JOC The Journal of Organic Chemistry

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Cobalt-Catalyzed Carbozincation of Ynamides

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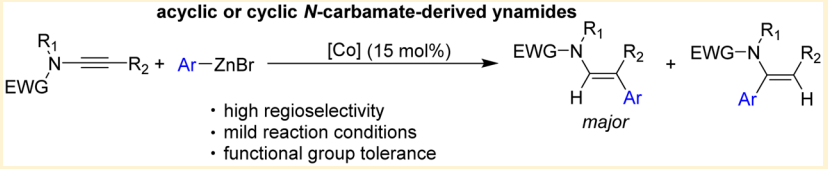
Supporting Information



ABSTRACT: An original cobalt-catalyzed ynamide carbozincation leading mainly to diverse 3-aryl enamides with mild reaction conditions and good functional-group tolerance has been developed. This reaction displays an excellent regio- and total stereoselectivity and opens the way to appealing synthetic applications. Moreover, this approach allows the selective synthesis of biologically relevant 3,5-disubstituted oxazolone frameworks.

Ynamide derivatives have been recognized as important intermediates in organic synthesis due to their synthetic versatility, in particular, as powerful precursors of nitrogen-containing reactive species such as enamides. In recent years, enamides have also shown valuable applications as useful building blocks to introduce nitrogen based functionalities into various aromatic or nonaromatic heterocycles.[1] Following our recent study on cobalt catalyzed carbozincation reactions,[2] and in our long-term quest for the metal mediated functionalization of enamides,[3] we disclose here a broadly applicable and original ynamide carbozincation. It is worth mentioning that carbometalation of alkynes,[4] and, in particular, carbozincation,[5] is one of the most important reactions due to the high functional group compatibility of organozinc reagents. Of particular interest is the cobalt-catalyzed carbometalation of alkynes, in view of the low cost and the low toxicity of cobalt. This catalytic reaction generally proceeds by *syn*-1,2-addition of organometallic species generated through transmetalation between organozinc and cobalt complexes across the carbon–carbon triple bond. Oshima[6] exploited the cobalt-catalyzed arylzincation of alkynes by using arylzinc–lithium complexes leading to the addition to symmetrical as well as unsymmetrical substituted internal alkynes. An interesting extension of this methodology was described by Yoshikai[7] involving a cobalt catalyzed addition/1,4 migratory arylzincation of internal alkynes. Trapping of the resulting *ortho*-alkenylarylzinc species with external electrophiles allows access to a variety of 1-alkenyl-arenes functionalized in the 2-position. The same group described the development of a cobalt/diphosphine catalyst which promotes stereoselective addition of alkenylzinc reagents to unfunctionalized internal alkynes.[8] Zhu achieved a Pd-catalyzed stereospecific *trans*-addition of boronic acids to ynamides, furnishing α,β-disubstituted enamides with excellent regio- and stereoselectivity.[9] Intramolecular copper-mediated carbomagnesiation and carbocupration of ynamides were also successfully described.[10] Recently, we reported the use of a shelf-stable $CoBr_2$(bipy) complex for the synthesis of arylzinc reagents and advantageously studied their reactivity in the carbozincation reaction.[2] Here we wish to report that cobalt salts can originally catalyze the arylzincation of ynamides (Scheme 1). Only one example of metal catalyzed carbozincation of ynamides has been reported in the literature so far using expensive rhodium as the catalyst and with poor regioselectivity.[11] In addition, a further advantage of this new method presented here is that it enables a novel access to multi-substituted enamides that would otherwise be difficult to prepare using alternative procedures.

We initiated our study by investigating the reaction of ynamide **1a** with 4-methoxyphenylzinc reagent **2a**. The latter was prepared from 4-bromoanisole and commercially available Zn powder in the presence of the cobalt catalyst in CH_3CN at room temperature for 1 h. At this stage, the presence of TFA was required for zinc activation and of allyl chloride to avoid the formation of reduced side products (Table 1).[12] After filtration of the mixture, ynamide **1a** was added, leading to the *syn*-addition product in 72% isolated yield as a α/β regioisomeric mixture, respectively **3aa** and **4aa**.[13] The regio- and stereochemistry were determined according to NMR experiments.[14] A subsequent study revealed that a higher regioselectivity was obtained by using phenantroline as a ligand (entries 1–3) and by conducting the reaction at low

Received: October 28, 2016
Published: December 27, 2016

DOI: 10.1021/acs.joc.6b02612
J. Org. Chem. 2017, 82, 1254–1259

Scheme 1. Metal-Catalyzed Ynamide Carbozincation

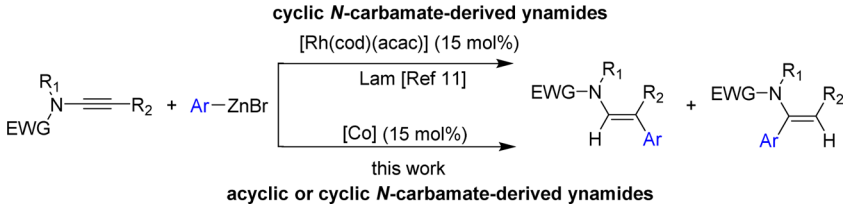
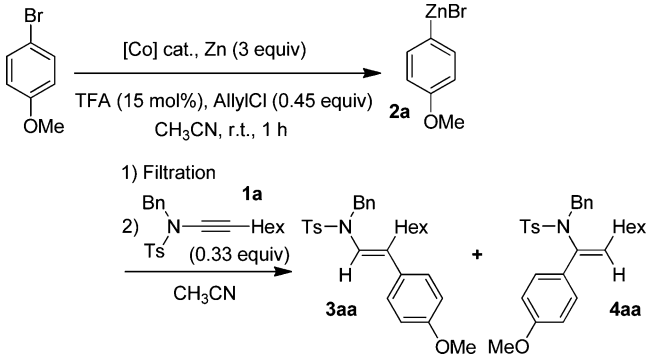


Table 1. Optimization of the Cobalt-Catalyzed Ynamide Carbozincation[a]



entry	catalyst	T (°C)	time (min)	yield[b] [%] (**3aa**:**4aa** ratio)[c]
1	[$CoBr_2$(bpy)]	rt	90	72 (65:35)
2	[$CoBr_2$(bpy)]	−10	90	0
3	[$CoBr_2$(phen)]	rt	90	74 (76:24)
4	[$CoBr_2$(phen)]	0	90	75 (79:21)
5	[$CoBr_2$(phen)]	−10	90	78 (82:18)
6[d]	[$CoBr_2$(phen)]	−10	90	0
7[e]	[$CoBr_2$(phen)]	−10	90	0
8	$CoBr_2$	−10	90	0
9[f]	[$CoBr_2$(phen)]	−10	90	69 (76:24)
10	[$CoBr_2$(phen)]	−10	60	57 (81:19)

[a]Reaction conditions unless otherwise specified: arylzinc reagent (5 mmol, 3 equiv), cobalt catalyst (15 mol %), CH_3CN (8 mL). [b]Isolated yield after purification by flash chromatography. [c]Determined by ^1H NMR of the crude product. [d]In situ formed [$CoBr_2$(phen)] complex (prepared from 15 mol % of $CoBr_2$ and 15 mol % of phenantroline) was used. [e]Arylzinc reagent (2 equiv). [f]Cobalt catalyst (10 mol %).

temperature (entries 4−5). It is noteworthy that no reaction occurred with the in situ formed [$CoBr_2$(phen)] complex (entry 6), by reducing the amount of aryl zinc reagent (entry 7), or by performing the reaction under ligand-free conditions (entry 8). It was also observed that a lower catalyst loading (entry 9) and a short reaction time (entry 10) decreased the efficiency of this transformation. In addition, we observed that the reaction was inhibited in the absence of a cobalt catalyst or by using a THF/MeCN solvent mixture. Prompted by these results, we sought to examine the scope of arylzinc reagents and ynamides. To the best of our knowledge, the Co-catalyzed arylzincation of ynamide is unprecedented and would constitute a powerful, selective, and atom-economic strategy to reach useful substituted enamide compounds.[1,15] The results are summarized in Tables 2 and 3. A variety of ynamides **1a−g** participated in the reaction with 4-methoxyphenyl zinc bromide **2a** to afford the corresponding regiosisomers 2-aryl- and/or 3-aryl enamides, respectively **3** and/or **4**, in moderate to good yields. By conducting the reaction at −10 °C, the carbometalation displayed excellent regio- and stereoselectivity with ynamides bearing an acyclic carbamate (**3ba**, **3ca**). However, as observed for the tosyl compound (**3aa**), lower regioselectivity was obtained in the case of ynamide bearing a cyclic carbamate group (**3da**) since a weakly coordinating directing group disfavors the stabilization of the orthoalkenylmetal intermediate (cf. **C** in the proposed mechanism in Scheme 3).

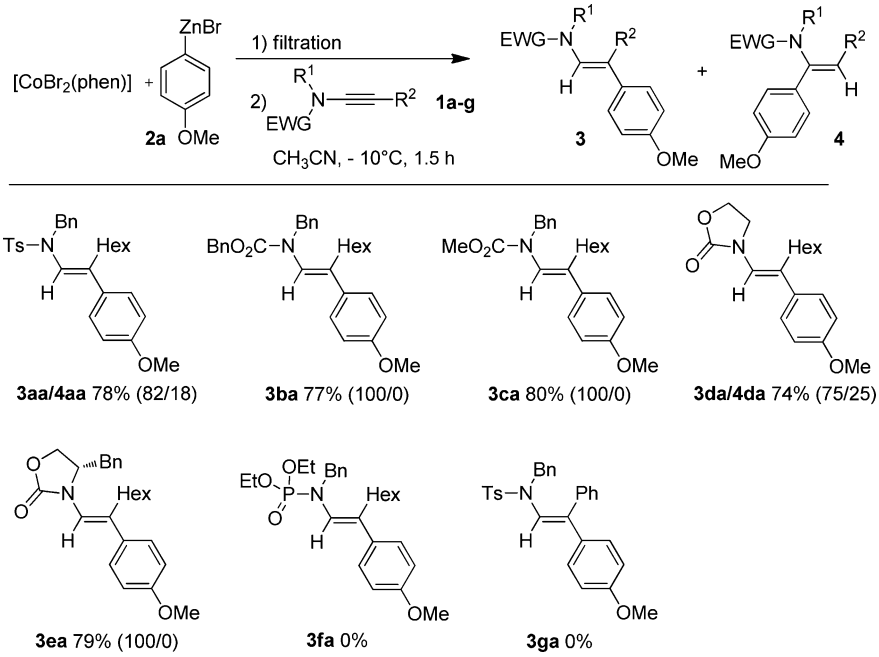
For cyclic carbamate **1e**, the high regioselectivity observed was governed by steric effects because of the presence of the hindered benzyl group leading to the formation of the sole 3-aryl regioisomers **3ea**. Moreover, with a sterically hindered phenyl substituent on the ynamide (R^2 = Ph), the reaction failed to give the desired enamide **3ga**, and an amide **5**, resulting from an hydratation process in the presence of TFA, was isolated in 61% yield instead (Scheme 2).[16]

The feasibility of the carbozincation reaction encouraged us to screen various typical organozinc reagents **2**. Ynamide **1b** that furnished one of the best yields with high regioselectivity was selected as the model substrate. As anticipated, carbometalation proceeded smoothly with a variety of arylzinc reagents to afford the corresponding 3-aryl enamides **3** in moderate to good yields as a single stereo- and regioisomer. Total regioselectivity was observed by conducting the reaction at −10 °C as previously demonstrated. Electron-donating (**3bb−3be**) and electron-withdrawing (**3bg−3bj**) functional groups and potentially sensitive functional groups including ester were tolerated; the efficiency of the reaction is directly correlated with the electron density on the aromatic ring. It is also noticeable that, in addition to an electronic effect, the carbozincation reaction is sensitive to steric hindrance which slows the reaction rate. The case of the amide formation from **1g** via a hydration process was already discussed above (eq 1, Scheme 2 and Table 2). However, while the reaction was performed with sterically hindered *ortho*-substituted arylzinc reagents, an oxazolone derivative **6** was isolated (eq 2, Scheme 2). No addition of the zinc reagent was observed. The formation of **6**, which results probably from the *in situ* formation of $ZnBr_2$, was surprising but quite promising, as it opens a new access to a range of 3,5-disubstituted oxazolone frameworks.[17] Some authors have already developed metal-catalyzed (e.g., Au, Pd, Cu) 5-endotrig cyclization of *N*-alkynyl *tert*-butyloxy-carbamates to synthesize this privileged structure.[18] However, to the best of our knowledge, no example with cobalt and/or zinc has been reported so far. Work is currently underway in our laboratory to determine the scope and limitations of this original reaction and will be reported in due course.

According to our observations and previously reported studies, cobalt-catalyzed ynamide carbozincation can be rationalized as depicted in Scheme 3. The neutral $CoBr_2$(ligand) complex is initially reduced to a Co(I) species while the remaining halide ion is abstracted by the Lewis acid $ZnBr_2$. Then, it can be envisioned as follows: (i) insertion of

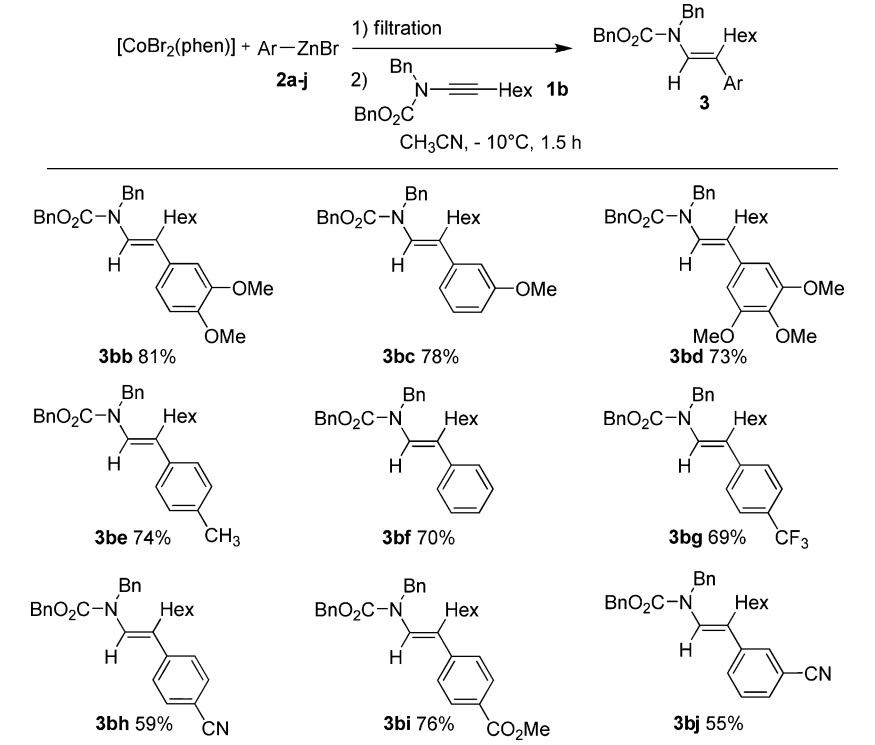
DOI: 10.1021/acs.joc.6b02612
J. Org. Chem. 2017, 82, 1254−1259

Table 2. Scope of the Cobalt-Catalyzed Ynamide Arylzincation Starting from 4-Methoxyphenyl Zinc Bromide 2a[a]



[a]Reaction conditions: **2a** (5 mmol, 3 equiv), cobalt catalyst (15 mol %), CH_3CN (8 mL), −10 °C, 1.5 h. Yields of isolated products are given.

Table 3. Cobalt-Catalyzed Ynamide Arylzincation with Various Organozinc Reagent[a]

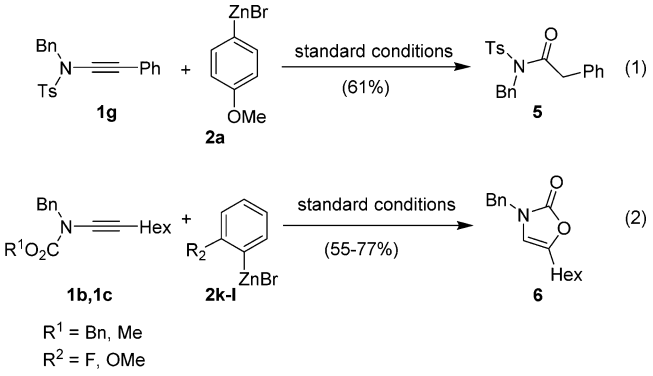


[a]Reaction conditions: **2a**–**j** (5 mmol, 3 equiv), cobalt catalyst (15 mol %), CH_3CN (8 mL), −10 °C, 1.5 h. Yields of isolated products are given.

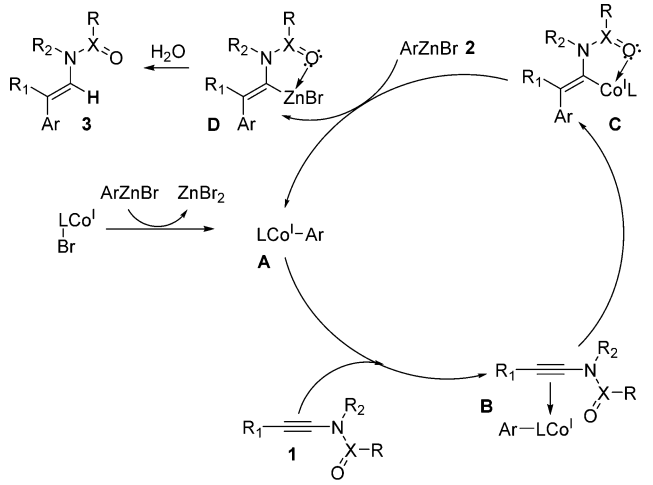
the ynamide **1** into an arylcobalt species **A** generated from the cobalt precatalyst and the arylzinc reagent; (ii) transmetalation between **C** and the arylzinc reagent **2** to afford an *ortho*-alkenylarylzinc intermediate and regenerate the arylcobalt species. The good regio- and stereoselectivity observed are both explained by an oxygen *syn* directed carbometalation[19] of the ynamide **1** with cobalt species leading to the α-alkenylcobalt intermediate **C** with the regioselectivity shown, thus overriding the intrinsic polarity of ynamides.[20] It should be pointed out that the intermediate **D** was then spontaneously quenched leading to the observed *syn* adduct **3**. A critical difference between the present reaction and the Rh-catalyzed carbozincation reaction reported in the literature[11] is that a range of acyclic or cyclic *N*-carbamate-derived ynamides could be used by conserving the same regioselectivity.

DOI: 10.1021/acs.joc.6b02612
J. Org. Chem. 2017, 82, 1254−1259

Scheme 2. Limitations of the Cobalt-Catalyzed Ynamide Arylzincation



Scheme 3. Proposed Mechanism for Ynamide Co-Catalyzed Carbozincation



In summary, we have developed an original cobalt-catalyzed ynamide carbozincation in the presence of arylzinc derivatives leading mainly to diverse 3-aryl enamides in moderate to good yields with high regio- and stereoselectivity and under mild reaction conditions. The reaction is sensitive to steric and electronic effects thus affording a hydration process while the use of *ortho*-substituted zinc derivatives leads to the formation of oxazolone frameworks present in natural products and/or bioactive compounds.

EXPERIMENTAL SECTION

General Experimental Methods. Acetonitrile and THF were purified with a dry station GT S100 immediately prior to use. The reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation and/or spraying with a solution of potassium permanganate, followed by charring at 150 °C. Flash column chromatography was performed on silica gel 60 (230−400 mesh, 0.040−0.063 mm). ^{1}H and ^{13}C NMR spectra were recorded on a spectrometer at 250 MHz (^{13}C, 62.9 MHz) or 400 MHz (^{13}C, 100 MHz). Chemicals shifts are given in parts per million from tetramethylsilane (TMS) as an internal standard. The following abbreviations are used for the proton spectra multiplicities: s.: singulet, d.: doublet, t.: triplet, m.: multiplet, br.: broad. Coupling constants (*J*) are reported in hertz (Hz). High-resolution accurate mass measurements (HRAM) were performed in positive mode with an ESI source on a Q-TOF mass spectrometer with an accuracy tolerance of 2 ppm by the "Fédération de Recherche" ICOA/CBM (FR2708) platform. All reagents were obtained from commercial suppliers unless otherwise stated.

General Procedure for Carbozincation of Ynamides. *Preparation of the Arylzinc.* To a solution of [$CoBr_2$(phen)] (0.75 mmol, 299 mg, 15 mol %) and Zn dust (15 mmol, 981 mg, 3 equiv) in MeCN (4 mL) were added allylCl (2.25 mmol, 0.20 mL, 0.45 equiv) and TFA (0.75 mmol, 0.06 mL, 15 mol %) under vigorous stirring. This caused a rise in temperature and a change of the color of the mixture from blue to orange and then to dark gray. Once the orange tinge of the mixture had disappeared, ArBr (5 mmol, 1 equiv) was added. The reaction was followed by GC-MS on iodolyzed aliquots. Once all the starting bromide was consumed, stirring was interrupted; the reaction medium was taken in a 10 mL syringe and filtered through a syringe filter. The starting flask was rinsed with MeCN (4 mL), which was filtered in the same manner, providing 8 mL of a cobalt-containing arylzinc bromide solution **2**.

Carbozincation. The solution of arylzinc bromide **2** was cooled to −10 °C and the ynamide **1**[21] (0.33 equiv vs ArZnBr) was added. The reaction was then stirred at −10 °C for 90 min. The reaction medium was diluted with ethyl acetate and filtered on a pad of silica (elution with EtOAc). The solvents were evaporated to afford the crude material, which was purified by flash column chromatography on silica gel using EtOAc/Petroleum Ether (90:10) as the eluent. The regioselectivity was determined on the crude ^{1}H NMR.

*N-Benzyl-4-methoxy-N-[(1E)-2-(4-methoxyphenyl)oct-1-en-1-yl]-benzene-1-sulfonamide (**3aa**).* 615 mg, 78% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) (major regioisomer) δ 7.68 (d, *J* = 7.5 Hz, 2H), 7.31−7.23 (m, 7H), 7.03 (d, *J* = 7.5 Hz, 2H), 6.78 (d, *J* = 10 Hz, 2H), 5.22 (s, 1H), 4.22 (s, 2H), 3.76 (s, 3H), 2.41−2.32 (m, 5H), 1.24−0.98 (m, 6H), 0.82−0.68 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) (major regioisomer) δ 159.2, 149.3, 143.4, 135.8, 131.7, 129.6, 129.3, 128.3, 127.9, 127.7, 121.3, 113.6, 55.2, 55.2, 31.6, 29.8, 29.4, 27.3, 22.5, 21.5, 14.0; HRMS (ESI+): calcd for $C_{29}H_{36}NO_3S^+$ [M + H]$^+$ 478.2410, found 478.2409.

*N-Benzyl-N-[(1Z)-1-(4-methoxyphenyl)oct-1-en-1-yl]-4-methyl-benzene-1-sulfonamide (**4aa**) (not isolated).* ^{1}H NMR (250 MHz, $CDCl_3$) (minor regioisomer) δ 7.81 (d, *J* = 3.75 Hz, 2H), 7.31−7.19 (m, 7H), 6.80−6.77 (m, 2H), 5.82 (d, *J* = 6.25 Hz, 2H), 5.08 (s, 1H), 4.22 (s, 2H), 3.74 (s, 3H), 2.44−2.36 (m, 5H), 1.24−1.03 (m, 6H), 0.92−0.79 (m, 5H).

*Benzyl N-Benzyl-N-[(1E)-2-(4-methoxyphenyl)oct-1-en-1-yl]-carbamate (**3ba**).* 580 mg, 77% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.19 (m, 12H), 6.86 (d, *J* = 8 Hz, 2H), 6.02 (s, 1H), 5.21 (s, 2H), 4.67 (s, 2H), 3.82 (s, 3H), 2.30 (s, 2H), 1.28−1.13 (m, 8H), 0.85 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 132.1, 128.4, 128.4, 127.9, 127.3, 113.6, 67.3, 55.2, 53.3, 31.5, 29.5, 29.4, 27.3, 22.5, 14.0; HRMS (ESI+): calcd for $C_{30}H_{36}NO_3^+$ [M + H]$^+$ 458.2690, found 458.2689.

*Methyl N-Benzyl-N-[(1E)-2-(4-methoxyphenyl)oct-1-en-1-yl]-carbamate (**3ca**).* 503 mg, 80% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.29−7.21 (m, 7H), 6.85−6.84 (m, 2H), 6.00 (br. s, 1H), 4.63 (s, 2H), 3.77 (s, 3H), 3.73 (s, 3H), 2.33−2.28 (m, 2H), 1.21−1.17 (m, 8H), 0.86−0.81 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 158.7, 156.6, 137.6, 132.0, 128.4, 128.2, 127.8, 127.3, 113.7, 55.2, 53.2, 52.9, 31.6, 29.4, 29.4, 27.3, 22.5, 14.0; HRMS (ESI+): calcd for $C_{24}H_{32}NO_3^+$ [M + H]$^+$ 382.2376, found 382.2377.

*3-[(1E)-2-(4-Methoxyphenyl)oct-1-en-1-yl]-1,3-oxazolidin-2-one (**3da**).* 370 mg, 74% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) (major regioisomer) δ 7.25−7.22 (m, 2H), 6.84−6.81 (m, 2H), 6.28 (s, 1H), 4.44−4.38 (m, 2H), 3.93−3.87 (m, 2H), 3.78 (s, 3H), 2.48 (t, *J* = 7.5 Hz, 2H), 1.30−1.21 (m, 8H), 0.86−0.80 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (major regioisomer) δ 158.9, 157.4, 133.2, 132.8, 127.7, 127.3, 127.1, 120.7, 113.7, 62.2, 55.2, 46.5, 31.6, 29.7, 29.4, 28.6, 22.5, 14.0; HRMS (ESI+): calcd for $C_{18}H_{26}NO_3^+$ [M + H]$^+$ 304.1907, found 304.1909.

*3-[(1E)-2-(4-Methoxyphenyl)oct-1-en-1-yl]-1,3-oxazolidin-2-one (**4da**).* ^{1}H NMR (250 MHz, $CDCl_3$) (minor regioisomer) δ 7.02 (d, *J* = 3.75 Hz, 2H), 6.80−6.75 (m, 2H), 5.81 (t, *J* = 7.5 Hz, 1H), 4.36−4.28 (m, 2H), 4.05−3.99 (m, 2H), 3.72 (s, 3H), 2.23 (t, *J* = 6.25 Hz, 2H), 1.23−1.17 (m, 8H), 0.81−0.75 (m, 3H).

DOI: 10.1021/acs.joc.6b02612
J. Org. Chem. 2017, 82, 1254−1259

*(4R)-4-Benzyl-3-[(1E)-2-(4-methoxyphenyl)oct-1-en-1-yl]-1,3-oxazolidin-2-one (**3ea**).* 512 mg, 79% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.31−7.12 (m, 7H), 6.85 (d, J = 10 Hz, 2H), 6.01 (s, 1H), 4.27−4.12 (m, 3H), 3.80 (s, 3H), 3.19−3.12 (m, 1H), 2.75−2.66 (m, 1H), 2.55−2.49 (m, 2H) 1.40−1.12 (m, 8H), 0.86−0.80 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 156.6, 140.1, 135.5, 132.0, 129.1, 128.9, 127.9, 127.2, 118.6, 113.7, 66.6, 59.0, 55.2, 38.6, 31.6, 30.2, 29.6, 27.7, 22.6, 14.0; HRMS (ESI+): calcd for $C_{25}H_{32}NO_3^+$ [M + H]$^+$ 394.2376, found 394.2374.

*Benzyl N-Benzyl-N-[(1E)-2-(3,4-dimethoxyphenyl)oct-1-en-1-yl]-carbamate (**3bb**).* 651 mg, 81% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.30−7.23 (m, 11H), 6.79 (s, 2H), 6.00 (s, 1H), 5.17 (s, 2H), 4.63 (s, 2H), 3.84 (s, 3H), 3.81 (s, 3H), 2.29 (s, 2H), 1.23−1.11 (m, 8H), 0.83−0.77 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.4, 128.4, 128.3, 110.3, 67.3, 55.9, 55.8, 31.5, 30.9, 29.4, 27.3, 22.5, 14.0; HRMS (ESI+): calcd for $C_{31}H_{38}NO_4^+$ [M + H]$^+$ 488.2795, found 488.2798.

*Benzyl N-Benzyl-N-[(1E)-2-(3-methoxyphenyl)oct-1-en-1-yl]-carbamate (**3bc**).* 588 mg, 78% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.31−7.16 (m, 12H), 6.82−6.76 (m, 2H), 6.06 (s, 1H), 5.17 (s, 2H), 4.64 (s, 2H), 3.76 (s, 3H), 2.27 (br.s, 2H), 1.19−1.09 (m, 8H), 0.80 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 141.4, 137.4, 136.6, 129.2, 128.4, 128.4, 127.9, 127.4, 119.4, 112.9, 112.5, 67.4, 55.1, 53.2, 31.5, 29.6, 29.4, 27.2, 22.5, 14.0; HRMS (ESI+): calcd for $C_{30}H_{36}NO_3^+$ [M + H]$^+$ 458.2690, found 458.2693.

*Benzyl N-Benzyl-N-[(1E)-2-(3,4,5-trimethoxyphenyl)oct-1-en-1-yl]carbamate (**3bd**).* 623 mg, 73% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.30−7.23 (m, 10H), 6.38 (s, 2H), 6.02 (s, 1H), 5.17 (s, 2H), 4.64 (s, 2H), 3.81 (s, 3H), 3.79 (s, 6H), 2.25 (s, 2H), 1.20−1.11 (m, 8H), 0.81 (t, J = 6.25 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 152.9, 128.7, 128.4, 128.4, 128.2, 128.1, 127.9, 127.4, 106.2, 105.6, 104.2, 67.5, 60.8, 56.1, 55.9, 31.4, 29.7, 29.4, 27.1, 22.5, 14.0; HRMS (ESI+): calcd for $C_{32}H_{40}NO_5^+$ [M + H]$^+$ 518.2901, found 518.2899.

*Benzyl N-Benzyl-N-[(1E)-2-(4-methylphenyl)oct-1-en-1-yl]-carbamate (**3be**).* 538 mg, 74% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.31−7.09 (m, 14H), 6.01 (s, 1H), 5.16 (s, 2H), 4.63 (s, 2H), 2.31−2.26 (m, 5H), 1.15−1.08 (m, 8H), 0.82−0.77 (t, J = 6.25 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2, 136.7, 129.0, 128.9, 128.4, 128.4, 127.9, 127.7, 127.3, 126.7, 67.3, 53.2, 31.5, 29.4, 29.4, 27.2, 22.5, 21.1, 14.0; HRMS (ESI+): calcd for $C_{30}H_{36}NO_2^+$ [M + H]$^+$ 442.2741, found 442.2740.

*Benzyl N-Benzyl-N-[(1E)-2-phenyloct-1-en-1-yl]carbamate (**3bf**).* 493 mg, 70% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.31−7.23 (m, 15H), 6.06 (s, 1H), 5.18 (s, 2H), 4.65 (s, 2H), 2.29 (s, 2H), 1.18−1.10 (m, 8H), 0.80 (t, J = 6.25 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 137.4, 136.6, 128.4, 128.4, 128.2, 127.9, 127.7, 127.4, 127.4, 126.9, 67.4, 53.2, 31.5, 29.5, 29.4, 27.2, 22.5, 14.0; HRMS (ESI+): calcd for $C_{29}H_{34}NO_2^+$ [M + H]$^+$ 428.2584, found 428.2585.

*Benzyl N-Benzyl-N-[(1E)-2-[4-(trifluoromethyl)phenyl]oct-1-en-1-yl]carbamate (**3bg**).* 564 mg, 69% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.52 (d, J = 10 Hz, 2H), 7.30−7.23 (m, 12H), 6.10 (s, 1H), 5.17 (s, 2H), 4.65 (s, 2H), 2.30 (s, 2H), 1.24−1.07 (m, 8H), 0.84−0.77 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.8, 128.5, 128.4, 128.0, 127.5, 127.1, 126.6 (q, $^1J_{C-F}$ = 258 Hz), 67.6, 53.1, 31.4, 29.5, 29.3, 27.1, 22.5, 14.0; HRMS (ESI+): calcd for $C_{30}H_{33}F_3NO_2^+$ [M + H]$^+$ 496.2458, found 496.2457.

*Benzyl N-Benzyl-N-[(1E)-2-(4-cyanophenyl)oct-1-en-1-yl]-carbamate (**3bh**).* 440 mg, 59% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.55 (d, J = 7.5 Hz, 2H), 7.30−7.23 (m, 12H), 6.14 (s, 1H), 5.18 (s, 2H), 4.66 (s, 2H), 2.31 (s, 2H), 1.24−1.08 (m, 8H), 0.80 (t, J = 6.25 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 132.1, 128.5, 128.5, 128.1, 127.9, 127.6, 127.4, 118.8, 110.9, 67.7, 53.1, 31.4, 29.7, 29.3, 27.1, 22.5, 14.0; HRMS (ESI+): calcd for $C_{30}H_{33}N_2O_2^+$ [M + H]$^+$ 453.2536, found 453.2533.

*Methyl 4-[(1E)-1-{Benzyl[(benzyloxy)carbonyl]amino}oct-1-en-2-yl]benzoate (**3bi**).* Isolated as a mixture in the presence of the dimeric biaryl compound in a 47/53 ratio. 376 mg, 47% yield (determined by ^{1}H NMR of the mixture), colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.94 (d, J = 7.5 Hz, 2H), 7.30−7.23 (m, 12H), 6.13 (s, 1H), 5.17 (s, 2H), 4.65 (s, 2H), 3.88 (s, 3H), 2.32 (s, 2H), 1.14−1.07 (m, 8H), 0.79 (t, J = 6.25 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 136.5, 135.7, 131.4, 130.2, 129.8, 129.6, 129.3, 128.5, 127.9, 127.5, 127.2, 126.8, 126.4, 123.0, 67.5, 52,4. 52.0, 31.6, 31.4, 29.7, 28.9, 22.5, 14.0; HRMS (ESI+): calcd for $C_{31}H_{36}NO_4^+$ [M + H]$^+$ 486.2639, found 486.2637.

*Benzyl N-Benzyl-N-[(1E)-2-(3-cyanophenyl)oct-1-en-1-yl]-carbamate (**3bj**).* 410 mg, 55% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.39−7.53 (m, 3H), 7.31−7.23 (m, 11H), 6.07 (s, 1H), 5.18 (s, 2H), 4.65 (s, 2H), 2.27 (s, 2H), 1.23−1.02 (m, 8H), 0.80 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 137.1, 130.4, 129.1, 128.5, 128.4, 128.1, 127.9, 127.6, 118.7, 112.5, 67.7, 53.0, 31.4, 29.4, 29.2, 27.1, 22.5, 13.9; HRMS (ESI$^+$): calcd for $C_{30}H_{33}N_2O_2^+$ [M + H]$^+$ 453.2537, found 453.2536.

*N-Benzyl-N-(4-methylbenzenesulfonyl)-2-phenylacetamide (**5**).*[16c] 381 mg, 61% yield, colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.64 (d, J = 7.5 Hz, 2H), 7.36−7.22 (m, 10H), 7.01−6.97 (m, 2H), 5.07 (s, 2H), 3.87 (s, 2H), 2.41 (s, 3H).

*3-Benzyl-5-hexyl-2,3-dihydro-1,3-oxazol-2-one (**6**).* 329 mg, 77% yield, white gum. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.35−7.23 (m, 5H), 5.99 (s, 1H), 4.66 (s, 2H), 2.33 (t, J = 8.75 Hz, 2H), 1.47−1.53 (m, 2H), 1.24−1.31 (m, 6H), 0.85 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 141.2, 135.6, 128.9, 128.2, 127.9, 109.0, 47.5, 31.3, 28.5, 26.4, 25.9, 22.4, 14.0; HRMS (ESI$^+$): calcd for $C_{16}H_{21}NO_2^+$ [M + H]$^+$ 260.1645, found 260.1648.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02612.

^{1}H and ^{13}NMR spectra for new compounds (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work has been partially supported by Université d'Orléans, CNRS, and LABEX SynOrg (ANR-11-LABX-0029) and Ecole polytechnique. R.S. thanks LABEX SynOrg for a postdoctoral fellowship. L.H. thanks the Region Centre Val de Loire, and M.C. thanks Ecole Polytechnique for a doctoral fellowship. The authors thank LABEX CHARMMMAT (ANR-11-LABX-0039) for support.

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