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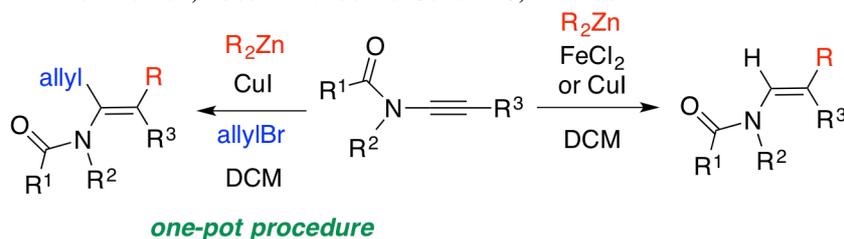
## Graphical Abstract

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### Iron(II)/copper(I)-mediated stereoselective carbozincation of ynamides. One-pot synthesis of $\alpha$ -allyl-tetrasubstituted-enamides.

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## Iron(II)/copper(I)-mediated stereoselective carbozincation of ynamides. One-pot synthesis of $\alpha$ -allyl-tetrasubstituted-enamides

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### ABSTRACT

The iron(II) chloride- and copper(I) iodide-mediated carbozincation of a panel of substituted ynamides is described in this article. The reaction is totally regio- and stereoselective. Experiments showed that the reaction mediated with Fe(II) was more substrate dependent than the reaction performed with Cu(I). Interestingly, in the presence of allylbromide, stereoselective carboallylation can be achieved for the first time in a one-pot procedure, leading to skipped dienamides.

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## 1. Introduction

Intermolecular carbometalation<sup>1</sup> of ynamides is one of the most flexible approaches for the enamide synthesis.<sup>2</sup> Marek and coworkers were the first to describe the carbocupration and the copper-catalyzed carbomagnesiation of ynamides.<sup>3</sup> Oshima and Yorimitsu have applied this methodology to prepare ynamides bearing an allyl group to perform subsequent aza-Claisen rearrangement.<sup>4</sup> Both carbozincation and carboboration of ynamides were achieved by Lam and coworkers, using a rhodium catalyst in the presence of dialkylzincs and arylboronic acids, respectively.<sup>5</sup> This process enables access to a range of multisubstituted enamides in a stereo- and regio-controlled fashion. This methodology was extended by Hou and coworkers to the alkylative carboxylation of ynamides in the presence of a CO<sub>2</sub> atmosphere,<sup>6</sup> in which a (NHC)-copper catalyst was used in place of the rhodium catalyst. The Pd-catalyzed addition of boronic acids has also been reported.<sup>7</sup> Recently, a cobalt-catalyzed carbocation of ynamides was described by Gosmini and Gillaizeau.<sup>8</sup> Intramolecular carbometalation of ynamides were also investigated to prepare indole and pyridine derivatives.<sup>9</sup>

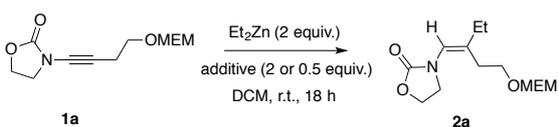
We have investigated FeCl<sub>2</sub> as a potential mediator for intermolecular ynamides carbocation.<sup>10</sup> Experiments conducted with Cu(I), a catalyst previously used for the carbocation of cyclopropenes<sup>11</sup> and alkynyl sulfoximines and sulfones<sup>12</sup> were carried out in parallel. This led us to propose a novel one-pot procedure for the regio- and stereoselective carbocation of ynamides leading to skipped dienamides.

## 2. Results and Discussion

In a blank experiment, ynamide **1a** was reacted with diethylzinc without any additive. After one night at room temperature the substrate was recovered and only a trace amount of the alkylated product **2a** was detected.<sup>13</sup> The use of 2 equivalents of iron(II) chloride allowed the formation of the expected compound in 91% yield (Table 1, entry 2).<sup>14</sup> In the presence of 0.5 equivalent of FeCl<sub>2</sub> the reaction was still efficient and the substrate was totally consumed to give **2a** in 73% isolated yield (Table 1, entry 3).

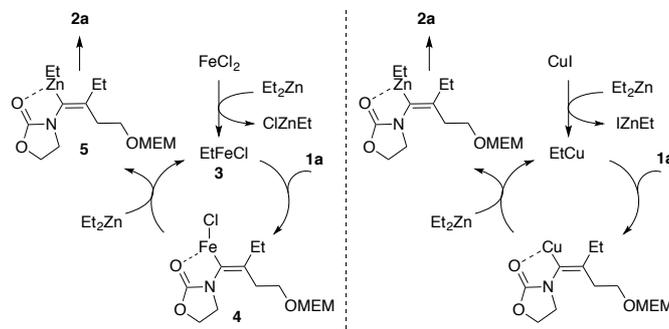
When CuI was used as the mediator, good results were obtained in the presence of either 2 or 0.5 equivalents of this transmetalation agent (Table 1, entries 4 and 5). The reaction was also conducted with 10 mol % of CuI. The substrate was totally consumed to give the desired enamide **2a** in 74% yield (Table 1, entry 6). In both cases, the monitoring of the reaction showed that the consumption of the substrate needed much more than 6 h to be completed at room temperature, for the sake of homogeneity, all the experiments were carried out over 18 h in the presence of 0.5 equivalents of the mediator.

**Table 1.** Ethylzincation of ynamide **1a** with FeCl<sub>2</sub> and CuI



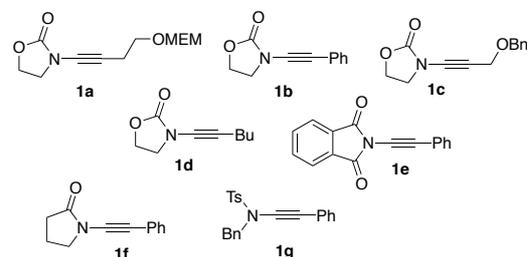
Entry	Additive (equiv.)	<b>2a</b> (isolated yield %)
1	-	Traces
2	FeCl <sub>2</sub> (2)	91
3	FeCl <sub>2</sub> (0.5)	73
4	CuI (2)	76
5	CuI (0.5)	83
6	CuI (0.1)	74

In each case carbometalation occurred with high regio- and stereoselectivity leading to a unique stereoisomer among the 4 possible ones. The regio- and stereoselectivity were the same as that observed by Marek and coworkers, and Lam and coworkers.<sup>3,5</sup> NOE and HMBC NMR experiments were performed to prove structural assignments. Iron(II) chloride was found as efficient as copper(I) iodide to perform this transformation.



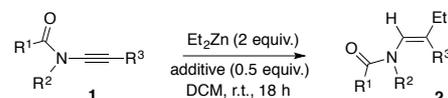
**Scheme 1.** Mechanism.

Since the use of 0.1 equivalent of the mediator was sufficient to perform the reaction, a possible catalytic cycle for these transformations is presented in Scheme 1. This mechanism is based on that proposed for copper-catalyzed carbomagnesiation.<sup>3</sup> The reaction of iron(II) chloride with diethylzinc would lead to an ethyliron species **3**. The carbocation would be directed by the coordination of iron(II) with the oxygen atom of the carbonyl group to regioselectively form the alkenyliron species **4**. Finally, transmetalation would occur between diethylzinc and **4** to give the alkenylzinc species **5** precursor of **2a** through hydrolysis. The observed reactivity relies on the ability of the substrate to form a five-membered chelated vinyl metal intermediate.



**Scheme 2.** Ynamides **1a-g**.

**Table 2.** Ethylzincation of ynamides **1**



Entry	<b>1</b>	Additive	<b>2</b> (isolated yield %)
1	<b>1a</b>	CuI	<b>2a</b> (83)
2	<b>1b</b>	CuI	<b>2b</b> (69)
3	<b>1c</b>	CuI	<b>2c</b> (65)
4	<b>1d</b>	CuI	<b>2d</b> (91)
5	<b>1e</b>	CuI	<b>2e</b> (80) <sup>[a]</sup>
6	<b>1f</b>	CuI	<b>2f</b> (65)
7	<b>1a</b>	FeCl <sub>2</sub>	<b>2a</b> (73)
8	<b>1b</b>	FeCl <sub>2</sub>	<b>2b</b> (25)
9	<b>1c</b>	FeCl <sub>2</sub>	<b>2c</b> (17)
10	<b>1d</b>	FeCl <sub>2</sub>	<b>2d</b> (60)
11	<b>1e</b>	FeCl <sub>2</sub>	<b>2e</b> (39)
12	<b>1f</b>	FeCl <sub>2</sub>	<b>2f</b> (77)

[a] Et<sub>2</sub>Zn (4 equiv.)

The scope of the process was explored with a panel of ynamides and dimethylzinc was also used in place of diethylzinc. The results are described in Tables 2 and 3. Ynamides **1** (Scheme 2) were prepared by slightly modifying known procedures.<sup>15,16,17</sup>

Ethylzincation was first applied to the oxazolidinone-derived ynamides **1a-d**. The reaction tolerated both alkyl (**1a**, **1c-d**) and aryl (**1b**) groups on the distal carbon of the ynamide. It led to the corresponding enamides **2a-d** in moderate to good yields with a total regioselectivity. Moreover, only one stereoisomer of the enamide was detected using either iron(II) or copper(I) (Table 2, entries 1-12). However, the reaction involving FeCl<sub>2</sub> seemed to be more dependant on the nature of the substrate than that mediated with copper(I).

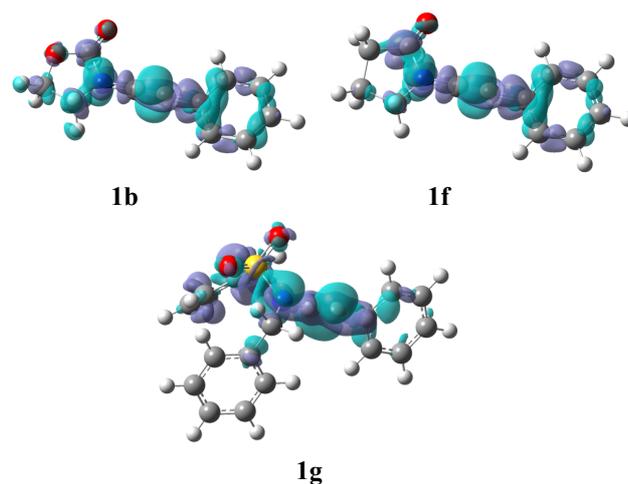
Ynamide **1e** derived from phthalimide showed to be the least reactive substrate and 4 equivalents of diethylzinc were necessary to obtain the corresponding ethylated enamide in 80% yield in the presence of copper(I) (Table 3, entry 5). In the presence of iron(II), the yield was lower whether using a large excess of diethylzinc or just 2 equivalents (entry 11). Ynamide **1f** derived from  $\gamma$ -lactam prove to be a good partner in these transformations (entries 6, 12). Finally, ynamide **1g** derived from *N*-benzyltosylamine failed to react either using CuI or FeCl<sub>2</sub>. Up to 80% of the starting material was recovered after workup. Ynamides are  $\pi$ -nucleophiles. Their nucleophilicity increases with the delocalization of the nitrogen electron pair towards the triple bond  $\pi$ -system. However, this electron-donating property is counterbalanced by the electron-withdrawing substituent at nitrogen, which improves their stability.<sup>2</sup> According to the scale established by Mayr,<sup>18</sup> ynamide **1g** is a better nucleophile than **1f** however, it is unreactive in carbocation processes. Conversely, *N*-tosylynamides were shown to be reactive in carbomagnesiation.<sup>3c</sup> The scale established from the kinetics of reactions with carbocations cannot be applied to the multistep carbometalation process. Rationalization is not straightforward.

B3LYP/6-31+G(d,p) calculations were performed on **1b**, **1f** and **1g** for the sake of collecting reactivity quantitative parameters (see: supplementary content). According to the global electrophilicity index defined by Parr,<sup>19</sup> the electrophilicity is low, it varies in the following order: **1g** ( $\omega=1.59$  eV) > **1f** ( $\omega=1.30$  eV) > **1b** ( $\omega=1.28$  eV), even though the gap between **1f** and **1b** is tiny. Not surprisingly, this sequence based on  $\omega$  correlates with the relative energies of the LUMOs, **1g** having the lowest LUMO in the series (LUMOs energies in eV: **1g** (-1.54) < **1f** (-1.15) < **1b** (-1.09). The nucleophilicity sequence should be the reversal (according to HOMOs energies in eV, the position of **1f** and **1g** should be reversed: **1f** (-5.85) > **1b** (-6.01) > **1g** (-6.10)).

Condensed Fukui's functions were also calculated using NPA charges.<sup>20</sup> The maps of Fukui's dual descriptors<sup>21</sup> are shown in **Erreur ! La référence est incorrecte pour un signet.** The values of condensed Fukui's function  $f^-$ , gives the following sequence of nucleophilicity for O, C $\alpha$  and C $\beta$  sites:

O : **1f** > **1b** > **1g**  
 C $\alpha$  : **1b** > **1f** >> **1g**  
 C $\beta$  : **1g** > **1f** > **1b**

According to condensed Fukui's function  $f^+$  C $\alpha$  is the most electrophilic site in **1f** and **1b**. Comparatively, this value is low in **1g**. The two components neutralize each other in  $f^{(2)}$  but the residual nucleophilicity is mainly localized at C $\beta$  as shown in Figure 1. No clean conclusion can be drawn from the examination of these quantitative parameters. The reactivity seems to increase as C $\beta$  nucleophilicity decreases.



<b>1b</b>	$f^-$	$f^+$	$f^{(2)}$
O	0.073	0.051	-0.022
C $\alpha$	0.126	0.107	-0.019
C $\beta$	0.120	0.000	-0.120

<b>1f</b>	$f^-$	$f^+$	$f^{(2)}$
O	0.093	0.085	-0.008
C $\alpha$	0.116	0.112	-0.004
C $\beta$	0.125	0.020	-0.105

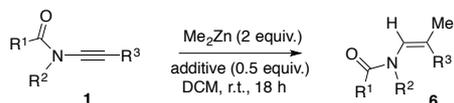
<b>1g</b>	$f^-$	$f^+$	$f^{(2)}$
O	0.033	0.035	0.002
C $\alpha$	0.077	0.044	-0.033
C $\beta$	0.191	0.031	-0.160

**Figure 1.** Maps of Fukui's dual descriptors for **1b**, **1f** and **1g** (more Nu than E zones in turquoise blue; more E than Nu zones in lavender-blue). Table of values of condensed Fukui functions  $f^-$  and  $f^+$  and dual descriptor  $f^{(2)}$ .

To date, the best rationale regarding the regioselectivity of the process has been proposed by Marek,<sup>3</sup> who pointed the major role of the oxygen atom in coordinating the metal and directing the metalation process. This is in agreement with the above discussed values of  $f^-$  condensed Fukui's function at oxygen. Additional calculations of the intermediate vinylzincs evidenced the stabilizing role of the carbonyl oxygen atom as an intramolecular ligand, which favors the transmetalation step and controls the overall enthalpy of the process. The electron density at the oxygen atom has a large impact on the stability of the putative vinylzinc intermediate. The overall reaction enthalpies for the formation of the vinylzinc intermediate from **1b**, **1f**, **1g** and Et<sub>2</sub>Zn were calculated at the B3LYP/6-31+G(d,p) level. They are -44.9, -44.3 and -33.8 kcal mol<sup>-1</sup>, respectively (see, supplementary content).

Methylzincation was achieved with dimethylzinc. In the presence of CuI, methylzincation and ethylzincation led to similar yields for all the ynamides investigated. Quite good yields and selectivity were observed with ynamides **1a-f**. Substrate **1g** failed to react. When the methylzincation was conducted with FeCl<sub>2</sub>, the results were significantly different. In most cases yields were far lower, except in the case of **1f**.

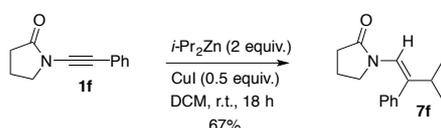
**Table 3.** Methylzincation of ynamides **1**



Entry	<b>1</b>	Additive	<b>6</b> (isolated yield %)
1	<b>1a</b>	CuI	<b>6a</b> (62)
2	<b>1b</b>	CuI	<b>6b</b> (77)
3	<b>1c</b>	CuI	<b>6c</b> (72)
4	<b>1d</b>	CuI	<b>6d</b> (74)
5	<b>1e</b>	CuI	<b>6e</b> (80)
6	<b>1f</b>	CuI	<b>6f</b> (87)
7	<b>1a</b>	FeCl <sub>2</sub>	<b>6a</b> (-) <sup>[a]</sup>
8	<b>1b</b>	FeCl <sub>2</sub>	<b>6b</b> (13)(25) <sup>[b]</sup>
9	<b>1c</b>	FeCl <sub>2</sub>	<b>6c</b> (54)
10	<b>1d</b>	FeCl <sub>2</sub>	<b>6d</b> (23)
11	<b>1e</b>	FeCl <sub>2</sub>	<b>6e</b> (35) <sup>[c]</sup>
12	<b>1f</b>	FeCl <sub>2</sub>	<b>6f</b> (91)

[a] The substrate was fully recovered, [b] 2 equivalents of FeCl<sub>2</sub> were used, [c] Me<sub>2</sub>Zn (5 equiv.)

An additional experiment was conducted in presence of diisopropylzinc with ynamide **1f** and CuI. It led to the expected enamide **7f** in 67% yield (Scheme 3).

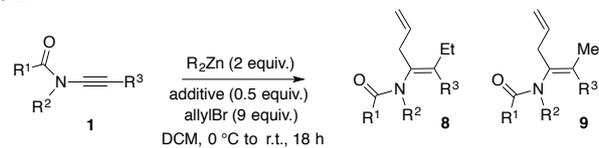


### Scheme 3. Isopropylzincation of **1f**.

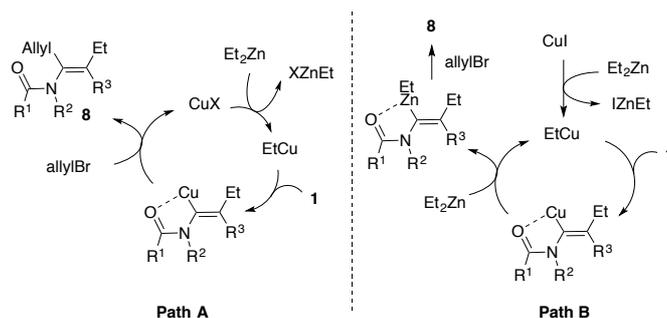
The trapping of the vinylzinc intermediate was achieved with ND<sub>4</sub>Cl, which led to a mixture of deuterated **10b** and non deuterated **2b** in a 89:11 ratio (60% yield). Similarly, it could be trapped by other electrophiles like PhSeCl. The corresponding vinylselenide was isolated in 50% isolated yield.

The synthesis of tetrasubstituted enamides was also envisaged by adding allylbromide in a sequential step. Substrate **1b** was reacted in the presence of CuI (0.5 equiv.) and diethylzinc for 18h. Allylbromide was then added to give after workup the desired allylenamide in moderate yield. The proton NMR spectrum of the crude reaction showed a mixture of allylated and non-allylated products (**8b:2b**, 73:27).<sup>22</sup> To our knowledge, the carboallylation of ynamides has only been reported in sequential procedures.<sup>3,5</sup> We have shown that far better yields could be obtained when the carboallylation was achieved in a one-pot procedure, by introducing directly allylbromide into the initial mixture (Table 4). Interestingly, the copper-mediated ethylallylation of ynamide **1b** led to the desired product **8b** with a quantitative yield, no competing side reaction was observed (Table 4, entry 1). The reaction was still efficient in the presence of 10 mol % of CuI (entry 2). Only one stereoisomer was detected from the analysis of the proton NMR spectrum of the crude reaction mixture. The same behavior was observed for the methylallylation of **1b** conducted in the presence of dimethylzinc (entry 4). Moving from copper(I) to iron(II) led to half the yield of **8b**, despite the use of 2 equivalents of iron(II) (entry 3). To widen the scope of this one-pot procedure, ynamides **1a**, **1d** and **1f** were submitted to the same experimental conditions. They led to the corresponding dienamides in good yields with a total stereoselectivity (entries 5-7).

**Table 4.** One-pot procedure for stereoselective carboallylation of ynamides **1**



Entry	<b>1</b>	Additive	R	<b>8/9</b> (isolated yield %)
1	<b>1b</b>	CuI	Et	<b>8b</b> (100)
2	<b>1b</b>	CuI (0.1)	Et	<b>8b</b> (70)
3	<b>1b</b>	FeCl <sub>2</sub>	Et	<b>8b</b> (46)
4	<b>1b</b>	CuI	Me	<b>9b</b> (93)
5	<b>1d</b>	CuI	Et	<b>8d</b> (76)
6	<b>1a</b>	CuI	Et	<b>8a</b> (47)
7	<b>1f</b>	CuI	Et	<b>8f</b> (53)



**Scheme 5.** Mechanism for the carboallylation of ynamides **1**

Two pathways can be envisaged to explain the formation of the allylated products (Scheme 5): the allylation of a vinylzinc intermediate (path B) or the direct allylation of a vinylcopper intermediate leading to the formation of CuBr that can participate in the catalytic cycle (path A).

### 3. Conclusions

In conclusion, the carbozincation of ynamides could be mediated either by CuI and FeCl<sub>2</sub>, two common and inexpensive reagents, to prepare regio- and stereoselectively trisubstituted enamides. The use of CuI proved to be more efficient and less substrate dependent in most cases. It enabled to develop an original one-pot procedure for the direct stereocontrolled formation of tetrasubstituted allylenamides.

### 4. Experimental Section

#### General.

Commercially available solvents were used as purchased. CH<sub>2</sub>Cl<sub>2</sub> (GC grade) was used as solvent; it was stored on molecular sieves. Analytical thin layer chromatography was performed on pre-coated silica gel plates. NMR spectra were recorded at 300 MHz and 400 MHz (<sup>1</sup>H) and 75 MHz and 100 MHz (<sup>13</sup>C) using CDCl<sub>3</sub> as the solvent. Chemical shifts (δ) are reported in ppm. Signals due to residual protonated solvent or to the deuterated solvent served as the internal standards to calibrate the spectra (<sup>1</sup>H NMR, CHCl<sub>3</sub>, 7.26 ppm; <sup>13</sup>C NMR, CDCl<sub>3</sub>, 77.16 ppm). One or more of the following descriptors indicate multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextuplet), sept (septet), m (multiplet), br (broad). The *J* values are given in Hz.

#### Computational details

All the calculations were performed with Gaussian 09 Rev. D01 package.<sup>23</sup> The geometries of **1b**, **1f** and **1g** were fully optimized at the B3LYP/6-31+G(d,p) level of theory. Vibrational frequency calculations were performed to insure that the geometries are minima (no imaginary frequency). The Fukui dual descriptors

were calculated using Multiwfn software<sup>24</sup> with the neutral, cation and anion wavefunctions (isodensity value=0.002).

### General procedure for ynamides synthesis.

In a two-neck round-bottom flask equipped with a stir-bar, CuCl<sub>2</sub> (0.2 equiv), oxazolidin-2-one (5.0 equiv), Na<sub>2</sub>CO<sub>3</sub> or Cs<sub>2</sub>CO<sub>3</sub> (2.0 equiv) and molecular sieve (4Å) were combined. The reaction flask was purged with oxygen for 15 minutes. A solution of pyridine (2.0 equiv) in dry toluene (0.2M) was added to the reaction flask via a syringe at room temperature. Two balloons filled with oxygen were connected to the reaction flask via a needle. The flask was placed in an oil-bath and heated to 70 °C. A solution of alkyne (1.0 equiv) in dry toluene was added over 4 h using a syringe pump. After the addition was completed, the reaction mixture was stirred at 70 °C for 8 h and then cooled to room temperature. The crude mixture was concentrated under vacuum and the residue was purified by flash chromatography on silica gel.

**3-{4-[(2-Methoxyethoxy)methoxy]but-1-yn-1-yl}-1,3-oxazolidin-2-one (1a).** The reaction was conducted according to the general procedure in the presence of CuCl<sub>2</sub> (1.0 mmol, 134.5 mg), oxazolidin-2-one (25.0 mmol, 2.18 g) Na<sub>2</sub>CO<sub>3</sub> (10.0 mmol, 1.27 g), a solution of pyridine (10.0 mmol, 0.95 ml) in dry toluene (30 mL) and 1-[(but-3-yn-1-yloxy) methoxy]-2-methoxyethane (5.0 mmol, 1.0 g) was added in dry toluene (20 mL). Purification by flash chromatography on silica gel (pentane/ethyl acetate (10/0 to 8/2)) led to ynamide **1a** (990 mg, 81% yield) as an oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 2.58 (t, *J* = 6.8, 2H), 3.36 (s, 3H), 3.55-3.57 (m, 2H), 3.69 (t, *J* = 6.8, 2H), 3.66-3.71 (m, 2H), 3.87 (t, *J* = 7.8, 2H), 4.40 (t, *J* = 7.8, 2H), 4.74 (s, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 20.0 (CH<sub>2</sub>), 46.9 (CH<sub>2</sub>), 59.1 (CH<sub>3</sub>), 63.0 (CH<sub>2</sub>), 66.1 (CH<sub>2</sub>), 66.9 (CH<sub>2</sub>), 68.1 (≡C), 71.0 (≡C), 71.8 (CH<sub>2</sub>), 95.5 (CH<sub>2</sub>), 156.6 (C=O). HRMS (ESI): *m/z*: calcd for [M+H<sup>+</sup>] C<sub>11</sub>H<sub>18</sub>NO<sub>5</sub>: 261.1145, found 261.1444.

**3-(2-Phenylethynyl)-1,3-oxazolidin-2-one (1b).**<sup>16</sup> The reaction was conducted according to the general procedure in the presence of CuCl<sub>2</sub> (0.2 mmol, 27.0 mg), oxazolidin-2-one (5.0 mmol, 435 mg), Na<sub>2</sub>CO<sub>3</sub> (2.0 mmol, 212 mg), a solution of pyridine (2.0 mmol) in dry toluene (5.0 mL) and phenylacetylene (1.0 mmol, 101 mg) was added in dry toluene (5.0 mL). Purification by flash chromatography on silica gel (pentane/ethyl acetate (9/1 to 6/4)) led to ynamide **1b** (170 mg, 91% yield) as a white powder. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 4.01 (pseudo t, *J* = 8.2, 2H), 4.50 (pseudo t, *J* = 8.2, 2H), 7.25-7.30 (m, 3H), 7.42-7.46 (m, 2H).

**3-[3-(Benzyloxy)prop-1-yn-1-yl]-1,3-oxazolidin-2-one (1c).**<sup>16</sup> The reaction was conducted according to the general procedure in the presence of CuCl<sub>2</sub> (1.1 mmol, 148.0 mg), oxazolidin-2-one (5.0 mmol, 435 mg), Cs<sub>2</sub>CO<sub>3</sub> (2.0 mmol, 651 mg), a solution of pyridine (2.0 mmol, 0.16 mL) in dry toluene (5 mL) and [(prop-2-yn-1-yloxy)methyl]benzene (1.0 mmol, 146 mg) was added in dry toluene (5 mL). Purification by flash chromatography on silica gel (pentane/ethyl acetate (10/0 to 7/3)) led to ynamide **1c** (205 mg, 89% yield) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 3.92 (pseudo t, *J* = 8.0, 2H), 4.33 (s, 2H), 4.44 (pseudo t, *J* = 8.0, 2H), 4.60 (s, 2H), 7.28-7.38 (m, 5H).

**3-(Hex-1-yn-1-yl)-1,3-oxazolidin-2-one (1d).**<sup>25</sup> The reaction was conducted according to the general procedure in the presence of CuCl<sub>2</sub> (0.2 mmol, 27.0 mg), oxazolidin-2-one (5.0 mmol, 435 mg), Na<sub>2</sub>CO<sub>3</sub> (2.0 mmol, 212 mg), a solution of pyridine (2.0 mmol) in dry toluene (5.0 mL) and butylacetylene (1.0 mmol, 0.114 mL) was added in dry toluene (5.0 mL). Purification by flash chromatography on silica gel (pentane/ethyl acetate (9/1 to 6/4)) led to ynamide **1d** (98 mg, 58% yield) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.90 (t, *J* = 7.3, 3H), 1.39 (sext, *J* =

7.1, 2H), 1.49 (quint, *J* = 7.1, 2H), 2.29 (t, *J* = 7.1, 2H), 3.86 (pseudo t, *J* = 8.0, 2H), 4.40 (pseudo t, *J* = 8.0, 2H).

### 2-(2-Phenylethynyl)-2,3-dihydro-1H-isoindole-1,3-dione

**(1e).**<sup>26</sup> The reaction was conducted according to the general procedure in the presence of Cu(OAc)<sub>2</sub> (3.9 mmol, 710 mg, 0.2 equiv), phthalimide (97.7 mmol, 14.38 g, 5.0 equiv), Na<sub>2</sub>CO<sub>3</sub> (39.1 mmol, 4.14 g, 2.0 equiv), a solution of pyridine (39.1 mmol, 3.15 mL, 2.0 equiv) in dry toluene (100 mL) and phenylacetylene (19.5 mmol, 2.15 mL, 1.0 equiv) was added in dry toluene (100 mL). Purification by flash chromatography on silica gel (pentane/ethyl acetate (100/0 to 95/5)) led to ynamide **1e** (860 mg, 18% yield) as colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 7.31-7.40 (m, 3H), 7.58 (dd, *J* = 6.6 and 3.0, 2H), 7.82 (dd, *J* = 5.5, 3.1, 2H), 7.96 (dd, *J* = 5.5 and 3.1, 2H).

**1-(2-Phenylethynyl)pyrrolidin-2-one (1f).**<sup>27</sup> In a 15 mL Schlenk flask, pyrrolidone (3.2 mmol, 244 μL, 1 equiv), 1,1-dibromo-1-alkene (4.8 mmol, 700 μL, 1.5 equiv), Cs<sub>2</sub>CO<sub>3</sub> (12.8 mmol, 4.2 g, 4 equiv) and copper(I) iodide (0.64 mmol, 122 mg, 0.2 equiv) were added. The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon. Dry 1,4-dioxane (3 mL), degassed with 3 freeze-pump-thaw cycles, and *N,N*-dimethylethylenediamine (0.13 mmol, 140 μL, 0.4 equiv) were next added under argon and the light blue-green suspension was heated at 60 °C for 24 h. The brownish suspension was cooled to rt. The crude reaction mixture was filtered over a plug of silica gel (washed with EtOAc) and concentrated. The crude residue was purified by flash chromatography on silica gel (pentane/ethyl acetate (10/0 to 7/3)) to give ynamide **1f** (345 mg, 58% yield) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 2.17 (quint, *J* = 7.4, 2H), 2.48 (t, *J* = 8.1, 2H), 3.78 (t, *J* = 8.1, 2H), 7.26-7.32 (m, 3H), 7.42-7.46 (m, 2H).

### *N*-Benzyl-4-methyl-*N*-(2-phenylethynyl)benzene-1-

**sulfonamide (1g).**<sup>28</sup> The reaction was conducted under argon in the presence of K<sub>2</sub>CO<sub>3</sub> (2.0 mmol, 276 mg, 2 equiv), *N*-benzyl-4-methylbenzene-1-sulfonamide (1.0 mmol, 261 mg, 1 equiv) and FeCl<sub>3</sub>·6H<sub>2</sub>O (0.1 mmol, 27 mg, 0.1 equiv) in toluene (5 mL). (2-Bromoethynyl)benzene (1.2 mmol, 217 mg, 1.2 equiv) and DMEDA (0.2 mmol, 21 μL, 0.2 equiv) were added. The reaction mixture was stirred at 90 °C for 12 h. The crude product was filtered on a silica pad and washed with diethyl ether. The filtrate was concentrated under vacuum and purified by flash chromatography on silica gel (pentane/diethyl ether (10/0 to 6/4)) to give the tosylynamide **1g** (0.68 mmol, 246 mg, 68% yield) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 2.45 (s, 3H), 4.59 (s, 2H), 7.24 (br s, 4H), 7.29-7.35 (m, 6H), 7.77-7.83 (m, 2H), 7.82 – 7.78 (m, 2H).

### General procedure for carbozincation reactions

**Method A:** Copper Iodide or Iron(II) chloride (0.5-2 equiv) was added under argon at room temperature to a solution of ynamide **1** (1 equiv, 0.2 M) in non-degassed dichloromethane. Dialkylzinc (1 M in hexane, 2 equiv) was added and the reaction was stirred for 18 h and quenched with saturated NH<sub>4</sub>Cl. The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (x3). The combined organic phases were dried over MgSO<sub>4</sub>, filtered on silica gel and concentrated under vacuum. Enamides **2/6/7** were purified by flash chromatography on silica gel (pentane/ethyl acetate).

**Method B:** Copper Iodide or Iron (II) chloride (0.5-2 equiv) and allylbromide (9 equiv) were added under argon at 0 °C to a solution of ynamide **1** (1 equiv, 0.2 M) in non-degassed dichloromethane. Dialkylzinc (1 M in hexane, 2 equiv) was added and the reaction was stirred at room temperature for 18 h and quenched with saturated NH<sub>4</sub>Cl. The layers were separated

and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (x3). The combined organic phases were dried over MgSO<sub>4</sub>, filtered on silica gel and concentrated under vacuum. Enamides **8/9** were purified by flash chromatography on silica gel (pentane/ethyl acetate).

**3-[(1Z)-2-Ethyl-4-[(2-methoxyethoxy)methoxy]but-1-en-1-yl]-1,3-oxazolidin-2-one (2a).** The reaction was conducted on 3-{4-[(2-methoxyethoxy)methoxy]but-1-yn-1-yl}-1,3-oxazolidin-2-one (0.44 mmol, 107 mg), **1a** according to *method A* with diethylzinc (880 μL) and **CuI** (0.22 mmol, 42 mg, 0.5 equiv) to give **2a** as colorless oil (0.37 mmol, 100 mg, 83%). The reaction was conducted on 3-{4-[(2-methoxyethoxy)methoxy]but-1-yn-1-yl}-1,3-oxazolidin-2-one (0.45 mmol, 110 mg) **1a** according to *method A* with diethylzinc (900 μL) and **FeCl<sub>2</sub>** (0.23 mmol, 29 mg, 0.5 equiv) to give **2a** as a colorless oil (0.33 mmol, 90 mg, 73%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 1.04 (t, *J* = 7.4, 3H), 2.09 (qd, *J* = 7.4 and 1.1, 2H), 2.42 (t, *J* = 7.0, 2H), 3.37 (s, 3H), 3.51-3.56 (m, 2H), 3.59 (t, *J* = 7.0, 2H), 3.61-3.68 (m, 2H), 3.83 (pseudo t, *J* = 8.6, 2H), 4.36 (pseudo t, *J* = 8.6, 2H), 4.68 (s, 2H), 5.99 (br s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 12.9 (CH<sub>3</sub>), 27.8 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 46.8 (CH<sub>2</sub>), 59.1 (CH<sub>3</sub>), 62.3 (CH<sub>2</sub>), 65.8 (CH<sub>2</sub>), 67.1 (CH<sub>2</sub>), 71.9 (CH<sub>2</sub>), 95.6 (CH<sub>2</sub>), 120.2 (=CH), 132.6 (=C), 157.6 (C=O). HRMS (ESI): *m/z*: calcd for [M+H<sup>+</sup>] C<sub>13</sub>H<sub>24</sub>NO<sub>5</sub>: 274.1649, found 274.1648.

**3-[(1Z)-2-Phenylbut-1-en-1-yl]-1,3-oxazolidin-2-one (2b).**<sup>5a</sup> The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.27 mmol, 50 mg) **1b** according to *method A* with diethylzinc (540 μL) and **CuI** (0.14 mmol, 27 mg, 0.5 equiv) to give **2b** as a colorless oil (0.19 mmol, 41 mg, 69%). The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.54 mmol, 100 mg) **1b** according to *method A* with diethylzinc (2.16 mL, 4 equiv) and **FeCl<sub>2</sub>** (0.27 mmol, 34 mg, 0.5 equiv) to give **2b** as a colorless oil (0.14 mmol, 30 mg, 25%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.99 (t, *J* = 7.4, 3H), 2.37 (q, *J* = 7.4, 2H), 3.03 (pseudo t, *J* = 7.9, 2H), 4.12 (pseudo t, *J* = 7.9, 2H), 6.55 (s, 1H), 7.19-7.22 (m, 2H), 7.25-7.37 (m, 3H).

**3-[(1Z)-2-[(Benzyloxy)methyl]but-1-en-1-yl]-1,3-oxazolidin-2-one (2c).** The reaction was conducted on 3-[3-(benzyloxy)prop-1-yn-1-yl]-1,3-oxazolidin-2-one (0.45 mmol, 103 mg) **1c** according to *method A* with diethylzinc (900 μL) and **CuI** (0.22 mmol, 42 mg, 0.5 equiv) to give **2c** as a colorless oil (0.29 mmol, 76 mg, 65%). The reaction was conducted on 3-[3-(benzyloxy)prop-1-yn-1-yl]-1,3-oxazolidin-2-one (0.37 mmol, 85 mg) **1c** according to *method A* with diethylzinc (740 μL) and **FeCl<sub>2</sub>** (0.19 mmol, 23 mg, 0.5 equiv) to give **2c** as a colorless oil (0.06 mmol, 16 mg, 17%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 1.07 (t, *J* = 7.4, 3H), 2.18 (qd, *J* = 7.4 and 0.9, 2H), 3.75 (pseudo t, *J* = 7.5, 2H), 4.04 (s, 2H), 4.26 (pseudo t, *J* = 7.5, 2H), 4.49 (s, 2H), 6.17 (br s, 1H), 7.27-7.40 (m, 5H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 13.1 (CH<sub>3</sub>), 27.3 (CH<sub>2</sub>), 46.3 (CH<sub>2</sub>), 62.3 (CH<sub>2</sub>), 66.8 (CH<sub>2</sub>), 72.6 (CH<sub>2</sub>), 121.9 (=CH), 128.0 (=CH), 128.1 (=CH), 128.6 (=CH), 129.1 (=C), 138.2 (=C), 157.1 (C=O). HRMS (ESI): *m/z*: calcd for [M+H<sup>+</sup>] C<sub>15</sub>H<sub>20</sub>NO<sub>3</sub>: 262.1438, found 262.1437.

**3-[(1Z)-2-Methylhex-1-en-1-yl]-1,3-oxazolidin-2-one (2d).** The reaction was conducted on 3-(hex-1-yn-1-yl)-1,3-oxazolidin-2-one (0.51 mmol, 85 mg) **1d** according to *method A* with diethylzinc (1.02 mL) and **CuI** (0.25 mmol, 48 mg, 0.5 equiv) to give **2d** (0.47 mmol, 92 mg, 91%) as a colorless oil. The reaction was conducted on 3-(hex-1-yn-1-yl)-1,3-oxazolidin-2-one (0.38 mmol, 64 mg) **1d** according to *method A* with diethylzinc (760 μL) and **FeCl<sub>2</sub>** (0.19 mmol, 24 mg, 0.5 equiv) to give **2d** as a colorless oil (0.23 mmol, 45 mg, 60%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 0.91 (t, *J* = 7.0, 3H), 1.04 (t, *J* = 7.4, 3H), 1.21-1.47 (m, 4H), 1.99-2.15 (m, 4H), 3.75 (pseudo t, *J* = 7.4, 2H), 4.36

(pseudo t, *J* = 7.4, 2H), 5.87 (s, 1H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 12.9 (CH<sub>3</sub>), 14.0 (CH<sub>3</sub>), 23.0 (CH<sub>2</sub>), 27.5 (CH<sub>2</sub>), 29.4 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 47.0 (CH<sub>2</sub>), 62.2 (CH<sub>2</sub>), 118.3 (=CH), 138.0 (=C), 157.6 (C=O). HRMS (ESI): *m/z*: calcd for [M+H<sup>+</sup>] C<sub>11</sub>H<sub>20</sub>NO<sub>2</sub>: 198.1489, found 198.1490.

**2-[(1Z)-2-Phenylbut-1-en-1-yl]-2,3-dihydro-1H-isoindole-1,3-dione (2e).** The reaction was conducted on 2-(2-phenylethynyl)-2,3-dihydro-1H-isoindole-1,3-dione **1e** (0.28 mmol, 70 mg) according to *method A* with diethylzinc (756 μL) and **CuI** (0.19 mmol, 36 mg, 0.5 equiv) to give **2e** as a colorless oil (0.19 mmol, 53 mg) with 65% yield. The reaction was conducted on 2-(2-phenylethynyl)-2,3-dihydro-1H-isoindole-1,3-dione **1e** (0.28 mmol, 70 mg) according to *method A* with diethylzinc (810 μL, 2.0 equiv) and **FeCl<sub>2</sub>** (0.14 mmol, 18 mg, 0.5 equiv) to give **2e** as a colorless oil (0.11 mmol, 30 mg) with 39% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.98 (t, *J* = 7.4, 3H), 2.59 (q, *J* = 7.4, 2H), 6.12 (s, 1H), 7.10-7.26 (m, 5H), 7.55-7.75 (m, 4H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 12.6 (CH<sub>3</sub>), 29.8 (CH<sub>2</sub>), 112.5 (=CH), 123.5 (=CH), 127.2 (=CH), 127.6 (=CH), 128.4 (=CH), 132.0 (=C), 134.1 (=CH), 138.6 (=C), 149.0 (=C), 167.2 (C=O). HRMS (ESI): *m/z*: calcd for [M+H<sup>+</sup>] C<sub>18</sub>H<sub>16</sub>NO<sub>2</sub>: 278.1176, found 278.1176.

**1-[(1Z)-2-Phenylbut-1-en-1-yl]pyrrolidin-2-one (2f).** The reaction was conducted on 1-(2-phenylethynyl)pyrrolidin-2-one (0.38 mmol, 70 mg) **1f** according to *method A* with diethylzinc (760 μL) and **CuI** (0.19 mmol, 36 mg, 0.5 equiv) to give **2f** as a colorless oil (0.25 mmol, 53 mg, 65%). The reaction was conducted on 1-(2-phenylethynyl)pyrrolidin-2-one (0.27 mmol, 50 mg) **1f** according to *method A* with diethylzinc (540 μL) and **FeCl<sub>2</sub>** (0.14 mmol, 17 mg, 0.5 equiv) to give **2f** as a colorless oil (0.21 mmol, 45 mg, 77%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.98 (t, *J* = 7.4, 3H), 1.78 (quint, *J* = 7.7, 2H), 2.33 (t, *J* = 8.2, 2H), 2.39 (q, *J* = 7.4, 2H), 2.87 (t, *J* = 7.2, 2H), 6.72 (s, 1H), 7.13-7.20 (m, 2H), 7.22-7.36 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 13.3 (CH<sub>3</sub>), 18.8 (CH<sub>2</sub>), 30.6 (CH<sub>2</sub>), 31.1 (CH<sub>2</sub>), 48.4 (CH<sub>2</sub>), 120.0 (=CH), 127.2 (=CH), 128.0 (=CH), 129.1 (=CH), 129.4 (=C), 139.8 (=C), 175.1 (C=O). HRMS (ESI): *m/z*: calcd for [M+H<sup>+</sup>] C<sub>14</sub>H<sub>18</sub>NO: 216.1383, found 216.1382.

**3-[(1Z)-4-[(2-Methoxyethoxy)methoxy]-2-methylbut-1-en-1-yl]-1,3-oxazolidin-2-one (6a).** The reaction was conducted on 3-{4-[(2-methoxyethoxy)methoxy]but-1-yn-1-yl}-1,3-oxazolidin-2-one **1a** according to *method A* with dimethylzinc (800 μL) and **CuI** (0.21 mmol, 40 mg, 0.5 equiv) to give **6a** as a colorless oil (0.14 mmol, 37 mg, 62%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 1.77 (s, 3H), 2.42 (t, *J* = 6.7, 2H), 3.39 (s, 3H), 3.54-3.57 (m, 2H), 3.65 (t, *J* = 6.9, 2H), 3.65-3.71 (m, 2H), 3.82 (pseudo t, *J* = 8.0, 2H), 4.37 (pseudo t, *J* = 8.0, 2H), 4.70 (s, 2H), 5.98 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 20.8 (CH<sub>3</sub>), 31.9 (CH<sub>2</sub>), 46.8 (CH<sub>2</sub>), 59.1 (CH<sub>3</sub>), 62.3 (CH<sub>2</sub>), 65.3 (CH<sub>2</sub>), 67.0 (CH<sub>2</sub>), 71.9 (CH<sub>2</sub>), 95.5 (CH<sub>2</sub>), 120.7 (=CH), 128.4 (=C), 157.5 (C=O). HRMS (ESI): *m/z*: calcd for [M+H<sup>+</sup>] C<sub>12</sub>H<sub>22</sub>NO<sub>5</sub>: 260.1492, found 260.1491.

**3-[(1Z)-2-Phenylprop-1-en-1-yl]-1,3-oxazolidin-2-one (6b).**<sup>29</sup> The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.53 mmol, 106 mg) **1b** according to *method A* with dimethylzinc (1.1 mL) and **CuI** (0.27 mmol, 51 mg, 0.5 equiv) to give **6b** as colorless oil (0.41 mmol, 84 mg, 77%). The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.27 mmol, 50 mg) **1b** according to *method A* with dimethylzinc (540 μL) and **FeCl<sub>2</sub>** (0.54 mmol, 63 mg, 2.0 equiv) to give **6b** as a colorless oil (0.07 mmol, 19.6 mg, 25%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 2.05 (s, 3H), 3.09 (t, *J* = 7.9, 2H), 4.14 (t, *J* = 7.9, 2H), 6.55 (s, 1H), 7.23-7.36 (m, 5H).

**3-[(1Z)-3-(benzyloxy)-2-methylprop-1-en-1-yl]-1,3-oxazolidin-2-one (6c).** The reaction was conducted on 3-[3-(benzyloxy)prop-1-yn-1-yl]-1,3-oxazolidin-2-one (0.30 mmol, 70 mg) **1c** (according to *method A* with dimethylzinc (600  $\mu$ L) and **CuI** (0.15 mmol, 28 mg, 0.5 equiv) to give **6c** as a colorless oil (0.22 mmol, 53.3 mg, 72%). The reaction was conducted on 3-[3-(benzyloxy)prop-1-yn-1-yl]-1,3-oxazolidin-2-one (0.26 mmol, 60 mg) **1c** according to *method A* with dimethylzinc (520  $\mu$ L) and **FeCl<sub>2</sub>** (0.13 mmol, 17 mg, 0.5 equiv) to give **6c** as a colorless oil (0.14 mmol, 35 mg, 54%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.84 (s, 3H), 3.70 (pseudo t,  $J = 8.0$ , 2H), 4.04 (s, 2H), 4.28 (pseudo t,  $J = 8.0$ , 2H), 4.50 (s, 2H), 6.10 (s, 1H), 7.29-7.34 (m, 5H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 19.7 (CH<sub>3</sub>), 46.3 (CH<sub>2</sub>), 62.2 (CH<sub>2</sub>), 67.9 (CH<sub>2</sub>), 72.3 (CH<sub>2</sub>), 121.9 (=CH), 125.1 (=C), 127.8 (=CH), 128.0 (=CH), 128.5 (=CH), 138.1 (=C), 157.1 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+Na<sup>+</sup>] C<sub>14</sub>H<sub>18</sub>NO<sub>3</sub>: 270.1101, found 270.1102.

**3-[(1Z)-2-methylhex-1-en-1-yl]-1,3-oxazolidin-2-one (6d).** The reaction was conducted on 3-(hex-1-yn-1-yl)-1,3-oxazolidin-2-one (0.68 mmol, 114 mg) **1d** according to *method A* with dimethylzinc (1.26 mL) and **CuI** (0.34 mmol, 65 mg, 0.5 equiv) to give **6d** (0.51 mmol, 94 mg, 75%) as a colorless oil. The reaction was conducted on 3-(hex-1-yn-1-yl)-1,3-oxazolidin-2-one (0.60 mmol, 100 mg) **1d** according to *method A* with dimethylzinc (1.2 mL) and **FeCl<sub>2</sub>** (0.30 mmol, 38 mg, 0.5 equiv) to give **6d** as a colorless oil (0.014 mmol, 25 mg, 23%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 0.91 (t,  $J = 7.2$ , 3H), 1.29-1.42 (m, 4H), 1.73 (s, 3H), 2.09 (t,  $J = 8.2$ , 2H), 3.74 (pseudo t,  $J = 8.0$ , 2H), 4.37 (pseudo t,  $J = 8.0$ , 2H), 5.84 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 14.0 (CH<sub>3</sub>), 20.5 (CH<sub>3</sub>), 22.9 (CH<sub>2</sub>), 29.8 (CH<sub>2</sub>), 31.2 (CH<sub>2</sub>), 47.0 (CH<sub>2</sub>), 62.2 (CH<sub>2</sub>), 118.8 (=CH), 135.5 (=C), 157.6 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+H<sup>+</sup>] C<sub>10</sub>H<sub>18</sub>NO<sub>2</sub>: 184.1332, found 184.1332.

**2-[(1Z)-2-Phenylprop-1-en-1-yl]-2,3-dihydro-1H-isoindole-1,3-dione (6e).** The reaction was conducted on 2-(2-phenylethynyl)-2,3-dihydro-1H-isoindole-1,3-dione **1e** (0.4 mmol, 100 mg) according to *method A* with dimethylzinc (810  $\mu$ L) and **CuI** (0.2 mmol, 38 mg, 0.5 equiv) to give **6e** as a colorless oil (0.32 mmol, 85 mg) with 80% yield. The reaction was conducted on 2-(2-phenylethynyl)-2,3-dihydro-1H-isoindole-1,3-dione **1e** (0.4 mmol, 100 mg) according to *method A* with dimethylzinc (810  $\mu$ L) and **FeCl<sub>2</sub>** (0.2 mmol, 26 mg, 0.5 equiv) to give **6e** as a colorless oil (0.05 mmol, 12.8 mg) with 12% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 2.25 (d,  $J = 1.6$ , 3H), 6.15 (q,  $J = 1.4$ , 1H), 7.15-7.25 (m, 5H), 7.65-7.67 (m, 2H), 7.74-7.76 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 22.9 (CH<sub>3</sub>), 113.2 (=CH), 123.6 (=CH), 126.8 (=CH), 127.8 (=CH), 128.5 (=CH), 132.0 (=C), 134.2 (=CH), 139.5 (=C), 142.8 (=C), 167.2 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+H<sup>+</sup>] C<sub>17</sub>H<sub>14</sub>NO<sub>2</sub>: 264.1019, found 264.1021.

**1-[(1Z)-2-Phenylprop-1-en-1-yl]pyrrolidin-2-one (6f).** The reaction was conducted on 1-(2-phenylethynyl)pyrrolidin-2-one (0.22 mmol, 40 mg) **1f** according to *method A* with dimethylzinc (430  $\mu$ L) and **CuI** (0.11 mmol, 21 mg, 0.5 equiv) to give **6f** as a colorless oil (0.19 mmol, 38 mg, 87%). The reaction was conducted on 1-(2-phenylethynyl)pyrrolidin-2-one (0.27 mmol, 50 mg) **1f** according to *method A* with dimethylzinc (540  $\mu$ L) and **FeCl<sub>2</sub>** (0.14 mmol, 17 mg, 0.5 equiv) to give **6f** as a colorless oil (0.24 mmol, 49 mg, 91%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.74 (quint,  $J = 7.6$ , 2H), 1.99 (s, 3H), 2.28 (t,  $J = 8.1$ , 2H), 2.93 (t,  $J = 8.1$ , 2H), 6.60 (s, 1H), 7.13-7.25 (m, 5H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 18.9 (CH<sub>2</sub>), 24.1 (CH<sub>3</sub>), 30.6 (CH<sub>2</sub>), 48.3 (CH<sub>2</sub>), 120.7 (=CH), 124.2 (=C), 127.3 (=CH), 128.2 (=CH), 128.4 (=CH),

140.8 (=C), 175.3 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+H<sup>+</sup>] C<sub>13</sub>H<sub>16</sub>NO: 202.1226, found: 202.1227.

**1-[(1Z)-3-methyl-2-phenylbut-1-en-1-yl]pyrrolidin-2-one (7f).** The reaction was conducted on 1-(2-phenylethynyl)pyrrolidin-2-one (0.22 mmol, 40 mg) **1f** according to *method A* with diisopropylzinc (440  $\mu$ L) and **CuI** (0.11 mmol, 21 mg, 0.5 equiv) to give **7f** as a colorless oil (0.15 mmol, 32 mg, 67%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.03 (d,  $J = 6.9$ , 6H), 1.74 (quint,  $J = 7.6$ , 2H), 2.30 (t,  $J = 8.2$ , 2H), 2.60 (sept,  $J = 6.9$ , 1H), 2.74 (t,  $J = 8.2$ , 2H), 6.75 (s, 1H), 7.09-7.15 (m, 2H), 7.24-7.32 (m, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 18.7 (CH<sub>2</sub>), 22.1 (CH<sub>3</sub>), 30.6 (CH<sub>2</sub>), 35.7 (CH), 48.4 (CH<sub>2</sub>), 119.8 (=CH), 127.1 (=CH), 127.7 (=CH), 129.9 (=CH), 133.1 (=C), 139.1 (=C), 175.1 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+H<sup>+</sup>] C<sub>15</sub>H<sub>20</sub>NO: 230.1539, found 230.1538.

**3-[(4Z)-5-Ethyl-7-[(2-methoxyethoxy)methoxy]hepta-1,4-dien-4-yl]-1,3-oxazolidin-2-one (8a).** The reaction was conducted on 3-{4-[(2-methoxyethoxy)methoxy]but-1-yn-1-yl}-1,3-oxazolidin-2-one (0.21 mmol, 50 mg) **1a** according to *method B* with diethylzinc (620  $\mu$ L) and **CuI** (0.31 mmol, 59 mg, 1.5 equiv) to give **8a** as a colorless oil (0.10 mmol, 31 mg, 47%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.05 (t,  $J = 7.6$ , 3H), 2.16 (q,  $J = 7.6$ , 2H), 2.40 (t,  $J = 7.0$ , 2H), 3.06 (d,  $J = 6.4$ , 2H), 3.39 (s, 3H), 3.52-3.58 (m, 2H), 3.60-3.74 (m, 6H), 4.33 (t,  $J = 7.7$ , 2H), 4.69 (s, 2H), 5.04-5.19 (m, 2H), 5.79 (ddt,  $J = 16.6$ , 9.9 and 6.5, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 13.2 (CH<sub>3</sub>), 24.4 (CH<sub>2</sub>), 31.6 (CH<sub>2</sub>), 34.3 (CH<sub>2</sub>), 47.0 (CH<sub>2</sub>), 59.2 (CH<sub>3</sub>), 62.3 (CH<sub>2</sub>), 66.0 (CH<sub>2</sub>), 67.1 (CH<sub>2</sub>), 72.0 (CH<sub>2</sub>), 95.7 (CH<sub>2</sub>), 117.1 (=CH<sub>2</sub>), 128.4 (=C), 135.0 (=CH), 139.4 (=C), 160.7 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+H<sup>+</sup>] C<sub>16</sub>H<sub>28</sub>NO<sub>5</sub>: 314.1962, found: 314.1963.

**3-[(4Z)-5-Phenylhepta-1,4-dien-4-yl]-1,3-oxazolidin-2-one (8b).** The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.27 mmol, 50 mg) **1b** according to *method B* with diethylzinc (540  $\mu$ L) and **CuI** (0.14 mmol, 27 mg, 0.5 equiv) to give **8b** as a colorless oil (0.27 mmol, 69 mg, 100%). The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.27 mmol, 50 mg) **1a** according to *method B* with diethylzinc (540  $\mu$ L) and **FeCl<sub>2</sub>** (0.54 mmol, 68 mg, 2 equiv) to give **8b** as a colorless oil (0.12 mmol, 32 mg, 73%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 0.94 (t,  $J = 7.5$ , 3H), 2.46 (q,  $J = 7.5$ , 2H), 3.10 (pseudo t,  $J = 8.5$ , 2H), 3.29 (d,  $J = 6.6$ , 2H), 3.94 (pseudo t,  $J = 8.5$ , 2H), 5.10 (dq,  $J = 10.0$  and 1.5, 1H), 5.19 (dq,  $J = 16.7$  and 1.5, 1H), 5.85 (ddt,  $J = 16.7$ , 10.0 and 6.7, 1H), 7.17-7.36 (m, 5H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 12.8 (CH<sub>3</sub>), 26.8 (CH<sub>2</sub>), 34.5 (CH<sub>2</sub>), 46.8 (CH<sub>2</sub>), 62.4 (CH<sub>2</sub>), 117.20 (=CH<sub>2</sub>), 127.5 (=CH), 128.0 (=CH), 128.6 (=CH), 129.0 (=C), 134.7 (=CH), 140.2 (=C), 142.3 (=C), 157.0 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+H<sup>+</sup>] C<sub>16</sub>H<sub>20</sub>NO<sub>2</sub>: 258.1489, found: 258.1487.

**3-[(4Z)-5-Ethylnona-1,4-dien-4-yl]-1,3-oxazolidin-2-one (8d).** The reaction was conducted on 3-(hex-1-yn-1-yl)-1,3-oxazolidin-2-one (0.30 mmol, 50 mg) **1d** according to *method B* with diethylzinc (600  $\mu$ L) and **CuI** (0.6 mmol, 114 mg, 2.0 equiv) to give **8d** as a colorless oil (0.23 mmol, 54 mg, 76%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 0.89 (t,  $J = 7.1$ , 3H), 1.02 (t,  $J = 7.6$ , 3H), 1.23-1.44 (m, 4H), 2.04 (distorted t,  $J = 7.7$ , 2H), 2.12 (q,  $J = 7.6$ , 2H), 3.04 (d,  $J = 6.6$ , 2H), 3.63 (pseudo t,  $J = 8.0$ , 2H), 4.31 (pseudo t,  $J = 8.0$ , 2H), 5.05 (dq,  $J = 10.0$  and 1.7, 1H), 5.12 (dq,  $J = 16.6$  and 1.7, 1H), 5.79 (ddt,  $J = 16.6$ , 10.0 and 6.6, 1H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 13.2 (CH<sub>3</sub>), 14.0 (CH<sub>3</sub>), 23.2 (CH<sub>2</sub>), 24.1 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 30.9 (CH<sub>2</sub>), 34.3 (CH<sub>2</sub>), 47.1 (CH<sub>2</sub>), 62.1 (CH<sub>2</sub>), 116.8 (=CH<sub>2</sub>), 126.3 (=C), 135.3 (=CH), 142.9 (=C), 157.0 (C=O). HRMS (ESI):  $m/z$ : calcd for [M+H<sup>+</sup>] C<sub>14</sub>H<sub>24</sub>NO<sub>2</sub>: 238.1802, found 238.1802

**1-[(4Z)-5-Phenylhepta-1,4-dien-4-yl]pyrrolidin-2-one (8f).** The reaction was conducted on 1-(2-phenylethynyl)pyrrolidin-2-one (0.25 mmol, 46 mg) **1f** according to *method B* with diethylzinc (500  $\mu$ L) and **CuI** (0.12 mmol, 24 mg, 0.5 equiv) to give **8f** as a colorless oil (0.13 mmol, 34 mg, 53%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 0.95 (t,  $J = 7.5$ , 3H), 1.63 (quint,  $J = 7.5$ , 2H), 2.16 (t,  $J = 8.0$ , 2H), 2.46 (q,  $J = 7.5$ , 2H), 2.94 (t,  $J = 6.9$ , 2H), 3.25 (d,  $J = 6.7$ , 2H), 5.08 – 5.04 (dq,  $J = 10.0$  and 1.6, 1H), 5.14 (dq,  $J = 17.1$  and 1.6, 1H), 5.83 (ddt,  $J = 16.8$ , 10.0 and 6.7, 1H), 7.34 – 7.16 (m, 5H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 13.1 ( $\text{CH}_3$ ), 19.4 ( $\text{CH}_2$ ), 26.7 ( $\text{CH}_2$ ), 31.4 ( $\text{CH}_2$ ), 35.0 ( $\text{CH}_2$ ), 50.1 ( $\text{CH}_2$ ), 116.9 ( $=\text{CH}_2$ ), 127.3 ( $=\text{CH}$ ), 128.1 ( $=\text{CH}$ ), 128.4 ( $=\text{CH}$ ), 131.1 ( $=\text{C}$ ), 135.1 ( $=\text{CH}$ ), 140.6 ( $=\text{C}$ ), 141.5 ( $=\text{C}$ ), 175.3 ( $\text{C}=\text{O}$ ). HRMS (ESI):  $m/z$ : calcd for  $[\text{M}+\text{H}^+]$   $\text{C}_{17}\text{H}_{22}\text{NO}$ : 256.1696, found 256.1696.

**3-[(2Z)-2-Phenylhexa-2,5-dien-3-yl]-1,3-oxazolidin-2-one (9b).** The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.27 mmol, 50 mg) **1b** according to *method B* with dimethylzinc (540  $\mu$ L) and **CuI** (0.14 mmol, 27 mg, 0.5 equiv) to give **9b** as a colorless oil (0.25 mmol, 62 mg, 93%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 2.09 (s, 3H), 3.12 (pseudo t,  $J = 8.6$ , 2H), 3.30 (d,  $J = 6.6$ , 2H), 3.98 (pseudo t,  $J = 8.6$ , 2H), 5.12 (dq,  $J = 10.0$  and 1.6, 1H), 5.19 (dq,  $J = 16.7$  and 1.6, 1H), 5.86 (ddt,  $J = 16.7$ , 10.0 and 6.6, 1H), 7.24-7.36 (m, 5H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 20.0 ( $\text{CH}_3$ ), 35.0 ( $\text{CH}_2$ ), 46.6 ( $\text{CH}_2$ ), 62.5 ( $\text{CH}_2$ ), 117.2 ( $=\text{CH}_2$ ), 127.4 ( $=\text{CH}$ ), 127.5 ( $=\text{CH}$ ), 128.6 ( $=\text{CH}$ ), 129.4 ( $=\text{C}$ ), 134.2 ( $=\text{CH}$ ), 136.1 ( $=\text{C}$ ), 141.6 ( $=\text{C}$ ), 157.2 ( $\text{C}=\text{O}$ ). HRMS (ESI):  $m/z$ : calcd for  $[\text{M}+\text{H}^+]$   $\text{C}_{15}\text{H}_{18}\text{NO}_2$ : 244.1332, found 244.1332.

**3-[(1Z)-2-phenyl(1- $^2\text{H}$ )but-1-en-1-yl]-1,3-oxazolidin-2-one (10b).** The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.27 mmol, 50 mg) **1b** according to *method A* with diethylzinc (540  $\mu$ L) and **CuI** (0.14 mmol, 27 mg, 0.5 equiv). The reaction was stirred for 18 h and quenched with saturated  $\text{ND}_4\text{Cl}$  to give **10b** as a colorless oil (0.16 mmol, 35 mg, 60%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 0.98 (t,  $J = 7.4$ , 3H), 2.36 (q,  $J = 7.4$ , 2H), 3.03 (pseudo t,  $J = 7.9$ , 2H), 4.12 (pseudo t,  $J = 7.9$ , 2H), 7.16-7.22 (m, 2H), 7.24-7.36 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 13.3 ( $\text{CH}_3$ ), 30.9 ( $\text{CH}_2$ ), 45.2 ( $\text{CH}_2$ ), 62.6 ( $\text{CH}_2$ ), 119.7 ( $=\text{CD}$ , t,  $J_D=27$ ), 127.4 ( $\text{CH}$ ), 128.1 ( $\text{C}$ ), 128.2 ( $\text{CH}$ ), 129.3 ( $\text{CH}$ ), 139.2 ( $=\text{C}$ ), 157.4 ( $\text{C}=\text{O}$ ). HRMS (ESI):  $m/z$ : calcd for  $[\text{M}+\text{H}^+]$   $\text{C}_{13}\text{H}_{15}\text{DNO}_2$ : 219.1238, found: 219.1240.

**(E)-3-(2-phenyl-1-(phenylselanyl)but-1-en-1-yl)oxazolidin-2-one (11b).** The reaction was conducted on 3-(2-phenylethynyl)-1,3-oxazolidin-2-one (0.27 mmol, 50 mg) **1b** according to *method A* with diethylzinc (540  $\mu$ L) and **CuI** (0.14 mmol, 27 mg, 0.5 equiv). The reaction was stirred for 18 h and  $\text{PhSeCl}$  (0.108 mmol, 207 mg) in DCM (0.4 ml) was added at 0  $^\circ\text{C}$ . reaction mixture was stirred for 10 h and quenched with saturated  $\text{NH}_4\text{Cl}$ . The layers were separated and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (x3). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered on silica gel and concentrated under vacuum and purified by flash chromatography on silica gel (pentane/ether) to give **11b** as colorless oil (0.134 mmol, 50%). NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 0.97 (t,  $J = 7.5$  Hz, 3H), 2.76 (q,  $J = 7.5$  Hz, 2H), 3.15 (t,  $J = 7.7$  Hz, 2H), 3.15 (pseudo t,  $J = 7.7$  Hz, 2H), 3.66 (pseudo t,  $J = 7.6$  Hz, 2H), 7.36 – 7.20 (m, 8H), 7.70 – 7.63 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 12.7 ( $\text{CH}_3$ ), 30.9 ( $\text{CH}_2$ ), 46.6 ( $\text{CH}_2$ ), 61.9 ( $\text{CH}_2$ ), 123.2 ( $=\text{C}$ ), 125.7 ( $\text{CH}$ ), 127.7 ( $\text{CH}$ ), 128.0 ( $=\text{C}$ ), 128.4 ( $\text{CH}$ ), 128.5 ( $\text{CH}$ ), 129.4 ( $\text{CH}$ ), 134.8 ( $\text{CH}$ ), 139.9 ( $=\text{C}$ ), 149.9 ( $=\text{C}$ ), 155.7 ( $\text{C}=\text{O}$ ).

**Supplementary content.** NMR spectra for all new compounds. Calculations of **1b**, **1g**, **1f**, the resulting vinylzincs and  $\text{Et}_2\text{Zn}$  at the B3LYP/6-31+G(d,p) level of theory. Condensed Fukui's functions  $f^-$ ,  $f^+$  and dual descriptor  $f^{(2)}$ : table of their values at O, C $\alpha$ , and C $\beta$ .

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