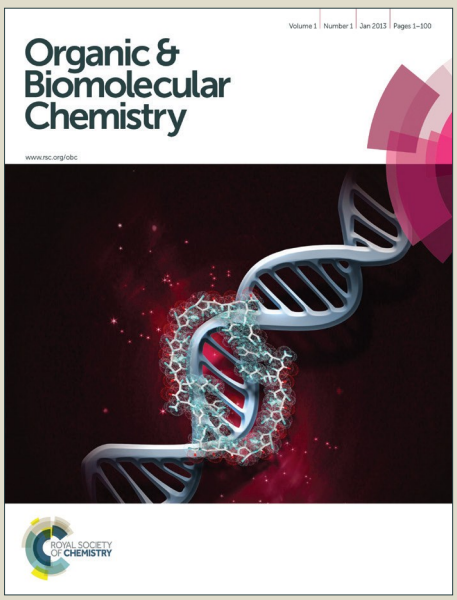
Organic & Biomolecular Chemistry

Accepted Manuscript



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ARTICLE

Hg/Pt-Catalyzed Conversion of Bromo Alkynamines/Alkynols to Saturated and Unsaturated γ-butyrolactams/lactones via Intramolecular Electrophilic Cyclization

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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A convenient and general Hg(II)/Pt(IV) catalyzed syntheses of γ-butyrolactams and α,β- unsaturated γ-butyrolactones/lactams are described *via* an intramolecular electrophilic cyclizations of bromoalkynes with tosylamino and hydroxyl tethers. The reaction features the use of wet solvents, the exclusion of any base and additive, mild conditions and practical yields. We also synthesised few chiral lactams through this pathway. Additionally, it is shown that NHTs group distanced farther from homopropargylic position assists for regioselective bromoalkyne hydration to yield useful α-bromoketones. Further, Boc protected bromo homo propargyl amines undergo 6-*endo-dig* cyclization through Boc oxygen to give bromomethylene substituted oxazinones.

Introduction

Five-membered lactams[1] and lactones[2] (both saturated and unsaturated) are prevalent sub structures frequently found in biologically as well as pharmaceutically interesting molecules. For instance, the molecules shown in Figure 1[3] are representative of biologically relevant compounds bearing the related skeletons. Further, they are often used as building blocks in the construction of larger molecules. Consequently, the development of synthetic approaches toward these scaffolds has been of broad interest for organic chemists from long ago.[4-5] On the other hand, since the last decade, an explosion of alkyne chemistry *via* electrophilic activation and subsequent intramolecular nucleophilic attack has led to the construction of numerous heterocycles with wide substitution patterns.[6] As part of our on-going program of unveiling the new reactions of functionalized alkynes, we also reported various such cyclic scaffolds in this way.[7] In an earlier attempt, we showed that the bromo alkynes with hydroxyl tether at proper distance would undergo an intramolecular nucleophilic attack by using an appropriate activating soft catalyst.[7i] We here in reveal some interesting results of study of activation/cyclization of bromo alkynes tethered with amino/hydroxyl group with and without propargylic hydroxyl function.

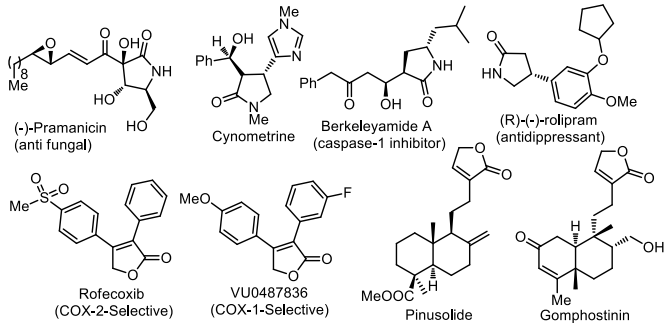

Figure 1. Some representative biologically active lactams/lactones

Results and Discussion

Initially, we synthesized tosyl amino tethered bromo alkyne **3a** from readily available aziridine **1**a *via* ring opening by TMS acetylide (to get **2a**) followed by Bromide-TMS group exchange. Activation (by a soft catalyst) of alkyne would lead to intramolecular hydroamination (**4**) with a regioselection of amine attack on bromide attached alkyne terminus (5-*endo-dig* cyclization). The intermediate would subsequently undergo hydrolysis to deliver the lactam **5a**. To test this, we treated **3a** with 10 mol% $AuCl_3$ in wet toluene (adding 3 equivalents of water to toluene) at room temperature (entry 1). As expected, the lactam **5a** was cleanly obtained in 70% yield. The other low valent Au-catalysts like AuCl and PPh_3AuCl were not very effective for the same conversion (entries 2-3). The change of solvent to CH_3CN proved to be negative for the reaction (entry 4). Next, we screened the reaction with wet-toluene/THF/DCE using $Hg(OTf)_2$ as catalyst but to obtain the product in unacceptable yields (entries 5-7).Pleasingly, the change of solvent to wet-CH_3CN furnished the product neatly in 95% yield

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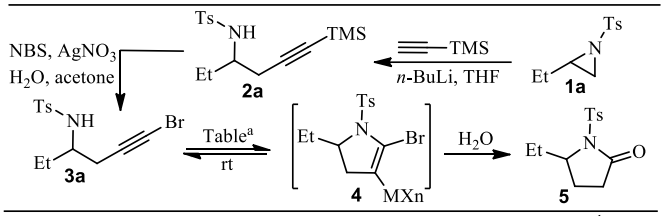
Electronic Supplementary Information (ESI) available: See
DOI: 10.1039/x0xx00000x

(entry 8). Increase of water equivalents (above 3 equiv) gradually decreased the yields and water as only solvent completely halted the reaction (entries 9-11). The yield was dropped to 50% when $HgCl_2$ was used instead of $Hg(OTf)_2$ (entry 12). $Cu(OTf)_2$ could not catalyse the reaction (entry 13).

Table 1. Optimization studies



Entry	Catalyst	Solvent	H_2O (equiv)	Yiled[b]
1	$AuCl_3$	toluene	3	80%
2	AuCl	toluene	3	45%
3	PPh_3AuCl	toluene	3	20%
4	$AuCl_3$	CH_3CN	3	30%
5	$Hg(OTf)_2$	toluene	3	40%
6	$Hg(OTf)_2$	THF	3	30%
7	$Hg(OTf)_2$	DCE	3	15%
8	**$Hg(OTf)_2$**	**CH_3CN**	3	**95%**
9	$Hg(OTf)_2$	CH_3CN	5	85%
10	$Hg(OTf)_2$	CH_3CN	10	75%
11	$Hg(OTf)_2$	H_2O	--	--[c]
12	$HgCl_2$	CH_3CN	3	50%
13	$Cu(OTf)_2$	CH_3CN	3	--[c]
14	$Hg(OTf)_2$	CH_3CN	--	--[c]
15[d]	$Hg(OTf)_2$	CH_3CN	3	--[c]
16	TfOH	CH_3CN	3	--[c]

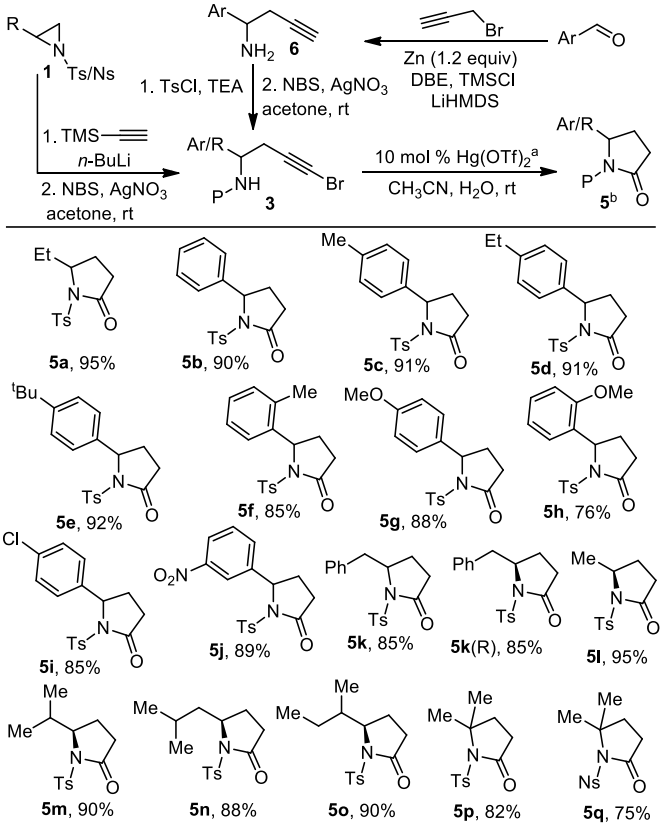
[a]Reaction conditions: **3a** (1.0 mmol), catalyst (10 mol %), H_2O (3 equiv), solvent (0.25 M), RT, 18 h, open air. [b]Isolated yield. [c]SM was recovered. [d]0.5 equivalents of 2,6-lutidine was used as base.

Interestingly, when we performed the reaction with $Hg(OTf)_2$ in the absence of water, starting material was recovered as such (entry 14). It suggests that the initial cyclization is reversible. It gets converted to product only in presence water. Surprisingly, use of 2,6-lutidine as base totally halted the reaction (entry 15). To verify whether TfOH (which may be released from $Hg(OTf)_2$) was responsible for the reaction *via* hydrolysis of the alkyne moiety, we conducted an experiment with 10 mol% TfOH (entry 16). No reaction occurred, demonstrating that the Hg-or Au-catalyst was necessary for activating alkyne for cyclization.

With the optimised conditions in hand, we turned to evaluate the generality of the method. First, a range of 4-bromo homopropargyl amides **3** were synthesized; few from benzaldehydes (**3b-j**) and others from readily available amino acids (**3k-o**).[8] As is evident from Table 2, a variety of substituents like alkyl, aryl, halogen, methoxy, and nitro groups were tolerated in the reaction to afford the products in excellent yields. Thus, the alkyl (Me, Et and t-But) tethered phenyl substituted lactam (**5b-f**) could be synthesized in excellent yields (85-92%). Electron rich phenyl substituted products (**5g-h**) were obtained with equal ease (76-88%). After the clean syntheses of 5f and 5h, it appears that steric factors from ortho substitution on phenyl rings showed negligible effect on the outcome of the reaction (only 6-12% reduction in yield). Notably, electronic factors were also not influencing the reaction as the electron deficient chloro- and nitro-phenyl substituted lactams (**5i-j**) were obtained in as good yields like their electron rich counterparts (**5c**-**h**). Next, we synthesized various 5-alkyl substituted adducts this way. Thus benzyl lactam **5k** was obtained in 85% yield.

Pleasingly, the same reaction when conducted on optically active **3k**(S) (obtained from L-phenyl alanine), the product **5k**(R) was obtained with excellent ee (>99.9, see Supporting Information for HPLC data). Similarly, several chiral pure bromo propargyl amides were synthesized from various amino acids and converted to the corresponding enantiomerically enriched lactam adducts (**5l-o**) in excellent yields (88-95%). Finally, the reaction could also be extended to the synthesis of 5,5-disubstituted γ-lactam **5p** in practical yield of 82%. To facilitate the liberation of free amide by easier deprotection, a nosyl protected lactam **5q** was also synthesized in the standard conditions.

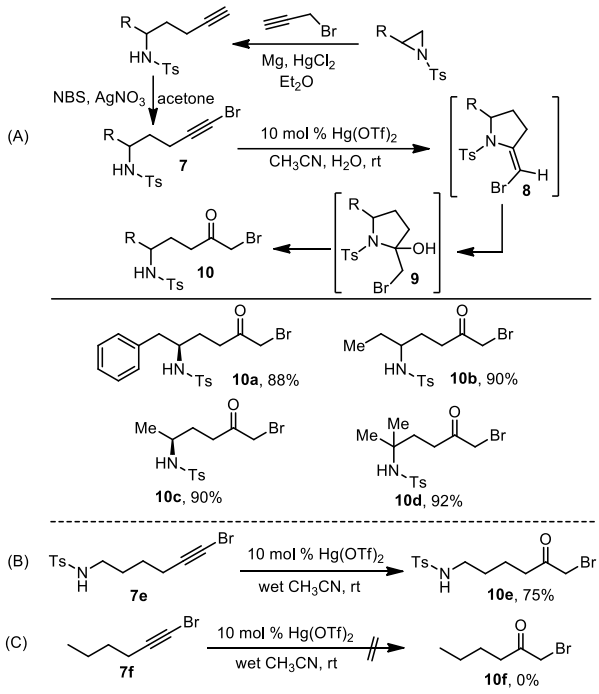
Table 2. Synthesis of butyrolactams **5** *via* electrophilic cyclization of **3**.



[a]Reaction conditions: **3a** (1.0 mmol), $Hg(OTf)_2$ (0.1 mmol), H_2O (3 equiv), CH_3CN (4 mL), RT, 18 h, open air. [b]Isolated yield.

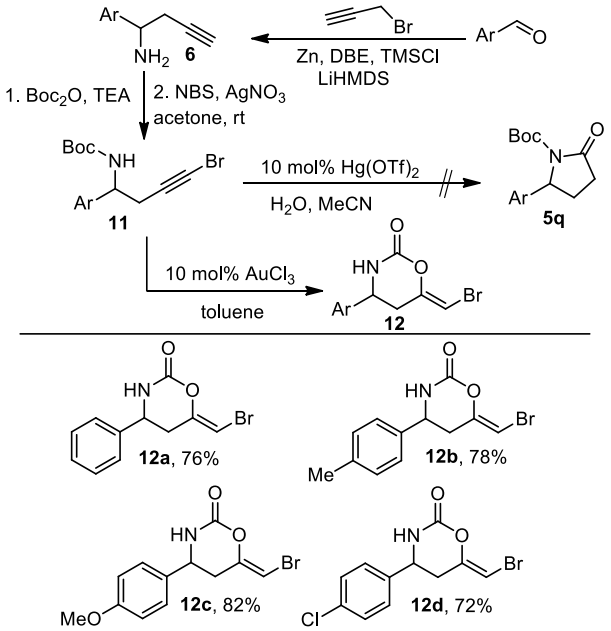
Excited with the above results, we moved on to the substrates with amine group distanced from bromo alkyne group by one carbon so that the cyclization (6-*endo-dig*) on to bromo attached alkyne group would lead to δ-lactams. Surprisingly, we observed the exclusive

formation (88%) regioselectively hydrolysed product α-bromoketone **10a** (Scheme 1). This must have happened through *5-exo-dig* cyclization followed by hydrolysis reaction. Tempted by the multifunctional nature of the products, and various literature uses of α-bromoketones,[9] we quickly checked this new reaction's generality. Thus, methyl-, ethyl- and dimethyl-substituted substrates were tested and smoothly converted to the corresponding α-bromoketones (**10b-d**). Next, the substrate **7e** with further parted amino group was subjected to the standard reaction conditions. Again, the reaction led to the selective hydrolysis via relatively less energetic *6-exo-dig* pathway (compared to other possible 7-*endo-dig* cyclization) to produce α-bromoketone **10e**. We next tested the reaction on substrate lacking the NHTs group **7f** so as to know its involvement/importance. As expected, **10f** was observed to be inert to the reaction suggesting that the assistance of NHTs was necessary to initiate the hydrolysis. This is the reminiscent of the work by Nishizawa et al where they showed the hydroxyl assisted hydrolysis of the alkyne group.[6c] What we have shown here is that not only NHTs group assists in such hydrolysis in similar way, but the sensitive bromide group survives the hydrolysis reaction and remains as a useful handle at alpha to the keto group in the product.



Scheme 1. NHTs assisted selective hydrolysis of bromoalkynes.

In parallel, we also studied the reactivity of Boc-protected substrates like **11** for the similar cyclizations (Scheme 2). Unfortunately, neither any product nor starting material was recovered. We attribute this to the Boc group sensitivity to the acidic conditions exerted by the presence of water with triflate (TfOH formation). Interestingly, when subjected the **11a** to the alternate reagent $AuCl_3$ (Table 1, entry 1), we obtained oxazinone **12a** via cyclization of Boc oxygen instead of NH group. This kind of cyclization on terminal and ester substituted alkynes were reported by Carretero et al.[10] Since this finding has a considerable variation in bringing bromomethylene substituted products staging a plat form for further manipulation via various metal mediated couplings of vinyl bromide group, we pursued for its generality. Similar to **12a**, methyl, methoxy and chloro substituted phenyl adducts (**12b-d**) were obtained in excellent yields (72-82%).

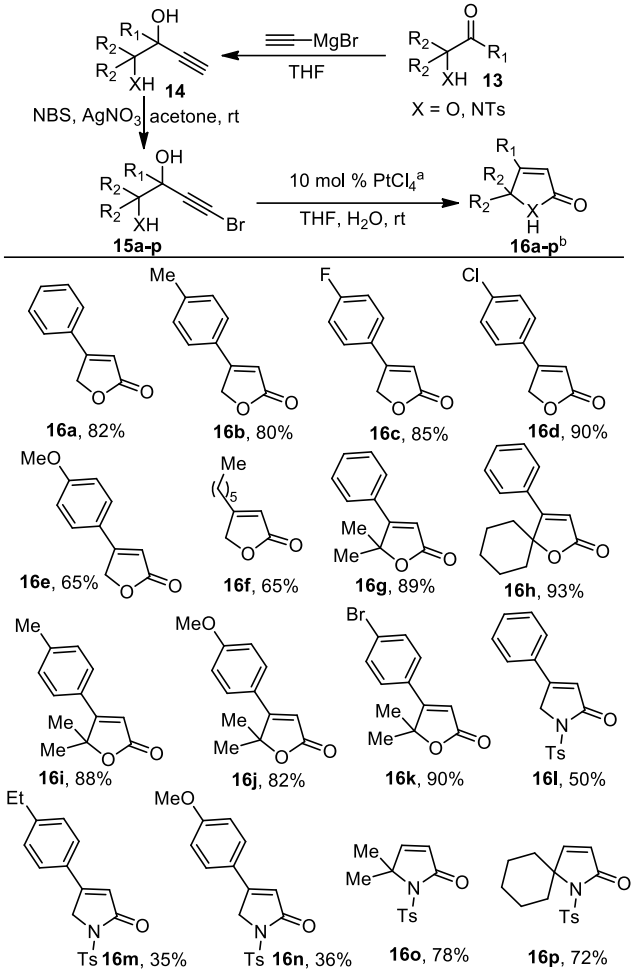


Scheme 2. Synthesis of oxazinones **12** via electrophilic cyclization.

We next became interested in studying the reactivity pattern of propargylic alcohol system which could lead to unsaturated cycles. We first prepared various 1,2-dihydroxy-4-bromo-3-ynes **15a-k** to see whether it would undergo the expected cascade reaction including electrophilic cyclization, hydrolysis followed by elimination of benzylic hydroxyl group to deliver the α,β-unsaturated γ-butyrolactone **16a-k**. An optimization study led to identify $PtCl_4$ as the most suitable catalyst for the transformation.[8] Thus, **15a** was converted to **16a** in 82% yield using 10 mol% $PtCl_4$ in wet THF with no assistance of any base or additive (Table 3). We first aimed at 5-unsubstituted adducts (like **16a-f**) as they are found in various applications in the literature through functionalization of both C5 acidic protons.[11] Thus, methyl, chloro and fluoro substituted phenyl adducts (**16b-d**) were synthesized in excellent yields (80-90%). Methoxyphenyl substituted lactone **16e** was obtained in lower yield of 65%. Further, 4-alkyl adduct **16f** was also synthesized in similar (65%). Next, 4,5-trisubstituted adducts were targeted. Thus, 4-phenyl-5,5-dimethyl product **16g** was produced in excellent yield of 89%. A variety of substitution (Me, OMe, Br) on phenyl ring was well tolerated (**16i-k** in 82-90% yields). Finally, 5-spiro substituted adduct **16h** was obtained in equal ease (93%). Next, similar cyclization for α,β-unsaturated γ-butyrolactam was tested. The reaction was found to be slightly less efficient compared to their lactone counterparts. Thus, 4-phenyl adduct **16l** was furnished in 50% yield. Electron rich phenyl substituted lactams like

16m and **16n** were obtained in 35% and 36% yields respectively where as halo- substitution on phenyl ring completely deterred the reaction. But, 5,5-disubstituted adducts **16o-p** in contrast were obtained in excellent yields (72-78%). The acidic protons in earlier cases might have assisted for some unwanted aromatizations.

Table 3. Synthesis of **16** *via* electrophilic cyclization.



[a]Reaction conditions: **15a** (1.0 mmol), $PtCl_4$ (0.1 mmol), H_2O (3 equiv), THF (4 mL), RT, 18 h, open air. [b]Isolated yield.

In summary, we have shown some interesting reactions of bromoalkynes tethered with hydroxyl or amino group. How the reaction pathway changes depending on the position of the tether and substitution on amino group, and based on the presence or absence of the propargyl hydroxyl group is well studied for the formation of various interesting scaffolds like saturated/unsaturated lactams, unsaturated lactones, oxazinones and α-bromoketones. Further, it is shown that the synthetic approach described here are equally potential for the synthesis of enantiopure adducts.

Experimental Section

General Information:

General Information: All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 400 MHz spectrometer for ^{1}H NMR, 100 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$/[D6]DMSO for ^{1}H and ^{13}C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), doublet (d), broad singlet (bs), doublet of doublets (dd), triplet (t), quartet (q), multiplet (m). HRMS were recorded by using QTof mass spectrometer. Column chromatography was performed with silica gel (100–200 mesh) as the stationary phase. All reactions were monitored by using TLC. The purity and characterization of compounds were further established by using HRMS.

2.1. General Procedure A, for the synthesis of 5 from 3:

To the substrate **3a** (165 mg, 0.5 mmol) dissolved in acetonitrile (2 ml) were added H_2O (27 mg, 3 equiv) and $Hg(OTf)_2$ (25 mg, 0.1 mmol). The mixture was stirred at room temperature till the completion of the reaction (TLC, 18 h). The reaction mixture was then added water (4 ml) followed by brine solution (4 ml) and extracted with ethyl acetate (3 x 6 ml). The combined extracts were dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography (silicagel, 10-20% EtOAc in hexanes) to get the pure product **5a** (123mg).

5-ethyl-1-tosylpyrrolidin-2-one (5a): 92% yield (123 mg); white solid; mp 117-119 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.94 (d, *J* = 8.2 Hz, 2H); 7.31 (d, *J* = 8.2 Hz, 2H); 4.37-4.31 (m, 1H); 2.55-2.46 (m, 1H); 2.42 (s, 3H); 2.36-2.29 (m, 1H); 2.21-2.11 (m, 1H); 2.05-1.95 (m, 1H); 1.88-1.81 (m, 1H); 1.75-1.64 (m, 1H); 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.6, 144.9, 136.1, 129.5, 128.3, 61.5, 30.8, 27.6, 23.0, 21.6, 9.3; IR (neat) *ν* 3030, 1610, 1365, 1219; HRMS (ESI-TOF) calcd for $C_{13}H_{18}NO_3S$ [M + H]$^+$ 268.1007, found 268.1002.

5-phenyl-1-tosylpyrrolidin-2-one (5b): 90% yield (142 mg); white solid; mp 146-148 °C; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.56 (d, *J* = 8.3 Hz, 2H); 7.31-7.26 (m, 3H); 7.17 (d, *J* = 8.3 Hz, 2H); 7.13-7.10 (m, 2H); 5.44 (dd, *J* = 8.5, 2.0 Hz, 1H); 2.74-2.46 (m, 3H); 2.39 (s, 3H); 2.01-1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 173.6, 144.9, 140.7, 135.5, 129.2, 128.8, 128.5, 128.1, 126.1, 63.1, 30.7, 28.4, 21.7; IR (neat) *ν* 3120, 1650, 1384, 1215; HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_3S$ [M + H]$^+$ 316.1007, found 316.1009.

5-p-tolyl-1-tosylpyrrolidin-2-one (5c): 91% yield (150 mg); white solid; mp 137-139 °C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.59 (d, *J* = 8.3 Hz, 2H); 7.17 (d, *J* = 8.3 Hz, 2H); 7.09 (d, *J* = 7.9 Hz, 2H); 7.01 (d, *J* = 7.9 Hz, 2H); 5.41 (dd, *J* = 8.2, 1.6 Hz, 1H); 2.72-2.44 (m, 3H); 2.39 (s, 3H); 2.34 (s, 3H); 1.98-1.92 (m,

1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.6, 144.8, 137.8, 137.7, 135.5, 129.4, 129.1, 128.5, 126.0, 62.9, 30.6, 28.4, 21.6, 21.1; IR (neat) *v* 3098, 1657, 1360, 1201; HRMS (ESI-TOF) calcd for $C_{18}H_{20}NO_3S$ [M + H]$^+$ 330.1164, found 330.1164.

5-(4-ethylphenyl)-1-tosylpyrrolidin-2-one (5d): 91% yield (156 mg); white solid; mp 145-147 °C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.55 (d, *J* = 8.3 Hz, 2H); 7.14 (d, *J* = 8.3 Hz, 2H); 7.10 (d, *J* = 8.1 Hz, 2H); 7.02 (d, *J* = 8.1 Hz, 2H); 5.41(dd, *J* = 8.4, 1.8 Hz, 1H); 2.70-2.48 (m, 5H); 2.38 (s, 3H); 2.00-1.94(m, 1H); 1.24 (t, *J* = 7.6 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.5, 144.7, 144.2, 137.8, 135.5, 129.0, 128.5, 128.2, 126.1, 62.9, 30.7, 28.5, 28.2, 21.6, 15.6; IR (neat) *v* 3120, 1632, 1399, 1253; HRMS (ESI-TOF) calcd for $C_{19}H_{22}NO_3S$ [M + H]$^+$ 344.1320, found 344.1320.

5-(4-tert-butylphenyl)-1-tosylpyrrolidin-2-one (5e): 92% yield (171 mg); white solid; mp 137-139 °C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.51 (d, *J* = 8.3 Hz, 2H); 7.28-7.26 (m, 2H); 7.11 (d, *J* = 8.3 Hz, 2H); 7.05-7.01 (m, 2H); 5.41 (dd, *J* = 8.6, 1.9 Hz, 1H); 2.27-2.48 (m, 3H); 2.34 (s, 3H); 2.02-1.96 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.5, 151.1, 144.6, 137.4, 135.6, 129.0, 128.4, 125.9, 125.6, 62.8, 34.5, 31.3, 30.8, 28.0, 21.6; IR (neat) *v* 2099, 1663, 1365, 1200; HRMS (ESI-TOF) calcd for $C_{21}H_{26}NO_3S$ [M + H]$^+$ 372.1633, found 372.1625.

5-o-tolyl-1-tosylpyrrolidin-2-one (5f): 85% yield (140 mg); white solid; mp 136-138 °C; R_f = 0.50 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.66 (d, *J* = 8.3 Hz, 2H); 7.22-7.15 (m, 4H); 7.01-6.97 (m, 1H); 6.80 (d, *J* = 7.7, 1H); 5.69 (dd, *J* = 8.1, 1.6 Hz, 1H); 2.69-2.44 (m, 3H); 2.41 (s, 6H); 1.88-1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.8, 144.9, 138.5, 135.4, 134.4, 131.0, 129.1, 128.7, 127.7, 126.1, 124.5, 59.4, 30.3, 27.3, 21.6, 19.1; IR (neat) *v* 3100, 1632, 1320, 1253; HRMS (ESI-TOF) calcd for $C_{18}H_{20}NO_3S$ [M + H]$^+$ 330.1164, found 330.1164.

5-(4-methoxyphenyl)-1-tosylpyrrolidin-2-one (5g): 88% yield (152 mg); white solid; mp 102-104 °C; R_f = 0.4 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.55 (d, *J* = 8.3 Hz, 2H); 7.16 (d, *J* = 8.3 Hz, 2H); 7.04 (d, *J* = 8.7 Hz, 2H); 6.80 (d, *J* = 8.7 Hz, 2H); 5.40 (dd, *J* = 8.6, 2.2 Hz, 1H); 3.81 (s, 3H); 2.73-2.45 (m, 3H); 2.38 (s, 3H); 1.98-1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.6, 159.5, 144.9, 135.7, 132.9, 129.2, 128.6, 127.5, 114.2, 62.7, 55.4, 30.8, 28.4, 21.7; IR (neat) *v* 3022, 1611, 1248, 1216; HRMS (ESI-TOF) calcd for $C_{18}H_{20}NO_4S$ [M + H]$^+$ 346.1113, found 346.1116.

5-(2-methoxyphenyl)-1-tosylpyrrolidin-2-one (5h): 76% yield (131 mg); white solid; mp 128-130 °C; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.51 (d, J = 8.3 Hz, 2H); 7.31-7.26 (m, 1H); 7.18-7.13 (m, 3H); 6.94-6.90 (m, 2H); 5.56 (dd, J = 8.1, 1.2 Hz, 1H); 3.46 (s, 3H); 2.76-2.49 (m, 3H); 2.39 (s, 3H); 2.02-1.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.3, 156.5, 144.3, 135.7, 129.4, 129.0, 128.9, 128.3, 127.9, 120.3, 110.7, 60.6, 54.7, 31.4, 25.6, 21.5; IR (neat) *v* 3054, 1653, 1324, 1231; HRMS (ESI-TOF) calcd for $C_{18}H_{20}NO_4S$ [M + H]$^+$ 346.1113, found 346.1116.

5-(4-chlorophenyl)-1-tosylpyrrolidin-2-one (5i): 85% yield (149 mg); white solid; mp 148-150 °C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.59 (d, *J* = 8.3 Hz, 2H); 7.27-7.22 (m, 2H); 7.19 (d, *J* = 8.3 Hz, 2H); 7.05 (d, *J* = 8.4 Hz, 2H); 5.38 (dd, *J* = 8.0, 1.8 Hz, 1H); 2.68-2.43 (m, 3H); 2.39 (s, 3H); 1.95-1.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.4, 145.2, 139.4, 135.5, 134.0, 129.4, 129.0, 128.5, 127.5, 62.4, 30.6, 28.3, 21.7; IR (neat) *v* 3022, 1603, 1386, 1215; HRMS (ESI-TOF) calcd for $C_{17}H_{17}ClNO_3S$ [M + H]$^+$ 350.0618, found 350.0615.

5-(3-nitrophenyl)-1-tosylpyrrolidin-2-one (5j): 89% yield (160 mg); white solid; mp 190-192 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 8.17-8.14 (m, 1H); 7.88 (t, *J* = 1.8 Hz, 1H); 7.64 (d, *J* = 8.3 Hz, 2H); 7.58-7.50 (m, 2H); 7.21 (d, *J* = 8.3 Hz, 2H); 5.51 (dd, *J* = 8.0, 2.7 Hz, 1H); 2.72-2.50 (m, 3H); 2.40 (s, 3H); 2.01-1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.1, 148.4, 145.6, 143.0, 135.2, 132.2, 130.0, 129.4, 128.2, 123.0, 120.8, 62.1, 30.3, 28.2, 21.6; IR (neat) *v* 3096, 1645, 1352, 1232; HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_5S$ [M + H]$^+$ 361.0858, found 361.0855.

(R)-5-benzyl-1-tosylpyrrolidin-2-one (5k): 85% yield (140 mg); white solid; mp 115-117 °C; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.98 (d, *J* = 8.3 Hz, 2H); 7.35-7.17 (m, 7H); 4.64-4.57 (m,. 1H); 3.31 (dd, *J* = 13.4, 3.3 Hz, 1H); 2.85 (dd, *J* = 13.4, 8.8 Hz, 1H); 2.42 (s, 3H); 2.18-1.92 (m, 3H); 1.88-1.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.6, 145.3, 136.5, 136.2, 129.7, 128.9, 128.6, 127.2, 61.1, 40.8, 30.6, 23.0, 21.8; IR (neat) *v* 3023, 1610, 1361, 1216; HRMS (ESI-TOF) calcd for $C_{18}H_{20}NO_3S$ [M + H]$^+$ 330.1164, found 330.1157.

(S)-5-methyl-1-tosylpyrrolidin-2-one (5l): 95% yield (120 mg); white solid; mp 140-142 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.94 (d, *J* = 8.3 Hz, 2H); 7.32 (d, *J* = 8.3 Hz, 2H); 4.56-4.47 (m, 1H); 2.60-2.49 (m, 1H); 2.42 (s, 3H); 2.38-2.22 (m, 2H); 1.74-1.67 (m, 1H); 1.46 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.3, 145.0, 136.2, 129.5, 128.3, 56.4, 30.6, 26.7, 21.7, 21.5; IR (neat) *v* 3030, 1610, 1365, 1219; HRMS (ESI-TOF) calcd for $C_{12}H_{16}NO_3S$ [M + H]$^+$ 254.0851, found 254.0851.

(R)-5-isopropyl-1-tosylpyrrolidin-2-one (5m): 90% yield (127 mg); white solid; mp 116-118 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.95 (d, *J* = 8.4 Hz, 2H); 7.31 (d, *J* = 8.4 Hz, 2H); 4.39-4.33 (m, 1H); 2.56-2.46 (m, 1H); 2.46-2.29 (m, 5H); 2.11-1.97 (m, 1H); 1.94-1.84 (m, 1H); 0.97 (d, *J* = 6.9 Hz, 3H); 0.71 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.1, 144.9, 136.0, 129.5, 128.4, 65.0, 31.7, 31.4, 21.7, 18.9, 18.5, 14.9; IR (neat) *v* 3022, 1603, 1386, 1215; HRMS (ESI-TOF) calcd for $C_{14}H_{20}NO_3S$ [M + H]$^+$ 282.1164, found 282.1154.

(R)-5-isobutyl-1-tosylpyrrolidin-2-one (5n): 88% yield (130 mg); white solid; mp 102-104 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.94 (d, *J* = 8.3 Hz, 2H); 7.32 (d, *J* = 8.3 Hz, 2H); 4.45-4.38 (m, 1H); 2.59-2.48 (m, 1H); 2.43 (s, 3H); 2.36-2.27 (m, 1H); 2.20-2.08 (m, 1H); 1.89-1.81 (m, 2H); 1.69-1.61 (m, 1H); 1.54-1.45 (m, 1H); 1.01 (d, *J* = 6.5 Hz, 3H); 0.96 (d, *J* = 6.5 Hz, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) *δ:* 173.4, 144.9, 136.3, 129.5, 128.4, 59.2, 43.2, 30.5, 25.4, 23.9, 23.8, 21.7, 21.3; IR (neat) *ν* 3020, 1610, 1385, 1220; HRMS (ESI-TOF) calcd for $C_{15}H_{22}NO_3S$ [M + H]$^+$ 296.1320, found 296.1321.

(R)-5-sec-butyl-1-tosylpyrrolidin-2-one (5o): 90% yield (133 mg); white solid; mp 132-134 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.95 (d, *J* = 8.3 Hz, 2H); 7.32 (d, *J* = 8.3 Hz, 2H); 4.48-4.44 (m, 1H); 2.47-2.32 (m, 5H); 2.31-2.23 (m, 1H); 2.10-1.99 (m, 1H); 1.90-1.82 (m, 1H); 1.43-1.32 (m, 1H); 1.29-1.17 (m, 1H); 0.99 (t, *J* = 7.3 Hz, 3H); 0.69 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.2, 144.9, 136.1, 129.5, 128.5, 63.8, 38.3, 31.8, 26.4, 21.7, 18.6, 12.4, 12.0; IR (neat) *ν* 3021, 1620, 1388, 1216; HRMS (ESI-TOF) calcd for $C_{15}H_{22}NO_3S$ [M + H]$^+$ 296.1320, found 296.1321.

5,5-dimethyl-1-tosylpyrrolidin-2-one (5p): 82% yield (110 mg); white solid; mp 112-114 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.94 (d, *J* = 8.3 Hz, 2H); 7.31 (d, *J* = 8.3 Hz, 2H); 2.42-2.37 (m, 5H); 1.92 (t, *J* = 8.2 Hz, 2H); 1.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.0, 144.7, 136.8, 129.8, 128.7, 67.1, 35.8, 30.0, 28.3, 21.7; IR (neat) *ν* 3021, 1620, 1388, 1216; HRMS (ESI-TOF) calcd for $C_{13}H_{18}NO_3S$ [M + H]$^+$ 268.1007, found 268.1016.

5,5-dimethyl-1-((4-nitrophenyl)sulfonyl)pyrrolidin-2-one (5q): 75% yield (112 mg); white solid; mp 168-170 °C; R_f = 0.20 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 8.36-8.33 (m, 2H); 8.26-8.23 (m, 2H); 2.43 (t, *J* = 8.1 Hz, 2H); 1.97 (t, *J* = 8.1 Hz, 2H); 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.2, 150.7, 144.9, 130.2, 124.0, 67.8, 35.8, 29.9, 28.4; IR (neat) *ν* 3068, 1636, 1394, 1210; HRMS (ESI-TOF) calcd for $C_{12}H_{15}N_2O_5S$ [M + H]$^+$ 299.0702, found 299.0692.

(R)-N-(6-bromo-5-oxo-1-phenylhexan-2-yl)-4-methylbenzenesulfonamide (10a): 88% yield (186 mg); white solid; mp 108-110 °C; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.65 (d, *J* = 8.2 Hz, 2H); 7.27 (d, *J* = 7.3 Hz, 2H); 7.23-7.19 (m, 3H); 6.97-6.94 (m, 2H); 4.36 (d, *J* = 8.8 Hz, 1H); 3.93-3.86 (m, 2H); 3.54-3.46 (m, 1H); 2.85-2.77 (m, 1H); 2.71-2.53 (m, 3H); 2.44 (s, 3H); 1.94-1.86 (m, 1H); 1.61-1.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 202.0, 143.5, 137.7, 136.6, 129.8, 129.4, 128.7, 127.0, 126.8, 54.3, 41.9, 35.9, 34.8, 28.5, 21.6; IR (neat) *ν* 3415, 1725, 1396, 668; HRMS (ESI-TOF) calcd for $C_{19}H_{23}BrNO_3S$ [M + H]$^+$ 424.0582, found 424.0580.

N-(7-bromo-6-oxoheptan-3-yl)-4-methylbenzenesulfonamide (10b): 90% yield (163 mg); colorless liquid; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.71 (d, *J* = 8.2 Hz, 2H); 7.28 (d, *J* = 8.2 Hz, 2H); 4.63 (d, *J* = 8.8 Hz, 1H); 3.93-3.86 (m, 2H); 3.18-3.09 (m, 1H); 2.82-2.73 (m, 1H); 2.69-2.61 (m, 1H); 2.41 (s, 3H); 1.89-1.81 (m, 1H); 1.56-1.47 (m, 1H); 1.37-1.24 (m, 2H); 0.66 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 202.1, 143.5, 138.2, 129.8, 127.1, 54.7, 35.9, 34.8, 28.7, 28.6, 21.6, 9.8; IR (neat) *ν* 3369, 1715, 1397, 675; HRMS (ESI-TOF) calcd for $C_{14}H_{21}BrNaNO_3S$ [M + Na]$^+$ 384.0245, found 384.0239.

(S)-N-(6-bromo-5-oxohexan-2-yl)-4-methylbenzenesulfonamide (10c): 90% yield (156 mg); white solid; mp 88-90 °C; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.73-7.69 (m, 2H); 7.31-7.28 (m, 2H); 4.38 (d, *J* = 8.9 Hz, 1H); 3.94-3.87 (m, 2H); 3.34-3.23 (m, 1H); 2.84-2.75 (m, 1H); 2.72-2.64 (m, 1H); 2.42 (s, 3H); 1.84-1.76 (m, 1H); 1.59-1.51 (m, 1H); 0.94 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 202.1, 143.6, 137.9, 129.9, 127.1, 49.5, 36.1, 34.8, 31.3, 22.1, 21.7; IR (neat) *ν* 3369, 1715, 1397, 675; HRMS (ESI-TOF) calcd for $C_{13}H_{19}BrNO_3S$ [M + H]$^+$ 348.0269, found 348.0255.

N-(6-bromo-2-methyl-5-oxohexan-2-yl)-4-methylbenzenesulfonamide (10d): 92% yield (166 mg); white solid; mp 116-118 °C; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.76 (d, *J* = 8.2 Hz, 2H); 7.28 (d, *J* = 8.2 Hz, 2H); 4.78 (s, 1H); 3.86 (s, 2H); 2.69 (t, *J* = 7.4 Hz, 2H); 2.42 (s, 3H); 1.84 (t, *J* = 7.4 Hz, 2H); 1.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 201.8, 143.2, 140.3, 129.7, 127.0, 56.4, 36.0, 34.9, 34.4, 27.9, 21.6; IR (neat) *ν* 3399, 1723, 1403, 682; HRMS (ESI-TOF) calcd for $C_{14}H_{20}BrNaNO_3S$ [M + Na]$^+$ 384.0245, found 384.0239.

N-(6-bromo-5-oxohexyl)-4-methylbenzenesulfonamide (10e): 75% yield (130 mg); white solid; mp 96-98 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.73 (d, *J* = 8.3 Hz, 2H); 7.30 (d, *J* = 8.3 Hz, 2H); 4.81 (t, *J* = 6.2 Hz, 1H); 3.84 (s, 2H); 2.91 (q, *J* = 6.4 Hz, 2H); 2.61 (t, *J* = 7.0 Hz, 2H); 2.41 (s, 3H); 1.64-1.56 (m, 2H); 1.51-1.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 201.9, 143.6, 136.9, 129.8, 127.2, 42.8, 39.0, 34.3, 28.8, 21.6, 20.6; IR (neat) *ν* 3396, 1710, 1403, 680; HRMS (ESI-TOF) calcd for $C_{13}H_{19}BrNO_3S$ [M + H]$^+$ 348.0269, found 348.0255.

tert-butyl (4-bromo-1-phenylbut-3-yn-1-yl)carbamate (11a): 80% yield (259 mg); white solid; mp 122-124 °C;R_f = 0.7 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.38-7.25 (m, 5H); 5.06 (s, 1H); 4.87 (s, 1H); 2.81-2.62 (m, 2H); 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 155.2, 128.7, 127.8, 126.4, 80.1, 76.2, 52.8, 41.3, 28.5, 27.9; IR (neat) *ν* 3460, 2198, 1721, 685; HRMS (ESI-TOF) calcd for $C_{15}H_{19}BrNO_2$ [M + H]$^+$ 326.0574, found 326.0564.

tert-butyl (4-bromo-1-(p-tolyl)but-3-yn-1-yl)carbamate (11b): 80% yield (270 mg); white solid; mp 115-117 °C; R_f = 0.70 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.21-7.13 (m, 4H); 5.03 (s, 1H); 4.82 (s, 1H); 2.79-2.62 (m, 2H); 2.33 (s, 3H); 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 155.1, 138.0, 137.4, 129.4, 126.3, 79.9, 76.4, 52.6, 41.1, 28.5, 27.9, 21.2; IR (neat) *ν* 3423, 2252, 1706, 650; HRMS (ESI-TOF) calcd for $C_{16}H_{21}BrNO_2$ [M + H]$^+$ 340.0735, found 340.0729.

tert-butyl (4-bromo-1-(4-methoxyphenyl)but-3-yn-1-yl)carbamate (11c): 75% yield (265 mg); white solid; mp 137-139 °C; R_f = 0.60

(SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.23 (d, *J* = 8.6 Hz, 2H); 6.87 (d, *J* = 8.6 Hz, 2H) 5.01 (s, 1H); 4.80 (s, 1H); 3.79 (s, 3H); 2.76-2.63 (m, 2H); 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 159.2, 155.2, 133.2, 127.6, 114.1, 79.9, 76.4, 55.4, 52.4, 41.1, 28.5, 27.8; IR (neat) *ν* 3490, 2310, 1725, 680; HRMS (ESI-TOF) calcd for $C_{16}H_{21}BrNO_3$ $[M + H]^+$ 356.0684, found 356.0673.

tert-butyl (4-bromo-1-(4-chlorophenyl)but-3-yn-1-yl)carbamate (11d): 78% yield (279 mg); white solid; mp 128-130 °C; R_f = 0.70 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7. 32 (d, *J* = 8.5 Hz, 2H); 7.24 (d, *J* = 8.5 Hz, 2H); 5.05 (s, 1H); 4.83 (s, 1H); 2.77-2.62 (m, 2H); 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 155.1, 139.7, 133.5, 128.8, 127.8, 80.2, 75.8, 52.3 41.8, 28.5, 27.7; IR (neat) *ν* 3432, 2260, 1706, 669; HRMS (ESI-TOF) calcd for $C_{15}H_{18}BrClNO_2$ $[M + H]^+$ 360.0189, found 360.0195.

2.2 General Procedure B, for the synthesis of 12 from 11:

To the substrate **11a** (160 mg, 0.5 mmol) dissolved in toluene (2 ml) was added $AuCl_3$ (16 mg, 0.1 mmol). The mixture was stirred at room temperature till the completion of the reaction (TLC, 16 h). The reaction mixture was then added water (4 ml) followed by brine solution (4 ml) and extracted with ethyl acetate (3 x 6 ml). The combined extracts were dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography (silicagel, 20-30% EtOAc in hexanes) to get the pure product **12a** (101 mg).

(Z)-6-(bromomethylene)-4-phenyl-1,3-oxazinan-2-one (12a): 76% yield (101 mg); white solid; mp 148-150 °C;R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.34-7.26 (m, 3H); 7.22-7.19 (m, 2H); 6.01 (s, 1H); 5.28-5.27 (m, 1H); 4.55-4.51 (m, 1H); 2.82-2.77 (m, 1H); 2.51-2.46 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 150.3, 147.5, 139.1, 129.3, 129.0, 126.1, 85.6, 53.8, 34.8; IR (neat) *ν* 3461, 3110, 1725, 623; HRMS (ESI-TOF) calcd for $C_{11}H_{11}BrNO_2$ $[M + H]^+$ 267.9973, found 267.9979.

(Z)-6-(bromomethylene)-4-(p-tolyl)-1,3-oxazinan-2-one (12b): 78% yield (110 mg); white solid; mp 157-159 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, DMSO-d_6) *δ:* 8.37 (s, 1H); 7.18 (d, *J* = 7.9 Hz, 2H); 7.15 (d, *J* = 7.9 Hz, 2H); 5.58 (s, 1H); 4.61-4.56 (m, 1H); 2.90 (dd, *J* = 14.5, 5.1 Hz, 1H); 2.62 (dd, *J* = 14.5, 5.8 Hz, 1H); 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) *δ:* 149.6, 148.9, 138.2, 137.4, 129.5, 126.4, 83.8, 51.8, 33.6, 21.1; IR (neat) *ν* 3465, 3012, 1723, 652; HRMS (ESI-TOF) calcd for $C_{12}H_{13}BrNO_2$ $[M + H]^+$ 282.0130, found 282.0125.

(Z)-6-(bromomethylene)-4-(4-methoxyphenyl)-1,3-oxazinan-2-one (12c): 82% yield (122 mg); white solid; mp 148-150 °C; R_f = 0.20 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.19 (d, *J* = 8.6 Hz, 2H); 6.91 (d, *J* = 8.6 Hz, 2H); 5.89 (s, 1H); 5.35 (s, 1H); 4.54 (dd, *J* = 8.6, 4.1 Hz, 1H); 3.81 (s, 3H); 2.82 (dd, *J* = 14.3, 4.1 Hz, 1H); 2.53 (dd, *J* = 14.3, 8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 160.0, 150.3, 147.6, 131.0, 127.4, 114.6, 85.4, 55.5, 53.3, 34.9; IR (neat) *ν* 3612, 3096, 1751, 682; HRMS (ESI-TOF) calcd for $C_{12}H_{13}BrNO_3$ $[M + H]^+$ 300.0058, found 300.0047.

(Z)-6-(bromomethylene)-4-(4-chlorophenyl)-1,3-oxazinan-2-one (12d): 72% yield (108 mg); white solid; mp 171-173 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, DMSO-d_6) *δ:* 8.42 (s, 1H); 7.45 (d, *J* = 8.4 Hz, 2H); 7.30 (d, *J* = 8.4 Hz, 2H); 5.60 (s, 1H); 4.68-4.64 (m, 1H); 2.92 (dd, *J* = 14.5, 5.1 Hz, 1H); 2.65 (dd, *J* = 14.5, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) *δ:* 149.5, 148.6, 140.2, 132.8, 128.9, 128.5, 84.1, 51.4, 33.4; IR (neat) *ν* 3419, 3021, 1741, 669; HRMS (ESI-TOF) calcd for $C_{11}H_{10}BrClNNaO_2$ $[M + Na]^+$ 323.9397, found 323.9390.

2.3 General Procedure C for the synthesis of 16 from 15:

To the substrate **15a** (120 g, 0.5 mmol) dissolved in THF (2 ml) were added H_2O (27 mg, 3 equiv) and $PtCl_4$ (17 mg, 0.1 mmol). The mixture was stirred at room temperature till the completion of the reaction (TLC, 18 h). The reaction mixture was then added water (4 ml) followed by brine solution (4 ml) and extracted with ethyl acetate (3 x 6 ml). The combined extracts were dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography (silicagel, 10-15% EtOAc in hexanes) to get the pure product **16a** (66 mg).

4-phenylfuran-2(5H)-one (16a): 82% yield (66 mg); white solid; mp 122-124 °C; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.53-7.45 (m, 5H); 6.38 (t, *J* = 1.8 Hz, 1H); 5.23 (d, *J* = 1.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.9, 164.0, 131.9, 129.8, 129.4, 126.6, 113.2, 71.1; IR (neat) *ν* 3019, 1740, 1643, 1215; HRMS (ESI-TOF) calcd for $C_{10}H_9O_2$ $[M + H]^+$ 161.0603, found 161.0601.

4-(p-tolyl)furan-2(5H)-one (16b): 80% yield (70 mg); white solid; mp 112-114 °C; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.42 (d, *J* = 8.2 Hz, 2H); 7.29 (d, *J* = 8.2 Hz, 2H); 6.33 (t, *J* = 1.7 Hz, 1H); 5.22 (d, *J* = 1.7 Hz, 2H); 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.2, 164.1, 142.6, 130.1, 126.9, 126.5, 112.0, 71.1, 21.7; IR (neat) *ν* 3021, 1745, 1622, 1216; HRMS (ESI-TOF) calcd for $C_{11}H_{11}O_2$ $[M + H]^+$ 175.0759, found 175.0748.

4-(4-fluorophenyl)furan-2(5H)-one (16c): 85% yield (76 mg); white solid; mp 120-122 °C; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.54-7.49 (m, 2H); 7.19-7.14 (m, 2H); 6.33 (t, *J* = 1.7 Hz, 1H); 5.20 (d, *J* = 1.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.8, 164.8 (d, *J* = 252 Hz), 162.7, 128.7 (d, *J* = 9 Hz), 126.2, 116.8 (d, *J* = 22 Hz), 113.0, 71.0; IR (neat) *ν* 3021, 1749, 1626, 1216; HRMS (ESI-TOF) calcd for $C_{10}H_8FO_2$ $[M + H]^+$ 179.0508, found 179.0505.

4-(4-chlorophenyl)furan-2(5H)-one (16d): 90% yield (88 mg); white solid; mp 158-160 °C; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.47-7.42 (m, 4H); 6.37 (t, *J* = 1.8 Hz, 1H); 5.19 (d, *J* = 1.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 173.6, 162.6, 138.1, 129.8, 128.3, 127.8, 113.7, 70.9; IR (neat) *ν* 3019, 1749, 1623, 1215; HRMS (ESI-TOF) calcd for $C_{10}H_8ClO_2$ $[M + H]^+$ 195.0213, found 195.0208.

4-(4-methoxyphenyl)furan-2(5H)-one (16e): 65% yield (62 mg); white solid; mp 129-131 °C; R_f = 0.30 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.45 (d, *J* = 8.0 Hz, 2H); 6.96 (d, *J* = 8.0 Hz, 2H); 6.23 (t, *J* = 4.0 Hz, 1H); 5.18 (d, *J* = 4.0 Hz, 2H); 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.4, 163.7, 162.5, 128.3, 122.4, 114.8, 110.7, 71.1, 55.6; IR (neat) *ν* 3025, 1749, 1625, 1220; HRMS (ESI-TOF) calcd for $C_{11}H_{11}O_3$ [M + H]$^+$ 191.0708, found 191.0710.

4-hexylfuran-2(5H)-one (16f): 65% yield (55 mg); red liquid; R_f = 0.30 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 5.82 (p, *J* = 1.7 Hz, 1H); 4.72 (d, *J* = 1.7 Hz, 2H); 2.42-2.36 (m, 2H); 1.61-1.53 (m, 2H); 1.39-1.26 (m, 6H); 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 174.3, 170.8, 115.5, 73.2, 31.5, 29.0, 28.7, 27.3, 22.6, 14.1; IR (neat) *ν* 1748, 1638, 1216; HRMS (ESI-TOF) calcd for $C_{10}H_{17}O_2$ [M + H]$^+$ 169.1229, found 169.1127.

5,5-dimethyl-4-phenylfuran-2(5H)-one (16g): 89% yield (84 mg); white solid; mp 95-97 °C; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.54-7.51 (m, 2H); 7.48-7.45 (m, 3H); 6.21 (s, 1H); 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 172.2, 171.5, 130.9, 130.4, 129.2, 127.6, 114.8, 87.4, 26.4; IR (neat) *ν* 3019, 1736, 1643, 1215; HRMS (ESI-TOF) calcd for $C_{12}H_{13}O_2$ [M + H]$^+$ 189.0916, found 189.0910

4-phenyl-1-oxaspiro[4.5]dec-3-en-2-one (16h): 93% yield (106 mg); colorless liquid; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.51-7.41 (m, 5H); 6.13 (s, 1H); 2.03-1.92 (m, 2H); 1.87-1.68 (m, 6H); 1.29-1.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 172.9, 171.8, 131.1, 130.4, 129.0, 127.6, 115.8, 89.5, 34.6, 24.6, 22.3; IR (neat) *ν* 3019, 1741, 1642, 1220; HRMS (ESI-TOF) calcd for $C_{15}H_{17}O_2$ [M + H]$^+$ 229.1229, found 229.1217.

5,5-dimethyl-4-(p-tolyl)furan-2(5H)-one (16i): 88% yield (89 mg); colorless liquid; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 7.34 (d, *J* = 8.2 Hz, 2H); 7.16 (d, *J* = 8.2 Hz, 2H); 6.08 (s, 1H); 2.30(s, 3H); 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 171.9, 171.6, 141.4, 129.8, 127.6, 127.2, 113.5, 87.2, 26.4, 21.4; IR (neat) *ν* 3019, 1740, 1640, 1225; HRMS (ESI-TOF) calcd for $C_{13}H_{15}O_2$ [M + H]$^+$ 203.1072, found 203.1070.

4-(4-methoxyphenyl)-5,5-dimethylfuran-2(5H)-one (16j): 82% yield (90 mg); colorless liquid; R_f = 0.30 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.52-7.49 (m, 2H); 6.97-6.94 (m, 2H); 6.12 (s, 1H); 3.84 (s, 3H); 1.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 171.8, 171.4, 161.7, 129.4, 122.3, 114.6, 112.0, 87.0, 55.5, 26.5; IR (neat) *ν* 3020, 1744, 1613, 1216; HRMS (ESI-TOF) calcd for $C_{13}H_{15}O_3$ [M + H]$^+$ 219.1021, found 219.1015.

4-(4-bromophenyl)-5,5-dimethylfuran-2(5H)-one (16k): 90% yield (120 mg); white solid; mp 134-136 °C; R_f = 0.40 (SiO_2, 20% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.60 (d, *J* = 8.6 Hz, 2H); 7.39 (d, *J* = 8.6 Hz, 2H); 6.20 (s, 1H); 1.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 171.0, 170.8, 132.5, 129.2, 129.0, 125.4, 87.2, 26.2; IR (neat) *ν* 3026, 1725, 1635, 1216; HRMS (ESI-TOF) calcd for $C_{12}H_{12}BrO_2$ [M + H]$^+$ 267.0021, found 267.0015.

4-phenyl-1-tosyl-1H-pyrrol-2(5H)-one (16l): 50% yield (78 mg); white solid; mp 168-170 °C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.99 (d, *J* = 8.2 Hz, 2H); 7.51-7.42 (m, 5H); 7.33 (d, *J* = 8.2 Hz, 2H); 6.30 (t, *J* = 1.4 Hz, 1H); 4.83 (d, *J* = 1.4 Hz, 2H); 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 168.7, 157.8, 145.3, 135.6, 131.7, 130.6, 129.9, 129.4, 128.1, 126.3, 118.8, 51.9, 21.8; IR (neat) *ν* 3030, 1636, 1402, 1217; HRMS (ESI-TOF) calcd for $C_{17}H_{16}NO_3S$ [M + H]$^+$ 314.0851, found 314.0841.

4-(4-ethylphenyl)-1-tosyl-1H-pyrrol-2(5H)-one (16m): 35% yield (60 mg); white solid; mp 150-152 °C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.98 (d, *J* = 8.3 Hz, 2H); 7.41 (d, *J* = 8.3 Hz, 2H); 7.33 (d, *J* = 8.1 Hz, 2H); 7.26 (d, *J* = 8.1 Hz, 2H); 6.25 (t, *J* = 1.4 Hz, 1H); 4.81 (d, *J* = 1.4 Hz, 2H); 2.68 (q, *J* = 7.5 Hz, 2H); 2.42 (s, 3H); 1.24 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 168.7, 157.8, 148.6, 145.0, 135.5, 129.7, 128.8, 127.9, 126.2, 117.6, 51.7, 28.8, 21.6, 15.2; IR (neat) *ν* 3019, 1701, 1167; HRMS (ESI-TOF) calcd for $C_{19}H_{20}NO_3S$ [M + H]$^+$ 342.1164, found 342.1161.

4-(4-methoxyphenyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (16n): 36% yield (63 mg); white solid; mp 142-144 °C; R_f = 0.30 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.98 (d, *J* = 7.7 Hz, 2H); 7.44 (d, *J* = 8.4 Hz, 2H); 7.33(d, *J* = 7.7 Hz, 2H); 6.93 (d, *J* = 8.4 Hz, 2H); 6.17 (s, 1H); 4.79 (s, 2H); 3.85 (s, 3H); 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 168.9, 162.3, 157.4, 144.9, 135.6, 129.7, 127.9, 127.9, 123.1, 116.3, 114.7, 55.5, 51.7, 21.6; IR (neat) *ν* 3022, 1660, 1217; HRMS (ESI-TOF) calcd for $C_{18}H_{18}NO_4S$ [M + H]$^+$ 344.0957, found 344.0951.

5,5-dimethyl-1-tosyl-1H-pyrrol-2(5H)-one (16o): 78% yield (104 mg); white solid; mp 133-135 °C; R_f = 0.50 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.97 (d, *J* = 8.3 Hz, 2H); 7.30 (d, *J* = 8.3 Hz, 2H); 7.02 (d, *J* = 6.0 Hz, 1H); 5.86 (d, *J* = 6.0 Hz, 1H); 2.41 (s, 3H); 1.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 168.4, 159.1, 144.8, 136.9, 129.4, 128.5, 122.5, 69.6, 25.0, 21.7; IR (neat) *ν* 3019, 1715, 1167; HRMS (ESI-TOF) calcd for $C_{13}H_{16}NO_3S$ [M + H]$^+$ 266.0851, found 266.0840.

1-tosyl-1-azaspiro[4.5]dec-3-en-2-one (16p): 72% yield (110 mg); white solid; mp 145-147 °C; R_f = 0.40 (SiO_2, 30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 7.96 (d, *J* = 8.3 Hz, 2H); 7.64 (d, *J* = 6.2 Hz, 1H); 7.29 (d, *J* = 8.3 Hz, 2H); 5.94 (d, *J* = 6.2 Hz, 1H); 2.89-2.81 (m, 2H); 2.41 (s, 3H); 1.93-1.79 (m, 3H); 1.69-1.66 (m, 2H); 1.55-1.37 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 168.3, 155.2, 144.6, 136.9, 129.2, 128.4, 123.4, 74.1, 34.1, 24.7, 24.2, 21.6; IR (neat) *ν* 2934, 1682, 1296, 1219; HRMS (ESI-TOF) calcd for $C_{16}H_{20}NO_3S$ [M + H]$^+$ 306.1164, found 306.1163.

Acknowledgements

YKK and GRK thank CSIR for the fellowships. We thank SAIF division CSIR-CDRI for the analytical support. We gratefully acknowledge the financial support by CSIR (THUNDER, BSC 0102) and DST (SB/FT/CS-102/2012). CDRI Communication No: (will be inserted if accepted)

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