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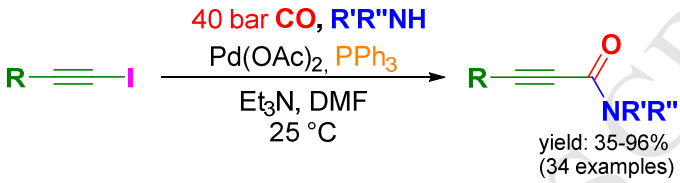
Graphical abstract



Efficient Synthesis of Alkynyl Amides via Aminocarbonylation of Iodoalkynes

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Abstract: Iodoethynylbenzene as iodoalkyne model compound was aminocarbonylated with *tert*-butylamine under carbon monoxide atmosphere in the presence of *in situ* palladium(0) catalysts. The formation of the unsaturated carboxamide (alkynyl amide) is always accompanied by that of the Glaser coupling product, diphenylbutadiyne. The yield of the amide-forming reaction was optimized by the systematic variation of the phosphine ligand, carbon monoxide pressure and temperature. The scope of the reaction was investigated by using various primary and secondary amines including amino acid methyl esters as N-nucleophiles.

17α-(Iodoethynyl)-testosterone was also functionalised by using this methodology providing the corresponding 17α-(carboxamidoethynyl)-testosterone derivatives in up to 96% yields. The reaction was extended to 1-(iodoethynyl)cyclohex-1-ene and 1-iodohex-1-yne. Ethyl iodopropiolate gave the enamine type product by the addition of amine to the alkyne functionality which was formed from the iodoalkyne via deiodination under standard aminocarbonylation conditions. The bromo analogue, bromoethynylbenzene has shown lower reactivity than the corresponding iodo derivative.

Key-words: iodoalkyne, palladium, carbon monoxide, aminocarbonylation, carboxamide

Introduction

Carboxamides are among the most investigated compounds with high synthetic significance discussed even in fundamental text-books.[1] The conventional carboxylic acid–acyl halide–carboxamide route can be circumvented by homogeneous catalytic methodologies which are based on finding applications in various types of transition metal catalysed reactions.[2] As a real breakthrough, the discovery of palladium-catalysed aminocarbonylation of haloaromatics (iodoarenes and bromoarenes) and that of their synthetic surrogates, aryl triflates, lead to the great variety of aromatic carboxamides.[3] Similarly, the reaction of iodoalkenes and their analogues, enoltriflates, provided the corresponding α,β-unsaturated carboxamides. The palladium-catalysed aminocarbonylation of both types of substrates was reviewed in many book-chapters and journal reviews.[4]

Although carboxamides, possessing carboxamido functionality attached to an sp^2-carbon, were synthesised in great variety, far less examples are known for the synthesis of carboxamides containing an *sp*-carbon—amide bond. As an obvious strategy, haloalkyne-based carbonylation reactions can be used. A halodecarboxylation protocol was reported for the synthesis of haloalkynes by using substituted propiolic acids.[5] N-Iodosuccinimide (NIS) was used for the synthesis of 17α-iodoethynyl-steroids.[6]

Arylalkynyl bromides were aminocarbonylated under mild conditions toward the corresponding carboxamides in the presence of dicobalt octacarbonyl as a CO source.[7] Alkynyl amides were synthesized in a palladium-catalyzed coupling reaction of alkynyl carboxylic acids and amines under carbon monoxide via decarboxylation of the substrate.[8] Propiolamides were synthesised via carbamoylation in the presence of copper catalysts.[9] Terminal alkynes were trasnsferred to the corresponding carboxamides via oxidative aminocarbonylation using Pd/C catalyst.[10] Aryl-substituted propiolamides were synthesised from iodopropiolamides and arylboronic acids via Suzuki-Miyaura reaction.[11]

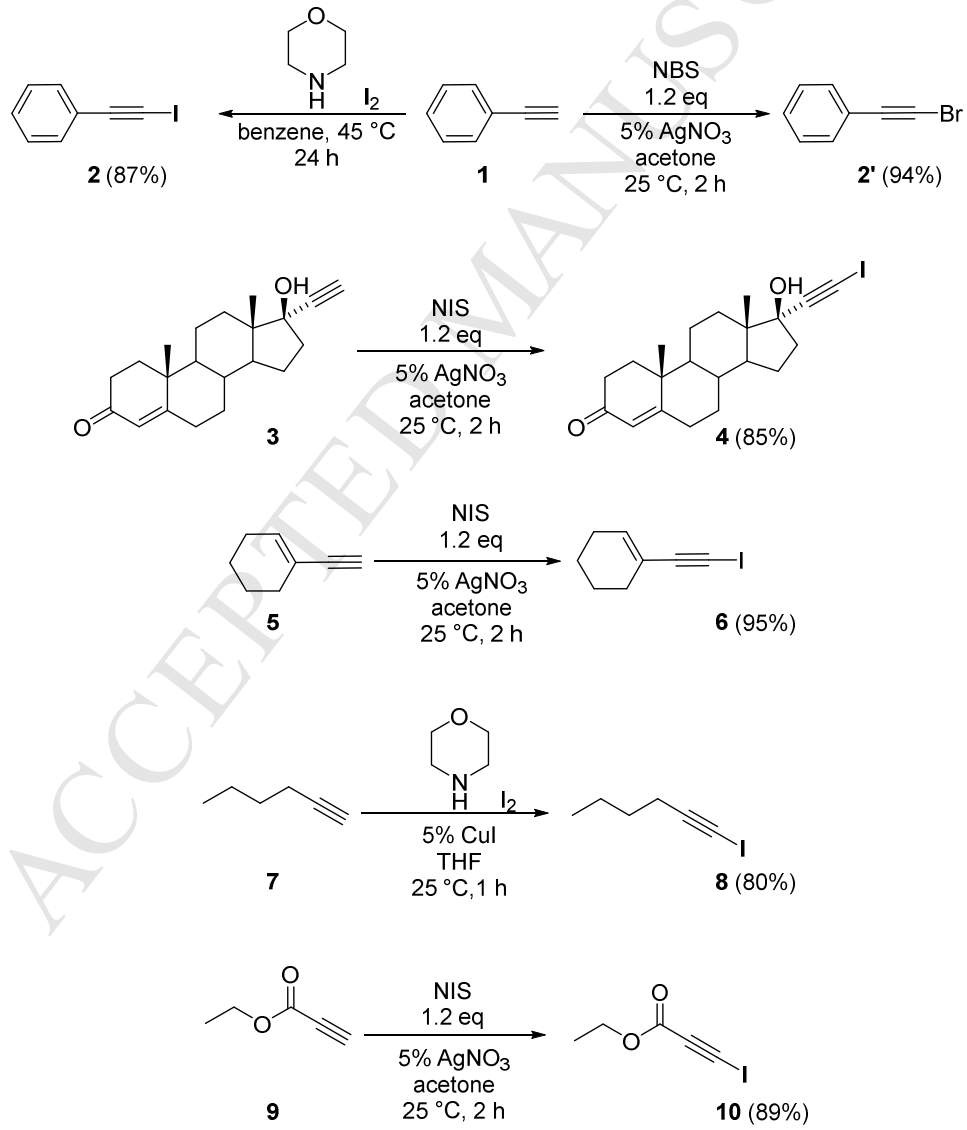
Hypervalent iodine(III) reagents/photoredox dual catalysis were used for the synthesis of alkynyl amide via radical ynonylation.[12] N-Aryl-substituted alkynyl amide underwent palladium-catalyzed domino carbopalladation/C-H activation/C-C bond-formation.[13] N,N-Disubstituted alkynyl amides were reacted with isolated diynes to yield benzamides with axial chirality in highly enantioselective cyclization reaction.[14]

Alkynyl amides represent an important family of unsaturated carboxamides due to their pharmacological importance.[15] Encouraged by their application as building blocks even in further transition metal catalysed reactions, we extended our systematic investigations in the field of carbonylation reactions to the investigation of iodoalkynes. This way, the high-yielding aminocarbonylation of iodoalkynes with various primary and secondary amines is reported here.

Results and Discussion

*Synthesis of iodoalkynes (**2, 4**, **6**, **8** and **10**)*

For the synthesis of iodoalkynyl substrates, applicable in further catalytic transformations, terminal alkynes such as ethynylbenzene (**1**), 17α-(ethynyl)-testosterone (**3**), 1-ethynylcyclohex-1-ene (**5**), 1-hexyne (**7**) and ethyl propiolate (**9**) were chosen as starting material. The non-functionalised iodoalkynes, iodoethynylbenzene (**2**) and 1-iodohex-1-yne (**8**) were obtained by direct iodination in the presence of iodomorpholinium iodide formed *in situ* from morpholine and iodine.[16] The three additional functionalised iodoalkynes, 7α-(iodoethynyl)-testosterone (**4**), 1-(iodoethynyl)cyclohexene (**6**) and ethyl iodopropiolate (**10**) were obtained in excellent yields by using *N*-iodosuccinimide (NIS) as iodination agent (*Scheme 1*).[4a] The bromoalkyne derivative (**2'**) was synthesised according to a similar methodology by using *N*-bromosuccinimide (NBS) as bromination agent.[6]



Scheme 1. Synthesis of iodoalkynes (**2**, **4**, **6, 8** and **10**) and bromoalkyne (**2'**) used as substrates in aminocarbonylations

*Aminocarbonylation of iodoalkyne (**2**) and bromoalkyne (**2'**)*

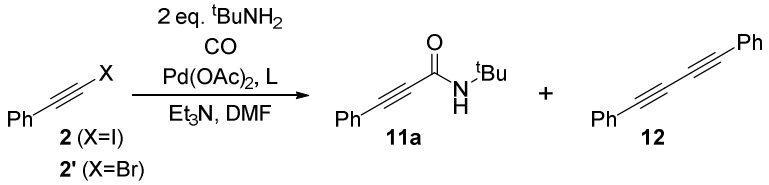
Iodoethynylbenzene (**2**) was reacted with *tert*-butylamine (**a**) and carbon monoxide under various conditions. Highly reactive palladium(0) catalysts, formed *in situ* from palladium(II) acetate and the appropriate monodentate (PPh_3, P^tBu_3, PCy_3, $P(OPh)_3$) or bidentate P-ligands (dppe, dppp, dppf, Xantphos), were used. The *in situ* reduction of Pd(II) to Pd(0) resulting in low-ligated, highly active palladium complexes was discussed previously.[17]

The formation of the target alkynyl amide (**11a**) is accompanied by that of the Glaser-coupling derivative, diphenylbutadiyne (**12**) (*Table 1*). Although the two products are formed in comparable amounts under atmospheric pressure, the chemoselectivity toward **11a** can be substantially increased by using higher CO pressures (entries 3 and 4). Higher temperatures favour direct coupling (the formation of **12**) at atmospheric pressure, *i.e.*, lower chemoselectivity toward **11a** was obtained (*compare entries 2, 5 and 6*). It has to be noted, that no similar effect was observed at high pressure. Similar **11a**/**12** ratios were obtained at 80 bar CO pressure at different temperatures (*entries 4 and 7*).

A similar effect of the pressure was observed using phosphines of high basicity, *i.e.*, in the presence of PBu_3 the higher CO pressure favours higher chemoselectivity towards amide (*entries 9 and 10*). A typical chemoselectivity of *ca*. 80% was observed also with PCy_3 (*entry 8*). The flexible diphosphines ($Ph_2P(CH_2)_nPPh_2$) gave much lower chemoselectivities (*entries 11-13*). The rigid diphosphines, dppf and Xantphos, especially, provided **11a**/**12** ratios similar to those obtained with monodentate ligands (*entries 14 and 15*). It is worth noting that even in case of Xantphos ligand the increase of the temperature resulted in similar chemoselectivity as with PPh_3 (compare *entries 5 and 16*). The tested phosphite ligand ($P(OPh)_3$) also formed active catalytic system with palladium, providing carboxamide yields similar to basic monodentate ligands (*entry 17*).

The bromoalkyne derivative (**2'**) shows much lower reactivity than the corresponding iodoalkyne substrate (**2**). Higher temperature and elevated reaction times are necessary to achieve conversions similar to **2** (*entry 18*).

Table 1. Aminocarbonylation of iodoethynylbenzene (**2**) in the presence of *tert*-butylamine as N-nucleophile (optimization of the reaction conditions)[a]



Entry	Ligand	T [°C]	p(CO) [bar]	R.time [h]	Ratio of **11a**/**12**[b]	Yield[e] (**11a**) [%]
1	PPh_3	25	1	2.5	50/50[c]	n.i.
2	PPh_3	25	1	20	70/30	62
3	PPh_3	25	40	2.5	91/9	85
4	PPh_3	25	80	2.5	88/12	68
5	PPh_3	50	1	2	52/48	45
6	PPh_3	70	1	1	29/71	10
7	PPh_3	70	80	2.5	89/11	68
8	$P(Cy)_3$	25	40	2.5	79/21	75
9	P^tBu_3	25	1	2.5	70/30	35
10	P^tBu_3	25	40	2.5	82/18	20
11	dppe	25	40	2.5	62/38[d]	n.i.
12	dppe	25	40	2.5	61/39	60
13	dppp	25	40	2.5	53/47	48
14	dppf	25	40	2.5	80/20	74
15	Xantphos	25	40	2.5	92/8	82
16	Xantphos	50	1	1	48/52	n.i.
17	$P(OPh)_3$	25	40	2.5	83/17	76
18[f]	PPh_3	50	1	8	70/30	n.i.

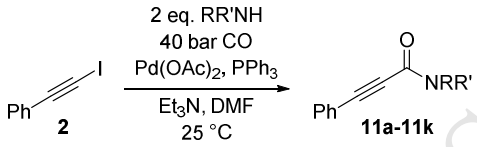
a) Reaction conditions: 1 mmol of substrate (**2**), 2 mmol of *tert*-butylamine nucleophile (**a**); 0.025 mmol of $Pd(OAc)_2$, 0.05 mmol monophosphine or $P(OPh)_3$, (or 0.025 mmol of diphosphine); 0.5 mL of Et_3N, 10 ml of DMF
b) Determined by GC and GC–MS. Conversion of 97-99% was achieved in all cases (unless otherwise stated).
c) Conversion: 42%
d) Conversion: 73%
e) Isolated yield based on the starting amount of the substrate (**2**)
f) **2'** was used as substrate

Aminocarbonylation of iodoalkynes using various N-nucleophiles

Iodoalkynes **2** and **4** were aminocarbonylated under optimised reaction conditions (40 bar CO, 25 °C) (*Table 2 and Table 3*, respectively). In addition to the *tert*-butylamine (**a**) discussed above, piperidine (**b**), morpholine (**c**), allylamine (**d**), methyl glycinate (**e**), methyl alaninate (**f**), methyl valinate (**g**), methyl prolinate

(**h**), methyl phenylalaninate (**i**), N,O-dimethylhydroxylamine (**j**) and (*S*)-2-methylbenzylamine (**k**) were used as N-nucleophile. Both substrates were practically fully converted to the carboxamides (**11a-k** and **13a-k**, respectively). Considering the whole range of amines (**a-k**) good to excellent yields (up to 96%) for the isolated carboxamides were obtained. Nucleophiles **d** and **i** gave the lowest isolated yields in both series of carboxamides (*entries 4 and 9* in both Tables) due to difficulties in chromatographic separation. It has to be noted that the corresponding carboxamides were formed in high yields even in these cases based on the NMR analysis of the crude reaction products.

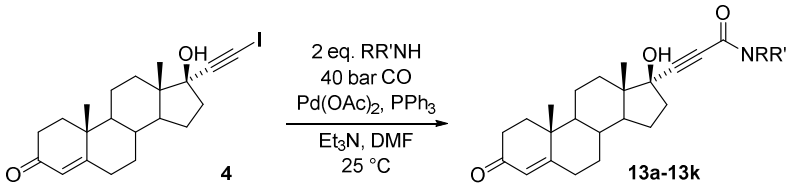
Table 2. Aminocarbonylation of **2** in the presence of various primary and secondary amines[a]



Entry	Amine		Yield[b] [%]
	R	R'	
1	H	*t*Bu	85 (**11a**)
2		$(CH_2)_5$	84 (**11b**)
3		$(CH_2)_2O(CH_2)_2$	81 (**11c**)
4	H	$CH_2CH{=}CH_2$	62 (**11d**)
5	H	CH_2COOCH_3	67 (**11e**)
6	H	$CH(CH_3)COOCH_3$	80 (**11f**)
7	H	$CH(CH(CH_3)_2)COOCH_3$	75 (**11g**)
8		$CH(COOCH_3)(CH_2)_3$	83 (**11h**)
9	H	$CH(CH_2Ph)COOCH_3$	59 (**11i**)
10	CH_3	OCH_3	63 (**11j**)
11	H	(*S*)-$CH(CH_3)Ph$	96 (**11k**)

a) Reaction conditions: 1 mmol of substrate, 2 mmol of amine nucleophile (**a-k**); 0.025 mmol of $Pd(OAc)_2$, 0.05 mmol of PPh_3, 0.5 mL of Et_3N, 10 ml of DMF, 40 bar CO, 25 ^oC.
b) Yield of the isolated product based on the starting amount of the substrate (**2**).

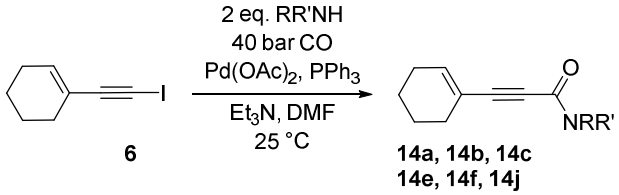
Table 3. Aminocarbonylation of **4** in the presence of various primary and secondary amines (for reaction conditions see Table 2)



Entry	Amine		Yield
	R	R'	[%]
1	H	*t*Bu	95 (**13a**)
2		$(CH_2)_5$	96 (**13b**)
3		$(CH_2)_2O(CH_2)_2$	96 (**13c**)
4	H	$CH_2CH=CH_2$	65 (**13d**)
5	H	CH_2COOCH_3	92 (**13e**)
6	H	$CH(CH_3)COOCH_3$	90 (**13f**)
7	H	$CH(CH(CH_3)_2)COOCH_3$	60 (**13g**)
8		$CH(COOCH_3)(CH_2)_3$	65 (**13h**)
9	H	$CH(CH_2Ph)COOCH_3$	56 (**13i**)
10	CH_3	OCH_3	75 (**13j**)
11	H	(*S*)-$CH(CH_3)Ph$	78 (**13k**)

To investigate the scope of the substrates in aminocarbonylation, **6** and **8** were aminocarbonylated using selected amines (**a-c**, **e**, **f**, **j**) (*Table 4 and 5*, respectively). The alkynyl amides were isolated in analytical purity and fully characterised in both cases. Moderate isolated yields were obtained. As above, it is worth noting that the relatively low yields are due to the loss of the products during isolation with column chromatography. The only side-product the Glaser-coupled diyne was formed in less than 3%. The diynes were even not detectable in the reaction mixture (isolated as crude products still containing the catalyst, ammonium salts and side-products, if any) with NMR. Excellent yields were obtained with nucleophiles **c** and **f** (*Table 5, entries 3 and 5*).

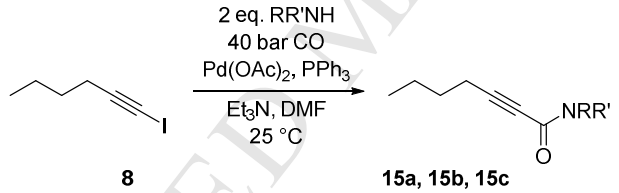
Table 4. Aminocarbonylation of **6** in the presence of various primary and secondary amines (for reaction conditions see *Table 2*)



6 **14a, 14b, 14c 14e, 14f, 14j**

Entry	Amine R	Amine R'	Yield [%]
1	H	*t*Bu	53 (**14a**)
2		$(CH_2)_5$	59 (**14b**)
3		$(CH_2)_2O(CH_2)_2$	55 (**14c**)
4	H	CH_2COOCH_3	59 (**14e**)
5	H	$CH(CH_3)COOCH_3$	47 (**14f**)
6	CH_3	OCH_3	35 (**14j**)

Table 5. Aminocarbonylation of **8** in the presence of various primary and secondary amines (for reaction conditions see Table 2)

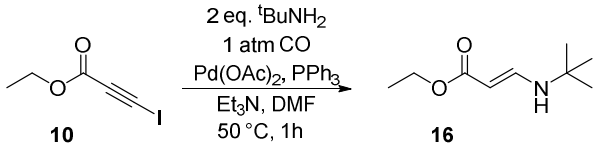


8 **15a, 15b, 15c 15e, 15f, 15j**

Entry	Amine R	Amine R'	Yield[b] [%]
1	H	*t*Bu	56 (**15a**)
2		$(CH_2)_5$	64 (**15b**)
3		$(CH_2)_2O(CH_2)_2$	95 (**15c**)
4	H	CH_2COOCH_3	53 (**15e**)
5	H	$CH(CH_3)COOCH_3$	86 (**15f**)
6	CH_3	OCH_3	52 (**15j**)

The third type of iodoalkyne, the activated ethyl iodopropiolate (**10**) gave the enamine type product (**16**) exclusively (*Scheme 2*) The loss of iodine from **10** resulting in ethyl propiolate took place under the reductive conditions used and was followed by the addition of amine to the alkyne functionality. Since no similar reaction(s) were detected, the following reaction sequence could be suggested in order to rationalize the formation of **16**. *tert*-Butylamine could serve as a hydrogen source for the hydrogenolysis of the iodoalkyne

moiety while corresponding hydrazines and ammonium iodides are formed. The addition of the amine (**a**) to the activated triple bond brings about enamine (**16**). As a consequence of the above preferred side-reactions the target alkynyl amide was formed only in traces (less than 1%) and was detected by GC-MS only.



Scheme 2. Reactions of **10** under aminocarbonylation conditions (formation of enamines accompanied by deiodination)

Conclusions

Iodoalkynes, easily accessible from alkynes, can be considered as appropriate starting materials for the synthesis of alkynyl amides. Under mild conditions the iodoalkyne substrate undergoes aminocabonylation reaction in the presence of carbon monoxide and primary and secondary amines. The amount of the most characteristic side product, the Glaser coupling derivative can be substantially reduced by the optimization of the reaction conditions (systematic variation of the phosphine ligand, carbon monoxide pressure and temperature).

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 residual $CHCl_3$ (7.26 and 77.00 ppm for ^{1}H and ^{13}C, respectively). 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}. MS measurements were carried out on an Agilent LC-MSD-TRAP-XCT apparatus in ESI (positive) mode. Samples of the catalytic reactions were analysed with a Hewlett Packard 5830A gas chromatograph fitted with a capillary column coated with OV-1.

The alkynes and N-nucleophiles were purchased from Sigma-Aldrich and were used without further purification. 2-Bromophenylacetylene (**2'**) substrate was synthesised according to a known procedure.[6] (*Caution!* 2-Bromophenylacetylene is a strong lacrimator (tear-producing compound).)

3.2. Aminocarbonylation experiments at normal pressure

In a typical experiment a solution of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PPh_3 (13.1 mg, 0.05 mmol) (or $P^tBu_3 \cdot HBF_4$ (14.5 mg, 0.05 mmol)), 1.0 mmol iodoethynylbenzene (**2**), 2.0 mmol *tert*-butylamine (**a**) were dissolved in 10 mL of DMF under argon. Triethylamine (0.5 mL) was added to the homogeneous yellow solution and the atmosphere was changed to carbon monoxide. The colour changed to dark red. The reaction was conducted for 24 hours at 25, 50 or 70 ^oC. Some metallic palladium was formed at the end of the reaction which was filtered off. (A sample of this solution was immediately analysed by GC-MS.) The mixture was then concentrated and evaporated to dryness. The residue was dissolved in chloroform (20 mL) and washed with water (20 mL). The organic phase was thoroughly washed twice with brine (20 mL), dried over Na_2SO_4 and concentrated to a red waxy material or a thick oil. Chromatography (silica, chloroform/hexane, chloroform/ethyl acetate) yielded the desired compounds as pale yellow solid.

3.3. Aminocarbonylation experiments at high pressure

The DMF solution (10 mL) of the catalyst precursor ($Pd(OAc)_2$ (5.6 mg, 0.025 mmol), 0.05 mmol monophosphine or $P(OPh)_3$, or 0.025 mmol of diphosphine) and the reactants (1.0 mmol of **2** or 0.5 mmol of **4** iodoalkyne substrate and 2 equivalents of *N*-nucleophile) and triethylamine (0.5 mL) was transferred under argon into a 100 mL stainless steel autoclave. The reaction vessel was pressurised up to 40 or 80 bar total pressure with carbon monoxide and the magnetically stirred mixture was heated in an oil bath at 50 or 70 ^oC or stirred at room temperature for 2.5 h. The work-up procedure is identical with that given above.

3.4. Characterization of the products

N-(tert-Butyl)-3-phenylpropiolamide (**11a**): Yield: 171 mg (85%); pale yellow solid material, mp. 76-77°C; R_f (5% EtOAc, 95% $CHCl_3$) 0.88; δ_H (500 MHz, $CDCl_3$) 7.54 (2H, d, *J*=7.2 Hz, Ar), 7.44-7.41 (1H, m, Ar), 7.38-7.35 (2H, m, Ar), 5.77 (1H, brs, N*H*), 1.44 (9H, s, C(C*H*$_3$)$_3$). δ_C (125.7 MHz, $CDCl_3$) 152.5, 132.4, 129.8, 128.5, 120.5, 84.1, 82.5, 52.4, 28.7. IR (KBr, ν (cm^{-1})): 3229 ν(NH), 3054 ν(CH, Ar), 2991, 2986, 2931, 2866 ν(CH_3), 2220 ν(C≡C), 1625 Amide I., 1551 Amide II., 757 γ(=CH). MS m/z (rel int.): 201 (14, M^+), 186 (25), 146 (16), 129 (100), 101 (8), 75 (13), 51 (5).

(3-Phenyl-propiolyl)-piperidine (**11b**): Yield: 179 mg (84%); off-white solid material, mp. 105 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.70; δ_H (500 MHz, $CDCl_3$) 7.58-7.56 (2H, m, Ar), 7.45-7.42 (1H, m, Ar), 7.40-7.37 (2H, m, Ar), 3.81-3.79 (2H, m), 3.66-3.64 (2H, m), 1.74-1.59 (6H, m). δ_C (125.7 MHz, $CDCl_3$) 153.0, 132.3, 129.9, 128.5, 120.8, 90.3, 81.5, 48.2, 42.4, 26.5, 25.4, 24.6. IR (KBr, ν (cm^{-1})): 2996, 2980, 2944 ν(CH_2), 2215 ν(C≡C), 1623 Amide I., 1488, 1464, 1456, 1438 ν(C=C), 765 γ(=CH). MS m/z (rel int.): 213 (46, M^+), 212 (50, M-1$^+$), 184 (26), 156 (10), 129 (100), 101 (13), 75 (18), 56 (6), 51 (8).

4-(3-Phenylpropiolyl)-morpholine (**11c**): Yield: 174 mg (81%); off-white solid material, mp. 58-59 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.42; δ_H (500 MHz, $CDCl_3$) 7.58-7.56 (2H, m, Ar), 7.47-7.43 (1H, m, Ar), 7.41-

7.38 (2H, m, Ar), 3.88-3.86 (2H, m), 3.78-3.76 (2H, m), 3.73 (4H, s). δ_C (125.7 MHz, $CDCl_3$) 153.2, 132.4, 130.2, 128.6, 120.3, 91.2, 80.8, 66.9, 66.5, 47.3, 42.0. IR (KBr, ν (cm^{-1})): 3057, 3045 ν(CH, Ar), 2973, 2923, 2898, 2862 ν(CH_2), 2217 ν(C≡C), 1620 Amide I., 1493, 1453, 1444, 1433 ν(C=C), 1111 ν(C-O-C), 766 γ(=CH). MS m/z (rel int.): 215 (29, M^+), 186 (12), 156 (10), 129 (100), 101 (11), 86 (18), 75 (19), 56 (18), 51 (7).

N-Allyl-3-phenylpropiolamide (**11d**): Yield: 115 mg (62%); yellow solid material, mp. 39-40 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.71; δ_H (500 MHz, $CDCl_3$) 7.57-7.53 (2H, m, Ar), 7.45-7.40 (1H, m, Ar), 7.38-7.35 (2H, m, Ar), 6.19 (1H, brs, N*H*), 5.89 (1H, ddd, *J*= 15.9 Hz, 10.7 Hz, 5.7 Hz, C*H*=CH_2), 5.28(1H, d, *J*= 15.9 Hz, CH=CH_2(*E*)), 5.25 (1H, d, *J*= 10.7 Hz, CH=CH_2(*Z*)), 3.99. δ_C (125.7 MHz, $CDCl_3$) 153.3, 133.2, 132.5, 130.1, 128.5, 120.2, 117.1, 84.9, 82.9, 42.9. IR (KBr, ν (cm^{-1})): 3282 ν(NH), 3079, 3066, 3053, 3012 ν(CH, Ar), 2980, 2920 ν(CH_2), 2222 ν(C≡C), 1637 Amide I., 1534 Amide II, 1483, 1443, 1413 ν(C=C), 759 γ(=CH). MS m/z (rel int.): 184 (21, M^+), 156 (46), 142 (15), 129 (100), 101 (13), 75 (22), 51 (8).

Methyl N-(3-phenyl-propiolyl)-glycinate (**11e**): Yield: 145 mg (67%); pale yellow solid material, mp. 95-96 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.48; δ_H (500 MHz, $CDCl_3$) 7.58-7.56 (2H, m, Ar), 7.47-7.44 (1H, m, Ar), 7.41-7.38 (2H, m, Ar), 6.54 (1H, brs, N*H*), 4.19 (2H, d, *J*= 5.2 Hz), 3.82 (3H, s, CH_3). δ_C (125.7 MHz, $CDCl_3$) 169.7, 153.3, 132.6, 130.3, 128.6, 120.0, 85.8, 82.4, 52.6, 41.5. (KBr, ν (cm^{-1})): 3274 ν(NH), 3063, 2993 ν(CH, Ar), 2949, 2954, 2819, 2756 ν(CH_2, CH_3), 2233 ν(C≡C), 1733 ν(C=O ester) 1626 Amide I., 1549 Amide II., 1446, 1433 ν(C=C), 1285 ν(C-O-C ester), 764 γ(=CH). MS m/z (rel int.): 217 (13, M^+), 158 (20), 129 (100), 101 (9), 75 (15), 51 (5).

Methyl N-(3-phenyl-propiolyl)-alaninate (**11f**): Yield: 185 mg (80%); viscous orange material; R_f (5% EtOAc, 95% $CHCl_3$) 0.68; δ_H (500 MHz, $CDCl_3$) 7.57-7.55 (2H, m, Ar), 7.46-7.43 (1H, m, Ar), 7.40-7.36 (2H, m, Ar), 6.63 (1H, d, *J*= 5.7 Hz, N*H*), 4.75-4.69 (1H, m, C*H*), 3.81 (3H, s, CH_3), 1.50 (3H, d, *J*= 7.2 Hz, CH_3). δ_C (125.7 MHz, $CDCl_3$) 172.8, 152.7, 132.6, 130.2, 128.5, 120.1, 85.4, 82.7, 52.7, 48.3, 18.4. (KBr, ν (cm^{-1})): 3259 ν(NH), 3057 ν(CH, Ar), 2952, 2876, 2844 ν(CH_2, CH_3), 2216 ν(C≡C), 1747 ν(C=O ester) 1655 Amide I., 1530 Amide II., 759 γ(=CH). MS m/z (rel int.): 231 (5, M^+), 172 (38), 129 (100), 101 (8), 75 (13), 51 (5).

Methyl N-(3-phenyl-propiolyl)-valinate (**11g**): Yield: 194 mg (75%); pale yellow solid material, mp. 62 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.77; δ_H (500 MHz, $CDCl_3$) 7.60-7.58 (2H, m, Ar), 7.48-7.44 (1H, m, Ar), 7.41-7.38 (2H, m, Ar), 6.46 (1H, d, *J*= 8.7 Hz, N*H*), 4.70 (1H, dd, *J*= 8.7 Hz, 5.0 Hz, NH(C*H)*), 3.81 (1H, s, CH_3), 2.26 (1H, dq, J=6.9 Hz, 5.0 Hz, $(CH_3)_2$C*H*), 1.03 (3H, d, J= 6.9 Hz, (CH)*C*H_3), 0.99 (3H, d, J= 6.9 Hz, (CH)*C*H_3). δ_C (125.7 MHz, $CDCl_3$) 171.9, 153.1, 132.6, 130.2, 128.6, 120.1, 85.6, 82.7, 57.4, 52.4, 31.5, 18.9, 17.9. IR (KBr, ν (cm^{-1})): 3201 ν(NH), 3031 ν(CH, Ar), 2974, 2946, 2908, 2879, 2838 ν(CH_2, CH_3), 2221 ν(C≡C), 1736 ν(C=O ester) 1627 Amide I., 1551 Amide II., 1285 ν(C-O-C ester), 767 γ(=CH). MS m/z (rel int.): 259 (3, M^+), 244 (7), 200 (31), 129 (100), 101 (7), 75 (10), 51 (3).

Methyl N-(3-phenyl-propiolyl)-prolinate (**rotamer A + rotamer B**) (**11h**): Yield: 213 mg (83%); viscous orange material; R_f (5% EtOAc, 95% $CHCl_3$) 0.75; δ_H (500 MHz, $CDCl_3$) 7.59-7.53 (2H, m, Ar), 7.47-7.43 (1H, m, Ar), 7.41-7.37 (2H, m, Ar), 4.80-4.59 (1H, m), 3.97-3.85 (1H, m), 3.79 (3H, s rotamer A), 3.78 (3H, s rotamer B), 3.75-3.66 (1H, m), 2.42-2.27 (1H, m), 2.21-1.97 (3H, m). δ_C (125.7 MHz, $CDCl_3$) rotamer A: 172.6, 152.9, 132.6, 130.3, 128.5, 120.2, 89.3, 82.1, 61.0, 52.6, 46.1, 30.8, 23.3; rotamer B: 172.0, 153.1, 132.5, 130.1, 128.6, 120.5, 89.6, 82.3, 58.2, 52.4, 48.5, 29.8, 24.2. IR (KBr, ν (cm^{-1})): 3056 ν(CH, Ar), 2980, 2952, 2879, 2844 ν(CH_2, CH_3), 2208 ν(C≡C), 1749 ν(C=O ester) 1613 Amide I., 760 γ(=CH). MS m/z (rel int.): 257 (7, M^+), 198 (43), 129 (100), 101 (7), 75 (22), 51 (8).

Methyl N-(3-phenyl-propiolyl)-phenylalaninate (**11i**): Yield: 181 mg (59%); pale yellow solid material, mp. 103-104 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.80; δ_H (500 MHz, $CDCl_3$) 7.57-7.56 (2H, m, Ar), 7.47-7.44 (1H, m, Ar), 7.41-7.38 (2H, m, Ar), 7,36-7.33 (2H, m, Ar), 7.31-7.28 (1H, m, Ar), 7.18-7.17 (2H, m, Ar), 6.45 (1H, d, *J*= 7.7 Hz, N*H*), 5.02 (1H, dt, *J*= 7.7 Hz, 5.6 Hz, C*H*), 3.79 (3H, s, CH_3), 3.28-3.18 (2H, m, CH_2). δ_C (125.7 MHz, $CDCl_3$) 171.3, 152.7, 135.5, 132.7, 130.2, 129.3, 128.7, 128.5, 127.3, 120.0, 85.6, 82.6, 53.6, 52.5, 37.8. IR (KBr, ν (cm^{-1})): 3296 ν(NH), 3082, 3063, 3031 ν(CH, Ar), 2946, 2838 ν(CH_2, CH_3), 2217 ν(C≡C), 1741 ν(C=O ester) 1634 Amide I., 1531 Amide II., 1486, 1436 ν(C=C), 1319 ν(C-O-C ester), 759 γ(=CH). MS m/z (rel int.): 307 (3, M^+), 248 (10), 162 (28), 129 (100), 101 (7), 91 (13), 77 (11), 51 (7).

N-Methoxy-N-methyl-3-phenylpropiolamide (**11j**): Yield: 119 mg (63%); light brown solid material, mp. 36 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.47; δ_H (500 MHz, $CDCl_3$) 7.59 (2H, d, *J*=7.3 Hz, Ar), 7.47-7.44 (1H, m, Ar), 7.41-7.31 (2H, m, Ar), 3.87 (3H, brs, OCH_3), 3.32 (3H, brs, NCH_3). δ_C (125.7 MHz, $CDCl_3$) 154.7, 132.6, 130.2, 128.5, 120.5, 90.4, 80.8, 62.2, 32.6. IR (KBr, ν (cm^{-1})): 3056, 3019 ν(CH, Ar), 2971 ν(CH_3), 2218 ν(C≡C), 1638 Amide I., 1492, 1472, 1461, 1447, 1415 ν(C=C), 1202 ν(C-O-C), 760 γ(=CH). MS m/z (rel int.): 189 (4, M^+), 159 (4), 129 (100), 101 (8), 75 (16), 51 (6).

(S)-3-Phenyl-N-(1-phenylethyl)propiolamide (**11k**): Yield: 239 mg (96%); pale yellow solid material, mp. 108 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.82; δ_H (500 MHz, $CDCl_3$) 7.56-7.29 (10 H, m, Ar), 6.24 (1H, brs, N*H*), 5.29-5.23 (1H, m, C*H*), 1.60 (3H, d, CH_3). δ_C (125.7 MHz, $CDCl_3$) 152.5, 142.3, 132.5, 130.3, 128.8, 128.5, 127.7, 126.3, 120.2, 84.7, 83.1, 49.4, 21.5. IR (KBr, ν (cm^{-1})): 3316 ν(NH) 3085, 3063, 3031 ν(CH, Ar), 2968, 2927, 2867 ν(CH_3, CH), 2215 ν(C≡C), 1623 Amide I., 1529 Amide II., 1495, 1451, 1445 ν(C=C), 762 γ(=CH). MS m/z (rel int.): 248 (21, M-1$^+$), 206 (23), 191 (15), 129 (100), 104 (15), 77 (17), 51 (12).

17β-Hydroxy-N-(terc-butyl)-17α-pregna-4-en-20-yn-3-one-20-carboxamide (**13a**): Yield: 195 mg (95%); light brown solid material, mp. 129-130 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.58; δ_H (500 MHz, $CDCl_3$) 5.75 (1H, s, 3-C*H*), 5.69 (1H, s, N*H*), 2.48-1.01 (19H, m skeleton protons), 1.38 (9H, s, $C(CH_3)_3$), 1.21 (3H, s, 19-CH_3), 0.92 (3H, s, 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.4, 170.9, 152.2, 124.0, 86.4, 81.5, 79.7, 53.0, 52.4, 50.1, 47.2, 38.7, 38.6, 36.3, 35.6, 33.9, 32.8, 32.7, 31.3, 28.6, 23.2, 20.7, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3325

ν(OH), 2965, 2945, 2873 ν(CH_2, CH_3), 2221 ν(C≡C), 1659 Amide I + ν(C=O) + ν(C=C), 1531 Amide II., 1069 ν(C-OH). MS (ESI) m/z (rel int.): 412.3 (100, $M+1^+$), MS^2 m/z (rel int.): 394.3 (21), 356.2 (100), 338.2 (29),

1-(17β-Hydroxy-17α-pregna-4-en-20-yn-3-one)carbonyl-piperidine (**13b**)*:*Yield: 203 mg (96%); off white solid material, mp. 116 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.50; δ_H (500 MHz, $CDCl_3$) 5.76 (1H, s, 3-C*H*), 3.72-3.64 (2H, m), 3.63-3.53 (2H, m), 2.48-1.01 (19H, m, skeleton protons), 1.72-1.57 (8H, m), 1.22 (3H, s, 19-CH_3), 0.94 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.3, 170.7, 152.5, 124.0, 94.3, 79.8, 78.9, 53.5, 50,4, 48.2, 47.4, 42.4, 38.7, 38.6, 36.2, 35.8, 33.9, 32.8, 32.7, 31.5, 26.4, 25.3, 24.5, 23.2, 20.7, 17.5, 12.7. IR (KBr, ν (cm^{-1})): 3304, 3259 ν(OH), 3008, 2972, 2939, 2857 ν(CH_2, CH_3), 2219 ν(C≡C), 1665 ν(C=C) + ν(C=O), 1603 Amide I., 1070 ν(C-OH). MS (ESI) m/z (rel int.): 424.3 (100, $M+1^+$), MS^2 m/z (rel int.): 406.3 (100), MS^3 m/z (rel int.): 388.3 (100), 321.2 (30), 251.1 (51), 209 (32), 138 (78).

4-(17β-Hydroxy-17α-pregna-4-en-20-yn-3-one)carbonyl-morpholine (**13c**) *:* Yield: 204 mg (96%); off white solid material, mp. 189-190 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.29; δ_H (500 MHz, $CDCl_3$) 5.75 (1H, s, 3-C*H*), 3.75-3.65 (8H, m), 2.48-0.98 (19H, m, skeleton protons), 1.21 (3H, s, 19-CH_3), 0.94 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.3, 170.6, 152.8, 124.0, 96.0, 79.9, 78.2, 66.8, 66.4, 53.4, 50,4, 47.4, 47.2, 42.0, 38.8, 38.6, 36.3, 35.7, 33.9, 32.9, 32.7, 31.5, 23.2, 20.7, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3375 ν(OH), 2940, 2857 ν(CH_2, CH_3), 2218 ν(C≡C), 1665 ν(C=C) + ν(C=O), 1603 Amide I., 1069 ν(C-OH). MS (ESI) m/z (rel int.):426.3 (100, $M+1^+$), MS^2 m/z (rel int.): 408.3 (100), MS^3 m/z (rel int.): 390.3 (100), 321.2 (71), 303.2 (71), 275.1 (74), 251.1 (79).

17β-Hydroxy-N-(allyl)-17α-pregna-4-en-20-yn-3-one-20-carboxamide (**13d**)*:*Yield: 128 mg (65%); off white solid material, mp. 201-202 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.43; δ_H (500 MHz, $CDCl_3$) 6.10 (1H, brs, N*H*), 5.90-5.80 (2H, ddd, J= 16.2 Hz, 10.4 Hz, 5.7 Hz C*H*=CH_2), 5.75 (1H, s, 3-C*H*), 5.25 (1H, d, *J*= 16.2 Hz CH=CH_2(*E*)), 5.19 (1H, d, *J*= 10.4 Hz CH=CH2(Z)), 3.93 (2H, t, *J*= 5.7 Hz, NCH_2), 2.48-0.99 (19H, m, skeleton protons), 1.21 (3H, s, 19-CH_3), 0.92 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.4, 170.9, 152.9, 133.2, 124.0, 117.3, 88.9, 80.4, 79.7, 53.1, 50.2, 47.3, 42.3, 38.7, 38.6, 36.3, 35.7, 33.9, 32.8, 32.7, 31.4, 23.2, 20.7, 17.5, 12.7. IR (KBr, ν (cm^{-1})): 3299 ν(OH), 2983, 2973, 2943, 2908, 2883, 2853 ν(CH_2, CH_3), 2220 ν(C≡C), 1652 Amide I + ν(C=O) + ν(C=C), 1520 Amide II., 1068 ν(C-OH). MS (ESI) m/z (rel int.):396.3 (100, $M+1^+$), MS^2 m/z (rel int.): 378.3 (100), MS^3 m/z (rel int.): 360.3 (45), 337.2 (100), 321.3 (26).

(17β-Hydroxy-17α-pregna-4-en-20-yn-3-one)carbonyl-glycine methyl ester (**13e**) *:* Yield: 196 mg (92%); pale yellow solid material, mp. 191 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.31; δ_H (500 MHz, $CDCl_3$) 6.75 (1H, brs, N*H*), 5.75 (1H, s, 3-C*H*), 4.11 (2H, d, J= 5.1 Hz), 3.80 (3H, s, CH_3), 2.48-0.99 (19H, m, skeleton protons), 1.21 (3H, s, 19-CH_3), 0.92 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.4, 170.9, 169.9, 153.1, 124.0, 90.1, 79.9, 79.6, 53.1, 52.6, 50.2, 47.3, 41.3, 38.6, 36.3, 35.6, 33.9, 32.8, 32.7, 31.4, 23.2, 20.7, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3331 ν(OH), 2975, 2949, 2887, 2862 ν(CH_2, CH_3), 2225 ν(C≡C), 1730 ν(C=O ester), 1667 ν(C=C) +

ν(C=O) + Amide I., 1539 Amide II., 1062 ν(C-OH). MS (ESI) m/z (rel int.):428.3 (100, $M+1^+$), MS^2 m/z (rel int.): 410.3 (100), 378.2 (28), 350.3 (13), 321.2 (13).

(17β-Hydroxy-17α-pregna-4-en-20-yn-3-one)carbonyl-L-alanine methyl ester (**13f**)*:* Yield: 199 mg (90%); light brown solid material, mp. 152-153 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.40; δ_H (500 MHz, $CDCl_3$) 6.88 (1H, d, J= 7.2 Hz, N*H*), 5.75 (1H, s, 3-C*H*), 4.68-4.62 (1H, m), 3.78 (3H, s, CH_3), 2.48-1.00 (19H, m, skeleton protons), 1.45 (3H, d, J= 7.2 Hz, CH_3), 1.21 (3H, s, 19-CH_3), 0.92 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.4, 173.2, 170.9, 152.6, 124.0, 89.7, 80.1, 79.6, 53.1, 52.7, 50.2, 48.3, 47.3, 38.7, 38.6, 36.3, 35.6, 33.9, 32.8, 32,7, 31.3, 23.2, 20.7, 18,2, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3360, 3309 ν(OH), 2976, 2946, 2878, 2860 ν(CH_2, CH_3, CH), 2220 ν(C≡C), 1743 ν(C=O ester), 1668, 1625 ν(C=C) + ν(C=O) + Amide I., 1529 Amide II., 1069 ν(C-OH). MS (ESI) m/z (rel int.):442.4 (100, $M+1^+$), MS^2 m/z (rel int.): 424.3 (100), 410.2 (11), 392.2 (56), 364.2 (57), 321.2 (12).

(17β-Hydroxy-17α-pregna-4-en-20-yn-3-one)carbonyl-L-valine methyl ester (**13g**) *:* Yield: 141 mg (60%); pale yellow solid material, mp. 169-170 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.53; δ_H (500 MHz, $CDCl_3$) 6.90 (1H, d, J= 9.0 Hz, N*H*), 5.76 (1H, s, 3-C*H*), 4.62 (1H, dd, J= 9.0 Hz, 5.2 Hz), 3.78 (3H, s, CH_3), 2.48-1.01 (19H, m, skeleton protons), 2.21 (1H, dq, J= 6.8 Hz, 5.2 Hz), 1.21 (3H, s, 19-CH_3), 0.99 (3H, d, J= 6.8 Hz), 0.97 (3H, d, J= 6.8 Hz), 0.93 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.5, 172.3, 171.0, 153.3, 124.0, 90.1, 80.1, 79.6, 57.4, 53.0, 52.4, 50.1, 47.2, 38.7, 38.6, 36.3, 35.6, 33.9, 32.8, 32.7, 31.4, 31.3, 23.3, 20.7, 18.9, 17.9, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3433, 3350 ν(OH), 2951, 2876 ν(CH_2, CH_3), 2223 ν(C≡C), 1736 ν(C=O ester), 1676 ν(C=C) + ν(C=O), 1639 Amide I., 1535 Amide II., 1069 ν(C-OH). MS (ESI) m/z (rel int.):470.4 (100, $M+1^+$), MS^2 m/z (rel int.): 452.3 (100), 438.3 (21), 420.3 (58), 410.3 (36), 392.3 (72), 321 (7).

(17β-Hydroxy-17α-pregna-4-en-20-yn-3-one)carbonyl-L-proline methyl ester (**rotamer A+ rotamer B***)* (**13h**)*:*Yield: 152 mg (65%); off white solid material, mp. 130-131 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.32; δ_H (500 MHz, $CDCl_3$) 5.76 (1H, s, 3-C*H*), 4.62-4.50 (1H, m, rotamer A+ rotamer B), 3.84-3.59 (6H, m), 3.77 (3H, s, rotamer A), 3.76 (3H, s, rotamer B), 2.49-0.97 (19H, m, skeleton protons), 1.22 (3H, s, 19-CH_3, rotamer A), 1.21 (3H, s, 19-CH_3, rotamer B), 0.94 (3H, s 18-CH_3, rotamer A), 0.92 (3H, s 18-CH_3, rotamer B). δ_C (125.7 MHz, $CDCl_3$) rotamer A+ rotamer B 199.4, 172.8, 172.0, 171.9, 170.9, 170.8, 152.6, 152.5, 124.0, 94.0, 93.7, 79.8, 79.7, 61.2, 58.2, 53.3, 53.1, 52.7, 52.4, 50.3, 50.2, 48.4, 47.3, 47.2, 46.1, 38.8, 38.6, 38.5, 36.2, 35.7, 34.0, 32.8, 32.7, 31.4, 31.3, 30.7, 29.7, 24.2, 23.3, 23.2, 23.1, 20.7, 17.4, 12.7, 12.6. IR (KBr, ν (cm^{-1})): 3257 ν(OH), 2974, 2945, 2914, 2891, 2859 ν(CH_2, CH_3), 2221 ν(C≡C), 1743 ν(C=O ester), 1714 ν(C=O), 1671 ν(C=C), 1608 Amide I., 1078 ν(C-OH). MS (ESI) m/z (rel int.):468.3 (100, $M+1^+$), MS^2 m/z (rel int.): 450.3 (100), 390.2 (15), MS^3 (450.3) m/z (rel int.): 390 (100), 321.2 (26), 303.2 (8)

(17β-Hydroxy-17α-pregna-4-en-20-yn-3-one)carbonyl-L-phenylalnine methyl ester (**13i**) *:* Yield: 145 mg (56%); pale yellow solid material, mp. 85-86 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.53; δ_H (500 MHz, $CDCl_3$)

7.32-7.25 (3H, m, Ar), 7.16-7.13 (2H, m, Ar), 6.81 (1H, d, J= 7.8 Hz), 5.76 (1H, s, 3-C*H*), 4.93-4.89 (1H, m), 3.74 (3H, s, CH_3), 3.17-3.08 (2H, m, Ph(CH_2)), 2.48-0.98 (19H, m, skeleton protons), 1.21 (3H, s, 19-CH_3), 0.91 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.5, 171.7, 171.1, 152.8, 135.5, 129.3, 128.6, 127.3, 123.9, 90.1, 79.9, 79.5, 53.6, 53.1, 52.5, 50.1, 47.3, 38.7, 38.6, 37.7, 36.2, 35.6, 33.9, 32.8, 32,7, 31.3, 23.2, 20.7, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3413 ν(OH), 3029, 3015 ν(CH, Ar), 2947, 2875, 2857 ν(CH_2, CH_3, CH), 2223 ν(C≡C), 1745 ν(C=O ester), 1659 ν(C=C) + ν(C=O) + Amide I., 1529 Amide II., 1069 ν(C-OH). MS (ESI) m/z (rel int.):518.3 (100, $M+1^+$), MS^2 m/z (rel int.): 500.3 (100), 486.3 (11), 468.3 (29), 458.2 (11), 440.3 (66). 321 (6).

17β-Hydroxy-(N-methyl-N-methoxy)-17α-pregna-4-en-20-yn-3-one-20-carboxamide (**13j**) *:* Yield: 150 mg (75%); light brown solid material, mp. 182 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.37; δ_H (500 MHz, $CDCl_3$) 5.76 (1H, s, 3-C*H*), 3.78 (3H, s, OCH_3), 3.25 (3H, brs, NCH_3), 2.47-0.97 (19H, m, skeleton protons), 1.22 (3H, s, 19-CH_3), 0.95 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.4, 170.8, 154.2, 124.0, 94.4, 79.8, 78.2, 62.2, 53.5, 50,3, 47.4, 38.7, 38.6, 36.2, 35.8, 33.9, 32.8, 32.7, 32.4, 31.5, 23.2, 20.7, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3351 ν(OH), 2974, 2946, 2882, 2857 ν(CH_2, CH_3), 2225 ν(C≡C), 1671 ν(C=O), 1639 ν(C=C), 1613 Amide I., 1069 ν(C-OH). MS (ESI) m/z (rel int.):400.3 (100, $M+1^+$), MS^2 m/z (rel int.): 382.3 (100), 321,2 (30), 293.2 (14).

17β-Hydroxy-N-((S)-1-phenylethyl)-17α-pregna-4-en-20-yn-3-one-20-carboxamide (**13k**)*:* Yield: 179 mg (78%); light brown solid material, mp. 119 °C; R_f (50% EtOAc, 50% $CHCl_3$) 0.48; δ_H (500 MHz, $CDCl_3$) 7.39-7.29 (5H, m, Ar), 6.23 (1H, d, *J*= 7.5 Hz, N*H*), 5.75 (1H, s, 3-C*H*), 5.17 (1H, dq, J= 7.5 Hz, 7.0 Hz, (CH_3)CH), 2.64-1.0 (19H, m, skeleton protons), 1.54 (3H, d, J= 7.0 Hz), 1.21 (3H, s, 19-CH_3), 0.92 (3H, s 18-CH_3). δ_C (125.7 MHz, $CDCl_3$) 199.5, 171.0, 152.1, 142.1, 128.8, 127.7, 126.4, 124.0, 88.70, 80.6, 79.8, 53.0, 50,1, 49.4, 47.3, 38.7, 38.6, 36.3, 35.6, 33.9, 32.8, 32.7, 31.3, 23.2, 21.3, 20.7, 17.4, 12.7. IR (KBr, ν (cm^{-1})): 3394, 3303 ν(OH), 3060, 3029 ν(CH Ar), 2974, 2945, 2873 ν(CH_2, CH_3), 2222 ν(C≡C), 1656 Amide I + ν(C=O) + ν(C=C), 1530 Amide II., 1069 ν(C-OH). MS (ESI) m/z (rel int.):460.3 (100, $M+1^+$), MS^2 m/z (rel int.): 356.2 (100), 338.3 (8), MS^3 (338.3) m/z (rel int.): 321.2 (100), 310.2 (75), 293.2 (29), 202.1 (33).

N-(tert-Butyl)-3-(cyclohex-1-en-1-yl)propiolamide (**14a**): Yield: 108 mg (53%); yellow solid material, mp. 78 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.91; δ_H (500 MHz, $CDCl_3$) 6.33 (1H, s, =C*H*), 5.64 (1H, brs, N*H*), 2.15-2.12 (4H, m), 1.68-1.58 (4H, m), 1.39 (9H, s, C(CH_3)$_3$) δ_C (125.7 MHz, $CDCl_3$) 153.0, 139.6, 118.8, 84.6, 82.0, 52.2, 28.6, 28.2, 25.8, 22.0, 21.2. IR (KBr, ν (cm^{-1})): 3241 ν(NH), 3052 ν(=CH), 2967, 2924, 2859 ν(CH_2, CH_3) 2208 ν(C≡C), 1620 ν(C=C) + Amide I., 1537 Amide II., 1454. MS m/z (rel int.): 205 (18, M^+), 190 (24), 175 (2), 161 (2), 150 (18), 133 (100), 105 (15), 77 (22), 51 (7).

3-(Cyclohex-1-en-1-yl)-1-(piperidin-1-yl)prop-2-yn-1-one (**14b**): Yield: 128 mg (59%); red oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.84; δ_H (500 MHz, $CDCl_3$) 6.37-6.34 (1H, m, =C*H*), 3.69 (2H, t, *J*= 5.6 Hz), 3.59 (2H, t, *J*= 5.6 Hz), 2.20-2.13 (4H, m), 1.68-1.65 (2H, m), 1.64-1.60 (2H, m), 1.58-1.54 (2H, m). δ_C (125.7 MHz,

$CDCl_3$) 153.4, 139.4, 119.2, 92.4, 79.3, 48.1, 42.3, 28.4, 26.4, 25.9, 25.4, 24.6, 22.0, 21.2. IR (KBr, ν (cm^{-1})): 2935, 2857 ν(CH_2) 2197 ν(C≡C), 1628 ν(C=C)+ Amide I., 1433. MS m/z (rel int.): 217 (100, M^+), 202 (42), 188 (52), 160 (29), 136 (48), 133 (93), 105 (42), 84 (57), 80 (63), 77 (78), 55 (26).

3-(Cyclohex-1-en-1-yl)-1-morpholinoprop-2-yn-1-one (**14c**): Yield: 120 mg (55%); yellow solid material, mp. 49 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.67; δ_H (500 MHz, $CDCl_3$) 6.37 (1H, m, =C*H*), 3.76-3.74 (2H, m), 3.71-3.70 (2H, m), 3.66 (4H, brs), 2.16-2.14 (4H, m), 1.68-1.58 (4H, m). δ_C (125.7 MHz, $CDCl_3$) 153.6, 140.2, 118.9, 93.3, 78.6, 66.9, 66.5, 47.2, 41.9, 28.3, 25.9, 21.9, 21.1. IR (KBr, ν (cm^{-1})): 2926, 2904, 2864 ν(CH_2), 2197 ν(C≡C), 1613 ν(C=C) + Amide I., 1427, 1271, 1253, 1113 ν(C-O-C). MS m/z (rel int.): 219 (48, M^+), 204 (5), 190 (12), 133 (100), 105 (26), 86 (48), 77 (45), 56 (33).

Methyl (3-(cyclohex-1-en-1-yl)propioloyl)glycinate (**14e**): Yield: 130 mg (59%); yellow oil; R_f (5% EtOAc, 95% $CHCl_3$); 0.67; δ_H (500 MHz, $CDCl_3$) 6.43 (1H, brs, N*H*), 6.39 (1H, brs, =C*H*), 4.11 (2H, d, *J*= 5.3 Hz), 3.79 (3H, s, CH_3), 2.17-2.14 (4H, m), 1.68-1.58 (4H, m). δ_C (125.7 MHz, $CDCl_3$) 169.8, 153.8, 140.8, 118.6, 87.9, 80.3, 52.5, 41.4, 28.2, 25.9, 21.9, 21.1. IR (KBr, ν (cm^{-1})): 3276 ν(NH), 2935, 2860 ν(CH_2, CH_3), 2206 ν(C≡C), 1745 ν(C=O ester), 1636 ν(C=C) + Amide I., 1533 Amide II., 1300, 1210 ν(C-O-C ester), 1180. MS m/z (rel int.): 221 (20, M^+), 206 (1), 190 (2), 162 (11), 133 (100), 105 (13), 77 (22), 51 (8).

Methyl (3-(cyclohex-1-en-1-yl)propioloyl)-L-alaninate (**14f**): Yield: 110 mg (47%); yellow oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.81; δ_H (500 MHz, $CDCl_3$) 6.44 (1H, d, *J*= 7.2 Hz, N*H*), 6.39 (1H, s, =C*H*), 4.69-4.63 (1H, m, C*H*), 3.79 (3H, s, CH_3), 2.17-2.14 (4H, m), 1.69-1.59 (4H, m), 1.46 (3H, d, *J*= 7.2 Hz, CH_3). (125.7 MHz, $CDCl_3$) 172.9, 153.1, 140.6, 118.6, 87.5, 80.5, 52.6, 48.3, 28.2, 25.9, 22.0, 21.1, 18.4. IR (KBr, ν (cm^{-1})): 3272 ν(NH), 3029 ν(=CH), 2987, 2934, 2860 ν(CH_2, CH_3), 2203 ν(C≡C), 1740 ν(C=O ester), 1645 ν(C=C) + Amide I., 1528 Amide II., 1213 ν(C-O-C ester), 1179. MS m/z (rel int.): 235 (7, M^+), 204 (1), 176 (43), 133 (100), 105 (9), 77 (17), 51 (6).

3-(Cyclohex-1-en-1-yl)-N-methoxy-N-methylpropiolamide (**14j**): Yield: 68 mg (35%); red oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.81; δ_H (500 MHz, $CDCl_3$) 6.42 (1H, brs, =C*H*), 3.80 (3H, s, -OCH_3), 3.26 (3H, brs, -NCH_3), 2.20-20.16 (4H, m), 1.68-1.62 (4H, m). δ_C (125.7 MHz, $CDCl_3$) 155.1, 140.7, 119.0, 92.8, 78.7, 61.9, 32.5, 28.3, 25.9, 22.0, 21.2. IR (KBr, ν (cm^{-1})): 2934, 2860 ν(CH_2, CH_3), 2205 ν(C≡C), 1642 ν(C=C) + Amide I., 1412, 1381 ν(C-O-C), 720 γ(=CH). MS m/z (rel int.): 193 (<1, M^+), 163 (75), 133 (100), 105 (46), 77 (57), 51 (24).

N-(tert-Butyl)hept-2-ynamide (**15a**)*:* Yield: 102 mg (56%); yellow solid material, mp. 32 °C; R_f (5% EtOAc, 95% $CHCl_3$) 0.85; δ_H (500 MHz, $CDCl_3$) 5.60 (1H, brs, N*H*), 2.28 (2H, t, *J*= 7.1 Hz), 1.57-1.50 (2H, m), 1.47-1.41 (2H, m), 1.38 (9H, s, C(CH_3)$_3$), 0.93 (3H, t, *J*= 7.3 Hz). δ_C (125.7 MHz, $CDCl_3$) 152.8, 85.1, 76.6, 52.1, 29.8, 28.6, 22.0, 18.2, 13.5. IR (KBr, ν (cm^{-1})): 3324 ν(NH), 2967, 2932, 2873 ν(CH_2, CH_3), 2239 ν(C≡C), 1638 Amide I., 1522 Amide II., 1451, 1288, 1221. MS m/z (rel int.): 181 (23, M^+), 166 (90), 152 (1), 138 (6), 126 (100), 109 (92), 79 (39), 58 (96).

1-(Piperidin-1-yl)hept-2-yn-1-one (**15b**)*:* Yield: 124 mg (64%); red oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.78; δ_H (500 MHz, $CDCl_3$) 3.70-3.67 (2H, m), 3.58-3.55 (2H, m), 2.36 (2H, t, *J*= 7.1 Hz), 1.67-1.64 (2H, m), 1.62-1.54 (6H, m), 1.48-1.40 (2H, m), 0.93 (3H, t, *J*= 7.3 Hz). δ_C (125.7 MHz, $CDCl_3$) 153.2, 93.1, 73.9, 48.1, 42.2, 29.9, 26.4, 25.4, 24.5, 22.0, 18.7, 13.5. IR (KBr, ν (cm^{-1})): 2939, 2858 ν(CH_2, CH_3), 2237 ν(C≡C), 1616 Amide I., 1435 Amide II., 1268, 732. MS m/z (rel int.): 193 (16, M^+), 178 (2), 164 (11), 150 (100), 136 (10), 109 (16), 84 (22), 79 (20), 67 (7), 53 (15).

1-Morpholinohept-2-yn-1-one (**15c**)*:* Yield: 185 mg (95%); red oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.64; δ_H (500 MHz, $CDCl_3$) 3.77-3.75 (2H, m), 3.72-3.70 (2H, m), 3.67-3.64 (4H, m), 2.37 (2H, t, *J*= 7.1 Hz), 1.62-1.55 (2H, m), 1.47-1.40 (2H, m), 0.93 (3H, t, *J*= 7.3 Hz). δ_C (125.7 MHz, $CDCl_3$) 153.4, 94.2, 73.3, 66.9, 66.5, 47.2, 41.8, 29.8, 22.0, 18.6, 13.5. IR (KBr, ν (cm^{-1})): 2960, 2931, 2860 ν(CH_2, CH_3), 2238 ν(C≡C), 1623 Amide I., 1429, 1276, 1247, 1150 ν(C-O-C), 1010, 732. MS m/z (rel int.): 195 (35, M^+), 180 (20), 166 (20), 152 (36), 109 (47), 86 (100), 56 (82)

Methyl hept-2-ynoylglycinate (**15e**)*:* Yield: 105 mg (53%); yellow oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.65; δ_H (500 MHz, $CDCl_3$) 6.38 (1H, brs, N*H*), 4.09 (2H, d, *J*= 5.1 Hz), 3.79 (3H, s, CH_3), 2.33 (2H, t, *J*= 7.1 Hz), 1.59-1.53 (2H, m), 1.48-1.40 (2H, m), 0.93 (3H, t, *J*= 7.3 Hz). δ_C (125.7 MHz, $CDCl_3$) 169.8, 153.5, 88.7, 74.9, 52.5, 41.3, 29.7, 21.9, 18.3, 13.5. IR (KBr, ν (cm^{-1})): 3301 ν(NH), 3054, 2958, 2874 ν(CH_2, CH_3), 2233 ν(C≡C), 1757 ν(C=O ester), 1653 Amide I., 1529 Amide II., 1287, 1212 ν(C-O-C ester), 1008, 744. MS m/z (rel int.): 197 (1, M^+), 182 (1), 168 (2), 155 (7), 138 (44), 109 (100), 79 (24), 66 (13), 52 (15).

Methyl hept-2-ynoyl-L-alaninate (**15f**)*:* Yield: 182 mg (86%); yellow oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.75; δ_H (500 MHz, $CDCl_3$) 6.41 (1H, brs, N*H*), 4.67-4.59 (1H, m), 3.78 (3H, s, OCH_3), 2.33-2.30 (2H, m), 1.59-1.53 (2H, m), 1.45-1.42 (5H, m), 0.95-0.91 (3H, m, CH_3). δ_C (125.7 MHz, $CDCl_3$) 172.9, 152.9, 88.2, 75.1, 52.6, 48.2, 29.7, 21.9, 18.3, 18.2, 13.5. IR (KBr, ν (cm^{-1})): 3289 ν(NH), 3041, 2958, 2874 ν(CH_2, CH_3), 2237 ν(C≡C), 1749 ν(C=O ester), 1636 Amide I., 1533 Amide II., 1456, 1271, 1213, 1162 ν(C-O-C ester), 744. MS m/z (rel int.): 211 (1, M^+), 196 (1), 173 (23), 152 (90), 109 (100), 79 (32), 53 (18).

N-Methoxy-N-methylhept-2-ynamide (**15j**)*:* Yield: 88 mg (52%); red oil; R_f (5% EtOAc, 95% $CHCl_3$) 0.75; δ_C (125.7 MHz, $CDCl_3$) 154.8, 93.7, 73.2, 62.0, 32.3, 29.8, 21.9, 18.7, 13.5. δ_H (500 MHz, $CDCl_3$) 3.78 (3H, s, -OCH_3), 3.24 (3H, brs, -NCH_3), 2.42-2.39 (2H, m), 1.62-1.56 (2H, m), 1.49-1.44 (2H, m), 0.96-0.92 (3H, m, CH_3). IR (KBr, ν (cm^{-1})): 2961, 2936, 2874 ν(CH_2, CH_3), 2237 ν(C≡C), 1644 Amide I., 1460, 1380 ν(C-O-C), 724. MS m/z (rel int.): 169 (2, M^+), 154 (<1), 141 (1), 127 (6), 109 (100), 79 (44), 66 (14), 53 (30).

Ethyl (E)-3-(tert-butylamino)acrylate (**16**): MS m/z (rel int.): 171 (M+, 65), 156 (11), 141 (97), 126 (100), 98 (65), 56 (48).

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Captions

Scheme 1. Synthesis of iodoalkynes (**2**, **4**, **6, 8** and **10**) and bromoalkyne (**2'**) used as substrates in further aminocarbonylations

Scheme 2. Reactions of **10** under aminocarbonylation conditions (formation of enamines accompanied by deiodination)