R_f (3% EtOH/$CHCl_3$; aluminium oxide) 0.64. δ_H (500 MHz, $CDCl_3$) 9.11 (1H, d, *J* 1.7 Hz, Py *CH*), 8.77 (1H, dd, *J* 4.8 Hz, 1.6 Hz, Py *CH*), 8.17 (1H, dt, *J* 7.9 Hz, 2.0 Hz, Py *CH*), 7.74 (1H, d, *J* 4.7 Hz, CO*NH*), 7.41 (1H, ddd, *J* 8.0 Hz, 3.8 Hz, 0.7 Hz, Py *CH*), 6.22 (1H, br s, CO*NH*-CH_2), 4.76 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.45-3.28 (2H, m, *CH_2*NH), 2.28 (1H, br d, *J* 13.3 Hz, lactam *CH*), 2.15-2.06 (1H, m, lactam *CH*), 1.97-1.88 (2H, m, lactam *CH* x2), 1.68-1.57 (1H, m, lactam *CH*), 1.54-1.43 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 175.3, 164.4, 152.4, 148.4, 134.8, 129.8, 123.4, 52.7, 42.3, 31.5, 28.9, 28.0. IR (KBr, ν (cm^{-1})): 3339, 3225 (NH), 1676 (lactam CON), 1644 (CON), 1529 (NH); MS m/z (rel. int.): 233 (23, M^+), 205 (9), 188 (13), 161 (5), 147 (24), 127 (33), 106 (29), 99 (35), 78 (100), 51 (23).

3.4.10. 2-Oxo-*N*-(2'-oxoazepan-3'-yl)-2-(pyridin-3-yl)acetamide (**8a'**), (ca. 2/3 mixture of two C(O)N rotamers)

Yield: 49 mg (38%), Yellow solid material, m.p. 111-112 °C; [Anal. Calcd. for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.87; H, 5.89; N, 16.01.]; R_f (3% EtOH/$CHCl_3$; aluminium oxide) 0.39. δ_H (500 MHz, $CDCl_3$) 9.52 (1H, s, Py *CH*), 8.85 (1H, d, *J* 3.6 Hz, Py *CH*), 8.17 (1H, dt, *J* 8.0 Hz, 1.8 Hz, Py *CH*), 8.39 (1H, d, *J* 5.4 Hz, CO*NH*), 7.41 (1H, dd, *J* 8.0 Hz, 3.8 Hz, Py *CH*), 6.74/6.44 (minor/major, 1H, br s, CO*NH*-CH_2), 4.63/4.48 (major/minor, 1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.41-3.32/3.31-3.22 (major/minor, 2H, m, *CH_2*NH), 2.24-2.16 (1H, m, lactam *CH*), 2.15-2.07 (1H, m, lactam *CH*), 1.96-1.87 (2H, m, lactam *CH* x2), 1.70-1.59 (1H, m, lactam *CH*), 1.55-1.44 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 186.1, 177.1/174.4 (minor/major), 160.2, 154.2, 152.2, 138.3, 129.3, 123.4, 53.3/52.4 (minor/major), 42.3/42.2 (minor/major), 32.0/31.0 (minor/major), 29.0/28.9 (minor/major), 28.1/28.0. IR (KBr, ν (cm^{-1})): 3355, 3217 (NH), 1667 (br, lactam CON, CO and CON), 1539 (NH); MS m/z (rel. int.): 233 (2, M^+-28), 191 (1), 155 (100), 127 (3), 106 (12), 84 (8), 79 (24), 69 (16), 51 (13).

3.4.11. *N*-(2'-Oxoazepan-3'-yl)thiophene-2-carboxamide (**9a**)

Yield: 81 mg (68%), White powder, m.p. 201-202 °C; [Anal. Calcd. for $C_{11}H_{14}N_2O_2S$: C, 55.44; H, 5.92; N, 11.76. Found: C, 55.52; H, 5.80; N, 11.59.]; R_f 2% MeOH/$CHCl_{3;}$) 0.50. δ_H (500 MHz, $CDCl_3$) 7.59 (1H, dd, *J* 3.8 Hz, 1.1 Hz, Tioph *CH*), 7.53 (1H, d, *J* 5.1 Hz, CO*NH*), 7.49 (1H, dd, *J* 5.1 Hz, 1.1 Hz, Tioph *CH*), 7.09 (1H, dd, *J* 5.2 Hz, 3.8 Hz, Tioph *CH*), 6.57 (1H, br s, CO*NH*-CH_2), 4.71 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.40-3.25 (2H, m, *CH_2*NH), 2.25 (1H, br d, *J* 13.7 Hz, lactam *CH*), 2.11-2.01 (1H, m, lactam *CH*), 1.97-1.84 (2H, m, lactam *CH* x2), 1.64-1.53 (1H, m, lactam *CH*), 1.51-1.39 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 175.5, 160.9, 139.0, 130.1, 128.2, 127.6, 52.6, 42.2, 31.7, 28.9, 28.0. IR (KBr, ν (cm^{-1})): 3254, 3204 (NH), 1670 (lactam CON), 1643(CON), 1546 (NH); MS m/z (rel. int.): 238 (17, M^+), 205 (3), 181 (4), 141 (3), 127 (16), 111 (100), 83 (17), 51 (5).

3.4.12. 2-Oxo-*N*-(2-oxoazepan-3-yl)-2-(thiophen-2-yl)acetamide (**9a'**)

Yield: 58 mg (44%), Yellow solid material, m.p. 187-188 °C; R_f 2% MeOH/$CHCl_{3;}$) 0.64. δ_H (500 MHz, $CDCl_3$) 8.54 (1H, d, *J* 5.1 Hz, CO*NH*), 8.38 (1H, dd, *J* 3.8 Hz, 1.1 Hz, Tioph *CH*), , 7.84 (1H, dd, *J* 5.1 Hz, 1.1 Hz, Tioph *CH*), 7.21 (1H, dd, *J* 5.2 Hz, 3.8 Hz, Tioph *CH*), 6.74 (1H, br s, CO*NH*-CH_2), 4.60 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.38-3.28 (2H, m, *CH_2*NH), 2.17 (1H, br d, *J* 13.7 Hz, lactam *CH*), 2.13-2.05 (1H, m, lactam *CH*), 1.95-1.82 (2H, m, lactam *CH* x2), 1.69-1.57 (1H, m, lactam *CH*), 1.54-1.41 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 177.9, 174.6, 160.1, 138.4, 137.7, 128.2, 52.5, 42.1, 31.0, 28.9, 28.1. IR (KBr, ν (cm^{-1})): 3333, 3203 (NH), 1687 (CO), 1669(lactam CON), 1653 (CON), 1495 (NH); MS m/z (rel. int.): 195 (1, M^+-71), 155 (100), 127 (3), 111 (36), 83 (10), 69 (15), 55 (4).

3.4.13. *N*-(2'-Oxoazepan-3'-yl)-1H-indole-5-carboxamide (**10a**)

Yield: 93 mg (69%), Beige solid material, m.p. 260-261 °C; [Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.47; H, 6.44; N, 15.37.]; R_f 5% MeOH/$CHCl_3$) 0.44. δ_H (500 MHz, DMSO-d6) 11.34 (1H, br s, indole-*NH*), 8.14 (1H, br s, Ar-H), 8.03 (1H, d, *J* 5.6 Hz, CO*NH*), 7.91 (1H, br s, CO*NH*-CH), 7.61 (1H, d, *J* 7.8 Hz, Ar-H), 7.45 (1H, d, *J* 7.8 Hz, Ar-H), 7.42 (1 H, s, Ar-H), 6.57 (1 H, br s, CO*NH*-CH_2), 4.72-4.57 (1H, m, *CH*NH), 3.19-3.01 (2H, br m, *CH_2*NH), 2.01-1.91 (2H, m, lactam *CH* x 2), , 1.88-1.67 (2H, br m, lactam *CH* x2), 1.63-1.49 (1H, br m, lactam *CH*), 1.36-1.24 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 175.1, 166.6, 137.9, 127.6, 127.2, 125.7, 120.7, 120.2, 111.5, 102.7, 52.3, 41.2, 31.5, 29.4, 28.2. IR (KBr, ν (cm^{-1})): 3377 (indole-NH), 3292, 3230 (NH), 1665 (lactam CON), 1634(CON), 1529 (NH); MS m/z (rel. int.): 271 (24, M^+), 207 (1), 160 (7), 144 (100), 127 (14), 116 (32), 89 (10), 56 (1).

3.4.14. *N*-(2'-Oxoazepan-3'-yl)-1H-indole-7-carboxamide (**11a**)

Yield: 100 mg (74%), Pale brown solid material, m.p. 186-187 °C; [Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.52; H, 6.38; N, 15.43.]; R_f 3% MeOH/$CHCl_3$;) 0.46. δ_H (500 MHz, $CDCl_3$) 10.39 (1 H, brs, indole-*NH*), 7.92 (1 H, d, *J* 4.7 Hz, CO*NH*), 7.83 (1H, d, *J* 7.8 Hz, Ar-H), 7.59 (1 H, d, *J* 7.7 Hz, Ar-H), 6.58 (1 H, dd, *J* 3.0 Hz, 2.3 Hz, indole-H), 7.35 (1H, dd, *J* 3.3 Hz, 2.8 Hz, indole-H), 6.81 (1H, br s, CO*NH*-CH_2), 6.61 (1H, dd, *J* 3.3 Hz, 2.8 Hz, indole-H), 4.81 (1H, ddd, *J* 11.3 Hz, 5.4 Hz, 1.4 Hz, *CH*NH), 3.45-3.25 (2H, br m, *CH_2*NH), 2.31 (1H, br d, *J* 13.0 Hz, lactam *CH*), 2.17-2.06 (1H, m, lactam *CH*), 2.01-1.87 (2H, m, lactam *CH* x2), 1.72-1.59 (1H, m, lactam *CH*), 1.55-1.41 (1H, m, lactam *CH*). δ_C NMR (125.7 MHz) 176.1, 167.0 135.4, 129.5, 125.5, 124.9, 119.7, 118.8, 115.7, 102.0, 52.4, 42.3, 31.7, 28.9, 28.1. IR (KBr, ν (cm^{-1})): 3410 (indole-NH), 3381, 3212 (NH), 1672 (lactam CON), 1637(CON), 1527 (NH); MS m/z (rel. int.): 271 (67, M^+), 225 (2), 198 (2), 171 (6), 160 (15), 143 (100), 127 (32), 116 (68), 89 (26), 56 (5).

3.4.15. *N*-(2'-Oxopiperidin-3'-yl)cyclohex-1-enecarboxamide (**1b**)

Yield: 83 mg (75%), White powder, m.p. 161-162 °C; [Anal. Calcd. for $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16; N, 12.60. Found: C, 64.80; H, 8.32; N, 12.52.]; R_f (5% MeOH/$CHCl_3$) 0.38. δ_H (500 MHz, $CDCl_3$) 6.74-6.69 (1H, m, *CH*=C), 6.68 (1H, d, *J* 4.8 Hz, CO*NH*), 6.19 (1H, br s, CO*NH*-CH_2), 4.31 (1H, dt, 11.5 Hz, 5.4 Hz, *CH*NH), 3.41-3.34 (2H, m, *CH_2*NH), 2.63 (1H, dq, 12.8 Hz, 4.6 Hz, NHCH-*CH_2*), 2.37-2.27 (1H, m, cyhex *CH*), 2.26-2.12 (3H, br m, cyhex *CH* x 3), 2.01-1.89 (2H, m, lactam *CH_2*), 1.67 (1H, tt, 12.4 Hz, 7.8 Hz, NHCH-*CH_2*), 1.74-1.68 (1H, m, cyhex *CH*), 1.74-1.65 (2H, m, cyhex *CH* x2), 1.64-1.49 (3H, br m, overlapping of cyhex *CH* x 2 and lactam *CH*). δ_C NMR (125.7 MHz) 172.1, 168.7, 134.2, 132.9, 50.7, 41.7, 27.2, 25.4, 24.2, 22.1, 21.5, 21.0. IR (KBr, ν (cm^{-1})): 3319, 3212 (NH), 1654 (lactam CON), 1632 (CON), 1614 (C=C), 1533 (NH); MS m/z (rel. int.): 222 (61, M^+), 204 (14), 177 (4), 150 (3), 126 (7), 113 (89), 109 (100), 98 (18), 81 (84), 71 (30), 53 (30.

3.4.16. 4-(*tert*-Butyl)-*N*-(2'-oxopiperidin-3'-yl)cyclohex-1-enecarboxamide (**2b**), (ca. 1/1 mixture of two epimers)

Yield: 101 mg (73%), White solid material, m.p. 216-217 °C; [Anal. Calcd. for $C_{16}H_{26}N_2O_2$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.10; H, 9.52; N, 9.89.]; R_f (5% MeOH/$CHCl_3$) 0.43. δ_H (500 MHz, $CDCl_3$) 6.72 (2H, br s, overlapping of CO*NH* and *CH*=C), 6.39 (1H, brs, CO*NH*-CH_2), 4.31 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.42-3.31 (2H, m, *CH_2*NH), 2.62 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-*CH_2*), 2.56-2.36 (1H, m, cyhex *CH*), 2.33-2.09 (2H, m, 2 x cyhex *CH*), 2.04-1.85 (4H, m, overlapping of 2 x lactam *CH* and 2 x cyhex *CH*), 1.56 (1H, tt, *J* 12.4 Hz, 7.8 Hz, NHCH-*CH_2*), 1.33-1.23 (1H, m, cyhex *CH*), 1.17 (1H, qd, *J* 12.1 Hz, 4.6 Hz, cyhex *CH*). δ_C NMR (125.7 MHz) 172.1, 168.5/168.4, 134.7, 132.7/132.6, 50.7/50.6, 43.4, 41.7,

32.1, 27.2, 27.1, 25.7, 25.6, 23.6, 21.0. IR (KBr, ν (cm^{-1})): 3280, 3256 (NH), 1675 (lactam CON), 1659 (CON), 1621 (C=C), 1547 (NH); MS m/z (rel. int.): 278 (79, M^+), 263 (10), 221 (25), 202 (8), 193 (3), 182 (6), 165 (58), 137 (6), 113 (92), 107 (100), 79 (44), 57 (60).

3.4.17. *N*-(2'-Oxopiperidin-3'-yl)androst-16-ene-17-carboxamide (**3b**), (ca. 1/1 mixture of two epimers)

Yield: 133 mg (67%), White powder, m.p. 209-210 °C; [Anal. Calcd. for $C_{25}H_{38}N_2O_2$: C, 75.33; H, 9.61; N, 7.03. Found: C, 75.22; H, 9.70; N, 6.91.]; R_f (5% MeOH/$CHCl_3$) 0.50. δ_H (500 MHz, $CDCl_3$) 6.73/6.71 (1H, d, *J* 5.1 Hz, CO*NH*), 6.47/6.40 (1H, dd, *J* 3.4 Hz, 1.7 Hz, *16 CH*=C), 6.42 (1H, br s, CO*NH*-CH_2), 4.30 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.40-3.29 (2H, m, *CH_2*NH), 2.64 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-*CH_2)*, 2.25-2.12 (2H, m, 2 x skeleton *CH*), 2.05-1.88 (3H, m, overlapping of lactam *CH_2* and skeleton *CH*), 1.73-0-73 (20H, br m, 19 x skeleton protons and lactam CH), 1.00/0.97 (3H, s, 18-*CH_3*), 0.83 (3H, s, 19-*CH_3*). δ_C NMR (125.7 MHz) 172.1, 166.3/166.0, 150.3/150.0, 137.1/136.8, 56.9/56.7, 55.1, 50.5, 47.2, 46.6/46.4, 41.7, 38.5, 36.5, 35.1/34.9, 33.8, 31.9, 31.7/31.6, 29.0, 28.9, 27.3/27.2, 26.8, 22.1, 21.0/20.9, 20.7, 16.6/16.5, 12.2. IR (KBr, ν (cm^{-1})): 3292, 3252 (NH), 1677 (lactam CON), 1653 (CON), 1521 (NH); MS m/z (rel. int.): 398 (100, M^+), 383 (85), 365 (8), 302 (4), 285 (47), 269 (95), 257 (56), 207 (9), 161 (19), 115 (42), 91 (35), 68 (30), 55 (37).

3.4.18. 1,7,7-Trimethyl-*N*-(2'-oxopiperidin-3'-yl)bicyclo[2.2.1]hept-2-ene-2-carboxamide (**4b**), (ca. 1/1 mixture of two epimers)

Yield: 103 mg (75%), White solid material, m.p. 153-154 °C; [Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.14. Found: C, 69.59; H, 8.66; N, 10.01.]; R_f (5% MeOH/$CHCl_3$) 0.43. δ_H (500 MHz, $CDCl_3$) 6.67 (1H, d, *J* 4.3 Hz, CO*NH*), 6.54/6.47 (1H, d, *J* 3.3 Hz, 3-*CH*=C), 6.44 (1H, br s, CO*NH*-CH_2), 4.26 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.36-3.28 (2H, m, *CH_2*NH), 2.58 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-*CH_2*), 2.42 (1H, dd, *J* 4.1 Hz, 3.2 Hz, 4-*CH*), 1.96-1.82 (3H, br m, overlapping of 2 x lactam CH and 5-CH_a*H_b*), 1.67-1.47 (2H, br m, overlapping of lactam NHCH-*CH_2* and 6-CH_a*H_b*), 1.31-1.21 (4H, s and m, overlapping of 8-CH_3 and 6-*CH_a*H_b), 0.99 (1H, ddd, *J* 12.1 Hz, 9.1 Hz, 3.5 Hz, 5-*CH_a*H_b), 0.79/0.78 (3H, s, 9-CH_3), 0.77 (3H, s, 10-CH_3). δ_C NMR (125.7 MHz) 177.2, 167.2/167.9, 144.9/144.6, 139.4/139.3, 56.8/56.5, 54.3, 51.9/51.8, 50.4/50.3, 41.6/41.5, 31.4/31.3, 27.4/27.2, 24.9/24.8, 21.0/20.9, 19.4, 19.1, 11.8/11.7. IR (KBr, ν (cm^{-1})): 3259, 3226 (NH), 1671 (lactam CON), 1629 (CON), 1539 (NH); MS m/z (rel. int.): 276 (21, M^+), 262 (7), 248 (7), 221 (2), 190 (1), 162 (100), 147 (60), 135 (44), 119 (56), 113 (23), 91 (36), 77 (10), 55 (11).

3.4.19. (E)-*N*-(2-Oxopiperidin-3-yl)non-2-enamide (**5b**)

Yield: 91 mg (72%), White powder, m.p. 218-219 °C; [Anal. Calcd. for $C_{14}H_{24}N_2O_2$: C, 66.63; H, 9.59; N, 11.10. Found: C, 66.52; H, 9.70; N, 11.03.]; R_f (5% MeOH/$CHCl_3$) 0.34. δ_H (500 MHz, $CDCl_3$) 6.85 (1H, dt, *J* 15.2 Hz, 7.1 Hz, =*CH*), 6.53 (1H, br s, CO*NH*), 6.16 (1H, br s, CH_2*NH*), 5.84 (1H, dt, *J* 15.3 Hz, 1.3 Hz, =*CH*), 4.35 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.41-3.32 (2H, m, CH_2NH), 2.64 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-CH_2), 2.19 (2H, q, J 7.1 Hz, CH_2CH_3), 2.02-1.85 (3H, br m, overlapping of lactam *CH* and chain CH_2), 1.57 (1H, tt, *J* 12.4 Hz, 7.8 Hz, NHCH-CH_2), 1.50-1.40 (2H, m, chain CH_2), 1.37-1.22 (6H, br m, 3 x chain CH_2), 0.90 (3H, t, *J* 7.1 Hz, CH_2*CH3*). δ_C NMR (125.7 MHz) 172.0, 166.3, 145.3, 123.3, 50.6, 41.7, 32.1, 31.6, 28.9, 28.2, 27.2, 22.6, 21.0, 14.1. IR (KBr, ν (cm^{-1})): 3306, 3203 (NH), 1690 (lactam CON), 1668 (CON), 1625 (C=C), 1541 (NH); MS m/z (rel. int.): 252 (35, M^+), 223 (1), 195 (12), 167 (22), 156 (15), 140 (48), 113 (100), 98 (19), 85 (24), 69 (59), 55 (87).

3.4.20. *N*-(2'-Oxopiperidin-3'-yl)benzamide (**6b**)

Yield: 64 mg (56%), White powder, m.p. 189-190 °C; [Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.15; H, 6.54; N, 12.70.]; R_f (5% MeOH/$CHCl_3$) 0.38. δ_H (500 MHz, $CDCl_3$) 7.85 (2H, d, *J* 7.4 Hz, CH_{ortho}(Ph)), 7.52 (1H, t, *J* 7.4Hz, CH_{para}(Ph)), 7.45 (2H, t, *J* 7.4 Hz, CH_{meta}(Ph)), 7.28 (1H, d, *J* 5.5 Hz, CO*NH*), 6.34 (1H, br s, CO*NH*-CH_2), 4.46 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.44-3.37 (2H, m, CH_2NH), 2.73 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-CH_2), 2.04-1.95 (2H, m, lactam CH_2), 1.67 (1H, tt, *J* 12.4 Hz, 7.8 Hz, NHCH-CH_2). δ_C NMR (125.7 MHz) 171.9, 167.6, 134.2, 131.6, 128.5, 127.1, 51.0, 41.7, 27.1, 21.0. IR (KBr, ν (cm^{-1})): 3310, 3206 (NH), 1687 (lactam CON), 1632 (CON), 1532 (NH); MS m/z (rel. int.): 218 (18, M^+), 196 (1), 173 (3), 161 (3), 133 (3), 113 (41), 105 (100), 77 (60), 51 (17).

3.4.21. *N*-(2'-Oxopiperidin-3'-yl)picolinamide (**7b**)

Yield: 84 mg (76%), Off white solid material, m.p. 141-142 °C; [Anal. Calcd. for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.18; H, 5.90; N, 19.03.]; R_f (6% EtOH/$CHCl_3$, aluminium oxide) 0.66. δ_H (500 MHz, $CDCl_3$) 8.71 (1H, d, *J* 6.5 Hz, CO*NH*), 8.56 (1H, d, *J* 4.6 Hz, Py CH), 8.17 (1H, d, *J* 7.8 Hz, Py CH), 7.83 (1H, dt, *J* 7.7, 1.6 Hz, Py *CH*), 7.44 (1H, dd, *J* 7.7 Hz, 4.8 Hz, 1.0 Hz, Py *CH*), 6.94 (1H, br s, CO*NH*-CH_2), 4.52 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.39-3.23 (2H, m, CH_2NH), 2.57 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-CH_2), 2.00-1.91 (2H, m, lactam CH_2), 1.74 (1H, tt, *J* 12.4 Hz, 7.8 Hz, NHCH-CH_2). δ_C NMR (125.7 MHz) 171.6, 164.5, 149.7, 148.2, 137.2, 126.2, 122.1, 50.4, 41.8, 27.5, 21.2. IR (KBr, ν (cm^{-1})): 3336, 3199 (NH), 1687 (lactam CON), 1648 (CON), 1521 (NH); MS m/z (rel. int.): 219 (29, M^+), 191 (4), 174 (11), 161 (13), 147 (11), 139 (5), 134 (19), 113 (60), 106 (30), 85 (41), 78 (100), 70 (29), 51 (29).

3.4.22. *N*-(2'-Oxopiperidin-3'-yl)nicotinamide (**8b**)

Yield: 39 mg (36%), Pale yellow solid material, m.p. 164-165 °C; [Anal. Calcd. for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.10; H, 6.01; N, 19.04.]; R_f (5% MeOH/$CHCl_3$; aluminium oxide) 0.30. δ_H (500 MHz, $CDCl_3$) 9.08 (1H, d, *J* 1.7 Hz, Py *CH*), 8.74 (1H, dd, *J* 4.8 Hz, 1.5 Hz, Py *CH*), 8.18 (1H, dt, *J* 7.9 Hz, 2.0 Hz, Py *CH*), 7.54 (1H, br s, CO*NH*), 7.40 (1H, ddd, *J* 8.0 Hz, 4.0 Hz, 0.8 Hz, Py *CH*), 6.36 (1H, br s, CO*NH*-CH_2), 4.48 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.46-3.34 (2H, m, *CH_2*NH), 2.67 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-*CH_2*), 2.05-1.97 (2H, m, lactam *CH_2*), 1.70 (1H, tt, *J* 12.4 Hz, 7.8 Hz, NHCH-*CH_2*). δ_C NMR (125.7 MHz) 171.6, 165.8, 152.3, 148.4, 135.1, 129.8, 123.4, 51.0, 41.8, 27.1, 21.1. IR (KBr, ν (cm^{-1})): 3321, 3264 (NH), 1669 (lactam CON), 1647 (CON), 1556 (NH); MS m/z (rel. int.): 219 (20, M^+), 191 (3), 174 (5), 161 (7), 149 (11), 123 (22), 113 (60), 106 (100), 78 (69), 70 (23), 51 (33).

3.4.23. *N*-(2'-Oxopiperidin-3'-yl)thiophene-2-carboxamide (**9b**)

Yield: 52 mg (46%), Beige solid material, m.p. 195-196 °C; [Anal. Calcd. for $C_{10}H_{12}N_2O_2S$: C, 53.55; H, 5.39; N, 12.49. Found: C, 53.40; H, 5.47; N, 12.33.]; R_f 6% EtOH/$CHCl_3$, aluminium oxide) 0.45. δ_H (500 MHz, $CDCl_3$) 7.58 (1H, dd, *J* 3.8 Hz, 1.1 Hz, Tioph *CH*), 7.49 (1H, dd, *J* 5.1 Hz, 1.1 Hz, Tioph *CH*), 7.19 (1H, d, *J* 3.8 Hz, CO*NH*), 7.08 (1H, dd, *J* 5.2 Hz, 3.8 Hz, Tioph *CH*), 6.19 (1H, br s, CO*NH*-CH_2), 4.43 (1H, dt, *J* 11.5 Hz, 5.4 Hz, *CH*NH), 3.44-3.38 (2H, m, *CH_2*NH), 2.67 (1H, dq, *J* 12.8 Hz, 4.6 Hz, NHCH-*CH_2*), 2.05-1.97 (2H, m, lactam *CH_2*), 1.71 (1H, tt, *J* 12.4 Hz, 7.8 Hz, NHCH-*CH_2*). δ_C NMR (125.7 MHz) 171.7, 162.2, 138.7, 130.2, 128.4, 127.6, 51.1, 41.8, 27.2, 21.1. IR (KBr, ν (cm^{-1})): 3288, 3194 (NH), 1682 (br, CON), 1540 (NH); MS m/z (rel. int.): 224 (20, M^+), 206 (2), 179 (3), 154 (2), 128 (3), 113 (33), 111 (100), 87 (10), 70 (14), 53 (3).

3.4.24. *N*-(2'-Oxopiperidin-3'-yl)-1H-indole-5-carboxamide (**10b**)

Yield: 91 mg (71%), Pale brown solid material, m.p. 220-221 °C; [Anal. Calcd. for $C_{14}H_{15}N_3O_2$: C, 65.35; H, 5.88; N, 16.33. Found: C, 65.19; H, 5.98; N, 16.18.]; R_f 5% MeOH/$CHCl_3$) 0.24. δ_H (500 MHz, DMSO-d6) 11.33 (1H, br s, indole-*NH*), 8.41 (1H, d, *J* 7.8 Hz, Ar-H), 8.15 (1H, s, Ar-H), 7.64 (1H, d, *J* 8.2 Hz, Ar-H), 7.62 (1H, br s, CO*NH*), 7.74-7.40 (2H, br s, overlapping of CO*NH*-CH_2 and Ar-H), 6.54 (1H, s, Ar-H), 4.47-4.34 (1H, m, *CH*NH), 3.19 (2H, br s, *CH_2*NH), 2.08-1.97 (1H, m, NHCH-*CH_2*), 1.89-1.69 (3H, br m, 3 x lactam *CH*). δ_C NMR (125.7 MHz) 170.7, 167.3, 137.9, 127.4, 127.1, 125.8, 121.0, 120.4, 111.3, 102.6, 49.9, 41.7, 28.3, 21.9. IR (KBr, ν (cm^{-1})): 3377 (indole-NH), 3324, 3212 (NH), 1674 (lactam CON), 1631 (CON), 1525 (NH); MS m/z (rel. int.): 257 (23, M^+), 207 (6), 160 (8), 144 (100), 116 (31), 89 (12), 51 (1).

3.4.25. *N*-(2'-Oxopyrrolidin-3'-yl)cyclohex-1-enecarboxamide (**1c**)

Yield: 53 mg (51%), White powder, m.p. 198-199 °C; [Anal. Calcd. for $C_{11}H_{16}N_2O_2$: C, 63.44; H, 7.74; N, 13.45. Found: C, 63.30; H, 7.91; N, 13.28.]; R_f (3% MeOH/$CHCl_3$) 0.28. δ_H (500 MHz, $CDCl_3$) 6.75-6.70 (1H, m, *CH*=C), 6.66 (1H, br s, CO*NH*-CH_2), 6.41 (1H, d, *J* 4.5 Hz, CO*NH* 1H, br s, CO*NH*-CH_2), 4.42 (1H, ddd, *J* 10.7 Hz, 8.2 Hz, 5.2 Hz, *CH*NH), 3.47-3.36 (2H, m, *CH_2*NH), 2.86-2.77 (1H, m, NHCH-*CH_2*), 2.36-2.21 (2H, br m, cyhex *CH_2*), 2.20-2.14 (2H,m, cyhex *CH_2*), 2.02-1.90 (1H, m, NHCH-*CH_2*), 1.74-1.65 (2H, m, cyhex *CH_2*), 1.64-1.57 (2H, m, cyhex *CH_2*). δ_C NMR (125.7 MHz) 176.1, 169.0, 134.7, 132.5, 50.9, 39.4, 30.2, 25.4, 24.2, 22.1, 21.5. IR (KBr, ν (cm^{-1})): 3248 (br, NH), 1701 (lactam CON), 1669 (CON), 1617 (C=C), 1558 (NH); MS m/z (rel. int.): 208 (57, M^+), 190 (39), 165 (5), 136 (1), 126 (19), 109 (100), 99 (25), 81 (79), 53 (25).

3.4.26. *N*-(2'-Oxopyrrolidin-3'-yl)androst-16-ene-17-carboxamide (**3c**), (ca. 1/1 mixture of two epimers)

Yield: 104 mg (54%), Beige solid material, m.p. 130-131 °C; [Anal. Calcd. for $C_{24}H_{36}N_2O_2$: C, 74.96; H, 9.44; N, 7.28. Found: C, 74.90; H, 9.53; N, 7.16.]; R_f (2% EtOH/$CHCl_3$, aluminium oxide) 0.40. δ_H (500 MHz, $CDCl_3$) 6.86/6.84 (1H, br s, CO*NH*), 6.46/6.40 (1H, dd, *J* 3.4 Hz, 1.7 Hz, *16 CH*=C), 6.42 (1H, br s, CO*NH*-CH_2), 4.39 (1H, ddd, *J* 10.7 Hz, 8.2 Hz, 5.2 Hz, *CH*NH), 3.47-3.33 (2H, m, *CH_2*NH), 2.80 (1H, m, NHCH-*CH_2*), 2.27-2.15 (2H, m, 2 x skeleton *CH*), 2.01-1.89 (2H, m, overlapping of lactam *CH* and skeleton *CH*), 1.73-0-76 (19H, br m, skeleton protons), 0.99/0.96 (3H, s, 18-*CH_3*), 0.82 (3H, s, 19-*CH_3*). δ_C NMR (125.7 MHz) 176.2, 168.6/168.4, 149.9/149.7, 137.2137.0, 56.8/56.7, 55.1, 50.7, 47.2, 46.7/46.6, 39.5, 28.5, 36.5, 35.1/34.9, 33.8, 32.0, 31.8/31.7, 30.3/30.2, 29.0, 28.9, 26.8, 22.1, 20.7/20.6, 16.6/16.5, 12.2. IR (KBr, ν (cm^{-1})): 3326 (br, NH), 1703 (lactam CON), 1655 (CON), 1530 (NH); MS m/z (rel. int.): 384 (62, M^+), 369 (52), 351 (6), 302 (6), 285 (37), 269 (100), 257 (59), 207 (4), 161 (14), 147 (18), 105 (20), 91 (24), 68 (20), 55 (20).

3.4.27. (E)-*N*-(2-Oxopyrrolidin-3-yl)non-2-enamide (**5c**)

Yield: 91 mg (72%), White powder, m.p. 209-210 °C; [Anal. Calcd. for $C_{13}H_{22}N_2O_2$: C, 65.51; H, 9.30; N, 11.75. Found: C, 65.40; H, 9.44; N, 11.63.]; R_f (4% MeOH/$CHCl_3$, aluminium oxide) 0.59. δ_H (500 MHz, $CDCl_3$) 6.89 (1H, dt, *J* 15.2 Hz, 7.1 Hz, *=CH*), 6.38 (1H, br s, CO*NH*), 6.31 (1H, br s, CO*NH*-CH_2), 5.84 (1H, dt, *J* 15.3 Hz, 1.3 Hz, *=CH*), 4.45 (1H, ddd, *J* 10.7 Hz, 8.2 Hz, 5.4 Hz, *CH*NH), 3.47-3.37 (2H, m, *CH_2*NH), 2.90-2.79 (1H, m, NHCH-*CH_2*), 2.19 (2H, q, J 7.1 Hz, *CH_2*CH_3), 2.04-1.93 (1H, m, NHCH-*CH_2*), 1.52-1.40 (2H, m, chain *CH_2*), 1.38-1.22 (6H, br m, 3 x chain *CH_2*), 0.90 (3H, t, *J* 7.1 Hz, CH_2*CH_3*). δ_C NMR (125.7 MHz) 175.8, 166.7, 145.9, 122.9, 50.9, 39.3, 32.1, 31.6, 30.3, 28.8, 28.2, 22.6, 14.1. IR (KBr, ν (cm^{-1})): 3276, 3199 (NH), 1695 (lactam CON), 1669 (CON), 1630 (C=C), 1560 (NH); MS m/z (rel. int.): 238 (14, M^+), 220 (3), 199 (7), 181 (9), 156 (59), 138 (47), 99 (54), 81 (27), 69 (45), 55 (100).

3.4.28. *N*-(2'-Oxopyrrolidin-3'-yl)benzamide (**6c**)

Yield: 48 mg (47%), White powder, m.p. 220-221 °C; [Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.61; H, 5.97; N, 13.55.]; R_f (5% MeOH/$CHCl_3$) 0.28. δ_H (500 MHz, $CDCl_3$) 7.84 (2H,

d, *J* 7.4 Hz, CH_{ortho}(Ph)), 7.52 (1H, t, *J* 7.4Hz, CH_{para}(Ph)), 7.46 (2H, t, *J* 7.4 Hz, CH_{meta}(Ph)), 6.90 (1H, d, *J* 3.4 Hz, CO*NH*), 6.22 (1H, br s, CO*NH*-CH_2), 4.56 (1H, ddd, *J* 10.7 Hz, 8.2 Hz, 5.2 Hz, *CH*NH), 3.53-3.44 (2H, m, CH_2NH), 3.01-289 (1H, m, NHCH-CH_2), 2.14-2.02 (1H, m, NHCH-CH_2). δ_C NMR (125.7 MHz) 175.6, 168.0, 133.7, 131.8, 128.6, 127.1, 51.2, 39.4, 30.3. IR (KBr, ν (cm^{-1})): 3252 (br, NH), 1695 (lactam CON), 1670 (CON), 1561 (NH); MS m/z (rel. int.): 204 (21, M^+), 186 (4), 161 (4), 143 (2), 122 (28), 106 (100), 99 (10), 77 (55), 51 (18).

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