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Pd/Cu-Catalyzed Tandem Head-to-Tail Dimerization/ Cycloisomerization of Terminal Ynamides for the Synthesis of 5-Vinyloxazolones

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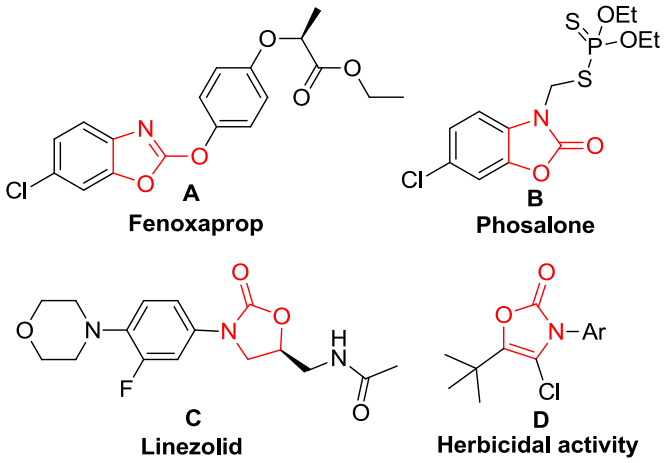
An attractive and novel methodology involving Pd/Cu-catalyzed tandem head-to-tail dimerization/cycloisomerization of terminal ynamides for the synthesis of 3,5-disubstituted oxazolones was developed. Under $Pd(PPh_3)_2Cl_2$/CuI cooperative catalyzed reaction conditions, it provided an efficient access to 5-vinyloxazolones with exceptional functional group tolerance and good chemoselectivity. The control experiments demonstrated that $Pd(PPh_3)_2Cl_2$ serves a key role in dimerization of terminal ynamides and shows low catalytic activity in the intramolecular cyclization. Moreover, hetero-Diels–Alder reaction of product 5-vinyloxazolones was also described, which provide the polycyclic oxazolones in good yield.

Introduction

Concurrent tandem catalysis (CTC),[1] which involves the cooperative action of two or more catalytic cycles in a single reactor without isolation and purification between steps,[2] has emerged as conceptually appealing transformations in organic synthesis. Obviously, there are two major benefits in CTC: 1) saving time by operating simultaneously, 2) reducing yield losses without purification of intermediates. However, each catalyst must be compatible with substrates, intermediates and other catalysts, as while as exhibit reaction sequence selectivity.[3] Therefore, designing and developing efficient CTC is of great necessity and yet remains a great challenge.

Oxazolone and its derivatives have received significant attention in recent years owing to their both biological properties and pharmaceutical applications (Scheme 1). They are widely used in medicine and pesticide as fenoxaprop (**A**),[4] phosalone (**B**)[5] and linezolid (**C**).[6] In addition, Noriaki Kudo reported that 4-halo-oxazolones (**D**) also show a wide range of herbicidal activity from broadleaf to narrowleaf weeds.[7] Therefore, the development of methods for the synthesis of different substituted oxazolones is important and currently attracting growing interest.



Scheme 1. Biologically Active and Pharmaceutically Important Oxazolone Derivatives.

During the past decade, tremendous efforts have been devoted to the development of versatile methods for constructing the multisubstituted oxazolones,[8] among which, the cycloisomerization of *N*-alkynyl *tert*-butyloxycarbamates was considered as a rapid and straightforward method to synthesize oxazolones. For instance, Gagosz's group[9] first reported Au-catalyzed cycloisomerization of ynamides in 2008, which provided an efficient and rapid process for the synthesis of 3,5-disubstituted oxazolones. Subsequently, many different types of metal catalysts such as palladium and copper had also been developed for the cycloisomerization of *N*-alkynyl *tert*-butyloxycarbamates (**Scheme 2**, a).[10] Recently, our group reported a novel method for the construction of 4-halo-oxazolones by the halopalladation type reaction.[11] Inspired by these excellent works and our interest in the exploration of the reactivity of ynamides,[12] we put further attention in the cycloisomerization of terminal ynamides. Although Yamamoto and Hsung's group reported their independent findings that head-to-tail dimerization of terminal

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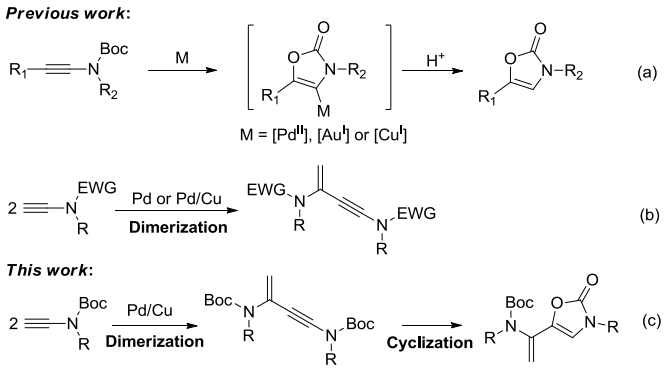
ynamides would generate en-ynamides based on totally different reaction conditions (**Scheme 2**, b),[13] we were still interested in exploring the activity of terminal ynamides containing nucleophilic group (e.g. Boc).[11, 14] What's more, no any proposed mechanism of the dimerization of terminal ynamides has been given. To the best of our knowledge, this is the first Pd/Cu-catalyzed tandem head-to-tail dimerization / cycloisomerization of terminal ynamides for synthesis of 5-vinyl-oxazolones based on CTC (**Scheme 2**, c).

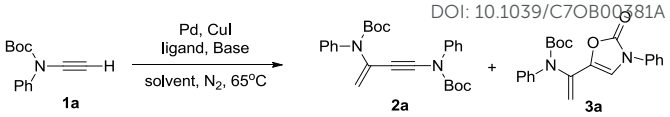


Scheme 2. Metal-catalyzed Cyclization of the *N*-Alkynyl alkyloxycarbamates.

Results and discussion

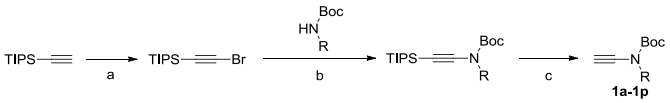
Initially, we investigated the cycloisomerization of *tert*-butyl ethynyl (phenyl)carbamate **1a** which was treated with 10 mol% of CuI, 5.0 mol% of $PdCl_2$, and 2.0 equiv of Et_3N in THF using P(2-$MeC_6H_4)_3$ as ligand. It was found that an unexpected *tert*-butyl (1-(2-oxo-3-phenyl-2,3-dihydrooxazol-5-yl)vinyl)(phenyl)-carbamate **3a** was obtained in 15% yield after 18 h (**Table 1**, entry 1). Then, different palladium catalysts, as $Pd(OAc)_2$, $Pd_2(dba)_3$, $Pd(PPh_3)_2Cl_2$, $Pd(PPh_3)_4$, were applied in this transformation. Among them, $Pd(PPh_3)_2Cl_2$ gave the best performance that product **3a** was obtained in 56% yield (**Table 1**, entries 2-4). It is worth mentioning that only head-to-tail dimerization product **2a** was obtained by using $Pd(PPh_3)_4$ as catalyst (**Table 1**, entry 5). The structure of **2a** was further confirmed by using single-crystal X-ray structure analysis (see **Figure 1**, 2a).[15] To further optimize the reaction, different ligands were examined and results demonstrated that ligands also had great effect on this reaction. For example, en-ynamide **2a** was obtained by utilizing DPEPhos and RuPhos as ligands (**Table 1**, entries 6-7). In contrast, only 5-vinyloxazolone **3a** could be obtained when PPh_3, $P(Cy)_3$, LB·Phos·HBF[16] and P(*t*-Bu)$_3$ were applied as ligand (**Table 1**, entries 8-11). Next, different bases were also examined in which DIPEA showed the best performance to give corresponding product **3a** in 62% yield (**Table 1**, entries 12-14). The less amount of corresponding product **3a** was provided in the absence of bases or ligands (**Table 1**, entries 15-16). Among the solvents screened, THF was superior to toluene and 1,4-dioxane (**Table 1**, entries 17-18). A blank experiment indicated that **1a** could produce **2a** in 36% yield and **3a** only in 11% yield without CuI loading (**Table 1**, entry 19). What's more, it could not generate the product **2a** or desired product **3a** in absence of Pd-catalyst (**Table 1**, entry 20).

Table 1. Optimization of Reaction Conditions.[a]



entry	Pd	base	ligand	**2a**/**3a** yield (%)
1	$PdCl_2$	Et_3N	P(2-$MeC_6H_4)_3$	--/15
2	$Pd(OAc)_2$	Et_3N	P(2-$MeC_6H_4)_3$	NR
3	$Pd_2(dba)_3$	Et_3N	P(2-$MeC_6H_4)_3$	--/23
4	$Pd(PPh_3)_2Cl_2$	Et_3N	P(2-$MeC_6H_4)_3$	--/56
5	$Pd(PPh_3)_4$	Et_3N	P(2-$MeC_6H_4)_3$	63/--
6	$Pd(PPh_3)_2Cl_2$	Et_3N	DPEPhos	41/25
7	$Pd(PPh_3)_2Cl_2$	Et_3N	RuPhos	46/24
8	$Pd(PPh_3)_2Cl_2$	Et_3N	PPh_3	--/40
9	$Pd(PPh_3)_2Cl_2$	Et_3N	$P(Cy)_3$	--/59
10	$Pd(PPh_3)_2Cl_2$	Et_3N	LB•Phos•HBF_4	--/38
11	$Pd(PPh_3)_2Cl_2$	Et_3N	P(*t*-Bu)$_3$	--/53
12	$Pd(PPh_3)_2Cl_2$	DIPEA	$P(Cy)_3$	--/62
13	$Pd(PPh_3)_2Cl_2$	DBU	$P(Cy)_3$	43/--
14	$Pd(PPh_3)_2Cl_2$	Py	$P(Cy)_3$	26/26
15	$Pd(PPh_3)_2Cl_2$	--	$P(Cy)_3$	--/14
16	$Pd(PPh_3)_2Cl_2$	DIPEA	--	25/19
17[b]	$Pd(PPh_3)_2Cl_2$	DIPEA	$P(Cy)_3$	--/50
18[c]	$Pd(PPh_3)_2Cl_2$	DIPEA	$P(Cy)_3$	--/41
19	--	DIPEA	$P(Cy)_3$	36/11
20[d]	$Pd(PPh_3)_2Cl_2$	DIPEA	$P(Cy)_3$	--/--

[a] The reaction was carried out with **1a** (0.3 mmol), Pd catalysts (5.0 mol%), bases (2.0 equiv), ligands (10 mol%) and CuI (10 mol%) in THF (2.0 mL) under N_2 atmosphere for 18 h; NR = No Reaction; [b] toluene was used as solvent; [c] 1,4-dioxane was used as solvent; [d] reaction was carried without CuI loading.

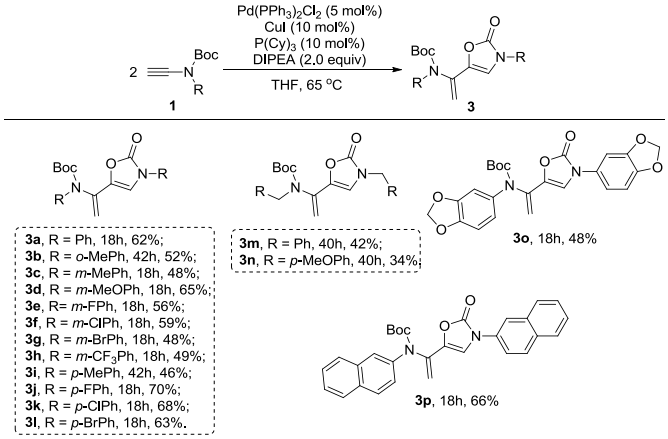


Scheme 3. Synthesis of Terminal Ynamides. a) NBS (1.25 equiv), $AgNO_3$ (5.0 mol%), acetone, rt; b) $CuSO_4·5H_2O$ (5.0 mol%), 1,10-Phen (10 mol%), K_3PO_4 (2.0 equiv), toluene, 85 °C; c) TBAF (1.1 equiv), THF, 0 °C-rt.

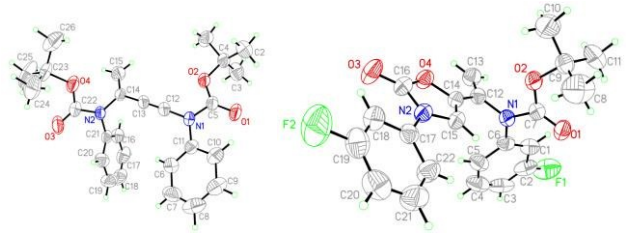
We first synthesized several terminal yanmides **1a**-**1p** to further examine the flexibility of this transition according to the previously reported methodology (Scheme 3).[12a, 17] Next, we tested the reactivity of those terminal ynamides **1a**-**1p** above in this transformation under the optimized reaction conditions (**Table 2**). First of all, methyl on the *ortho*-position of *N*-aryl ring was tolerated and produced the corresponding oxazolones **3b** in 52% yield after 42 h (**Table 2**, 3b). Next, ynamides with electron-donating groups, such as Me and MeO on the *meta*-position of *N*-aryl ring, gave the corresponding products in 48-65% yields (**Table 2**, 3c-3d). In addition, ynamides with electron-withdrawing groups on the *meta*-position of the *N*-aryl ring, such as F, Cl, Br, and CF_3, were also tolerated and generated the corresponding 5-vinyloxazolones in 48-59% yields (**Table 2**, 3e-3h). In general, ynamides bearing electron-withdrawing groups gave lower yields than those bearing electron-donating groups on the *meta*-position. The structure of **3e** was

further confirmed by using single-crystal X-ray structure analysis (see **Figure 1**, 3e).[15] Meanwhile, groups on the *para*-position of the *N*-aryl ring were also tested, the yields of the desired products were in 46%-70% yields. And the *para*-effect demonstrated that electron-withdrawing groups gave higher yields (**Table 2**, 3i-3l). Furthermore, ynamides with *N*-benzyl also successfully produced the desired 5-vinyloxazolones in acceptable yields (**Table 2**, 3m-3n). Finally, substrates possessing benzo[*d*][1,3]dioxol-5-yl and 2-naphthyl groups on N atom supplied the products in 48-66% yields (**Table 2**, 3o-3p).

Table 2. Pd/Cu-Catalyzed Formation of 5-Vinyloxazolones.[a]



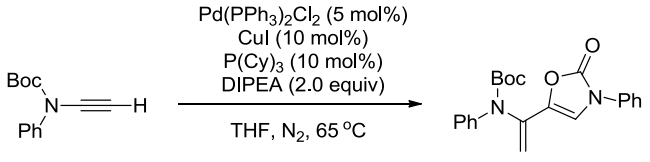
[a] Reaction conditions: **1a**-**1p** (0.3 mmol), $Pd(PPh_3)_2Cl_2$ (5.0 mol %), CuI (10 mol%), $P(Cy)_3$ (10 mol%), DIPEA (2.0 equiv) in THF (2.0 mL) at 65 °C.



2a **3e**

Figure 1. Single-crystal X-ray Structure of 2a and 3e.

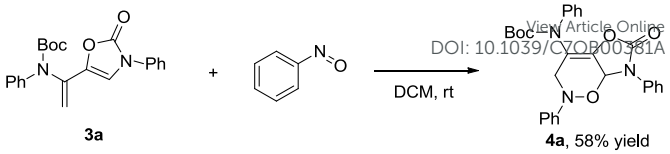
To demonstrate the synthetic potential of this strategy, **1a** (1.05 g, 5.0 mmol) was allowed to react under the optimized conditions. This reaction could be scaled up to 5.0 mmol with comparable efficiency in a moderate yield, illustrating its potential industrial applications in the future (**Scheme 4**).



1a (5.0 mmol, 1.05 g) **3a** (0.56 g, 61% yield)

Scheme 4. Scale-up Experiment.

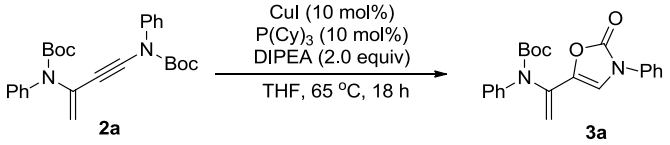
The Diels-Alder reaction of 5-vinyl-oxazolones **3a** with nitrosobenzene was next investigated, which could provide the corresponding polycyclic product **4a** in 58% yield with high regioselecttivity under the mild conditions (**Scheme 5**).



Scheme 5. Diels-Alder Reaction of 5-Vinyloxazolones.

As we confirmed, this tandem reaction would lose efficiency whatever in absence of Pd(II) or CuI (**Table 1**, entries 19-20). To further understand the mechanism of this reaction, control experiments were conducted for the cycloisomerization of en-ynamide **2a** (**Table 3**). Although Zhu's group reported that cycloisomerization of *N*-alkynyl *tert*-butyloxycarbamates could provide oxazolones efficiently only rely on simplex copper salts or palladium salts,[10b-10c] we still wanted to figure out what is essential in the second step of this tandem reaction. The final product **3a** was generated in 74% yield by utilizing CuI as catalyst in presence of ligand and base (**Table 3**, entry 1). However, next control experiment using $Pd(PPh_3)_2Cl_2$ as catalyst for the cycloisomerization of en-ynamide **2a** were carried out, which only afforded **3a** in 38% yield (**Table 3**, entry 2). These results suggested that the second step cycloisomerization was primarily promoted by CuI. What's more, it is demonstrated that both of ligand and base also have an important effect on the second cycloisomerization (**Table 3**, entries 3-4).

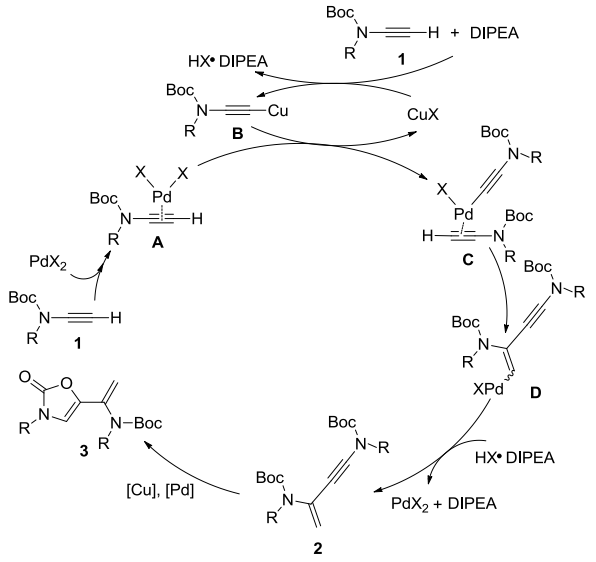
Table 3. **Control Experiments for the Cyclization of 2a**.[a]



entry	deviation from standard conditions	yield (%)
1	none	74
2	$PdCl_2(PPh_3)_2$ (5 mol%) instead of CuI (10 mol%)	38
3	without $P(Cy)_3$	21
4	without $P(Cy)_3$, DIPEA	24

[a] Reaction conditions: **2a** (0.3 mmol), CuI (10 mol%), $P(Cy)_3$ (10 mol%), DIPEA (2.0 equiv) in THF (2.0 mL) at 65 °C for 18h.

Based on the experimental results and the reported literature, a proposed mechanism for this Pd/Cu-catalyzed tandem head-to-tail dimerization/cycloisomerization of terminal ynamides is shown in **Scheme 6**. The activation of the triple bond in terminal ynamides **1** with Pd(II) produces the intermediate **A**.[18] At the same time, copper acetylide **B** is generated from a second molecule of terminal ynamide **1** with CuX in the presence of DIPEA. Then, Intermediate **A** undergos a transmetallation with copper acetylide **B** leading to the alkynyl palladium complex **C**, which provides *σ*-vinylpalladium intermediate **D** *via* a followed carbometalation.[19] The following protonation of intermediate **D** gives the dimerization product **2** and regenerates Pd(II) species.[19b] Finally, the corresponding 5-vinyl-oxazolones **3** are produced mainly by CuI-catalyzed cycloisomerization of en-ynamides **2**.[10a-10c]



Scheme 6. Proposed Mechanism for This Transformation.

Conclusions

In summary, we have developed a one-pot procedure for synthesis of 5-vinyloxazolones from readily available terminal ynamides by Pd/Cu-catalyzed tandem head-to-tail dimerization/ cycloisomerization. This method not only comprehensively reported the cyclization of terminal ynamides to oxazolones for the first time, but also tolerated a wide range of functional groups on the ynamide components under Pd/Cu cooperative conditions. The application of this protocol toward the synthesis of polycyclic oxazolones based on Diels-Alder reaction was also demonstrated. Further studies to find more efficient metal-catalyzed functionalization of ynamides for the synthesis of significant heterocyclic compounds are underway.

Acknowledgements

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Experimental

General Methods

All reactions were performed in reaction tubes under nitrogen atmosphere. ^{1}H NMR and ^{13}C NMR were recorded at, respectively, 400 and 100 MHz using $CDCl_3$ as solvent. The following abbreviations are used to describe peak patterns where appropriate: b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets. Coupling constants are reported in hertz (Hz). Chemical shifts are reported in ppm relative to the internal standard tetramethylsilane (δ = 0 ppm) for ^{1}HNMR and deuteriochloroform (δ = 77.00 ppm) for ^{13}C NMR. High-resolution mass spectra (HRMS) were recorded on an ESI-TOF (time-of-flight) mass spectrometer. Melting points were measured with a micro melting point apparatus.

Preparation of terminal ynamides

Procedure A: 1-bromo-2-triisopropylsilylacetylene was prepared according to Hofmeister's procedure.[20] A solution of ethynyltriisopropylsilane (50 mmol) in acetone (60 mL) is treated at rt with N-bromosuccinimide (NBS, 55 mmol) and $AgNO_3$ (2.5 mmol). After 2h, the reaction mixture is concentrated in vacuum. The crude products were purified by silica gel flash chromatography on a silica gel column with petroleum ether (PE) as eluent to afford the 1-bromo-2-triisopropylsilylacetylene.

Procedure B: TIPS-substituted ynamides were prepared according to a modified version of Hsung's procedure.[21] To a stirred solution of the appropriate amide (1.0 equiv, 1.0 M in toluene) were added K_3PO_4 (2.0 equiv), $CuSO_4$•$5H_2O$ (10 mol%), 1,10-phenanthroline (20 mol%) and 1-bromo-2-triisopropylsilylacetylene (1.25 equiv). The reaction was capped under a blanket of nitrogen and heated at 85 ^oC for 48 h while monitored with TLC analysis. Upon completion, the reaction mixture was cooled to room temperature and diluted with EtOAc and filtered through celite, and the filtrate was concentrated in vacuum. The crude products were purified by silica gel flash chromatography on a silica gel column with petroleum ether (PE) and ethyl acetate (EA) as eluent to afford directing products.

Procedure C: Terminal ynamides **1a**-**1p** were prepared by the modified version of Oestreich's procedure.[17] To a stirred solution of the appropriate TIPS-substituted ynamide (1.0 equiv, 0.2 M in THF) cooled to 0 °C was added a solution of TBAF (1.2 equiv, 1.0 M in THF). After 1h stirring at 0 °C, the reaction was allowed to warm to room temperature and then quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with Et_2O (x 3). The combined organics were washed with brine (x 2), dried (Na_2SO_4), filtered and the solvents were evaporated under reduced pressure to afford the crude product **1a**-**1p**.

***tert*-butyl ethynyl(4-fluorophenyl)carbamate (1j)**: Yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 60:1); 1H NMR (400 Hz, $CDCl_3$) δ 7.43-7.40 (m, 2 H), 7.08-7.03 (m, 2 H), 2.87(s, 1 H), 1.53 (s, 9 H); 13C NMR (100 Hz, $CDCl_3$) δ 161.1 (d, J = 244.6 Hz), 153.1 (d, J = 2.6 Hz), 126.7 (d, J = 8.8 Hz), 115.7 (d, J = 22.8 Hz), 83.9, 58.3, 27.9; HRMS (ESI) exact mass calcd for $C_{13}H_{14}FNO_2$ [M + Na]+ m/z 258.0906, found 258.0916.

General Procedure for 5-vinyloxazolones

Terminal ynamides **1** (0.3 mmol), $Pd(PPh_3)_2Cl_2$ (0.015 mmol), CuI (0.03 mmol), $P(Cy)_3$ (0.03 mol), DIPEA (0.6 mmol), and THF (2.0 mL) were placed into a 10 mL Schlenk tube, and then the temperature was heated to 65 °C. The solution was stirred under an N_2 atmosphere for 18-45 h and monitored by TLC. After being cooled to room temperature, the reaction mixture was quenched with ethyl acetate (15 mL) and washed with water (30 mL). The aqueous phase was extracted twice with EtOAc (3 × 10 mL), and the combined organic layer was dried over anhydrous Na_2SO_4. After evaporation of the solvents under vacuum, the crude products were purified by flash chromatography on a silica gel column with petroleum ether (PE) and ethyl acetate (EA) as the eluent to afford the desired product.

***di-tert*-Butyl but-3-en-1-yne-1,3-diylbis(phenylcarbamate) (2a)**: yield 63% (42.9 mg); yellow solid; mp 89-90 ^oC (*n*-hexane/ethyl acetate); R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.34-7.27 (m, 8 H), 7.23-7.17 (m, 2 H), 5.40 (s, 1 H), 5.32 (s,

1 H), 1.52 (s, 9 H), 1.43 (s, 9H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 153.0, 152.5, 141.8, 139.1, 130.0, 128.7, 128.6, 128.5, 126.6, 126.5, 126.0, 124.3, 117.1, 83.6, 82.8, 81.2, 68.3, 28.1, 27.9; IR *v* (KBr, cm^{-1}) 2975, 2927, 2852, 2241, 1716, 1595, 1495, 1368, 1301, 1250, 1152, 757, 691; HRMS (ESI) exact mass calcd for $C_{26}H_{30}N_2O_6$ $[M + Na]^+$ m/z 457.2103, found 457.2107.

***tert*-Butyl (1-(2-oxo-3-phenyl-2,3-dihydrooxazol-5-yl)vinyl) (phenyl)carbamate (3a)**: yield 62% (34.9 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.49 (d, *J* = 7.6 Hz, 2 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.39-7.26 (m, 5 H), 7.21-7.14 (m, 1 H), 6.77 (s, 1 H), 5.79 (s, 1 H), 5.31 (s, 1 H), 1.48 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 153.2, 152.0, 141.3, 137.8, 135.1, 134.6, 129.5, 128.9, 126.8, 125.8, 124.7, 121.0, 114.0, 111.1, 82.0, 28.1; IR *v* (KBr, cm^{-1}) 3139, 2986, 2927, 1779, 1698, 1594, 1494, 1358, 1163, 1065, 758, 670; HRMS (ESI) exact mass calcd for $C_{22}H_{22}N_2O_4$ $[M + Na]^+$ m/z 401.1477, found 401.1502.

***tert*-Butyl (1-(2-oxo-3-(o-tolyl)-2,3-dihydrooxazol-5-yl)vinyl) (o-tolyl)carbamate (3b)**: yield 52% (63.5 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.34-7.18 (m, 8 H), 6.62 (s, 1 H), 5.50 (s, 1 H), 4.99 (d, *J* = 0.8 Hz, 1 H), 2.32 (s, 3 H), 2.30 (s, 3 H), 1.44 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 153.0, 152.7, 140.8, 137.9, 135.6, 135.3, 135.0, 133.6, 131.5, 131.1, 129.2, 127.4, 127.1, 127.0, 126.7, 113.4, 110.1, 81.5, 28.1, 18.1, 17.8; IR *v* (KBr, cm^{-1}) 3112, 2978, 2929, 1780, 1679, 1614, 1498, 1598, 1453, 1367, 1227, 1159, 753; HRMS (ESI) exact mass calcd for $C_{24}H_{26}N_2O_4$ $[M + Na]^+$ m/z 429.1790, found 429.1787.

***tert*-butyl (1-(2-oxo-3-(m-tolyl)-2,3-dihydrooxazol-5-yl)vinyl) (m-tolyl)carbamate (3c)**: yield 48% (59.7 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ7.33-7.15 (m, 6 H), 7.10 (d, J = 7.6 Hz, 1 H), 7.00 (d, *J* = 7.2 Hz, 1 H), 5.76 (s, 1 H), 5.28 (s, 1 H), 2.38 (s, 3 H), 2.34 (s, 3 H), 1.48 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 153.3, 152.2, 141.3, 139.7, 138.8, 137.9, 135.2, 134.9, 129.3, 128.6, 127.6, 126.7, 125.3, 121.9, 121.7, 118.1, 113.7, 111.3, 81.8, 28.2, 21.5, 21.4; IR *v* (KBr, cm^{-1}) 2976, 2924, 2853, 1771, 1714, 1607, 1493, 1368, 1324, 1159, 866, 779, 691; HRMS (ESI) exact mass calcd for $C_{24}H_{26}N_2O_4$ $[M + Na]^+$ m/z 429.1790, found 429.1829.

***tert*-Butyl(3-methoxyphenyl)(1-(3-(3-methoxyphenyl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3d)**: yield 65% (88.4 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.32 (t, *J* = 8.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1 H), 7.13 (t, *J* = 2.0 Hz, 1 H), 7.01 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1 H), 6.96 (dd, J_1 =1.6 Hz, J_2 = 7.6 Hz, 1 H), 6.93 (t, *J* = 1.6 Hz, 1 H), 6.82 (dd, J_1 = 2.4 Hz, J_2 =8.4 Hz, 1 H), 6.76 (s, 1 H), 6.73 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1 H), 5.78 (s, 1 H), 5.30 (s, 1 H), 3.81 (d, *J* = 11.2 Hz, 6 H), 1.48 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 160.3, 159.9, 153.1, 151.9, 142.4, 137.7, 136.2, 134.6, 130.2, 129.4, 117.0, 114.0, 112.8, 112.3, 111.1, 110.9, 110.8, 107.0, 81.9, 55.5, 55.3, 28.1; IR *v* (KBr, cm^{-1}) 2975, 2933, 2837, 1770, 1715, 1603, 1495, 1456, 1368, 1320, 1164, 1046, 771, 705; HRMS (ESI) exact mass calcd for $C_{24}H_{26}N_2O_6$ $[M + Na]^+$ m/z 461.1689, found 461.1720.

***tert*-Butyl (3-fluorophenyl)(1-(3-(3-fluorophenyl)-2-oxo-2,3-dihydrooxazol-5-yl) vinyl)carbamate (3e)**: yield 56% (69.5 mg); yellow solid, mp 145-146 °C (*n*-hexane/ethyl acetate); R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.40 (dd, J_1 =2.0 Hz, J_2 = 8.0 Hz, 1 H), 7.36 (td, J_1 =2.0 Hz, J_2 = 10.0 Hz, 1 H), 7.32 -7.24 (m, 2 H), 7.16 (d, *J* = 7.6 Hz, 2 H), 6.99 (dt, J_1 = 2.4 Hz, J_2 = 8.0 Hz,1 H), 6.89 (dt, J_1 = 1.6 Hz, J_2 = 6.8 Hz, 1 H), 6.75 (s, 1 H), 5.84 (s, 1 H), 5.34 (s, 1 H), 1.49 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 163.0 (d, *J* = 246.7 Hz), 162.7 (d, *J* = 244.3 Hz), 152.8, 151.6, 142.7 (d, *J* = 9.3 Hz), 137.8, 136.4 (d, *J* = 9.8 Hz), 134.1, 130.8 (d, *J* = 8.9 Hz), 129.9 (d, *J* = 9.0 Hz), 119.6 (d, *J* = 2.8 Hz), 115.9 (d, *J* = 3.5 Hz), 115.0, 113.7 (d, *J* = 20.8 Hz), 112.6 (d, *J* = 21.4 Hz), 111.7 (d, *J* = 24.5 Hz), 110.5, 108.4 (d, *J* = 25.3 Hz), 82.6, 28.1; IR *v* (KBr, cm^{-1}) 3136, 3005, 2981, 1775, 1709, 1614, 1591, 1498, 1371, 1335, 1223, 1169, 780, 711; HRMS (ESI) exact mass calcd for $C_{22}H_{20}F_2N_2O_4$ $[M + Na]^+$ m/z 437.1289, found 437.1319.

***tert*-Butyl(3-chlorophenyl)(1-(3-(3-chlorophenyl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3f)**: yield 59% (79.6 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.56 (t, *J* = 2.0 Hz, 1 H), 7.42-7.38 (m, 2 H), 7.35 (d, *J* = 8.0 Hz, 1 H), 7.29-7.25 (m, 3 H), 7.19-7.13 (m, 1 H), 6.75 (s, 1 H), 5.83 (s, 1 H), 5.33 (d, J = 0.8 Hz, 1 H), 1.48 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 152.7, 151.6, 142.3, 137.9, 136.1, 135.3, 134.4, 134.1, 130.5, 129.8, 127.0, 125.8, 124.4, 122.4, 121.0, 118.7, 115.0, 110.5, 82.6, 28.1; IR *v* (KBr, cm^{-1}) 3127, 2978, 2928, 2835, 1779, 1731, 1594, 1484, 1368, 1232, 1157, 777, 681; HRMS (ESI) exact mass calcd for $C_{22}H_{20}Cl_2N_2O_4$ $[M + K]^+$ m/z 485.0437, found 485.0857.

***tert*-Butyl(3-bromophenyl)(1-(3-(3-bromophenyl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3g)**: yield 48% (76.7 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.70 (t, *J* = 1.6 Hz, 1 H), 7.56 (t, *J* = 1.6 Hz, 1 H), 7.47-7.40 (m, 2 H), 7.31 (d, *J* = 8.4 Hz, 3 H), 7.20 (t, *J* = 7.6 Hz, 1 H), 6.75 (s, 1 H), 5.83 (s, 1 H), 5.33 (s, 1 H), 1.48 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 152.7, 151.5, 142.5, 137.8, 136.2, 134.1, 130.7, 130.0, 129.9, 128.8, 127.3, 123.8, 123.0, 122.9, 122.3, 119.3, 115.0, 110.5, 82.6, 28.1; IR *v* (KBr, cm^{-1}) 3128, 2977, 2928, 1769, 1730, 1588, 1517, 1481, 1369, 1232, 1156, 871, 776, 679; HRMS (ESI) exact mass calcd for $C_{22}H_{20}Br_2N_2O_4$ $[M + Na]^+$ m/z 556.9688, found 556.9712.

***tert*-Butyl(1-(2-oxo-3-(3-(trifluoromethyl)phenyl)-2,3-dihydrooxazol-5-yl)vinyl)(3-(trifluoromethyl)phenyl) carbamate (3h)**: yield 48% (76.7 mg); yellow solid; mp 121-122 °C (*n*-hexane/ethyl acetate); R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.77 (s, 1 H), 7.74 (dt, J_1 = 2.0 Hz, J_2 = 3.6 Hz, 1 H), 7.67 (s, 1 H), 7.60-7.54 (m, 3 H), 7.49-7.44 (m, 2 H), 6.81 (s, 1 H), 5.88 (s, 1 H), 5.36 (s, 1 H), 1.49 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 152.7, 151.6, 141.8, 138.0, 135.6, 134.1, 132.2 (d, *J* = 32.6 Hz), 131.4 (d, *J* = 32.4 Hz), 130.3, 129.5, 127.3, 125.0 123.9, 123.45 (m), 123.4 (d, *J* = 271.6 Hz), 122.3 (m), 121.2 (d, *J* = 4.8 Hz), 117.6 (q, *J* = 4.0 Hz), 115.4, 110.4, 82.9, 28.1; IR *v* (KBr, cm^{-1}) 3148, 2980, 1794, 1710, 1593, 1496, 1465, 1332, 1255, 1120, 792, 696; HRMS (ESI) exact mass calcd for $C_{24}H_{20}F_6N_2O_4$ $[M + Na]^+$ m/z 537.1225, found 537.1259.

***tert*-Butyl (1-(2-oxo-3-(p-tolyl)-2,3-dihydrooxazol-5-yl)vinyl) (p-tolyl)carbamate (3i)**: yield 46% (56.4 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (100 Hz, $CDCl_3$) δ 7.36 (d, *J* = 8.4 Hz, 3 H), 7.24-7.20 (m, 4 H), 7.12 (d, *J* = 8.0 Hz, 3 H), 6.73 (s, 1 H), 5.75 (s, 1 H), 5.28 (s, 1 H), 2.36 (s, 3 H), 2.32 (s, 3 H), 1.47 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 153.4, 152.2, 138.8, 137.7, 136.8, 135.7, 134.9, 132.7, 130.0, 129.4, 124.7, 121.0, 113.5, 111.4, 81.7, 28.2, 20.9, 20.8; IR *v* (KBr, cm^{-1}) 2976, 2925, 1765, 1713, 1613, 1514, 1367, 1253, 1161, 816; HRMS (ESI) exact mass calcd for $C_{24}H_{26}N_2O_4$ $[M + Na]^+$ m/z 437.1289, found 437.1320.

***tert*-Butyl(4-fluorophenyl)(1-(3-(4-fluorophenyl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3j)**: yield 70% (87.6 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.49-

7.45 (m, 2 H), 7.34-7.30 (m, 2 H), 7.13 (t, *J* = 8.4 Hz, 2 H), 7.03 (t, *J* = 8.4 Hz, 2 H), 6.72 (s, 1 H), 5,77 (s, 1 H), 5.29 (s, 1 H), 1.47 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 161.0 (d, *J* = 246.4 Hz), 160.4 (d, *J* = 243.6 Hz), 153.2, 152.1, 137.7, 137.3 (d, *J* = 3.1 Hz), 134.6, 131.1 (d, *J* = 3.2 Hz), 126.5 (d, *J* = 8.9 Hz), 123.1 (d, *J* = 9.1 Hz), 116.4 (d, *J* = 23.3 Hz), 115.7 (d, *J* = 22.5 Hz), 114.1, 111.2, 82.1, 28.1; IR *v* (KBr, cm^{-1}) 3144, 2988, 2928, 1770, 1703, 1606, 1509, 1458, 1368, 1330, 1226, 1159, 1120, 1066, 835; HRMS (ESI) exact mass calcd for $C_{22}H_{20}F_2N_2O_4$ [M + Na]$^+$ m/z 437.1289, found 437.1320.

***tert*-Butyl(4-chlorophenyl)(1-(3-(4-chlorophenyl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3k)**: yield 68% (90.9 mg); yellow solid; mp 167-168 °C (*n*-hexane/ethyl acetate); R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.48-7.38 (m, 4 H), 7.30 (s, 4 H), 6.71 (s, 1 H), 5.81 (s, 1 H), 5.31 (s, 1 H), 1.47 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 152.9, 151.7, 139.8, 137.8, 134.3, 133.6, 132.4, 131.2, 129.6, 129.0, 125.7, 122.1, 114.6, 110.7, 82.4, 28.1; IR *v* (KBr, cm^{-1}) 3148, 3000, 2979, 2920, 1764, 1704, 1598, 1499, 1458, 1367, 1324, 1159, 1076, 832; HRMS (ESI) exact mass calcd for $C_{22}H_{20}Cl_2N_2O_4$ [M + Na]$^+$ m/z 469.0698, found 469.0722.

***tert*-Butyl(4-bromophenyl)(1-(3-(4-bromophenyl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3l)**: yield 63% (101.2 mg); yellow solid; mp 122-123 °C (*n*-hexane/ethyl acetate); R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.56 (d, *J* = 8.8 Hz, 2 H),7.44 (d, *J* = 8.4 Hz, 2 H), 7.39 (d, *J* = 9.2 Hz, 2 H), 7.25 (d, *J* = 8.8 Hz, 2 H), 6.71 (s, 1 H), 5.81 (s, 1 H), 5.31 (s, 1 H), 1.47 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 152.8, 151.6, 140.3, 137.8, 134.2, 134.1, 132.6, 132.0, 126.0, 122.3, 120.2, 119.0, 114.8, 110.6, 82.5, 28.1; IR *v* (KBr, cm^{-1}) 3152, 3119, 2983, 2966, 2927, 1791, 1703, 1591, 1489, 1454, 1368, 1327, 1162, 1061, 823; HRMS (ESI) exact mass calcd for $C_{22}H_{20}Br_2N_2O_4$ [M + Na]$^+$ m/z 556.9688, found 556.9721.

***tert*-Butyl benzyl(1-(3-benzyl-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3m)**: yield 42% (51.4 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.40-7.30 (m, 4 H), 7.25-7.17 (m, 6 H), 5.92 (s, 1 H), 5.43 (s ,1 H), 4.91 (s, 1 H), 4.64 (s, 2 H), 4.53 (s, 2 H), 1.32 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 154.6, 154.3, 138.0, 137.2, 135.0, 134.7, 129.0, 128.4, 128.3, 128.0, 127.6, 111.3, 111.0, 80.9, 53.1, 47.7, 28.1; IR *v* (KBr, cm^{-1}) 3127, 2980, 2928, 1760, 1684, 1603, 1497, 1454, 1367, 1352, 1161, 1128, 1065, 737, 699; HRMS (ESI) exact mass calcd for $C_{24}H_{26}N_2O_4$ [M + Na]$^+$ m/z 429.1790, found 429.1818.

***tert*-Butyl(4-methoxybenzyl)(1-(3-(4-methoxybenzyl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3n)**: yield 34% (49.8 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.19-7.12 (m, 4 H), 6.88 (dt, J_1 = 2.0 Hz, J_2 = 8.8 Hz,2 H), 6.78 (dt, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 2 H), 5.91 (s, 1 H), 5.42 (s, 1 H), 4.87 (s, 1 H), 4.58 (s, 2 H), 4.46 (s, 2 H), 3.81 (s, 3 H), 3.78 (s, 3 H), 1.32 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 159.7, 159.0, 154.5, 154.2, 137.2, 134.6, 130.2, 129.8, 129.4, 127.0, 114.4, 113.7, 111.3, 110.8, 80.7, 55.3, 55.2, 52.4, 47.3, 28.1; IR *v* (KBr, cm^{-1}) 2933, 2837, 1768, 1699, 1611, 1514, 1456, 1367, 1249, 1175, 1033, 819, 765; HRMS (ESI) exact mass calcd for $C_{26}H_{30}N_2O_6$ [M + Na]$^+$ m/z 489.2002, found 489.2038.

***tert*-Butylbenzo[*d*][1,3]dioxol-5-yl](1-(3-(benzo[*d*][1,3]dioxol-5-yl)-2-oxo-2,3-dihydrooxazol-5-yl)vinyl)carbamate (3o)**: yield 48% (66.2 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.04 (d, *J* = 2.0 Hz, 1 H), 6.88-6.82 (m, 3 H), 6.80-6.72 (m, 2 H), 6.68 (s, 1 H), 6.00 (s, 2 H), 5.97 (s, 2 H), 5.71 (s, 1 H), 5.26 (s, 1 H), 1.46 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 153.4, 152.2, 148.3, 147.8, 146.5, 145.8, 137.4, 135.3, 135.0, 129.2, 118.6, 115.0, 113.3, 111.8, 108.4, 107.9, 107.0, 103.7, 101.8, 101.5, 81.8, 28.1; IR *v* (KBr, cm^{-1}) 2981, 2934, 1804, 1719, 1598, 1495, 1372, 1338, 1104, 757; HRMS (ESI) exact mass calcd for $C_{24}H_{22}N_2O_8$ [M + Na]$^+$ m/z 489.1274, found 489.1274.

***tert*-Buty lnaphthalen-2-yl(1-(3-(naphthalen-2-yl)-2-oxo-2,3-dihydrooxazol-5-yl) vinyl) carbamate (3p)**: yield 66% (121.8 mg); colorless oil; R_f 0.25 (v_{PE}/v_{EA} = 15:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.94 (d, *J* = 2.0 Hz, 1 H), 7.88 (d, *J* = 8.8 Hz, 1 H), 7.85-7.77 (m, 6 H), 7.62-7.42 (m, 6 H), 6.93 (s, 1 H), 5.87 (s, 1 H), 5.39 (s, 1 H), 1.52 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 153.4, 152.2, 138.9, 138.0, 134.8, 133.5, 133.3, 132.5, 131.7, 131.4, 129.6, 128.6, 127.9, 127.7, 127.5, 127.1, 126.5, 126.4, 125.9, 123.8, 122.0, 119.4, 119.0, 114.2, 111.4, 82.2, 31.6, 28.2, 22.7, 14.1; IR *v* (KBr, cm^{-1}) 3128, 2978, 2929, 1735, 1692, 1599, 1545, 1368, 1230, 1162, 1056, 814, 743; HRMS (ESI) exact mass calcd for $C_{30}H_{26}N_2O_4$ [M + Na]$^+$ m/z 501.1790, found 501.1788.

Diels-Alder reaction of 5-vinyloxazolone 3a

In a 10 mL flame-dried Schlenk tube under air condition, tert-Butyl (1-(2-oxo-3-phenyl-2, 3-dihydrooxazol-5-yl)vinyl)(phenyl) carbamate **3a** (0.3 mmol) and nitrosobenzene (0.33 mmol) were dissolved in toluene (2.0 mL). Then the reaction solution was kept stirring for 12 h under air condition and monitored by TLC. Upon completion, the reaction mixture was filtered and the filtrate was concentrated in vacuum to give a crude product, which was purified by silica gel column chromatography to afford ***tert*-butyl(6-*oxo*-2,7-diphenyl-3,6,7,7a-tetrahydro-2*H*-oxazolo [5, 4e] [1,2] oxazin-4-yl)(phenyl) carbamate** (**4a**): yield 58% (70.2 mg); yellow oil; R_f 0.25 (v_{PE}/v_{EA} = 10:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 7.67 (d, *J* = 7.6 Hz, 2 H), 7.47 (t, *J* = 7.6 Hz, 2 H), 7.40-7.23 (m, 7 H), 7.10-7.04 (m, 3 H), 6.37 (t, *J* = 2.4 Hz, 1 H), 4.28 (d, *J* = 14.0 Hz, 1 H), 3.88 (dd, J_1 = 2.4 Hz, J_2 = 14.4 Hz, 1 H), 1.51 (s, 9 H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 152.4, 151.0, 148.4, 139.5, 139.1, 135.9, 129.4, 129.1, 126.6, 126.5, 125.9, 123.7, 121.0, 116.0, 113.6, 85.6, 82.2, 54.5, 28.1; IR *v* (KBr, cm−1) 2976, 2925, 1802, 1749, 1694, 1599, 1492, 1351, 1298, 1120, 753; HRMS (ESI) exact mass calcd for $C_{28}H_{27}N_3O_5$ [M + Na]$^+$ m/z 508.1848, found 508.1882.

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