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

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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

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Five-membered lactams¹ and lactones² (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 1³ 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



Figure 1. Some representative biologically active lactams/lactones

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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.⁷¹ 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.

Results and Discussion

Initially, we synthesized tosyl amino tethered bromo alkyne 3a from readily available aziridine 1a 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% AuCl₃ 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 PPh₃AuCl were not very effective for the same conversion (entries 2-3). The change of solvent to CH₃CN proved to be negative for the reaction (entry 4). Next, we screened the reaction with wettoluene/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-CH₃CN furnished the product neatly in 95% yield

⁺ Contributed equally.

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(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 | | | | |
|------------------------------------------------------------------------------------|-----------------------|------------------------------|-------------------------------------------|---------------------------------------------------------------------------------------|
| NBS, AgNO ₃ H ₂ O, acetone Ts NH Et 3a | Br Table ^a | TMS Ts Et V 4 M2 | $\frac{-TMS}{I-BuLi, THF}$ $Br H_2O$ Xn | $\begin{bmatrix} T_{s} \\ T_{a} \\ T_{a} \\ Et \\ T_{s} \\ Et \\ 5 \end{bmatrix} = 0$ |
| Entry | Catalyst | Solvent | H ₂ O (equiv) | Yiled ^b |
| 1 | AuCl ₃ | toluene | 3 | 80% |
| 2 | AuCl | toluene | 3 | 45% |
| 3 | PPh3AuCl | toluene | 3 | 20% |
| 4 | AuCl ₃ | CH ₃ CN | 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 ₃ CN | 3 | 95% |
| 9 | Hg(OTf) ₂ | CH ₃ CN | 5 | 85% |
| 10 | Hg(OTf) ₂ | CH ₃ CN | 10 | 75% |
| 11 | Hg(OTf) ₂ | H_2O | | c |
| 12 | HgCl ₂ | CH ₃ CN | 3 | 50% |
| 13 | Cu(OTf) ₂ | CH ₃ CN | 3 | c |
| 14 | Hg(OTf) ₂ | CH ₃ CN | | c |
| 15 ^d | Hg(OTf) ₂ | CH ₃ CN | 3 | c |
| 16 | TfOH | CH ₃ CN | 3 | c |

^aReaction conditions: **3a** (1.0 mmol), catalyst (10 mol %), H₂O (3 equiv), solvent (0.25 M), RT, 18 h, open air. ^bIsolated yield. ^cSM was recovered. ^d0.5 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 (**5I-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.



^aReaction conditions: **3a** (1.0 mmol), Hg(OTf)₂ (0.1 mmol), H₂O (3 equiv), CH₃CN (4 mL), RT, 18 h, open air. ^bIsolated 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

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formation (88%) regioselectively hydrolysed product αbromoketone 10a (Scheme 1). This must have happened through 5exo-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 AuCl₃ (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 as plat torm 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 bv elimination of benzylic hydroxyl group to deliver the α , β unsaturated y-butyrolactone 16a-k. An optimization study led to identify PtCl₄ as the most suitable catalyst for the transformation.⁸ Thus, 15a was converted to 16a in 82% yield using 10 mol% PtCl₄ 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, 5spiro 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 16 was furnished in 50% yield. Electron rich phenyl substituted lactams like

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General Information:

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 **160-p** in contrast were obtained in excellent yields (72-78%). The acidic protons in earlier cases might have assisted for some unwanted aromatizations.



 $^aReaction conditions:$ 15a (1.0 mmol), PtCl4 (0.1 mmol), H2O (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

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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 ¹H NMR, 100 MHz for ¹³C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethylsilane in CDCl₃ or deuterated solvent CDCl₃/[D6]DMSO for ¹H and ¹³C 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; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3030, 1610, 1365, 1219; HRMS (ESI-TOF) calcd for C₁₃H₁₈NO₃S [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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3120, 1650, 1384, 1215; HRMS (ESI-TOF) calcd for C₁₇H₁₈NO₃S [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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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,

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1H); ¹³C NMR (100 MHz, CDCl₃) 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) ν 3098, 1657, 1360, 1201; HRMS (ESI-TOF) calcd for C₁₈H₂₀NO₃S [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; $R_f = 0.50$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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);¹³C NMR (100 MHz, CDCl₃) 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 C₁₉H₂₂NO₃S [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; $R_f = 0.50$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) ν 2099, 1663, 1365, 1200; HRMS (ESI-TOF) calcd for C₂₁H₂₆NO₃S [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; $R_f = 0.50$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₈H₂₀NO₃S [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; $R_f = 0.4$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) ν 3022, 1611, 1248, 1216; HRMS (ESI-TOF) calcd for C₁₈H₂₀NO₄S [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 (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₈H₂₀NO₄S [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 (SiO₂, 30% ECOAč/Hč(aRed)?⁵M NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₇H₁₇CINO₃S [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; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₇H₁₇N₂O₅S [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; $R_f = 0.40$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) ν 3023, 1610, 1361, 1216; HRMS (ESI-TOF) calcd for C₁₈H₂₀NO₃S [M + H]⁺ 330.1164, found 330.1157.

(S)-5-methyl-1-tosylpyrrolidin-2-one (5I): 95% yield (120 mg); white solid; mp 140-142 °C; R_f = 0.30 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₂H₁₆NO₃S [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; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₄H₂₀NO₃S [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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C

View Article Online DOI: 10.1039/C5OB02125A 1715, 1397, 675; HRMS (ESI-TOF) calcd for C14H21BrNaNO3S [M +

NMR (100 MHz, CDCl₃) 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) v 3020, 1610, 1385, 1220; HRMS (ESI-TOF) calcd for C₁₅H₂₂NO₃S [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; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3021, 1620, 1388, 1216; HRMS (ESI-TOF) calcd for C₁₅H₂₂NO₃S [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; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 174.0, 144.7, 136.8, 129.8, 128.7, 67.1, 35.8, 30.0, 28.3, 21.7; IR (neat) v 3021, 1620, 1388, 1216; HRMS (ESI-TOF) calcd for C₁₃H₁₈NO₃S [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; $R_f = 0.20$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 174.2, 150.7, 144.9, 130.2, 124.0, 67.8, 35.8, 29.9, 28.4; IR (neat) v 3068, 1636, 1394, 1210; HRMS (ESI-TOF) calcd for C₁₂H₁₅N₂O₅S [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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) *v* 3415, 1725, 1396, 668; HRMS (ESI-TOF) calcd for C₁₉H₂₃BrNO₃S [M + H]⁺ 424.0582, found 424.0580.

N-(7-bromo-6-oxoheptan-3-yl)-4-methylbenzenesulfonamide

(10b): 90% yield (163 mg); colorless liquid; $R_f = 0.40$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3369,

(S)-N-(6-bromo-5-oxohexan-2-yl)-4-methylbenzenesulfonamide

(10c): 90% yield (156 mg); white solid; mp 88-90 °C; $R_f = 0.40$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3369, 1715, 1397, 675; HRMS (ESI-TOF) calcd for C₁₃H₁₉BrNO₃S [M + H]⁺ 348.0269, found 348.0255.

N-(6-bromo-2-methyl-5-oxohexan-2-yl)-4-

Na]⁺ 384.0245, found 384.0239.

methylbenzenesulfonamide (10d): 92% yield (166 mg); white solid; mp 116-118 °C; R_f = 0.40 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) *v* 3399, 1723, 1403, 682; HRMS (ESI-TOF) calcd for C₁₄H₂₀BrNaNO₃S [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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3396, 1710, 1403, 680; HRMS (ESI-TOF) calcd for C₁₃H₁₉BrNO₃S [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 (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ: 155.2, 128.7, 127.8, 126.4, 80.1, 76.2, 52.8, 41.3, 28.5, 27.9; IR (neat) v 3460, 2198, 1721, 685; HRMS (ESI-TOF) calcd for C₁₅H₁₉BrNO₂ [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; $R_f = 0.70$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3423, 2252, 1706, 650; HRMS (ESI-TOF) calcd for C₁₆H₂₁BrNO₂ [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; $R_f = 0.60$

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(SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) *v* 3490, 2310, 1725, 680; HRMS (ESI-TOF) calcd for C₁₆H₂₁BrNO₃ [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 (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3432, 2260, 1706, 669; HRMS (ESI-TOF) calcd for C₁₅H₁₈BrCINO₂ [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 AuCl₃ (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 Na₂SO₄, 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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 150.3, 147.5, 139.1, 129.3, 129.0, 126.1, 85.6, 53.8, 34.8; IR (neat) v 3461, 3110, 1725, 623; HRMS (ESI-TOF) calcd for C₁₁H₁₁BrNO₂ [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; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H 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); ¹³C 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) v 3465, 3012, 1723, 652; HRMS (ESI-TOF) calcd for C₁₂H₁₃BrNO₂ [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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 160.0, 150.3, 147.6, 131.0, 127.4, 114.6, 85.4, 55.5, 53.3, 34.9; IR (neat) v 3612, 3096, 1751, 682; HRMS (ESI-TOF) calcd for C₁₂H₁₃BrNO₂ [M₁+ H]⁺ 300.0058, found 300.0047. DOI: 10.1039/C5OB02125A

(Z)-6-(bromomethylene)-4-(4-chlorophenyl)-1,3-oxazinan-2-one

(12d): 72% yield (108 mg); white solid; mp 171-173 °C; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H 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); ¹³C 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) v 3419, 3021, 1741, 669; HRMS (ESI-TOF) calcd for C₁₁H₁₀BrCINNaO₂ [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 PtCl₄ (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 Na₂SO₄, 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 (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) δ: 7.53-7.45 (m, 5H); 6.38 (t, *J* = 1.8 Hz, 1H); 5.23 (d, *J* = 1.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ: 173.9, 164.0, 131.9, 129.8, 129.4, 126.6, 113.2, 71.1; IR (neat) *v* 3019, 1740, 1643, 1215; HRMS (ESI-TOF) calcd for C₁₀H₉O₂ [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; $R_f = 0.40$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ: 174.2, 164.1, 142.6, 130.1, 126.9, 126.5, 112.0, 71.1, 21.7; IR (neat) v 3021, 1745, 1622, 1216; HRMS (ESI-TOF) calcd for C₁₁H₁₁O₂ [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 (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3021, 1749, 1626, 1216; HRMS (ESI-TOF) calcd for C₁₀H₈FO₂ [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; $R_f = 0.40$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) δ : 7.47-7.42 (m, 4H); 6.37 (t, J = 1.8 Hz, 1H); 5.19 (d, J = 1.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ : 173.6, 162.6, 138.1, 129.8, 128.3, 127.8, 113.7, 70.9; IR (neat) v 3019, 1749, 1623, 1215; HRMS (ESI-TOF) calcd for C₁₀H₈ClO₂ [M + H]⁺ 195.0213, found 195.0208.

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4-(4-methoxyphenyl)furan-2(5H)-one (16e): 65% yield (62 mg); white solid; mp 129-131 °C; $R_f = 0.30$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 174.4, 163.7, 162.5, 128.3, 122.4, 114.8, 110.7, 71.1, 55.6; IR (neat) v 3025, 1749, 1625, 1220; HRMS (ESI-TOF) calcd for C₁₁H₁₁O₃ [M + H]⁺ 191.0708, found 191.0710.

4-hexylfuran-2(5H)-one (16f): 65% yield (55 mg); red liquid; $R_f = 0.30$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 174.3, 170.8, 115.5, 73.2, 31.5, 29.0, 28.7, 27.3, 22.6, 14.1; IR (neat) v 1748, 1638, 1216; HRMS (ESI-TOF) calcd for C₁₀H₁₇O₂ [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 (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) δ : 7.54-7.51 (m, 2H); 7.48-7.45 (m, 3H); 6.21 (s, 1H); 1.70 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ : 172.2, 171.5, 130.9, 130.4, 129.2, 127.6, 114.8, 87.4, 26.4; IR (neat) v 3019, 1736, 1643, 1215; HRMS (ESI-TOF) calcd for C₁₂H₁₃O₂ [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; $R_f = 0.40$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) *v* 3019, 1741, 1642, 1220; HRMS (ESI-TOF) calcd for C₁₅H₁₇O₂ [M + H]⁺ 229.1229, found 229.1217.

5,5-dimethyl-4-(p-tolyl)furan-2(5H)-one (16i): 88% yield (89 mg); colorless liquid; $R_f = 0.40$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 171.9, 171.6, 141.4, 129.8, 127.6, 127.2, 113.5, 87.2, 26.4, 21.4; IR (neat) v 3019, 1740, 1640, 1225; HRMS (ESI-TOF) calcd for C₁₃H₁₅O₂ [M + H]⁺ 203.1072, found 203.1070.

4-(4-methoxyphenyl)-5,5-dimethylfuran-2(5H)-one (16j): 82% yield (90 mg); colorless liquid; $R_f = 0.30$ (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 171.8, 171.4, 161.7, 129.4, 122.3, 114.6, 112.0, 87.0, 55.5, 26.5; IR (neat) v 3020, 1744, 1613, 1216; HRMS (ESI-TOF) calcd for C₁₃H₁₅O₃ [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 (SiO₂, 20% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ : 171.0, 170.8, 132.5, 129.2, 129.0, 125.4, 87.2, 26.2;

IR (neat) v 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; $R_f = 0.50$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) v 3030, 1636, 1402, 1217; HRMS (ESI-TOF) calcd for C₁₇H₁₆NO₃S [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 (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) *v* 3019, 1701, 1167; HRMS (ESI-TOF) calcd for C₁₉H₂₀NO₃S [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; $R_f = 0.30$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); 7.34 (d, J = 8.4 Hz, 2H); 3.85 (s, 3H); 2.42 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 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) v 3022, 1660, 1217; HRMS (ESI-TOF) calcd for C₁₈H₁₈NO₄S [M + H]⁺ 344.0957, found 344.0951.

5,5-dimethyl-1-tosyl-1H-pyrrol-2(5H)-one (160): 78% yield (104 mg); white solid; mp 133-135 °C; $R_f = 0.50$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₃H₁₆NO₃S [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; $R_f = 0.40$ (SiO₂, 30% EtOAc/Hexanes); ¹H NMR (400 MHz, CDCl₃) 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); 2.41 (s, 3H); 1.93-1.79 (m, 3H); 1.69-1.66 (m, 2H); 1.55-1.37 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) 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) v 2934, 1682, 1296, 1219; HRMS (ESI-TOF) calcd for C₁₆H₂₀NO₃S [M + H]⁺ 306.1164, found 306.1163.

Acknowledgements

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