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Zinc Chloride-Mediated Synthesis of 1,4-Oxazepines from *N*-Propargylic β-Enaminones

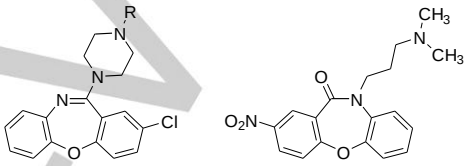
Yilmaz Kelgokmen,[a] Yasemin Cayan[a] and Metin Zora*[a]

Dedication ((optional))

Abstract: An efficient and general method for the synthesis of 1,4-oxazepines is described. When reacted with $ZnCl_2$ in DCM at 40 ºC or $CHCl_3$ at 61 ºC, *N*-propargylic β-enaminones undergo 7-exo-dig cyclization to afford 2-methylene-2,3-dihydro-1,4-oxazepines in good to high yields. This cyclization has been found to be general for a diverse range of *N*-propargylic β-enaminones with high efficiency and broad functional group tolerance. The reactions in refluxing $CHCl_3$ produced 1,4-oxazepines in comparatively shorter reaction times and better yields as compared to those in refluxing DCM. This operationally easy method may provide quick access to a library of functionalized 1,4-oxazepine derivatives of pharmacological interest.

Introduction

1,4-Oxazepines possess a unique position in the design and synthesis of novel biologically active agents that exhibit noteworthy medicinal activities.[1] In fact, 1,4-oxazepines have been extensively studied in the last decades as an intriguing class of heterocycles and still receive considerable attention for their interesting biological and pharmaceutical activities.[2] The most well-known examples of 1,4-oxazepines include half and fully saturated (i.e. dihydro, tetrahydro and perhydro), benzo-, dibenzo- and pyrido-fused, and/or oxo derivatives. 1,4-Oxazepine derivatives have been reported to display a wide range of biological properties, including analgesic,[3] antiallergic,[4] antibacterial,[5] anticonvulsant,[6] antidepressant,[7,8] antihistaminic,[8, 9] antiinflammatory,[10] antipsychotic,[11] anxiolytic,[12] antiulcer[13] and antitumor[14,15] activities. They have also been often used as histamine H_4 receptor (H_4R) agonist,[16] progesterone receptor agonists,[17] calcium antagonist,[18] PGE_2 antagonist,[3] non-nucleoside inhibitor of HIV-1 reverse transcriptase[19] and PI3Ka selective inhibitor.[15] In addition, 1,4-oxazepine derivatives have proven to be useful for the treatment of various diseases, including allergic bronchitis,[20] bronchial asthma,[20] breast cancer,[21] epilepsy and trigeminal neuralgia,[22] and psychotic disorders.[11] Furthermore, 1,4-oxazepines are frequently employed as building blocks and scaffolds for pharmaceutical research since they are present in the structures of a variety of drugs, including antidepressants *Amoxapine*[23] and *Sintamil* (Nitroxazepine),[24] and antipsychotic *Loxapine*[25] (Figure 1), the latter being used primarily in the treatment of schizophrenia as well. For the synthesis of substituted 1,4-oxazepines, many fruitful methods have been developed for decades and new variants also continue to emerge since their biological activity has made them a focus of medicinal chemistry over the years.



Amoxapine (R = H)
Loxapine (R = CH_3)

Sintamil
(Nitroxazepine)

Figure 1. Representative 1,4-oxazepine-containing drugs.

Noticeably, half and fully unsaturated monocyclic 1,4-oxazepines are relatively less explored. In particular, the fully unsaturated monocyclic derivatives are very rare. Indeed, very few strategies to synthesize these scaffolds have been reported. First examples of fully unsaturated monocyclic 1,4-oxazepines were reported by the Tsuchiya research group in 1986.[26] Photolysis of 3-oxa-6-aza-tricyclo[3.2.0.$0^{2,4}$]hept-6-enes, prepared from pyridines via five steps, resulted in valence isomerization with ring opening to afford 1,4-oxazepines (Scheme 1a). It was mentioned that as a result of having an antiaromatic ring system with 8π-electrons, the obtained 1,4-oxazepines were relatively unstable and readily decomposed during isolation by column chromatography.[27] Loreau and Taran have reported a method for the preparation of 2,3-dihydro-1,4-oxazepines via a phosphine-mediated tandem aza Wittig reaction of α,β-alkynic ketones with 2-azidoalcohols and intramolecular cyclization (Scheme 1b).[28]

Recently, *N*-propargylic β-enaminones have been recognized as valuable substrates in organic synthesis since, when treated with proper reagents, they afford a variety of heterocycles,[29] including pyrroles and pyridines.[30] It is noteworthy that mostly five- and six-membered heterocycles resulted from the cyclizations of *N*-propargylic β-enaminones. Although *N*-propargylic β-enaminones could serve as potential precursors for the synthesis of seven-membered ring systems such as 1,4-oxazepines, to our knowledge, very few reports have appeared until now. Cheng and Cui have shown that under strong basic conditions, *N*-propargylic β-enaminones have produced in situ 1,4-oxazepines, which undergo a series of rearrangements and concomitant reactions with heteroaromatic nitrogen nucleophiles to afford N-heteroarene-substituted pyridines (Scheme 1c).[31] When the reactions have been

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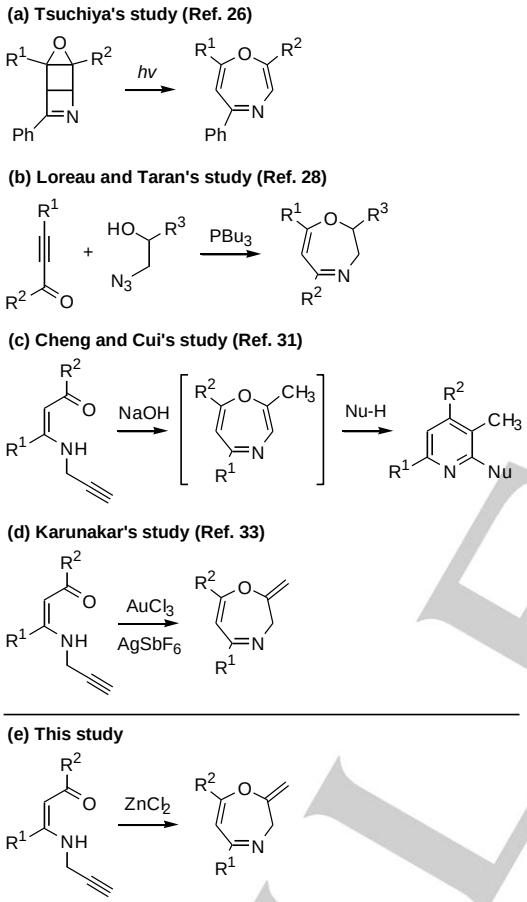
stopped after few minutes, the corresponding 1,4-oxazepine derivatives could be isolated in low to good yields. By using similar strategies, they have also described the synthesis of 2-(1*H*-pyrrol-1-yl)pyridines, 2-alkoxy/2-sulfenylpyridines and dihydrofuro[2,3-b]pyridines from *N*-propargylic β-enaminones, which proceed via the intermediacy of the corresponding 1,4-oxazepines.[32] Karunakar and coworkers have reported a gold-catalyzed intramolecular cyclization of *N*-propargylic β-enaminones, leading to the formation of 2-methylene-2,3-dihydro-1,4-oxazepine derivatives (Scheme 1d).[33] This method has been recently applied to the synthesis of 3-methylene-3,4-dihydrobenzo[b]oxepin-5-ones.[34]



Scheme 1. Strategies for the synthesis of 1,4-oxazepines.

Cyclizations involving metal-catalyzed activation of alkynes are mostly carried out by precious metals such as gold, palladium, platinum or rhodium. Accordingly, the use of inexpensive catalysts or mediators for such benefits attracts great attention since they could provide economically better alternatives and/or different reaction outcomes. Our continued interest in the synthesis of new heterocyclic compounds as potential pharmaceuticals and scaffolds has prompted us to investigate new reactivity patterns of *N*-propargylic β-enaminones. In this regard, we have recently shown that when treated with molecular iodine in the presence of sodium bicarbonate, *N*-propargylic β-enaminones undergo electrophilic cyclization to afford iodo-substituted pyridines in good to high yields with a broad range of functional group tolerability.[35] Iodopyridines have been further elaborated to more complex structures by metal-catalyzed coupling reactions such as Suzuki–Miyaura and Sonogashira reactions.[36] We have anticipated that other metal Lewis acids, particularly inexpensive ones, could affect the intramolecular cyclization of *N*-propargylic β-enaminones to generate seven-membered ring systems. Recently, zinc Lewis acids and salts have proven to be valid catalysts or mediators to accomplish a series of organic and organometallic reactions, including aldol- and Mannich-type reactions, cycloaddition, Michael addition, cross-coupling and Henry reactions.[37] We have found that the reactions of *N*-propargylic β-enaminones with zinc halides such as $ZnCl_2$ afford 2-methylene-2,3-dihydro-1,4-oxazepines (Scheme 1e). Herein, we report the results of this study.

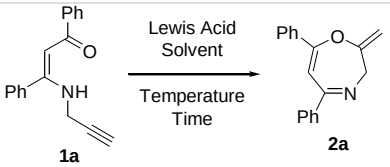
Results and Discussion

First, we synthesized the requisite *N*-propargylic β-enaminones according to a recent report.[35] Conjugate addition of propargylamine to α,β-alkynic ketones provided *N*-propargylic β-enaminones in good to excellent yields (61-98%). In fact, we prepared 21 kinds of *N*-propargylic β-enaminone derivatives, 16 of which have been synthesized for the first time (For identity of R groups and yields, see Experimental Section).

With *N*-propargylic β-enaminones in hand, we next investigated their Lewis acid promoted electrophilic cyclizations. In order to test seven-membered ring formation and optimize its conditions, we first studied the cyclization of *N*-propargylic β-enaminone **1a** with a variety of transition or post-transition metal Lewis acids as depicted in Table 1. When the reaction was performed with $FeCl_3$, $InCl_3$, $NiCl_2$, $PdCl_2(PPh_3)_2$, $HfCl_4$ or AuCl in refluxing DCM, no reaction was observed and the starting β-enaminone **1a** was recovered by some decomposition (Table 1, Entries 1-6). However, the reaction with $AuCl_3$ under same conditions yielded 2-methylene-2,3-dihydro-1,4-oxazepine (**2a**) in trace amount (Table 1, Entry 7). When the same reaction was carried out in refluxing DCE, instead of DCM, **2a** was isolated in 15% yield (Table 1, Entry 8). Subsequently, we tested the reaction with equimolar amounts of ZnI_2, $ZnBr_2$ and $ZnCl_2$ in refluxing DCM, which afforded 2-methylene-2,3-dihydro-1,4-oxazepine (**2a**) in 40, 85 and 95% yields, respectively (Table 1, Entries 9-11), the latter giving the highest yield of **2a**. Next we determined the effective number of equivalents of $ZnCl_2$ in the reaction. When the reaction was performed in turn with 0.2, 0.5 and 1.5 equivalents of $ZnCl_2$, it produced 1,4-oxazepine **2a** in 22, 52 and 95% yields, respectively (Table 1, Entries 12-14). Noticeably, the lower number of equivalents (0.2 and 0.5 equiv.) of $ZnCl_2$ significantly decreased the yield of **2a** while a higher number of equivalents (1.5 equiv) did not improve the yield. Hence the reactions were carried out with 1.0 equiv of $ZnCl_2$. The same reaction was also tried in $CHCl_3$ at 61 °C and DCE at 84 °C, which yielded 1,4-oxazepine **2a** in 95 and 76% yields,

respectively (Table 1, Entries 15 and 16). Notably, the former reaction not only produced 1,4-oxazepine **2a** with the highest yield (95%), as in case of DCM at 40 °C (Table 1, Entry 11), but it also reduced the reaction time from 9.0 to 1.5 h. Finally, the reaction was carried out with Zn dust but no reaction occurred (Table 1, Entry 17). In summary, the reactions performed with 1.0 equiv of $ZnCl_2$ in refluxing DCM and $CHCl_3$, i.e. the conditions in entries 11 and 15 of Table 1, respectively, gave the highest yield of **2a**. Thus, the reactions were conducted under both conditions. It is noteworthy that in most cases, the reactions in refluxing $CHCl_3$ provided 2-methylene-2,3-dihydro-1,4-oxazepines (**2**) in relatively higher yields and shorter reaction times as compared to those in refluxing DCM. However, in few cases, the reactions in refluxing DCM gave comparatively better yields of **2**, as it will be discussed later. The results from a systematic study are shown in Table 2.

Table 1. Optimization of the reaction conditions.[a]



1a **2a**

Entry	Lewis acid (equivalent)	Solvent	Temp. (°C)	Time (h)	Yield (%)[b][c]
1	$FeCl_3$ (1.0)	DCM	40	5.0	NR
2	$InCl_3$ (0.05)	DCM	40	11.5	NR
3	$NiCl_2$ (1.0)	DCM	40	3.0	NR
4	$PdCl_2(PPh_3)_2$ (0.05)	DCM	40	7.0	NR
5	$HfCl_4$ (0.1)	DCM	40	7.0	NR
6	AuCl (0.05)	DCM	40	11.5	NR
7	$AuCl_3$ (0.05)	DCM	40	15.0	trace
8	$AuCl_3$ (0.05)	DCE	84	12.0	15
9	ZnI_2 (1.0)	DCM	40	11.0	40
10	$ZnBr_2$ (1.0)	DCM	40	7.5	85
11	**$ZnCl_2$ (1.0)**	**DCM**	**40**	**9.0**	**95**
12	$ZnCl_2$ (0.2)	DCM	40	17.0	22
13	$ZnCl_2$ (0.5)	DCM	40	17.0	52
14	$ZnCl_2$ (1.5)	DCM	40	8.0	95
15	**$ZnCl_2$ (1.0)**	**$CHCl_3$**	**61**	**1.5**	**95**
16	$ZnCl_2$ (1.0)	DCE	84	3.5	76
17	Zn dust (1.0)	DCM	40	9.0	NR

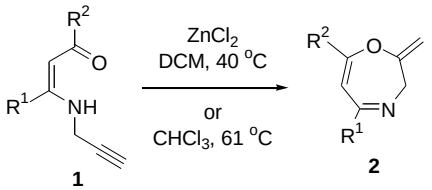
[a] Reactions were carried out on a scale of 0.3 mmol of *N*-propargylic β-enaminone **1a** in 5 mL of solvent under argon with the indicated conditions. For work-up and purification, see Experimental Section.
[b] Isolated yield.
[c] NR = no reaction.

As depicted in Table 2, a diverse range of 2-methylene-2,3-dihydro-1,4-oxazepines (**2**) were synthesized by employing a variety of *N*-propargylic β-enaminones **1**. Most of the cyclizations proceeded efficiently in both conditions and afforded the corresponding 1,4-oxazepines **2** in good to high yields (55-95%), except that oxazepines **2b**, **2f** and **2l** were obtained in moderate yields (40-47%). Notably, in many cases, the cyclizations in $CHCl_3$ at 61 °C afforded the corresponding 1,4-oxazepines in comparatively higher yields and shorter reaction times. However, the cyclizations in DCM at 40 °C produced 1,4-oxazepines **2f**, **2r**, **2t** and **2u** in relatively better yields as compared to those in $CHCl_3$ at 61 °C. Two derivatives of 5-alkyl-substituted 1,4-oxazepines, **2k**, and **2l**, were synthesized in 40-72% yields (Table 2). It should be noted that along with 1,4-oxazepines **2k** and **2l**, pyrrole derivatives **3k** and **3l** were also isolated, respectively, from these reactions but in low yields (9-20%), the structures of which are given in Figure 2. Interestingly, the analyses of the crude reaction mixtures by ^{1}H NMR did not at all reveal the formation of these pyrrole derivatives. We have, however, found that under flash-chromatography conditions on silica gel, 1,4-oxazepines **2k** and **2l** were not so stable that they were converted into the corresponding pyrroles and/or decomposed to some extent. For instance, when a pure amount of **2k** was rechromatographied under the same conditions on silica gel, it produced pyrrole **3k** in 9% yield while 72% of **2k** was recovered. The remaining 19% of **2k** was presumably decomposed during isolation. In brief, pyrroles **3k** and **3l** forms via silica gel-catalyzed rearrangement as will be shown in the proposed mechanism. It is noteworthy that the incorporation of fluorine-bearing groups into organic compounds could result in beneficial biological and medicinal properties.[38] Thus, five derivatives of fluorine-containing 2-methylene-2,3-dihydro-1,4-oxazepines, **2h**, **2i**, **2s**, **2t** and **2u**, were synthesized in 77-92% yields (Table 2). Briefly, this cyclization was found to be general for a diversity of *N*-propargylic β-enaminones **1** and demonstrated good tolerance to a variety of substituents, including electron-donating and electron-withdrawing groups.

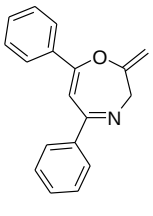
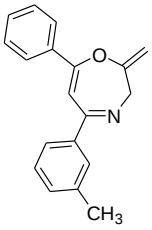
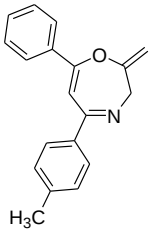
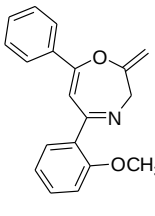
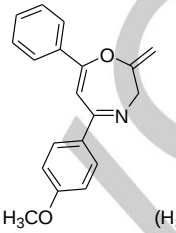
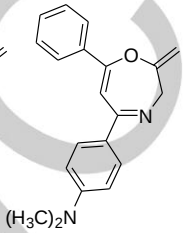
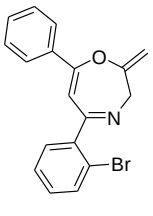
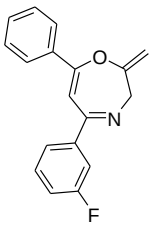
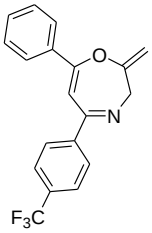
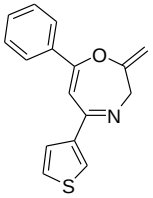
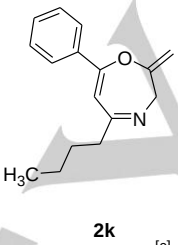
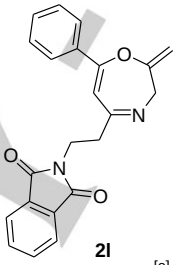
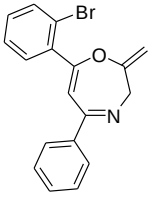
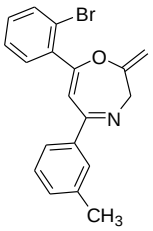
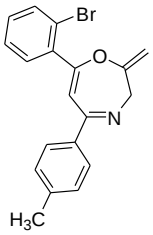
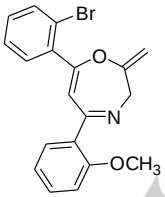
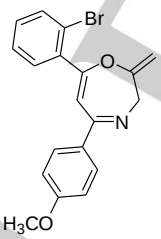
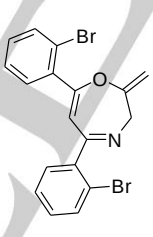
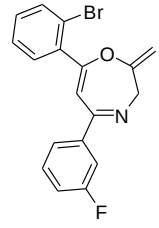
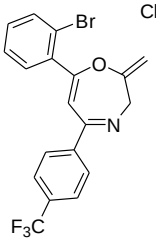
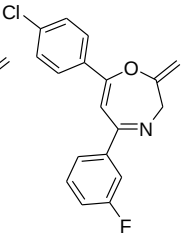
A possible mechanism for the formation of 2-methylene-2,3-dihydro-1,4-oxazepines **2** is outlined in Scheme 2. First, interaction of zinc chloride with alkyne moiety of **1** gives **4**, which enhances the electrophilicity of alkyne unit. Subsequent coordination of carbonyl oxygen to zinc through vinylogous amido-imido tautomerization generates intermediate **5**, bringing the carbonyl and alkyne functionalities in close proximity. Then intramolecular 7-exo-dig electrophilic cyclization takes place to produce vinyl zinc intermediate **6**. Finally, hydrolysis with HCl generated in situ affords 1,4-oxazepine derivatives **2** (Scheme 2).

The mechanism proposed for the formation of pyrroles **3** is depicted in Scheme 3. First, activation of vinylogous imine functionality in **2** with silica gel generates intermediate **7**, which enables conjugate addition of water to give hemiketal **8**. Ring opening affords dienol intermediate **9**, which, upon tautomerization, converts into keto-enol derivative **10**. Subsequently, cyclization takes place to furnish aldol product **11**. Water elimination via intermediate **12** produces 2*H*-pyrrole **13**. Finally, isomerization affords pyrrole derivatives **3** (Scheme 3).

Table 2. Synthesis of 2-methylene-2,3-dihydro-1,4-oxazepine derivatives.[a][b]



1 **2**

						
2a (95%, 9.0 h) [95%, 1.5 h]	**2b** (43%, 9.0 h) [74%, 1.5 h]	**2c** (62%, 9.0 h) [74%, 2.0 h]	**2d** (63%, 9.0 h) [66%, 6.0 h]	**2e** (66%, 9.0 h) [73%, 3.0 h]	**2f** (47%, 10.0 h) [40%, 1.5 h]	**2g** (63%, 20.0 h) [73%, 12.0 h]
						
2h (86%, 9.0 h) [90%, 2.0 h]	**2i** (80%, 9.0 h) [82%, 2.0 h]	**2j** (74%, 9.0 h) [84%, 2.0 h]	**2k** (59%, 24.0 h)[c] [72%, 5.0 h][d]	**2l** (40%, 20.0 h)[e] [40%, 9.0 h][f]	**2m** (80%, 9.0 h) [81%, 1.5 h]	**2n** (55%, 9.0 h) [95%, 1.5 h]
						
2o (70%, 9.0 h) [90%, 2.0 h]	**2p** (81%, 15.0 h) [88%, 6.0 h]	**2q** (70%, 9.0 h) [90%, 2.5 h]	**2r** (77%, 9.0 h) [68%, 5.0 h]	**2s** (79%, 9.0 h) [86%, 1.5 h]	**2t** (92%, 9.0 h) [91%, 3.0 h]	**2u** (89%, 9.0 h) [77%, 3.0 h]

[a] Reaction conditions: *N*-propargylic β-enaminone **1** (0.30 mmol), $ZnCl_2$ (0.30 mmol), DCM (5 mL) at 40 ºC or $CHCl_3$ (5 mL) at 61 ºC, under argon. For the full procedure including work-up and purification, see Experimental Section.
[b] Yields and reaction times in DCM at 40 ºC are shown in parentheses while those in $CHCl_3$ at 61 ºC are depicted in square brackets. All yields are of isolated products.
[c] Along with **2k**, pyrrole **3k** was also isolated in 14% yield from this reaction (see Figure 2 for its structure).
[d] Along with **2k**, pyrrole **3k** was also isolated in 9% yield from this reaction (see Figure 2 for its structure).
[e] Along with **2l**, pyrrole **3l** was also isolated in 20% yield from this reaction (see Figure 2 for its structure).
[f] Along with **2l**, pyrrole **3l** was also isolated in 12% yield from this reaction (see Figure 2 for its structure).

We have also examined one example of the reaction of *N*-propargylic β-enaminone that contains internal alkyne functionality, such as **14** (Scheme 4). Interestingly, the reaction of β-enaminone **14** under both conditions did not produce any 1,4-oxazepine derivative such as **16**, presumably to steric and/or electronic effects; instead, it gave a pyridine derivative, **15**, via 6-endo-dig cyclization but in low yields (25-28%) (Scheme 4). Since the formation of pyridines from *N*-propargylic β-enaminones is well documented,[30,35] we have not investigated their formation further.

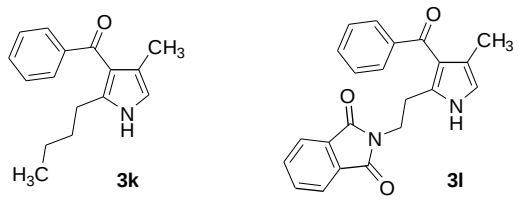
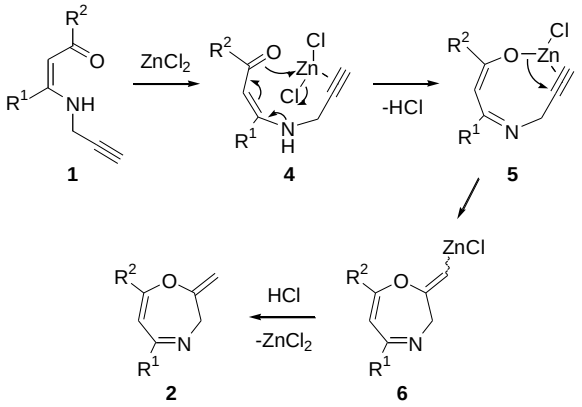
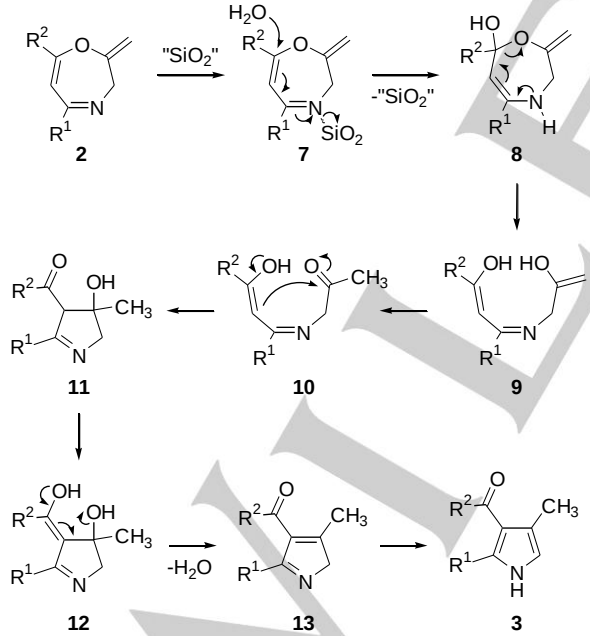


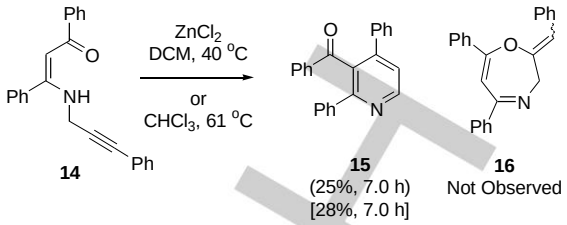
Figure 2. Structures of pyrrole derivatives isolated along with 1,4-oxazepines.



Scheme 2. Proposed mechanism for the synthesis of 2-methylene-2,3-dihydro-1,4-oxazepines



Scheme 3. Proposed mechanism for the formation of pyrroles.



Scheme 4. Formation of pyridines from internal alkyne-tethered *N*-propargylic β-enaminone (Yields and reaction times in DCM are depicted in parentheses while those in $CHCl_3$ are shown in square brackets).

Conclusions

In summary, we have developed a new robust method for the synthesis of 1,4-oxazepines. When treated with $ZnCl_2$ in refluxing DCM or $CHCl_3$, *N*-propargylic β-enaminones have produced 2-methylene-2,3-dihydro-1,4-oxazepines in good to high yields via electrophilic cyclization. Reaction has been found to be general for a variety of *N*-propargylic β-enaminones and tolerated a broad range of functional groups with electron-donating and electron-withdrawing substituents. In most cases, the reactions carried out in $CHCl_3$ have provided 1,4-oxazepines in higher yields and shorter reaction times. In conclusion, we anticipate that the efficiency and operational simplicity of the method could make it potentially attractive for the library construction of 1,4-oxazepines, particularly in the area of pharmaceuticals.

Experimental Section

General information. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts are reported in parts per million (ppm) relative to $CDCl_3$ (7.26 and 77.16 ppm in ^1H and ^{13}C NMR, respectively). Coupling constants (*J*) are reported in Hertz (Hz), and spin multiplicities are presented by the following symbols: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet). DEPT ^{13}C NMR information is given in parentheses as C, CH, CH_2 and CH_3. Infrared spectra (IR) were recorded by using attenuated total reflection (ATR). Band positions are reported in reciprocal centimeters (cm^{-1}). Mass spectra (MS) and high resolution mass spectra (HRMS) were obtained by using Electrospray Ionization (ESI) with Micro-Tof; *m/z* values are reported (For each measurement, the mass scale was recalibrated with sodium formate clusters, and samples were dissolved and measured in MeOH or CH_3CN). Flash chromatography was performed using thick-walled glass columns and "flash grade" silica gel (230-400 mesh) or aluminium oxide (neutral, 70-230 mesh). Thin layer chromatography (TLC) was performed by using commercially prepared 0.25 mm silica gel or aluminium oxide (neutral) plates and visualization was effected with short wavelength UV lamp (254 nm). The relative proportions of solvents in chromatography solvent mixtures refer to the volume:volume ratio. All commercially available reagents were used directly without purification unless otherwise stated. All solvents used in reactions and chromatography were distilled and/or dried properly for purity. The inert atmosphere was created by slight positive pressure (ca. 0.1 psi) of argon. All glassware was dried in oven prior to use.

α,β-Alkynic ketones were synthesized from commercially available terminal alkynes and acyl chlorides according to standard

protocols.[30,35,39] *N*-Propargylic β-enaminones **1** were synthesized by conjugate addition of propargylamine to α,β-alkynic ketones according to recent literature procedures.[30,35] *N*-Propargylic β-enaminone **14** was prepared from β-enaminone **1a** and iodobenzene by a coupling procedure.[30,35]

General Procedure for the synthesis of *N*-propargylic β-enaminones 1. To a stirred solution of the corresponding α,β-alkynic ketone (2.5 mmol) in absolute MeOH (10 mL) was added propargylamine (3.0 mmol) and the resulting mixture was heated at 65 °C for approximately 6 h (Note that the progress of the reaction was monitored by routine TLC for the disappearance of alkynic ketone). After the reaction was over, the solvent was removed on a rotary evaporator, and ethyl acetate (50 mL) and a saturated NaCl solution (50 mL) were added. After the layers were separated, the aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over $MgSO_4$ and evaporated on a rotary evaporator to give the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9:1 followed by 4:1) as the eluent to afford the corresponding β-enaminone **1**.

1,3-Diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1a). 1,3-Diphenylprop-2-yn-1-one (515.6 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 640.3 mg (98%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.33 (br s, 1H), 7.95-7.87 (m, 2H), 7.55-7.37 (m, 8H), 5.85 (br s, 1H), 3.95 (dd, *J* = 6.3, 2.5 Hz, 2H), 2.31 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.3 (C=O), 166.0 (C), 140.1 (C), 135.1 (C), 131.1 (CH), 130.0 (CH), 128.8 (CH), 128.4 (CH), 128.0 (CH), 127.3 (CH), 94.8 (CH), 79.9 (C), 72.6 (CH), 34.3 (CH_2). The spectral data were in agreement with those reported previously for this compound.[30,35]

1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(*m*-tolyl)prop-2-en-1-one (1b). 1-Phenyl-3-*m*-tolylprop-2-yn-1-one (550.7 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 653.9 mg (95%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.40 (br t, *J* = 6.0 Hz, 1H), 7.97-7.89 (m, 2H), 7.48-7.24 (m, 7H), 5.86 (s, 1H), 3.93 (dd, *J* = 6.3, 2.5 Hz, 2H), 2.41 (s, 3H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8 (C=O), 165.9 (C), 139.8 (C), 138.4 (C), 134.6 (C), 130.8 (CH), 130.4 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 127.0 (CH), 124.7 (CH), 94.3 (CH), 79.8 (C), 72.4 (CH), 34.0 (CH_2), 21.2 (CH_3); IR (neat): 3224, 3055, 2113, 1667, 1594, 1550, 1476, 1324, 1270, 1226, 1173, 1134, 1054, 1024, 789, 733 cm^{-1}; MS (ESI, m/z): 276.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{18}NO$: 276.1383 $[M+H]^+$, found: 276.1380.

1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(*p*-tolyl)prop-2-en-1-one (1c). 1-Phenyl-3-p-tolylprop-2-yn-1-one (550.7 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 633.3 mg (92%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.40 (br t, *J* = 5.6 Hz, 1H), 7.97-7.89 (m, 2H), 7.49-7.37 (m, 5H), 7.28 (d, *J* = 7.9 Hz, 2H), 5.87 (s, 1H), 3.96 (dd, *J* = 6.3, 2.5 Hz, 2H), 2.42 (s, 3H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (C=O), 166.1 (C), 140.0 (C), 131.9 (C), 130.9 (C), 129.3 (CH), 128.2 (CH), 127.7 (CH), 127.1 (CH), 94.5 (CH), 79.9 (C), 72.4 (CH), 34.1 (CH_2), 21.3 (CH_3) (Note that two CH peaks overlap on each other). The spectral data were in agreement with those reported previously for this compound.[35]

3-(2-Methoxyphenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1d). 3-(2-Methoxyphenyl)-1-phenylprop-2-yn-1-one (590.7 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 582.7 mg (80%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.51 (br s, 1H), 7.96-7.86 (m, 2H), 7.48-7.35 (m, 4H), 7.31 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 5.79 (s, 1H), 4.00-3.70 (m, 5H), 2.27 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8 (C=O), 163.3 (C), 156.0 (C), 140.1 (C), 131.2 (CH), 130.7 (CH), 129.8 (CH), 128.1 (CH), 127.1 (CH), 123.6 (C), 120.9 (CH), 110.8 (CH), 94.0 (CH), 79.4 (C), 72.1 (CH), 55.5 (OCH_3), 33.8 (CH_2); IR (neat): 3285, 2935, 1732, 1594, 1567, 1482, 1455, 1326, 1241, 1145, 1114, 1056, 1023, 808, 753, 692 cm^{-1}; MS (ESI, m/z): 292.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{18}NO_2$: 292.1332 $[M+H]^+$, found: 292.1341.

3-(4-Methoxyphenyl)-1-phenyl-3-(prop-2-ynylamino)prop-2-en-1-one (1e). 3-(4-Methoxyphenyl)-1-phenylprop-2-yn-1-one (590.7 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 713.8 mg (98%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.35 (br s, 1H), 7.94-7.87 (m, 2H), 7.48-7.37 (m, 5H), 7.02-6.96 (m, 2H), 5.84 (s, 1H), 3.98 (dd, *J* = 6.3 and 2.5 Hz, 2H), 3.86 (s, 3H), 2.32 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0 (C=O), 166.0 (C), 161.0 (C), 140.2 (C), 131.0 (CH), 129.6 (CH), 128.3 (CH), 127.3 (CH), 114.2 (CH), 94.7 (CH), 80.1 (C), 72.5 (CH), 55.5 (OCH_3), 34.4 (CH_2) (Note that two C peaks overlap on each other). The spectral data were in agreement with those reported previously for this compound.[35]

3-(4-(Dimethylamino)phenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1f). 3-(4-(Dimethylamino)phenyl)-1-phenylprop-2-yn-1-one (623.3 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 639.2 mg (84%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (br t, *J* = 5.5 Hz, 1H), 7.93 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.48-7.35 (m, 5H), 6.72 (d, *J* = 8.8 Hz, 2H), 5.88 (s, 1H), 4.05 (dd, *J* = 6.2, 2.4 Hz, 2H), 2.99 (s, 6H), 2.34 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2 (C=O), 166.9 (C), 151.4 (C), 140.4 (C), 130.6 (CH), 129.2 (CH), 128.1 (CH), 127.0 (CH), 121.7 (C), 111.5 (CH), 94.0 (CH), 80.3 (C), 72.3 (CH), 40.1 ($N(CH_3)_2$), 34.4 (CH_2); IR (neat): 3208, 2884, 2805, 2111, 1614, 1579, 1502, 1481, 1446, 1328, 1264, 1233, 1194, 1141, 1054, 928, 815, 797, 743, 729 cm^{-1}; MS (ESI, m/z): 305.17 $[M+H]^+$; HRMS (ESI) calcd. for $C_{20}H_{21}N_2O$: 305.1648 $[M+H]^+$, found: 305.1653.

3-(2-Bromophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1g). 3-(2-Bromophenyl)-1-phenylprop-2-yn-1-one (712.8 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 714.4 mg (84%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.19 (br s, 1H), 7.82-7.69 (m, 2H), 7.52-7.46 (m, 1H), 7.34-7.20 (m, 5H), 7.18-7.12 (m, 1H), 5.62 (s, 1H), 3.78 (ddd, *J* = 17.7, 4.9, 2.5 Hz, 1H), 3.58 (ddd, *J* = 17.6, 7.1, 2.4 Hz, 1H), 2.14 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.2 (C=O), 163.2 (C), 139.6 (C), 135.5 (C), 132.9 (CH), 131.0 (CH), 130.8 (CH), 129.8 (CH), 128.2 (CH), 127.6 (CH), 127.1 (CH), 121.4 (CBr), 93.9 (CH), 79.0 (C), 72.6 (CH), 33.6 (CH_2); IR (neat): 3291, 1732, 1595, 1572, 1549, 1462, 1322, 1306, 1254, 1145, 1054, 1024, 944, 853, 749 cm^{-1}; MS (ESI, m/z): 340.03 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}{}^{79}BrNO$: 340.0332 $[M+H]^+$, found: 340.0329.

3-(3-Fluorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1h). 3-(3-Fluorophenyl)-1-phenylprop-2-yn-1-one (560.6 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 628.4 mg (90%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.27 (br s, 1H), 7.98-7.88 (m, 2H), 7.55-7.39 (m, 4H), 7.33-7.14 (m, 3H), 5.86 (s, 1H), 3.95 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.5 (C=O), 164.2 (C), 162.7 (d, ^1J = 248.4 Hz, CF), 139.8 (C), 137.0 (d, ^3J = 7.6 Hz, C), 131.3 (CH), 130.6 (d, ^3J = 8.2 Hz, CH), 128.4 (CH), 127.3 (CH), 123.8 (d, ^4J = 3.1 Hz, CH), 116.9 (d, ^2J = 21.0 Hz, CH), 115.2 (d, ^2J = 22.7 Hz, CH), 94.8 (CH), 79.7 (C), 72.8 (CH), 34.3 (CH_2); IR (neat): 3222, 1600, 1570, 1549, 1520, 1474, 1431, 1323, 1299, 1284, 1265, 1250, 1226, 1203, 1025, 1000, 965, 876, 788 cm^{-1}; MS (ESI, m/z): 280.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}FNO$: 280.1132 $[M+H]^+$, found: 280.1134.

1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (1i). 1-Phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (685.6 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 666.9 mg (81%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.27 (br t, *J* = 5.6 Hz, 1H), 7.90 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.49-7.36 (m, 3H), 5.83 (s, 1H), 3.87 (dd, *J* = 6.4, 2.4 Hz, 2H), 2.33 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4 (C=O), 164.0 (C), 139.6 (C), 138.4 (C), 131.8 (q, ^{2}J = 32.7 Hz, C), 131.3 (CH), 128.4 (CH), 128.3 (CH), 127.2 (CH), 125.7 (q, ^{3}J = 3.7 Hz, CH), 123.8 (q, ^{1}J = 272.4 Hz, CF_3), 94.9 (CH), 79.5 (C), 72.8 (CH), 34.2 (CH_2); IR (neat): 3055, 2116, 1600, 1583, 1548, 1502, 1430, 1321, 1294, 1240, 1225, 1163, 1104, 1072, 1050, 1015, 925, 849, 737 cm^{-1}; MS (ESI, m/z): 330.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{15}F_3NO$: 330.1100 $[M+H]^+$, found: 330.1100.

1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(thiophen-3-yl)prop-2-en-1-one (1j). 1-Phenyl-3-(thiophen-3-yl)prop-2-yn-1-one (530.7 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 628.3 mg (94%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.44 (br t, *J* = 6.1 Hz, 1H), 7.95-7.86 (m, 2H), 7.59 (dd, *J* = 2.9, 1.1 Hz, 1H), 7.46-7.32 (m, 4H), 7.24 (dd, *J* = 5.0, 1.0 Hz, 1H), 5.92 (s, 1H), 3.97 (dd, *J* = 6.4, 2.4 Hz, 2H), 2.38 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.5 (C=O), 160.3 (C), 139.6 (C), 135.1 (C), 130.7 (CH), 128.0 (CH), 127.0 (CH), 126.9 (CH), 126.5 (CH), 126.1 (CH), 93.9 (CH), 79.9 (C), 72.6 (CH), 33.9 (CH_2). The spectral data were in agreement with those reported previously for this compound.[35]

1-Phenyl-3-(prop-2-yn-1-ylamino)hept-2-en-1-one (1k). 1-Phenylhept-2-yn-1-one (465.7 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 555.1 mg (92%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (br s, 1H), 7.89-7.83 (m, 2H), 7.46-7.36 (m, 3H), 5.75 (s, 1H), 4.08 (dd, *J* = 6.2, 2.5 Hz, 2H), 2.42-2.35 (m, 2H), 2.32 (t, *J* = 2.5 Hz, 1H), 1.67-1.57 (m, 2H), 1.44 (sextet, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8 (C=O), 168.2 (C), 140.4 (C), 130.7 (CH), 128.2 (CH), 127.1 (CH), 92.2 (CH), 79.2 (C), 72.5 (CH), 32.3 (CH_2), 31.9 (CH_2), 30.2 (CH_2), 22.7 (CH_2), 13.9 (CH_3). The spectral data were in agreement with those reported previously for this compound.[35]

2-(5-Oxo-5-phenyl-3-(prop-2-yn-1-ylamino)pent-3-en-1-yl)isoindoline-1,3-dione (1l). 2-(5-Oxo-5-phenylpent-3-yn-1-yl)isoindoline-1,3-dione (758.3 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 546.5 mg (61%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.30 (br t, *J* = 5.8 Hz, 1H), 7.86-7.72 (m, 4H), 7.70-7.61 (m, 2H), 7.43-7.29 (m, 3H), 5.76 (s, 1H), 4.21 (dd, *J* = 6.2, 2.4 Hz, 2H), 4.03-3.87 (m, 2H), 2.85-2.70 (m, 2H), 2.35 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0 (C=O), 167.9 (C), 162.8 (C=O), 139.7 (C), 134.1 (CH), 131.9 (CH), 130.9 (C), 128.2 (CH), 127.0 (CH), 123.4 (CH), 93.0 (CH), 79.2 (C), 72.8 (CH), 36.0 (CH_2), 32.4 (CH_2), 30.8 (CH_2); IR (neat): 3260, 1775, 1713, 1594, 1580, 1392, 1337, 1247, 1188, 1098, 970, 753 cm^{-1}; MS (ESI, m/z): 359.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{22}H_{19}N_2O_3$: 359.1390 $[M+H]^+$, found: 359.1399.

1-(2-Bromophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1m). 1-(2-Bromophenyl)-3-phenylprop-2-yn-1-one (712.8 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 740.0 mg (87%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.10 (br s, 1H), 7.56 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.52-7.40 (m, 6H), 7.30 (td, *J* = 7.5, 1.1 Hz, 1H), 7.21-7.15 (m, 1H), 5.47 (s, 1H), 3.96 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.33 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1 (C=O), 165.8 (C), 143.1 (C), 134.4 (C), 133.4 (CH), 130.3 (CH), 130.1 (CH), 129.2 (CH), 128.8 (CH), 127.9 (CH), 127.2 (CH), 119.5 (CBr), 98.4 (CH), 79.6 (C), 72.8 (CH), 34.4 (CH_2); IR (neat): 3290, 1731, 1588, 1560, 1483, 1461, 1427, 1317, 1244, 1145, 1082, 1023, 949, 751 cm^{-1}; MS (ESI, m/z): 340.03 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}{}^{79}BrNO$: 340.0332 $[M+H]^+$, found: 340.0333.

1-(2-Bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(*m*-tolyl)prop-2-en-1-one (1n). 1-(2-Bromophenyl)-3-(*m*-tolyl)prop-2-yn-1-one (747.9 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 770.5 mg (87%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.12 (br s, 1H), 7.57 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.50-7.44 (m, 1H), 7.38-7.24 (m, 5H), 7.22-7.16 (m, 1H), 5.47 (s, 1H), 3.98 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.40 (s, 3H), 2.36 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.9 (C=O), 166.1 (C), 143.0 (C), 138.5 (C), 134.2 (C), 133.3 (CH), 130.8 (CH), 130.2 (CH), 129.1 (CH), 128.5 (CH), 128.3 (CH), 127.1 (CH), 124.8 (CH), 119.4 (CBr), 98.1 (CH), 79.6 (C), 72.7 (CH), 34.3 (CH_2), 21.4 (CH_3); IR (neat): 3289, 1731, 1561, 1479, 1359, 1256, 1082, 1023, 758 cm^{-1}; MS (ESI, m/z): 354.05 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO$: 354.0488 $[M+H]^+$, found: 354.0490.

1-(2-Bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(*p*-tolyl)prop-2-en-1-one (1o). 1-(2-Bromophenyl)-3-(*p*-tolyl)prop-2-yn-1-one (747.9 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 752.8 mg (85%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.13 (br s, 1H), 7.58 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.48 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.32 (td, *J* = 7.5, 1.1 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 2H), 7.20 (td, *J* = 7.7, 1.7 Hz, 1H), 5.48 (s, 1H), 4.00 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.41 (s, 3H), 2.36 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.9 (C=O), 166.1 (C), 143.2 (C), 140.3 (C), 133.4 (CH), 131.5 (C), 130.3 (CH), 129.4 (CH), 129.3 (CH), 127.9 (CH), 127.2 (CH), 119.5 (CBr), 98.3 (CH), 79.8 (C), 72.7 (CH), 34.4 (CH_2), 21.4 (CH_3); IR (neat): 3280, 1586, 1571, 1492, 1310, 1256, 1046, 1080, 1021, 827, 791, 757 cm^{-1}; MS (ESI, m/z): 354.05 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO$: 354.0488 $[M+H]^+$, found: 354.0489.

1-(2-Bromophenyl)-3-(2-methoxyphenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1p). 1-(2-Bromophenyl)-3-(2-methoxyphenyl)prop-2-yn-1-one (787.9 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 703.5 mg (76%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.21 (br s, 1H), 7.57 (dd, *J* = 8.0, 0.7 Hz, 1H), 7.49 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.46-7.40 (m, 1H), 7.35-7.27 (m, 2H), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H), 7.03 (t, *J* = 7.2 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 5.40 (br s, 1H), 4.02-3.77 (m, 2H), 3.88 (s, 3H), 2.28 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8 (C=O), 163.4 (C), 156.1 (C), 143.2 (C), 133.4 (CH), 131.5 (CH), 130.2 (CH), 130.0 (CH), 129.4 (CH), 127.1 (CH), 123.4 (C), 121.0 (CH), 119.6 (CBr), 111.0 (CH), 98.0 (CH), 79.3 (C), 72.3 (CH), 55.7 (OCH_3), 34.1 (CH_2); IR (neat): 3247, 2190, 1587, 1536, 1485, 1461, 1328, 1237, 1163, 1084, 1065, 1023, 796, 753 cm^{-1}; MS (ESI, m/z): 370.04 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO_2$: 370.0437 $[M+H]^+$, found: 370.0440.

1-(2-Bromophenyl)-3-(4-methoxyphenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1q). 1-(2-Bromophenyl)-3-(4-methoxyphenyl)prop-2-yn-1-one (787.9 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 703.5 mg (76%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.11 (br s, 1H), 7.56 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.50-7.41 (m, 3H), 7.30 (td, *J* = 7.5, 1.1 Hz, 1H), 7.21-7.15 (m, 1H), 6.98-6.92 (m, 2H), 5.45 (br s, 1H), 4.00 (dd, *J* = 6.4, 2.5 Hz, 2H), 3.83 (s, 3H), 2.34 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8 (C=O), 165.9 (C), 161.1 (C), 143.3 (C), 133.4 (CH), 130.3 (CH), 129.6 (CH), 129.3 (CH), 127.2 (CH), 126.7 (C), 119.5 (CBr), 114.2 (CH), 98.3 (CH), 79.9 (C), 72.7 (CH), 55.5 (OCH_3), 34.50 (CH_2); IR (neat): 3286, 1587, 1558, 1490, 1323, 1296, 1247, 1174, 1083, 1021, 873, 759 cm^{-1}; MS (ESI, m/z): 370.04 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO_2$: 370.0437 $[M+H]^+$, found: 370.0440.

1,3-Bis(2-bromophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1r). 1,3-Bis(2-bromophenyl)prop-2-yn-1-one (910.1 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 901.1 mg (86%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.02 (br t, *J* = 5.5 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.39-7.31 (m, 2H), 7.30-7.23 (m, 2H), 7.15 (td, *J* = 8.0, 1.6 Hz, 1H), 5.34 (s, 1H), 3.92 (ddd, *J* = 17.7, 5.0, 2.5 Hz, 1H), 3.72 (ddd, *J* = 17.7, 7.0, 2.4 Hz, 1H), 2.28 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2 (C=O), 163.2 (C), 142.6 (C), 135.0 (C), 133.2 (CH), 132.8 (CH), 130.9 (CH), 130.3 (CH), 129.6 (CH), 129.0 (CH), 127.6 (CH), 127.0 (CH), 121.2 (CBr), 119.3 (CBr), 97.7 (CH), 78.6 (C), 72.8 (CH), 33.7 (CH_2); IR (neat): 3291, 1704, 1586, 1548, 1457, 1426, 1355, 1255, 1074, 1023, 750 cm^{-1}; MS (ESI, m/z): 417.94 and 419.94 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}{}^{79}Br_2NO$: 417.9437 $[M+H]^+$, found: 417.9442; calcd. for $C_{18}H_{14}{}^{79}Br^{81}Br$ NO: 419.9417 $[M+H]^+$, found: 419.9420.

1-(2-Bromophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1s). 1-(2-Bromophenyl)-3-(3-fluorophenyl)prop-2-yn-1-one (787.9 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 850.7 mg (95%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.01 (br s, 1H), 7.57 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.48-7.39 (m, 2H), 7.35-7.26 (m, 2H), 7.25-7.12 (m, 3H), 5.47 (s, 1H), 3.95 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.4 (C=O), 164.2 (C), 162.6 (d, ^1J = 248.4 Hz, CF), 142.9 (C), 136.4 (d, ^3J = 7.6 Hz, C), 133.5 (CH), 130.6 (d, ^3J = 8.2 Hz, CH), 130.5 (CH), 129.3 (CH), 127.3 (CH), 123.8 (d, ^4J = 3.1 Hz, CH), 119.5 (CBr), 117.1 (d, ^2J = 21.0 Hz, CH), 115.3 (d, ^2J = 22.9 Hz, CH), 98.5 (CH), 79.5 (C), 73.0 (CH), 34.4 (CH_2); IR (neat): 3294, 1562, 1477, 1321, 1224, 1197, 1079, 1023, 872, 790, 758 cm^{-1}; MS (ESI, m/z): 358.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}{}^{79}BrFNO$: 358.0237 $[M+H]^+$, found: 358.0239.

1-(2-Bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (1t). 1-(2-Bromophenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (882.8 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 898.1 mg (88%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.02 (br t, *J* = 5.8 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.55 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.30 (td, *J* = 7.5, 1.0 Hz, 1H), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H), 5.46 (s, 1H), 3.91 (dd, *J* = 6.5, 2.5 Hz, 2H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3 (C=O), 163.8 (C), 142.6 (C), 137.9 (C), 133.4 (CH), 131.9 (q, ^2J = 32.8 Hz, C), 130.5 (CH), 129.2 (CH), 128.4 (CH), 127.2 (CH), 125.7 (q, ^3J = 3.7 Hz, CH), 123.7 (q, ^1J = 272.4 Hz, CF_3), 119.3 (CBr), 98.6 (CH), 79.3 (C), 73.0 (CH), 34.3 (CH_2); IR (neat): 3297, 1587, 1561, 1319, 1167, 1125, 1063, 1018, 849, 740 cm^{-1}; MS (ESI, m/z): 408.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{14}{}^{79}BrF_3NO$: 408.0205 $[M+H]^+$, found: 408.0206.

1-(4-Chlorophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (1u). 1-(4-Chlorophenyl)-3-(3-fluorophenyl)prop-2-yn-1-one (646.7 mg, 2.5 mmol) and propargylamine (165.3 mg, 3.0 mmol) were employed to afford 713.8 mg (91%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.27 (br s, 1H), 7.90-7.80 (m, 2H), 7.51-7.42 (m, 1H), 7.41-7.34 (m, 2H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.26-7.15 (m, 2H), 5.79 (s, 1H), 3.94 (dd, *J* = 6.2, 2.2 Hz, 2H), 2.35 (t, *J* = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9 (C=O), 164.6 (C), 162.7 (d, ^1J = 248.5 Hz, CF), 138.1 (C), 137.4 (C), 136.8 (d, ^3J = 7.8 Hz, C), 130.6 (d, ^3J = 8.3 Hz, CH), 128.7 (CH), 128.6 (CH), 123.7 (d, ^4J = 3.0 Hz, CH), 117.0 (d, ^2J = 21.1 Hz, CH), 115.2 (d, ^2J = 22.9 Hz, CH), 94.4 (CH), 79.5 (C), 72.9 (CH), 34.3 (CH_2); IR (neat): 3232, 1570, 1545, 1473, 1325, 1282, 1265, 1231, 1092, 1065, 878, 764 cm^{-1}; MS (ESI, m/z): 314.07 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}ClFNO$: 314.0743 $[M+H]^+$, found: 314.0746.

General Procedure for the synthesis of 2-methylene-2,3-dihydro-1,4-oxazepines (2) (Table 2). To a stirred solution of the corresponding *N*-propargylic β-enaminone **1** (0.30 mmol) in DCM (5 mL) or in $CHCl_3$ (5 mL) at room temperature under argon were added $ZnCl_2$ (0.30 mmol). The resulting mixture was then refluxed at 40 °C (DCM) or at 61 °C ($CHCl_3$) (Note that reaction was continued until *N*-propargylic β-enaminone **1** was completely consumed as monitored by routine TLC). After the reaction was over, the solvent was removed on a rotary evaporator, and ethyl acetate (40 mL) and a saturated aqueous solution of NH_4Cl (15 mL) were added. After the layers were separated, the aqueous layer was extracted with ethyl acetate (2 x 30 mL). The combined organic layers were dried over $MgSO_4$ and evaporated on a rotary evaporator to give the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9:1 followed by 4:1) as the eluent to afford the corresponding 1,4-oxazepine derivative **2.**

2-Methylene-5,7-diphenyl-2,3-dihydro-1,4-oxazepine (2a). 1,3-Diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1a**) (78.4 mg, 0.30 mmol) and $ZnCl_2$ (40.9 mg, 0.30 mmol) were employed to afford the indicated product (74.5 mg (95%) in refluxing DCM; 74.5 mg (95%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.72 (m, 4H), 7.51-7.38 (m, 6H), 6.41 (s, 1H), 4.76 (d, *J* = 1.4 Hz 1H), 4.57 (s, 2H), 4.40 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (C), 159.0 (C), 158.2 (C), 139.8 (C), 135.2 (C), 130.2 (CH), 130.1 (CH), 128.7 (CH), 128.4 (CH), 127.5 (CH), 126.4 (CH), 99.8 (CH), 94.0 (CH_2), 55.6 (CH_2); IR (neat): 3104, 3059, 2994, 2955, 2837, 1656, 1627, 1587, 1570, 1491, 1446, 1361, 1313, 1290, 1260, 1230, 1191, 1176, 1110, 1076, 1055, 1027, 999, 946, 926, 882, 832, 804, 762 cm^{-1}; MS (ESI, m/z): 262.12 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{16}NO$: 262.1226 $[M+H]^+$, found: 262.1236. The spectral data were in agreement with those reported previously for this compound.[33]

2-Methylene-7-phenyl-5-(*m*-tolyl)-2,3-dihydro-1,4-oxazepine (2b). 1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(*m*-tolyl)prop-2-en-1-one (**1b**) (90.9 mg, 0.33 mmol) and $ZnCl_2$ (45.0 mg, 0.33 mmol) were employed to afford the indicated product (39.1 mg (43%) in refluxing DCM; 67.3 mg (74%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.77 (m, 2H), 7.67 (s, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.51-7.42 (m, 3H), 7.37-7.24 (m, 2H), 6.43 (s, 1H), 4.79 (d, *J* = 0.9 Hz, 1H), 4.59 (s, 2H), 4.42 (d, *J* = 1.5 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3 (C), 158.9 (C), 158.2 (C), 139.7 (C), 138.1 (C), 135.3 (C), 130.9 (CH), 130.2 (CH), 128.7 (CH), 128.3 (CH), 128.0 (CH), 126.4 (CH), 124.7 (CH), 99.9 (CH), 93.9 (CH_2), 55.5 (CH_2), 21.5 (CH_3); IR (neat): 3056, 3026, 2920, 1707, 1657, 1622, 1596, 1546, 1491, 1447, 1373, 1315, 1260, 1198, 1067, 1044, 1024, 999, 907, 831, 787, 764 cm^{-1}; MS (ESI, m/z): 276.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{18}NO$: 276.1383 $[M+H]^+$, found: 276.1394.

2-Methylene-7-phenyl-5-(*p*-tolyl)-2,3-dihydro-1,4-oxazepine (2c). 1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(*p*-tolyl)prop-2-en-1-one (**1c**) (88.1 mg, 0.32 mmol) and $ZnCl_2$ (43.6 mg, 0.32 mmol) were employed to afford the indicated product (54.6 mg (62%) in refluxing DCM; 65.2 mg (74%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.74 (m, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.48-7.41 (m, 3H), 7.22 (d, *J* = 8.0 Hz, 1H), 6.40 (s, 1H), 4.75 (s, 1H), 4.55 (s, 2H), 4.39 (d, *J* = 1.5 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9 (C), 158.8 (C), 158.4 (C), 140.2 (C), 137.1 (C), 135.3 (C), 130.1 (CH), 129.1 (CH), 128.6 (CH), 127.4 (CH), 126.3 (CH), 100.0 (CH), 93.7 (CH_2), 55.4 (CH_2), 21.4 (CH_3); IR (neat): 3112, 3055, 3025, 3000, 2962, 2836, 1659, 1624, 1584, 1561, 1508, 1492, 1446, 1362, 1316, 1292, 1264, 1229, 1198, 1179, 1109, 1063, 1028, 950, 882, 854, 812, 758 cm^{-1}; MS (ESI, m/z): 276.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{18}NO$: 276.1383 $[M+H]^+$, found: 276.1386.

5-(2-Methoxyphenyl)-2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepine (2d). 3-(2-Methoxyphenyl)-1-phenyl-3-(prop-2-yn-1-

ylamino)prop-2-en-1-one (**1d**) (110.7 mg, 0.38 mmol) and $ZnCl_2$ (51.8 mg, 0.38 mmol) were employed to afford the indicated product (69.7 mg (63%) in refluxing DCM; 73.1 mg (66%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.69 (m, 2H), 7.51 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.43-7.34 (m, 4H), 7.03-6.97 (m, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.37 (s, 1H), 4.77 (d, *J* = 0.9 Hz, 1H), 4.56 (s, 2H), 4.40 (d, *J* = 1.3 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7 (C), 157.8 (C), 157.3 (C), 156.8 (C), 135.5 (C), 130.8 (CH), 130.3 (CH), 130.0 (CH), 128.6 (CH), 126.4 (CH), 120.9 (CH), 111.6 (CH), 102.6 (CH), 94.2 (CH_2), 55.9 (OCH_3), 55.7 (CH_2) (Note that one C and one CH peak overlap on each other); IR (neat): 3059, 2937, 2836, 1731, 1710, 1657, 1623, 1597, 1567, 1487, 1461, 1434, 1365, 1321, 1241, 1179, 1161, 1120, 1063, 1046, 1020, 904, 813, 751 cm^{-1}; MS (ESI, m/z): 292.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{18}NO_2$: 292.1332 $[M+H]^+$, found: 292.1345.

5-(4-Methoxyphenyl)-2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepine (2e). 3-(4-Methoxyphenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1e**) (131.1 mg, 0.45 mmol) and $ZnCl_2$ (61.3 mg, 0.45 mmol) were employed to afford the indicated product (86.5 mg (66%) in refluxing DCM; 95.7 mg (73%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.74 (m, 4H), 7.46-7.41 (m, 3H), 6.95-6.89 (m, 2H), 6.39 (s, 1H), 4.73 (d, *J* = 1.1 Hz, 1H), 4.53 (s, 2H), 4.38 (d, *J* = 1.5 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4 (C), 161.4 (C), 158.9 (C), 158.6 (C), 135.4 (C), 132.4 (C), 130.2 (CH), 129.1 (CH), 128.7 (CH), 126.4 (CH), 113.8 (CH), 99.9 (CH), 93.7 (CH_2), 55.5 (OCH_3), 55.3 (CH_2); IR (neat): 3081, 3052, 2996, 2953, 2835, 1656, 1630, 1604, 1586, 1562, 1510, 1492, 1462, 1432, 1367, 1315, 1299, 1254, 1199, 1172, 1109, 1063, 1029, 999, 869, 856, 820, 762 cm^{-1}; MS (ESI, m/z): 292.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{18}NO_2$: 292.1332 $[M+H]^+$, found: 292.1346.

***N,N*-Dimethyl-4-(2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepin-5-yl)aniline (2f).** 3-(4-(Dimethylamino)phenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1f**) (91.3 mg, 0.30 mmol) and $ZnCl_2$ (40.9 mg, 0.30 mmol) were employed to afford the indicated product (42.9 mg (47%) in refluxing DCM; 36.5 mg (40%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.75 (m, 2H), 7.74-7.70 (m, 2H), 7.46-7.40 (m, 3H), 6.75-6.65 (m, 2H), 6.43 (s, 1H), 4.70 (d, *J* = 1.0 Hz, 1H), 4.51 (s, 2H), 4.37 (d, *J* = 1.4 Hz, 1H), 3.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4 (C), 159.0 (C), 158.5 (C), 151.8 (C), 135.5 (C), 130.0 (CH), 128.7 (CH), 128.6 (CH), 127.2 (C), 126.3 (CH), 111.5 (CH), 100.3 (CH), 93.2 (CH_2), 54.9 (CH_2), 40.4 ($N(CH_3)_2$); IR (neat): 2891, 2828, 1737, 1646, 1629, 1606, 1578, 1548, 1523, 1490, 1447, 1357, 1317, 1267, 1189, 1107, 1059, 811, 758, 683 cm^{-1}; MS (ESI, m/z): 305.17 $[M+H]^+$; HRMS (ESI) calcd. for $C_{20}H_{21}N_2O$: 305.1648 $[M+H]^+$, found: 305.1662.

5-(2-Bromophenyl)-2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepine (2g). 3-(2-Bromophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1g**) (112.3 mg, 0.33 mmol) and $ZnCl_2$ (45.0 mg, 0.33 mmol) were employed to afford the indicated product (70.7 mg (63%) in refluxing DCM; 82.0 mg (73%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.67 (m, 2H), 7.60 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.48-7.32 (m, 5H), 7.27-7.20 (m, 1H), 6.13 (s, 1H), 4.84 (d, *J* = 1.0 Hz, 1H), 4.58 (s, 2H), 4.44 (d, *J* = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6 (C), 157.9 (C), 157.2 (C), 142.0 (C), 135.0 (C), 133.2 (CH), 130.2 (CH), 130.2 (CH), 130.1 (CH), 128.6 (CH), 127.5 (CH), 126.4 (CH), 121.3 (CBr), 101.4 (CH), 95.2 (CH_2), 56.1 (CH_2); IR (neat): 3058, 1657, 1623, 1597, 1571, 1464, 1365, 1318, 1294, 1257, 1193, 1153, 1119, 1066, 1045, 1024, 848, 826, 757 cm^{-1}; MS (ESI, m/z): 340.03 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}{}^{79}BrNO$: 340.0332 $[M+H]^+$, found: 340.0330.

5-(3-Fluorophenyl)-2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepine (2h). 3-(3-Fluorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1h**) (89.4 mg, 0.32 mmol) and $ZnCl_2$ (43.6 mg, 0.32 mmol) were employed to afford the indicated product (76.9 mg (86%) in refluxing DCM; 80.5 mg (90%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.74 (m, 2H), 7.59-7.56 (m, 1H), 7.55-7.51 (m, 1H), 7.48-7.41 (m, 3H), 7.37 (td, *J* = 8.0, 5.8 Hz, 1H), 7.13 (tdd, *J* = 8.3, 2.6, 0.8 Hz, 1H), 6.35 (s, 1H), 4.78 (d, *J* = 0.4 Hz, 1H), 4.56 (s, 2H), 4.41 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (C), 162.9 (d, ^1J = 246.2 Hz, CF), 159.5 (C), 158.0 (C), 142.1 (d, ^3J = 7.1 Hz, C), 135.1 (C), 130.4 (CH), 130.0 (d, ^3J = 8.0 Hz, CH), 128.7 (CH), 126.4 (CH), 123.2 (d, ^4J = 2.5 Hz, CH), 116.7 (d, ^2J = 21.6 Hz, CH), 114.5 (d, ^2J = 22.7 Hz, CH), 99.2 (CH), 94.4 (CH_2), 55.6 (CH_2). IR (neat): 3102, 2993, 2951, 2837, 1731, 1704, 1656, 1624, 1569, 1483, 1447, 1431, 1361, 1313, 1296, 1261, 1248, 1196, 1174, 1104, 1077, 1055, 874, 825, 790, 762 cm^{-1}; MS (ESI, m/z): 280.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}FNO$: 280.1132 $[M+H]^+$, found: 280.1137.

2-Methylene-7-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1,4-oxazepine (2i). 1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**1i**) (98.8 mg, 0.30 mmol) and $ZnCl_2$ (40.9 mg, 0.30 mmol) were employed to afford the indicated product (79.0 mg (80%) in refluxing DCM; 81.0 mg (82%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.1 Hz, 2H), 7.80-7.74 (m, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.50-7.41 (m, 3H), 6.36 (s, 1H), 4.80 (d, *J* = 1.1 Hz, 1H), 4.59 (s, 2H), 4.42 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (C), 159.8 (C), 157.8 (C), 143.1 (C), 135.0 (C), 131.9 (q, ^2J = 32.4 Hz, C), 130.5 (CH), 128.8 (CH), 127.9 (CH), 126.5 (CH), 125.4 (q, ^3J = 3.7 Hz, CH), 124.2 (q, ^1J = 272.2 Hz, CF_3), 99.0 (CH), 94.7 (CH_2), 55.8 (CH_2); IR (neat): 3109, 3085, 3054, 3039, 1660, 1623, 1586, 1565, 1491, 1446, 1408, 1365, 1326, 1315, 1264, 1201, 1183, 1153, 1105, 1067, 1014, 947, 884, 861, 819, 759 cm^{-1}; MS (ESI, m/z): 330.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{15}F_3NO$: 330.1100 $[M+H]^+$, found: 330.1101.

2-Methylene-7-phenyl-5-(thiophen-3-yl)-2,3-dihydro-1,4-oxazepine (2j). 1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(thiophen-3-yl)prop-2-en-1-one (**1j**) (82.9 mg, 0.31 mmol) and $ZnCl_2$ (42.3 mg, 0.31 mmol) were employed to afford the indicated product (61.3 mg (74%) in refluxing DCM; 69.6 mg (84%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81-7.72 (m, 2H), 7.68 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.56 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.48-7.40 (m, 3H), 7.31 (dd, *J* = 5.1, 3.0 Hz, 1H), 6.41 (s, 1H), 4.75 (br s, 1H), 4.53 (s, 2H), 4.40 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (C), 158.6 (C), 158.1 (C), 142.9 (C), 135.2 (C), 130.2 (CH), 128.7 (CH), 126.9 (CH), 126.4 (CH), 126.0 (CH), 125.7 (CH), 99.5 (CH), 94.1 (CH_2), 55.4 (CH_2); IR (neat): 3098, 2989, 2954, 2832, 1656, 1626, 1577, 1492, 1448, 1352, 1312, 1283, 1261, 1194, 1110, 1057, 1028, 872, 764, 689 cm^{-1}; MS (ESI, m/z): 268.08 $[M+H]^+$; HRMS (ESI) calcd. for $C_{16}H_{14}NOS$: 268.0791 $[M+H]^+$, found: 268.0791.

5-Butyl-2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepine (2k) and (2-butyl-4-methyl-1*H*-pyrrol-3-yl)(phenyl)methanone (3k). 1-Phenyl-3-(prop-2-yn-1-ylamino)hept-2-en-1-one (**1k**) (72.4 mg, 0.30 mmol) and $ZnCl_2$ (40.9 mg, 0.30 mmol) were employed. Chromatographic purification of crude product on silica gel produced a mixture of two compounds. The mixture was then rechromatographed on aluminium oxide (neutral), which afforded two fractions. The product in the first fraction was identified as 5-butyl-2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepine (**2k**) (42.7 mg (59%) in refluxing DCM; 52.1 mg (72%) in refluxing $CHCl_3$). The product in the second fraction was assigned as (2-butyl-4-methyl-1*H*-pyrrol-3-yl)(phenyl)methanone (**3k**) (10.1 mg (14%) in refluxing DCM; 6.5 mg (9%) in refluxing $CHCl_3$).

2k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.63 (m, 2H), 7.44-7.35 (m, 3H), 5.88 (s, 1H), 4.68 (d, *J* = 1.1 Hz, 1H), 4.31 (s, 3H), 2.43-2.34 (m, 2H), 1.60 (tt, *J* = 7.8, 6.5 Hz, 2H), 1.37 (sextet, *J* = 7.3 Hz, 2H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (C), 157.8 (C), 157.1 (C), 135.2 (C), 130.0 (CH), 128.6 (CH), 126.3 (CH), 100.9 (CH), 93.8 (CH_2),

55.2 (CH_2), 40.3 (CH_2), 29.9 (CH_2), 22.5 (CH_2), 14.1 (CH_3); IR (neat): 3268, 2957, 2928, 2870, 1703, 1623, 1596, 1450, 1428, 1378, 1266, 1175, 1107, 1072, 1025, 767, 699 cm^{-1}; MS (ESI, m/z): 242.15 $[M+H]^+$; HRMS (ESI) calcd. for $C_{16}H_{20}NO$: 242.1539 $[M+H]^+$, found: 242.1541.

3k: ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (br s, 1H), 7.47-7.31 (m, 5H), 6.56 (dd, *J* = 2.2, 1.0 Hz, 1H), 2.39-2.31 (m, 2H), 2.26 (d, *J* = 0.8 Hz, 3H), 1.51-1.42 (m, 2H), 1.10 (sextet, *J* = 7.4 Hz, 2H), 0.73 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8 (C=O), 136.6 (C), 133.7 (C), 129.2 (CH), 128.6 (CH), 128.5 (CH), 122.2 (C), 121.8 (C), 117.0 (CH), 42.2 (CH_2), 27.2 (CH_2), 22.4 (CH_2), 13.9 (CH_3), 12.6 (CH_3); IR (neat): 3467, 3194, 3056, 2954, 2928, 1708, 1679, 1622, 1450, 1421, 1402, 1340, 1281, 1060, 768, 696 cm^{-1}; MS (ESI, m/z): 242.16 $[M+H]^+$; HRMS (ESI) calcd. for $C_{16}H_{20}NO$: 242.1539 $[M+H]^+$, found: 242.1551.

2-(2-Methylene-7-phenyl-2,3-dihydro-1,4-oxazepin-5-yl)isoindoline-1,3-dione (2l) and 2-(2-(3-benzoyl-4-methyl-1*H*-pyrrol-2-yl)ethyl)isoindoline-1,3-dione (3l). 2-(5-Oxo-5-phenyl-3-(prop-2-yn-1-ylamino)pent-3-en-1-yl)isoindoline-1,3-dione (**1l**) (75.1 mg, 0.21 mmol) and $ZnCl_2$ (28.6 mg, 0.21 mmol) were employed. Chromatographic purification of crude product on silica gel produced a mixture of two compounds. The mixture was then rechromatographed on aluminium oxide (neutral), which afforded two fractions. The product in the first fraction was identified as 2-(2-methylene-7-phenyl-2,3-dihydro-1,4-oxazepin-5-yl)isoindoline-1,3-dione (**2l**) (30.0 mg (40%) in refluxing DCM; 30.0 mg (40%) in refluxing $CHCl_3$). Second fraction produced a mixture of 1,4-oxazepine **2l** and pyrrole **3l**. Spectroscopic identification of pyrrole **3l** was made by peak picking of ^1H NMR spectrum of the mixture (see Figure S87 on page S45 of Supporting Information). The yield of pyrrole **3l** was calculated by the integration of the related ^1H NMR peaks of the mixture, which was found to be 20% (equivalent to 15.0 mg) in refluxing DCM and 12% (equivalent to 9.0 mg) in refluxing $CHCl_3$.

2l: ^1H NMR (400 MHz, $CDCl_3$) δ ^1H NMR (400 MHz, CDCl3) δ 7.83-7.79 (m, 2H), 7.69-7.65 (m, 2H), 7.65-7.62 (m, 2H), 7.41-7.34 (m, 3H), 5.87 (s, 1H), 4.67 (d, *J* = 1.0 Hz, 1H), 4.27 (s, 2H), 4.24 (d, *J* = 1.4 Hz, 1H), 4.02 (t, *J* = 7.3 Hz, 2H), 2.77 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2 (C=O), 158.1 (C), 157.0 (C), 134.9 (C), 133.9 (CH), 132.6 (CH), 132.3 (C), 130.2 (C), 128.6 (CH), 126.4 (CH), 123.3 (CH), 100.4 (CH), 94.6 (CH_2), 55.2 (CH_2), 38.4 (CH_2), 36.0 (CH_2); IR (neat): 3393, 3180, 2917, 2848, 1764, 1698, 1644, 1596, 1468, 1419, 1400, 1362, 1319, 1258, 1091, 992, 829, 760, 718 cm^{-1}; MS (ESI, m/z): 359.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{22}H_{19}N_2O_3$: 359.1390 $[M+H]^+$, found: 359.1400.

3l: ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (br s, 1H), in 7.84-7.75 (m, 2H), in 7.69-7.65 (m, 2H), in 7.41-7.34 (m, 5H), 6.55 (dd, *J* = 2.2, 1.0 Hz, 1H), 3.92 (t, *J* = 7.5 Hz, 2H), in 2.84-2.74 (m, 2H), 2.26 (d, *J* = 0.9 Hz, 3H). As mentioned above, pyrrole **3l** could not be isolated in pure state from flash column chromatography. That's why; further characterization of this compound could not be achieved.

7-(2-Bromophenyl)-2-methylene-5-phenyl-2,3-dihydro-1,4-oxazepine (2m). 1-(2-Bromophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1m**) (88.5 mg, 0.26 mmol) and $ZnCl_2$ (35.4 mg, 0.26 mmol) were employed to afford the indicated product (70.8 mg (80%) in refluxing DCM; 71.7 mg (81%) in refluxing $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76-7.70 (m, 2H), 7.57 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.38-7.27 (m, 4H), 7.23-7.16 (m, 1H), 5.95 (s, 1H), 4.60 (s, 3H), 4.29 (d, *J* = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8 (C), 159.7 (C), 158.9 (C), 139.2 (C), 137.9 (C), 133.5 (CH), 130.9 (CH), 130.8 (CH), 130.3 (CH), 128.5 (CH), 127.54 (CH), 127.47 (CH), 122.1 (CBr), 104.7 (CH), 94.2 (CH_2), 55.6 (CH_2); IR (neat): 3246, 3055, 2966, 2841, 1655, 1629, 1587, 1563, 1485, 1464, 1434, 1360, 1313, 1253, 1189, 1180, 1114, 1077, 1064, 1025, 953, 857, 831, 755 cm^{-1}; MS (ESI, m/z): 340.03 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}{}^{79}BrNO$: 340.0332 $[M+H]^+$, found: 340.0332.

7-(2-Bromophenyl)-2-methylene-5-(*m*-tolyl)-2,3-dihydro-1,4-oxazepine (2n). 1-(2-Bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(*m*-tolyl)prop-2-en-1-one (**1n**) (77.9 mg, 0.22 mmol) and $ZnCl_2$ (30.0 mg, 0.22 mmol) were employed to afford the indicated product (42.8 mg (55%) in refluxing DCM; 74.0 mg (95%) in refluxing $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.75-7.50 (m, 4H), 7.47-7.17 (m, 4H), 6.06 (s, 1H), 4.71 (s, 3H), 4.40 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9 (C), 159.5 (C), 158.9 (C), 139.1 (C), 138.2 (C), 137.8 (C), 133.5 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 128.3 (CH), 128.0 (CH), 127.5 (CH), 124.6 (CH), 122.1 (CBr), 104.8 (CH), 94.1 (CH_2), 55.5 (CH_2), 21.5 (CH_3); IR (neat): 3021, 2921, 2855, 1653, 1632, 1592, 1572, 1466, 1355, 1310, 1255, 1184, 1106, 1066, 1039, 1021, 951, 862, 831, 796, 757 cm^{-1}; MS (ESI, m/z): 354.05 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO$: 354.0488 $[M+H]^+$, found: 354.0495.

7-(2-Bromophenyl)-2-methylene-5-(*p*-tolyl)-2,3-dihydro-1,4-oxazepine (2o). 1-(2-Bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(*p*-tolyl)prop-2-en-1-one (**1o**) (102.7 mg, 0.29 mmol) and $ZnCl_2$ (39.5 mg, 0.29 mmol) were employed to afford the indicated product (71.9 mg (70%) in refluxing DCM; 92.4 mg (90%) in refluxing $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.57 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.44-7.37 (m, 1H), 7.33-7.27 (m, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.06 (s, 1H), 4.70 (s, 3H), 4.40 (br s, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6 (C), 159.5 (C), 159.0 (C), 140.5 (C), 137.8 (C), 136.3 (C), 133.4 (CH), 130.9 (CH), 130.8 (CH), 129.2 (CH), 127.5 (CH), 127.4 (CH), 122.1 (CBr), 104.8 (CH), 94.0 (CH_2), 55.4 (CH_2), 21.5 (CH_3); IR (neat): 2951, 2920, 2839, 1656, 1626, 1610, 1589, 1562, 1509, 1467, 1434, 1353, 1310, 1277, 1252, 1181, 1107, 1071, 1040, 1030, 861, 812, 754 cm^{-1}; MS (ESI, m/z): 354.05 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO$: 354.0488 $[M+H]^+$, found: 354.0489.

7-(2-Bromophenyl)-5-(2-methoxyphenyl)-2-methylene-2,3-dihydro-1,4-oxazepine (2p). 1-(2-Bromophenyl)-3-(2-methoxyphenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1p**) (74.0 mg, 0.20 mmol) and $ZnCl_2$ (27.3 mg, 0.20 mmol) were employed to afford the indicated product (59.9 mg (81%) in refluxing DCM; 65.1 mg (88%) in refluxing $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.55 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.49 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.41-7.33 (m, 2H), 7.30-7.25 (m, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.02 (s, 1H), 4.71 (s, 2H), 4.70 (s, 1H), 4.38 (d, *J* = 1.3 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5 (C), 158.9 (C), 157.2 (C), 157.1 (C), 138.1 (C), 133.3 (CH), 130.83 (CH), 130.77 (CH), 130.7 (CH), 130.3 (CH), 129.6 (C) 127.4 (CH), 122.2 (CBr), 120.9 (CH), 111.4 (CH), 107.7 (CH), 93.8 (CH_2), 55.9 (OCH_3), 55.8 (CH_2); IR (neat): 2962, 2831, 1656, 1630, 1591, 1569, 1486, 1465, 1433, 1360, 1313, 1300, 1253, 1189, 1162, 1113, 1076, 1027, 943, 872, 851, 832, 751 cm^{-1}; MS (ESI, m/z): 370.04 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO_2$: 370.0437 $[M+H]^+$, found: 370.0440.

7-(2-Bromophenyl)-5-(4-methoxyphenyl)-2-methylene-2,3-dihydro-1,4-oxazepine (2q). 1-(2-Bromophenyl)-3-(4-methoxyphenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1q**) (74.0 mg, 0.20 mmol) and $ZnCl_2$ (27.3 mg, 0.20 mmol) were employed to afford the indicated product (51.8 mg (70%) in refluxing DCM; 66.6 mg (90%) in refluxing $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.84-7.77 (m, 2H), 7.67 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.56 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.40 (td, *J* = 7.5, 1.0 Hz, 1H), 7.33-7.27 (m, 1H), 6.97-6.90 (m, 2H), 6.05 (s, 1H), 4.68 (s, 3H), 4.38 (d, *J* = 0.8 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9 (C), 161.4 (C), 159.33 (C), 159.30 (C), 137.9 (C), 133.4 (CH), 131.9 (C), 130.87 (CH), 130.83 (CH), 129.0 (CH), 127.5 (CH), 122.1 (CBr), 113.7 (CH), 104.8 (CH), 93.7 (CH_2), 55.4 (OCH_3), 55.3 (CH_2); IR (neat): 2993, 2952, 2835, 1656, 1627, 1603, 1587, 1569, 1510, 1492, 1461, 1361, 1312, 1192, 1168, 1107, 1072, 1028, 1000, 945, 855, 821, 759 cm^{-1}; MS (ESI, m/z): 370.04

$[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}{}^{79}BrNO_2$: 370.0437 $[M+H]^+$, found: 370.0442.

5,7-Bis(2-bromophenyl)-2-methylene-2,3-dihydro-1,4-oxazepine (2r). 1,3-Bis(2-bromophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1r**) (83.8 mg, 0.20 mmol) and $ZnCl_2$ (27.3 mg, 0.20 mmol) were employed to afford the indicated product (64.5 mg (77%) in refluxing DCM; 57.0 mg (68%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.60 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.54 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.36 (td, *J* = 7.5, 1.2 Hz, 2H), 7.31-7.21 (m, 2H), 5.78 (s, 1H), 4.79 (s, 1H), 4.72 (s, 2H), 4.43 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6 (C), 158.7 (C), 158.1 (C), 141.4 (C), 137.6 (C), 133.4 (CH), 133.2 (CH), 130.9 (CH), 130.6 (CH), 130.4 (CH), 130.2 (CH), 127.6 (CH), 127.5 (CH), 122.1 (CBr), 121.3 (CBr), 106.3 (CH), 95.1 (CH_2), 56.1 (CH_2); IR (neat): 3055, 2973, 1656, 1629, 1589, 1577, 1562, 1466, 1428, 1360, 1316, 1300, 1247, 1190, 1117, 1075, 1024, 943, 854, 828, 753 cm^{-1}; MS (ESI, m/z): 417.94 and 419.94 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}{}^{79}Br_2NO$: 417.9437 $[M+H]^+$, found: 417.9432; calcd. for $C_{18}H_{14}{}^{79}Br^{81}Br$ NO: 419.9417 $[M+H]^+$, found: 419.9417.

7-(2-Bromophenyl)-5-(3-fluorophenyl)-2-methylene-2,3-dihydro-1,4-oxazepine (2s). 1-(2-Bromophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1s**) (96.7 mg, 0.27 mmol) and $ZnCl_2$ (36.8 mg, 0.27 mmol) were employed to afford the indicated product (76.4 mg (79%) in refluxing DCM; 83.2 mg (86%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.53-7.48 (m, 1H), 7.48-7.42 (m, 2H), 7.34-7.25 (m, 2H), 7.24-7.17 (m, 1H), 7.07-7.01 (m, 1H), 5.90 (s, 1H), 4.62 (d, *J* = 1.4 Hz, 1H), 4.60 (s, 2H), 4.31 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7 (C), 162.9 (d, ^1J = 246.2 Hz, CF), 160.2 (C), 158.5 (C), 141.3 (d, ^3J = 7.7 Hz, C), 137.6 (C), 133.5 (CH), 131.1 (CH), 130.8 (CH), 130.0 (d, ^3J = 8.1 Hz, CH), 127.6 (CH), 123.2 (d, ^4J = 2.5 Hz, CH), 122.0 (CBr), 117.21 (d, ^2J = 21.4 Hz, CH), 114.4 (d, ^2J = 22.8 Hz, CH), 104.1 (CH), 94.7 (CH_2), 55.5 (CH_2); IR (neat): 3063, 2959, 1657, 1625, 1571, 1484, 1468, 1439, 1359, 1309, 1297, 1277, 1258, 1241, 1194, 1161, 1110, 1072, 1042, 1027, 1010, 981, 945, 897, 857, 786, 756 cm^{-1}; MS (ESI, m/z): 358.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}{}^{79}BrFNO$: 358.0237 $[M+H]^+$, found: 358.0242.

7-(2-Bromophenyl)-2-methylene-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1,4-oxazepine (2t). 1-(2-Bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**1t**) (93.9 mg, 0.23 mmol) and $ZnCl_2$ (31.4 mg, 0.23 mmol) were employed to afford the indicated product (86.4 mg (92%) in refluxing DCM; 85.4 mg (91%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 3H), 7.57 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.41 (td, *J* = 7.5, 1.1 Hz, 1H), 7.32 (td, *J* = 7.7, 1.7 Hz, 1H), 6.03 (s, 1H), 4.75 (s, 1H), 4.74 (s, 2H), 4.43 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6 (C), 160.2 (C), 158.5 (C), 142.5 (C), 137.6 (C), 133.5 (CH), 131.9 (q, ^2J = 32.5 Hz, C), 131.1 (CH), 130.7 (CH), 127.8 (CH), 127.6 (CH), 125.4 (q, ^3J = 3.7 Hz, CH), 124.1 (q, ^1J = 272.3 Hz, CF_3), 122.0 (CBr), 104.0 (CH), 94.8 (CH_2), 55.8 (CH_2); IR (neat): 3054, 2985, 1650, 1632, 1595, 1571, 1467, 1443, 1408, 1359, 1320, 1256, 1185, 1173, 1119, 1105, 1071, 1062, 1029, 1013, 954, 853, 767 cm^{-1}; MS (ESI, m/z): 408.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{14}{}^{79}BrF_3NO$: 408.0205 $[M+H]^+$, found: 408.0213.

7-(4-Chlorophenyl)-5-(3-fluorophenyl)-2-methylene-2,3-dihydro-1,4-oxazepine (2u). 1-(4-Chlorophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**1u**) (72.2 mg, 0.23 mmol) and $ZnCl_2$ (31.4 mg, 0.23 mmol) were employed to afford the indicated product (64.3 mg (89%) in refluxing DCM; 55.6 mg (77%) in refluxing $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73-7.66 (m, 2H), 7.55 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.53-7.48 (m, 1H), 7.44-7.33 (m, 3H), 7.17-7.09 (m, 1H), 6.31 (s, 1H), 4.77 (d, *J* = 1.2 Hz, 1H), 4.55 (s, 2H), 4.41 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (C), 162.9 (d, ^1J = 246.3 Hz, CF), 158.4 (C), 157.8 (C), 141.9 (d, ^3J = 7.1 Hz, C), 136.5 (C), 133.5 (C), 130.0 (d, ^3J = 8.1 Hz, CH), 128.9 (CH), 127.7 (CH), 123.2 (d, ^4J = 2.6 Hz, CH), 117.10 (d, ^2J = 21.5 Hz, CH), 114.5 (d, ^2J = 22.7 Hz, CH), 99.3 (CH), 94.7 (CH_2), 55.5 (CH_2); IR (neat): 3297, 2997, 1657, 1623, 1591, 1573, 1484, 1439, 1402, 1362, 1314, 1259, 1178, 1090, 1055, 1010, 984, 881, 819, 783 cm^{-1}; MS (ESI, m/z): 314.08 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}ClFNO$: 314.0743 $[M+H]^+$, found: 314.0750.

Synthesis of 1,3-diphenyl-3-((3-phenylprop-2-yn-1-yl)amino)prop-2-en-1-one (14). To a stirred solution of 1,3-diphenyl-3-(prop-2-ynylamino)prop-2-en-1-one (**1a**) (156.9 mg, 0.6 mmol) in DMF (0.15 mL) at room temperature under argon was added $(i\text{-Pr})_2NH$ (1.2 mL), $PdCl_2(PPh_3)_2$ (8.6 mg, 0.012 mmol) and CuI (2.3 mg, 0.012 mmol) in turn and the reaction mixture was stirred for 10 min. Iodobenzene (190.4 mg, 0.93 mmol) was then added and the resulting mixture was stirred at room temperature for approximately 3-5 h (Note that stirring was continued until β-enaminone **1a** was completely consumed as monitored by routine TLC). After the reaction was over, ethyl acetate (18 mL) was added, and the resulting solution was washed with 0.1 N HCl (4 mL) and subsequently with a saturated NH_4Cl solution (4 mL) in a separatory funnel. After the layers were separated, organic phase was dried over $MgSO_4$ and evaporated on a rotary evaporator to give the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9:1 followed by 4:1) as the eluent to afford 178.2 mg (88%) of the indicated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (br s, 1H), 7.96-7.87 (m, 2H), 7.57-7.52 (m, 2H), 7.51-7.47 (m, 3H), 7.46-7.38 (m, 5H), 7.35-7.28 (m, 3H), 5.87 (s, 1H), 4.18 (d, *J* = 6.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0 (C=O), 165.9 (C), 140.1 (C), 135.1 (C), 131.7 (CH), 130.9 (CH), 129.8 (CH), 128.7 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.2 (CH), 122.6 (C), 94.6 (CH), 85.2 (C), 84.2 (C), 35.0 (CH_2). The spectral data were in agreement with those reported previously for this compound.[35]

Reaction of *N*-propargylic β-enaminone 14 with $ZnCl_2$. To a stirred solution of 1,3-diphenyl-3-((3-phenylprop-2-yn-1-yl)amino)prop-2-en-1-one (**14**) (57.4 mg, 0.17 mmol) in DCM (3 mL) or in $CHCl_3$ (3 mL) at room temperature under argon were added $ZnCl_2$ (23.2 mg, 0.17 mmol). The resulting mixture was then refluxed at 40 °C (DCM) or at 61 °C ($CHCl_3$) (Note that reaction was continued until *N*-propargylic β-enaminone **14** was completely consumed as monitored by routine TLC). After the reaction was over, the solvent was removed on a rotary evaporator, and ethyl acetate (25 mL) and a saturated aqueous solution of NH_4Cl (10 mL) were added. After the layers were separated, the aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over $MgSO_4$ and evaporated on a rotary evaporator to give the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9:1 followed by 4:1) as the eluent to afford 14.3 mg (25%) in refluxing DCM and 16.0 mg (28%) in refluxing $CHCl_3$ of (2,4-diphenylpyridin-3-yl)(phenyl)methanone (**15**). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 5.1 Hz, 1H), 7.59-7.54 (m, 2H), 7.54-7.49 (m, 2H), 7.39 (d, *J* = 5.0 Hz, 1H), 7.39-7.34 (m, 1H), 7.30-7.19 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3 (C=O), 157.2 (C), 149.9 (CH), 149.3 (C), 139.6 (C), 137.9 (C), 137.7 (C), 133.7 (C), 133.3 (CH), 129.4 (CH), 129.3 (CH), 128.8 (CH), 128.7 (CH), 128.5 (2 x CH), 128.4 (CH), 128.3 (CH), 123.2 (CH); IR (neat): 3054, 1663, 1595, 1538, 1492, 1441, 1384, 1293, 1248, 1178, 1155, 1026, 921, 858, 753, 695 cm^{-1}; MS (ESI, m/z): 336.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}NO$: 336.1383 $[M+H]^+$, found: 336.1398. The spectral data were in agreement with those reported previously for this compound.[40]

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[1] G. V. Boyd, in *Houben-Weyl Methods of Organic Chemistry*, Hetarenes III, Part 4; (Eds.: K. H. Büchel, J. Falbe, H. Hagemann, M. Hanack, D. Klamann, R. Kreher, H. Kropf, M. Regitz, E. Schaumann), George Thieme Verlag: Stuttgart, **1998**; Vol. E9d, pp 299–323.

[2] (a) I. Ninomiya, T. Naito, O. Miyata, in *Comprehensive Heterocyclic Chemistry II*; (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven, G. R. Newkome), Pergamon: Oxford, **1996**; Vol. 9, Chapter 9.09, pp 217–231. (b) W. Dehaen, T. H. Ngo, in *Comprehensive Heterocyclic Chemistry III* (Eds.: A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven, R. J. K.. Taylor, G. R. Newkome), Pergamon: Oxford, **2008**; Vol. 13, Chapter 13.09, pp 255–298. (c) H. Kwiecien, M. Smist, A. Wrzesniewska, *Curr. Org. Synth.* **2012**, *9*, 828-850. (d) N. Zaware, M. Ohlmeyer, *Heterocycl. Commun.* **2014**, *20*, 251–256.

[3] (a) H. Toshiyuki, I. Takahiro, Y. Hisao, *Ger. Offen.* 2 014 223, **1969**. (b) R. T. Standridge, *US Patent* 4125538, **1978**; *Chem. Abstr.* **1979**, *90*, 72246r. (c) E. A. Hallinan, T. J. Hagen, R. K. Husa, S. Tsymbalov, S. N. Rao, J. P. vanHoeck, M. F. Rafferty, A. Stapelfeld, M. A. Savage, M. Reichman, *J. Med. Chem.* **1993**, *36*, 3293. (d) E. A. Hallinan, A. Stapelfeld, M. A. Savage, M. Reichman, *Bioorg. Med. Chem. Lett.* **1994**, *4*, 509. (e) E. A. Hallinan, T. J. Hagen, S. Tsymbalov, R. K. Husa, A. C. Lee, A. Stapelfeld, M. A. Savage, *J. Med. Chem.* **1996**, *39*, 609. (f) E. A. Hallinan, T. J. Hagen, S. Tsymbalov, A. Stapelfeld, M. A. Savage, *Bioorg. Med. Chem.* **2001**, *9*, 1.

[4] G. Walther, C. Schneider, K. H. Weber, A. Fuegner, *Chem. Abstr.* **1983**, *98*, 198233; *DE Patent* 3134672.

[5] H. Hamidi, M. M. Heravi, M. Tajbakhsh, M. Shiri, H. A. Oskooie, S. A. Shintre, N. A. Koorbanally, *J. Iran. Chem. Soc.* **2015**, *12*, 2205.

[6] W. E. Coyne, J. W. Cusic, *J. Med. Chem.* **1968**, *11*, 1158.

[7] (a) K. Nagarajan, J. David, R. S. Grewal, T. R. Govindachari, *Ind. J. Exp. Biol.* **1974**, *12*, 217. (b) K. Nagarajan, A. Venkateswarlu, C. L. Kulkarni, G. A. Nagana, R. K. Shah, *Ind. J. Chem.* **1974**, *12*, 236. (c) E. F. Coccaro, L. J. Siever, *J. Clin. Pharmacol.* **1985**, *25*, 241. (d) K. Nagarajan, J. David, Y. S. Kulkarni, S. B. Hendi, S. J. Shenoy, P. Upadhyaya, *Eur. J. Med. Chem. Chim. Ther.* **1986**, *21*, 21.

[8] (a) W. J. Van der Burg, R. R. M. Salsmans, *Chem. Abstr.* **1976**, *85*, 160191; *DE Patent* 2548045. (b) W. J. Van der Burg, R. R. M. Salsmans, *US Patent* 4039558, **1977**.

[9] (a) F. G. Sulman, Y. Pfeifer, E. Superstine, *Arzneimittelforschung* **1981**, *31*, 109. (b) G. Walther, H. Daniel, W. D. Bechtel, K. Brandt, *Arzneimittelforschung* **1990**, *40*, 440.

[10] J. K. Chakrabarti, T. A. Hicks, *Eur. J. Med. Chem.* **1987**, *22*, 161.

[11] Y. Liao, B. J. Venhuis, N. Rodenhuis, W. Timmerman, H. Wikstrom, E. Meire, G. D. Bartoszyk, H. Bottcher, C. A. Seyfried, S. Sundell, *J. Med. Chem.* **1999**, *42*, 2235.

[12] W. J. Van der Burg, *Chem. Abstr.* **1974**, *81*, 3986; *DE Patent* 2347727.

[13] W. J. Van der Burg, *Chem. Abstr.* **1973**, *79*, 5339; *DE Patent* 2248477.

[14] M. Binaschi, A. Boldetti, M. Gianni, C. A. Maggi, M. Gensini, M. Bigioni, M. Parlani, A. Giolitti, M. Fratelli, C. Valli, M. Terao, E. Garattini, *ACS Med. Chem. Lett.* **2010**, *1*, 411.

[15] Y. Yin, Y. Q. Zhang, B. Jin, S. Sha, X. Wu, C. B. Sangani, S. F. Wang, F. Qiao, A. M. Lu, P. C. Lv, H. L. Zhu, *Bioorg. Med. Chem.* **2015**, *23*, 1231.

[16] R. A. Smits, H. D. Lim, B. Stegink, R. A. Bakker, I. J. P. de Esch, R. Leurs, *J. Med. Chem.* **2006**, *49*, 4512.

[17] P. P. M. A. Dols, B. J. B. Folmer, H. Hamersma, C. W. Kuil, H. Lucas, L. Ollero, J. B. M. Rewinkel, P. H. H. Hermkens, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1461.

[18] R. Li, P. S. Farmer, J. Wang, R. J. Boyd, T. S. Cameron, M. A. Quilliam, J. A. Walter, S. E. Howlett, *Drug. Des. Discov.* **1995**, *12*, 337.

[19] (a) J. M. Klunder, K. D. Hargrave, M. West, E. Cullen, K. Pal, M. L. Behnke, S. R. Kapadia, D. W. McNeil, J. C. Wu, G. C. Chow, J. Adams, *J. Med. Chem.* **1992**, *35*, 1887. (b) K. Nagarajan, *J. Ind. Chem. Soc.* **1997**, *74*, 831. (c) F. Aiello, A. Brizzi, A. Garofalo, F. Grande, G. Ragno, R. Dayam, N. Neamati, *Bioorg. Med. Chem.* **2004**, *12*, 4459.

[20] G. Walther, C. S. Schneider, K. H. Weber, A. Fuegner, *Chem. Abstr.* **1982**, *96*, 6777; *DE Patent* 3008944.

[21] (a) M. Diaz-Gavilan, F. Rodritimeguez-Serrano, J. A. Gomez-Vidal, J. A. Marchal, A. Aranega, M. A. Gallo, A. Espinosa, J. M. Campos, *Tetrahedron* **2004**, *60*, 11547. (b) J. M. Mulligan, L. M. Greene, S. Cloonan, M. M. Mc Gee, V. Onnis, G. Campiani, C. Fattorusso, M. Lawler, D. C. Williams, D. M. Zisterer, *Mol. Pharmacol.* **2006**, *70*, 60. (c) K. Samanta, B. Chakravarti, J. K. Mishra, S. K. D. Dwivedi, L. V. Nayak, P. Choudhry, H. K. Bid, R. Konwar, N. Chattopadhyay, P. Panda, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 283.

[22] H. L. Yale, *J. Med. Chem.* **1968**, *11*, 396.

[23] (a) T. A. Ban, M. Fujimori, W. M. Petrie, M. Ragheb, W. H. Wilson, *Int. Pharmacopsych.* **1982**, *17*, 18. (b) B. M. Cohen, P. Q. Harris, R. I. Altesman, J. O. Cole, *Am. J. Psychiatry* **1982**, *139*, 1165. (c) S. Kapur, R. Cho, C. Jones, G. McKay, R. B. Zipursky, *Biol. Psychiatry* **1999**, *45*, 1217.

[24] (a) B. Blackwell, *Br. J. Psychiatry* **1976**, *129*, 513. (b) J. M. Klunder, K. D. Hargrave, M. West, E. Cullen, K. Pal, M. L. Behnke, S. R. Kapadia, D. W. McNeil, J. C. Wu, G. C. Chow, *J. Med. Chem.* **1992**, *35*, 1887. (c) N. D. Balani, S. M. Parhate, V. R. Thawani, A. M. Deshpande, *Ind. J. Physiol. Pharmacol.* **1995**, *39*, 293.

[25] (a) R. C. Heel, R. N. Brogden, T. M. Speight, G. S. Avery, *Drugs* **1978**, *15*, 198. (b) H. Umemiya, H. Fukasawa, M. Ebisawa, L. Eyrolles, E. Kawachi, G. Eisenmann, H. Gronemeyer, Y. Hashimoto, K. Shudo, H. Kagechika, *J. Med. Chem.* **1997**, *40*, 4222 and references cited therein. (c) A. Chakrabarti, A. M. Bagnall, P. Chue, M. Fenton, V. Palanisamy, W. Wong, J. Xia, *Cochrane Database of Systematic Reviews* **2007**, Issue 4, Art. No. CD001943. (d) S. H. Schultz, S. W. North, C. G. Shields, *Am. Fam. Phy.* **2007**, *75*, 1821. (e) A. Chakrabarti, A. M. Bagnall, P. Chue, M. Fenton, V. Palaniswamy, W. Wong, J. Xia, *The Cochrane Collaboration*, John Wiley & Sons: New York, **2012**.

[26] J. Kurita, K. Iwata, T. Tsuchiya, *J. Chem. Soc., Chem. Commun.* **1986**, 1188.

[27] J. Kurita, K. Iwata, T. Tsuchiya, *Chem. Pharm. Bull.* **1987**, *35*, 3166.

[28] C. Francois-Endelmond, T. Carlin, P. Thuery, O. Loreau, F. Taran, *Org. Lett.* **2010**, *12*, 40.

[29] (a) C. Jiang, M. Xu, S. Wang, H. Wang, Z. Y. Yao, *J. Org. Chem.* **2010**, *75*, 4323. (b) N. Fei, Q. Hou, S. Wang, H. Wang, Z. Y. Yao, *Org. Biomol. Chem.* **2010**, *8*, 4096. (c) Z. He, H. Li, Z. Li, *J. Org. Chem.* **2010**, *75*, 4636. (d) Z. He, W. Liu, Z. Li, *Chem. Asian J.* **2011**, *6*, 1340. (e) N. Fei, H. Yin, S. Wang, H. Wang, Z. Y. Yao, *Org. Lett.* **2011**, *13*, 4208. (f) H. Yin, F. Kong, S. Wang, Z. Y. Yao, *Tetrahedron Lett.* **2012**, *53*, 7078. (g) K. Goutham, N. S. V. M. R. Mangina, S. Suresh, P. Raghavaiah, G. V. Karunakar, *Org. Biomol. Chem.* **2014**, *12*, 2869. (h) K. Goutham, V. Nagaraju, S. Suresh, P. Raghavaiah, G. V. Karunakar, *RSC Adv.* **2014**, *4*, 21054. (i) S. Arshadi, E. Vessally, L. Edjlali, E. Ghorbani-Kalhor, R. Hosseinzadeh-Khanmiri, *RSC Adv.* **2017**, *7*, 13198.

[30] S. Cacchi, G. Fabrizi, E. Filisti, *Org. Lett.* **2008**, *10*, 2629.

[31] G. Cheng, Y. Weng, X. Yang, X. Cui, *Org. Lett.* **2015**, *17*, 3790.

[32] (a) J. Shen, X. Yang, F. Wang, Y. Wang, G. Cheng, X. Cui, *RSC Adv.* **2016**, *6*, 48905. (b) G. Cheng, L. Xue, Y. Weng, X. Cui, *J. Org. Chem.* **2017**, *82*, 9515.

[33] K. Goutham, D. A. Kumar, S. Suresh, B. Sridhar, R. Narender, G. V. Karunakar, *J. Org. Chem.* **2015**, *80*, 11162.

[34] N. S. V. M. R. Mangina, V. Kadiyala, R. Guduru, K. Goutham, B. Sridhar, G. V. Karunakar, *Org. Lett.* **2017**, *19*, 282.

[35] S. Karabiyikoglu, Y. Kelgokmen, M. Zora, *Tetrahedron* **2015**, *71*, 4324.

[36] (a) E. Karadeniz, M. Zora, N. Z. Kilicaslan, *Tetrahedron* **2015**, *71*, 8943. (b) Y. Kelgokmen, M. Zora, *RSC Adv.* **2016**, *6*, 4608.

[37] (a) M. Hatano, K. Ishihara, in *Acid Catalysis in Modern Organic Synthesis* (Eds.: H. Yamamoto, K. Ishihara), Wiley-VCH: Weinheim, **2008**; Vol. 1, Chapter 4, pp 135–186. (b) *Zinc Catalysis: Applications in Organic Synthesis* (Eds.: S. Enthaler, X. F. Wu), Wiley-VCH: Weinheim, **2015**.

[38] (a) B. K. Park, N. R. Kitteringham, P. M. O'Neill, *Annu. Rev. Pharmacol. Toxicol.* **2001**, *41*, 443. (b) R. Filler, R. Saha, *Future Med. Chem.* **2009**, *1*, 777. (c) T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem. Int. Ed.* **2013**, *52*, 8214. (d) J. Wang, M. Sanchez-Rosello, J. L. Acena, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, *Chem. Rev.* **2014**, *114*, 2432.

[39] J. P. Waldo, S. Mehta, B. Neuenswander, G. H. Lushington, R. C. Larock, *J. Comb. Chem.* **2008**, *10*, 658.

[40] Z. Song, X. Huang, W. Yi, W. Zhang, *Org. Lett.* **2016**, *18*, 5640.

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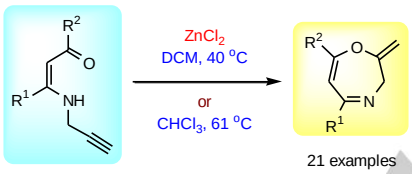
Layout 1:

FULL PAPER

A new robust method is described for the synthesis of 2-methylene-2,3-dihydro-1,4-oxazepines via $ZnCl_2$-mediated cyclization of *N*-propargylic β-enaminones



R^1 = aryl, heteroaryl, alkyl
R^2 = aryl

21 examples
up to 95% yield

1,4-Oxazepines

*Yilmaz Kelgokmen, Yasemin Cayan, Metin Zora**

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Zinc Chloride-Mediated Synthesis of 1,4-Oxazepines from *N*-Propargylic β-Enaminones

*one or two words that highlight the emphasis of the paper or the field of the study