JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Palladium-Catalyzed Intermolecular Oxidative Cyclization of Allyltosylamides with AcOH: Assembly of 3-Pyrrolin-2-ones

Jiuzhong Huang, Jia Zheng, Wanqing Wu, Jianxiao Li, Zhiqiang Ma,* Yanwei Ren, and Huanfeng Jiang*

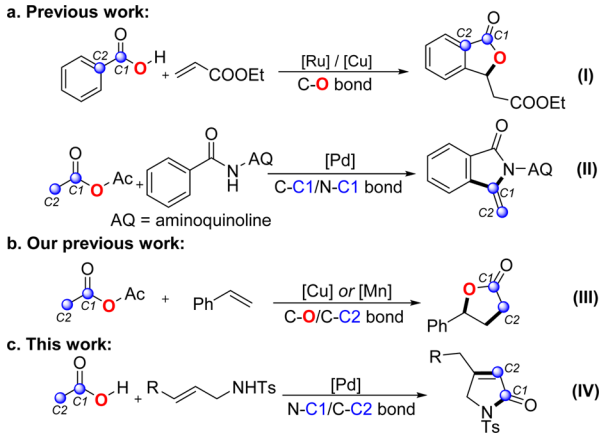
Key Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510640, P. R. China

Supporting Information

ABSTRACT: The first example of Pd-catalyzed oxidative cyclization of allyltosylamides with acetic acid is reported. This transformation involved C−N/C−C bond formation and provided 3-pyrrolin-2-ones in a one-pot manner with easy-operation, excellent atom economy and good yields. Mechanistic studies indicate that the reaction proceeds through intermolecular aminopalladation, migratory insertion, reinsertion and β-hydride elimination processes.

Transition metal-catalyzed oxidative coupling reactions have drawn increasing attention as powerful synthetic strategy for the formation of C−C/C−X (X = O, N, S···) bonds over the past decade.[1] Especially, Pd-catalyzed oxidative cyclizations of alkenes to construct functionalized molecules have been well explored.[2] In this regard, as commercial materials, carboxylic acids/anhydrides have been extensively explored in alkenyl C−H bond functionalization for the synthesis of heterocycles, in which they are generally used as synthons by offering one or two bonding sites.[3] For instance, Ackermann reported the Ru-catalyzed C−H bond alkenylation between benzoic acids and active alkenes with the formation of C−O bond (Scheme 1, I).[3a] Recently, Wei and colleagues have successfully constructed C−C1/N−C1 bonds at C1 position via Pd-catalyzed C−H functionalization of acrylamides (Scheme 1, II).[3c] In the aspect of C2 position as bonding site, our group utilized the anhydrides to construct C−O/C−C1 bonds in Cu-catalyzed[3d] and Mn-promoted[3e] carboesterification of alkenes (Scheme 1, III). Considering our interests in Pd-catalyzed oxidation cyclization reactions[4] and expanding the scope of synthetic applications of carboxylic acids/anhydrides, we are the first to disclose AcOH as a C2 synthon to enable rapid assembly of various 3-pyrrolin-2-ones.

Scheme 1. Transition Metal-Catalyzed Intermolecular Cyclization Reactions Involving Carboxylic Acids/Anhydrides



3-Pyrrolin-2-one skeleton is an important moiety in natural products and pharmaceuticals. For example, NMDA receptor glycine antagonist[5a] and NK1 receptor antagonist[5b] are the potential therapeutic drugs of chronic pain and CNS diseases (Figure 1). As synthons,[6] 3-pyrrolin-2-one skeleton has been modified to diverse functionalized molecules. However, examples of one-step approaches from readily available starting materials are still rare.[7] Generally, 3-pyrrolin-2-ones could be obtained by the reduction of maleimide[8] and the oxidation of pyrrole.[9] More convenient and versatile methods for constructing functionalized 3-pyrrolin-2-ones are still reckoned as a challenging task.

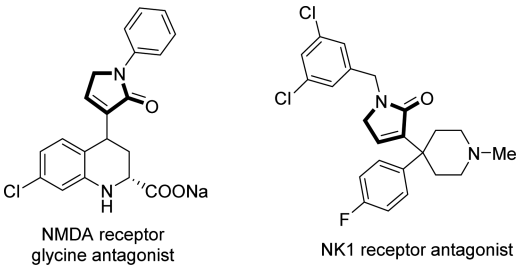
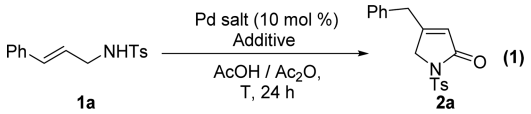


Figure 1. Selected biological active molecules containing 3-pyrrolin-2-one motifs.

Received: April 6, 2017
Published: July 7, 2017

DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198

Table 1. Optimization of Reaction Conditions[a]



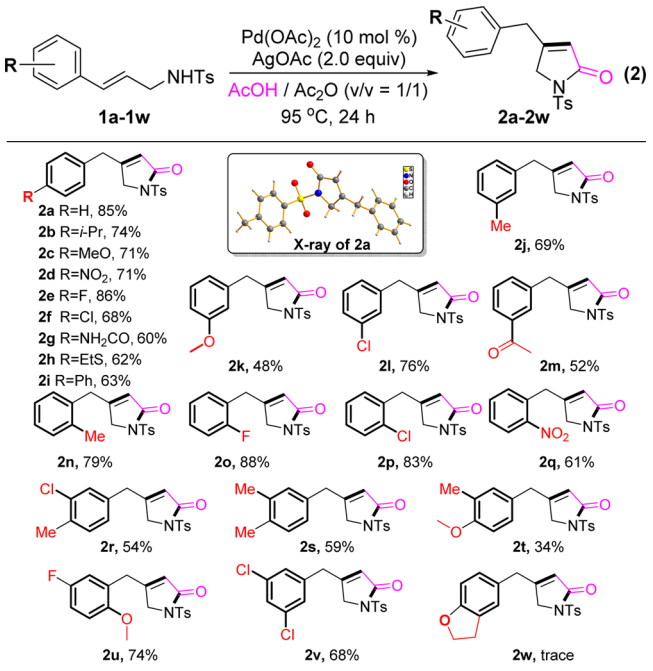
entry	catalyst (10 mol%)	additive (2.0 equiv)	$AcOH:Ac_2O$	T (°C)	yield (%)[b]
1	$Pd(OAc)_2$	$Cu(OAc)_2$	1:1	95	68 (63)
2	$PdCl_2$	$Cu(OAc)_2$	1:1	95	8
3	$Pd(CH_3CN)_2Cl_2$	$Cu(OAc)_2$	1:1	95	11
4	$Pd(TFA)_2$	$Cu(OAc)_2$	1:1	95	45
5	$Pd(OAc)_2$	$CuCl_2$	1:1	95	23
6	$Pd(OAc)_2$	CuCl	1:1	95	14
7	$Pd(OAc)_2$	$Cu(OTf)_2$	1:1	95	45
8	$Pd(OAc)_2$	$Fe(NO_3)_3$	1:1	95	23
9	$Pd(OAc)_2$	$Fe(acac)_3$	1:1	95	34
10	$Pd(OAc)_2$	$Fe(OAc)_2$	1:1	95	28
11	$Pd(OAc)_2$	$AgNO_3$	1:1	95	n.d.
12	$Pd(OAc)_2$	$AgNO_2$	1:1	95	61
13	$Pd(OAc)_2$	Ag_2O	1:1	95	72
14	$Pd(OAc)_2$	AgOAc	1:1	95	89 (85)
15[c]	$Pd(OAc)_2$	AgOAc	1:1	95	n.r.
16	$Pd(OAc)_2$	AgOAc	1:1	115	68
17	$Pd(OAc)_2$	AgOAc	1:1	65	32
18[d]	$Pd(OAc)_2$	AgOAc	1:1	95	45
19[e]	$Pd(OAc)_2$	AgOAc	1:1	95	acetylation
20	$Pd(OAc)_2$	AgOAc	0:1	95	8
21	$Pd(OAc)_2$	AgOAc	1:0	95	18

[a]Reaction conditions: **1a** (0.1 mmol), catalyst (10 mol%), additive (2.0 equiv), Ac_2O (0.6 mL), AcOH (0.6 mL) under air for 24 h. [b]Yield determined by ^1H NMR with CH_2BrCl as internal standard; Isolated yield is in the parentheses. n.d. = not detected; n.r. = not reaction. [c]20 mol% of 1,10-phenanthroline was added. [d]2.0 equiv of KOAc was added. [e]1.2 equiv of AgOAc was added; Ts = *p*-Tosyl, acac = acetylacetonato.

At the outset of this investigation, we employed cinnamyltosylamides as available substrates. In the presence of 10 mol% $Pd(OAc)_2$ and 2.0 equiv of $Cu(OAc)_2$ at 95 °C, 63% yield of **2a** was obtained in the reaction of cinnamyltosylamide with $AcOH/Ac_2O$ (Table 1, entry 1). The catalyst screening showed that other palladium salts, such as $PdCl_2$, $Pd(CH_3CN)_2Cl_2$, and $Pd(TFA)_2$, were less effective (Table 1, entries 2−4). Further examinations of different additives revealed that Ag salts promoted this reaction efficiently (Table 1, entries 11−14). To our delight, the yield increased to 89% when using 2.0 equiv of AgOAc (Table 1, entry 14). The reaction was totally inhibited when 20 mol% of 1,10-phenanthroline was added as ligand (Table 1, entry 15). Increasing or decreasing the reaction temperature showed no obvious beneficial effect (Table 1, entries 16 and 17). It is noteworthy that the *N*-acetylation of substrate **1a** was observed when decreasing the amount of AgOAc to 1.2 equiv (entry 19). Without AcOH or Ac_2O, product **2a** could be obtained in low yields (Table 1, entries 20 and 21). On the basis of above investigations, the optimal reaction conditions for this transformation is $Pd(OAc)_2$ (10 mol%), AgOAc (2.0 equiv) in $AcOH/Ac_2O$ (1/1, v/v) at 95 °C for 24 h.

With the optimized conditions in hand, various *N*-cinnamyltosylamides were examined (Table 2). It was found that most substrates with electron-deficient and electron-rich functional groups, including isopropyl, methoxy, nitro, fluoro, chloro, ethylthio, acetyl, and phenyl, were successfully transformed to the desired 3-pyrrolin-2-ones in moderate yields (**2a−2f**, **2h−2m**). However, the nitrile group could not be tolerated but hydrolyzed into the corresponding amide group under the standard conditions (**2g**). The reaction rate of

Table 2. Pd-Catalyzed Intermolecular Oxidative Cyclizations of Cinnamyltosylamides with AcOH[a,b]



[a]Reaction conditions: **1** (0.10 mmol), $Pd(OAc)_2$ (10 mol%), AgOAc (0.20 mmol), AcOH (0.6 mL), Ac_2O (0.6 mL) at 95 °C for 24 h. [b]Yields referred to isolated yield.

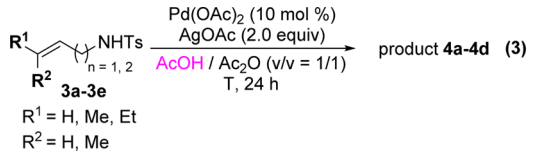
substrate with electron-donating group was faster than that with electron-withdrawing group, but they transformed into the

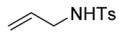
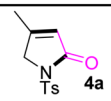
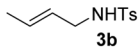
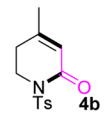
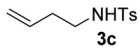
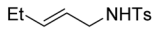
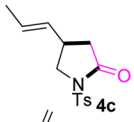
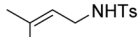
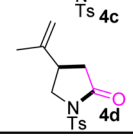
DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198

corresponding products in similar yields at last (**2c**, **2d**), which might be attributed to the slight decomposition of products with EDG under the standard conditions. Moreover, *ortho*-substituted cinnamyltosylamides (**2n**−**2q**) were transferred to the target products in similar yields with *para*- and *meta*-substituted ones. Gratifyingly, most of disubstituted substrates exhibited good compatibility in this reaction (**2s**, **2s**, **2u**), but 3-methyl-4-methoxy substrate afforded the product in lower yield (**2t**). Unfortunately, dihydrobenzofuran moiety was not tolerated under the current conditions. The electronic effects may still be a major reason. In addition, the structure of **2a** was confirmed by X-ray crystallographic analysis.

To our delight, the reaction of allyltosylamide **3a** also proceeded smoothly to provide the corresponding 5-membered ring product **4a** (Table 3, See X-ray of **4a** in SI).[9] Due to low

Table 3. Pd-Catalyzed Intermolecular Oxidative Cyclization of (Homo)Allyltosylamides with AcOH[a,b]



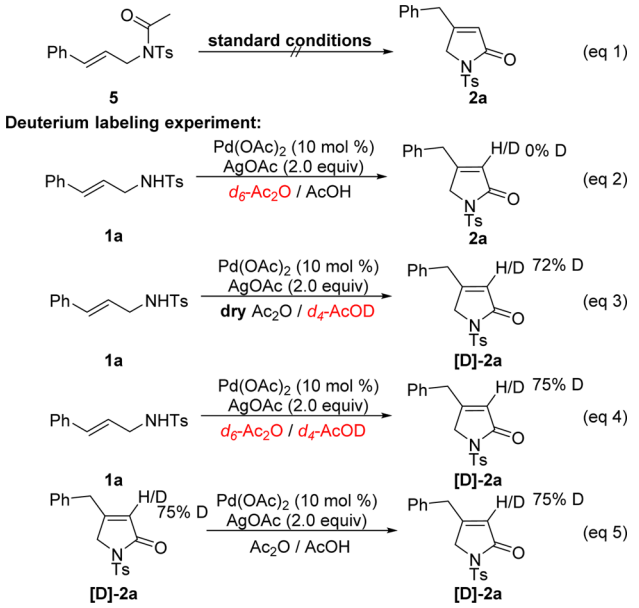
entry	substrate	T (°C)	product	yield
1	 **3a**	95	 **4a**	52%
2	 **3b**	110	 **4b**	68%
3	 **3c**	110		69%
4	 **3d**	110	 **4c**	53%
5	 **3e**	130	 **4d**	47%

[a]Reaction conditions: **3** (0.10 mmol), $Pd(OAc)_2$ (10 mol%), AgOAc (0.20 mmol), AcOH (0.6 mL), Ac_2O (0.6 mL) for 24 h. [b]Yields referred to isolated yield.

conversion rate under the standard conditions (95 °C), crotyltosylamide **3b** and 4-butenyl tosylamide **3c** transformed into 6-membered ring product **4b** at 110 °C via 6-*endo* cyclization, in which **3b** should undergo isomerization of olefin before cyclization. Meanwhile, (*E*)-3-pentenyl tosylamide **3d** and 3-methyl-3-butenyl tosylamide **3e** gave 2-pyrrolidone derivates containing exocyclic double bond **4c** and **4d** at higher temperature, respectively. On the basis of the current results, it is difficult to control the formation of 5- or 6-membered ring for the nature of substrates.

To gain further insights into this reaction, first, we subjected the *N*-acetylation byproduct **5** (Table 1, entry 21) to the standard reaction conditions, which failed to provide the corresponding product (Scheme 2, eq 1). Next, a series of deuterium labeling experiments were carried out. When the reaction was used AcOH/d_6-Ac_2O as solvent, no deuterated product was provided (eq 2). However, in the case of **1a** in d_4-AcOD/dry Ac_2O, product [**D**]-**2a** was obtained with 72% D

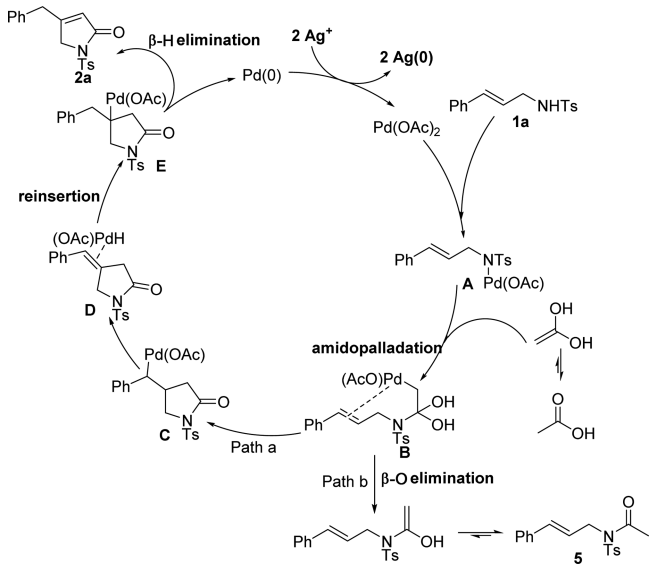
Scheme 2. Control Experiments



(eq 3). The low level of deuterium incorporation was caused by $Pd(OAc)_2$, AgOAc. Furthermore, [**D**]-**2a** with 75% D was afforded in d_6-Ac_2O/d_4-AcOD, which is near to the result of eq 3 (eq 4). It is noteworthy that the deuterated product [**D**]-**2a** (75% deuterium) was stable under the standard conditions[10] (eq 5), which indicated H/D exchange is impossible after formation of **2a**. Hence, it is supposed that AcOH was the only source of product **2a**. Nevertheless, the role of anhydride as solvent was still not very clear. And when propionic acid instead of AcOH was used in the reaction, the desired product could not be detected.

On the basis of the above results and previous works,[11] a tentative mechanism for the Pd-catalyzed oxidative cyclization between allyltosylamides and AcOH is proposed in Scheme 3. First, intermediate **A** is formed by the reaction of $Pd(OAc)_2$ and *N*-tosylamide.[2c,4b,12] Then the N−Pd species **A** inserts to the alkene isomer of AcOH,[13] followed by the intermolecular

Scheme 3. Proposed Mechanism



DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198

aminopalladation to generate the intermediate **B**.[14] Subsequent 1,2-migratory insertion offers intermediate **C** (path a). A sequence of β-hydride elimination and reinsertion provides the intermediate **E**.[15] Finally, β-hydride elimination of complex **E** releases product **2a** and Pd(0). The catalyst is regenerated by oxidation of AgOAc.[16] Additionally, the intermediate **B** can undergo β-oxygen elimination to afford the *N*-acetylation byproduct **5**.[17]

In conclusion, this method affords the desired 3-pyrrolin-2-ones with good yields and group tolerance. The reaction mechanism consists of intermolecular aminopalladation, migratory insertion, reinsertion and β-hydride elimination processes. Furthermore, we have developed a new and convenient palladium-catalyzed oxidative cyclization of allyltosylamides and acid as C2 synthon.

EXPERIMENTAL SECTION

General Method. ^{1}H and ^{13}C NMR spectra were recorded on BRUKER DRX-400 spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a BRUKER TENSOR 27 spectrometer. Melting points were determined with Büchi Melting Point B-545 instrument. Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification.

Synthesis of (*E*)-*N*-(3-Chloroallyl)-4-methylbenzenesulfonamide.[20] $TsNH_2$ (10.0 mmol), K_2CO_3 (6.0 mmol), CH_3CN (40 mL), and (*E*)-1,3-dichloroprop-1-ene (5.0 mmol) were successively added to 100 mL round-bottomed flask with magnetic stirrer bar. The mixture was stirred at 60 °C (oil bath temperature) for 16 h. The reaction was quenched with saturated NH_4Cl aq. and extracted with EtOAc (3 × 50 mL), washed with brine (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude product was purified via column chromatography (EtOAc/hexanes = 1/3) on silica gel to afford the product as white solid (759 mg, 62% yield).

Representative Procedure for *N*-Cinnamyltosylamides Derivatives (1a−1w). (*E*)-*N*-(3-Chloroallyl)-4-methylbenzenesulfonamide (1.0 mmol), aryl boric acid (1.2 mmol), K_2CO_3 (2.5 mmol), $Pd(dppf)Cl_2$ (0.1 mmol), EtOH (3 mL), and toluene (3 mL) were successively added to 25 mL seal tube, then was evacuated and filled with N_2 for three times. The mixture was stirred at 60 °C (oil bath temperature) overnight. The reaction was quenched with saturated NH_4Cl aq. and extracted with EtOAc (3 × 20 mL), washed with brine (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude product was purified via column chromatography (EtOAc/hexanes = 1/3−1/2) on silica gel. The characterization data of **1a**,[21a] **1c**,[21b] **1e**,[21b] **1f**,[21b] **1p**[21a] were consistent with the reported literatures.

Representative Procedure for (homo)Allyltosylamides Derivatives (3a−3e). $TsNH_2$ (2.0 mmol), K_2CO_3 (2.4 mmol), CH_3CN (8 mL), and (homo)allyl bromide (2.0 mmol) were successively added to 25 mL round-bottomed flask with magnetic stirrer bar. The mixture was stirred at 60 °C (oil bath temperature) for 16 h. The reaction was quenched with saturated NH_4Cl (aq.) and extracted with EtOAc (3 × 15 mL), washed with brine (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude product was purified via column chromatography (EtOAc/hexanes = 1/4) on silica gel. The characterization data of **3a**,[22a] **3b**,[22a] **3c**,[22b] **3d**,[22c] **3e**[20d] were consistent with the reported literatures.

Representative Procedure for 3-Pyrrolin-2-ones Derivatives. Allyltosylamide (0.10 mmol), $Pd(OAc)_2$ (0.01 mmol), AgOAc (0.20 mmol) in AcOH (0.6 mL), Ac_2O (0.6 mL) were added to a 20 mL tube with magnetic stirrer bar. The mixture was stirred at 90−130 °C (oil bath temperature) for 24 h under open air. After the reaction was finished (monitored by TLC), the mixture was cooled to room temperature. The reaction was neutralized with saturated $NaHCO_3$ aq. and extracted with EtOAc (3 × 15 mL), washed with brine (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude product was purified via column chromatography (EtOAc/hexanes = 1/3) on silica gel.

Analytical Characterization Data of Substrates and Products. *(E)-N-(3-(4-Isopropylphenyl)allyl)-4-methylbenzenesulfonamide (**1b**).* Purified via flash column chromatography with 25% ethyl acetate/petroleum ether, yielding 65% (213 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 7.16 (q, J = 8.3 Hz, 4H), 6.41 (d, J = 15.8 Hz, 1H), 5.96 (dt, J = 15.7, 6.4 Hz, 1H), 4.54 (s, 1H), 3.74 (t, J = 5.8 Hz, 2H), 2.87 (dt, J = 13.8, 6.9 Hz, 1H), 1.23 (d, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 143.5, 137.1, 133.7, 133.1, 129.7, 127.2, 126.6, 126.4, 123.1, 45.6, 33.8, 23.9, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{23}NO_2SNa$ 352.1342; found 352.1344.

*(E)-4-Methyl-N-(3-(4-nitrophenyl)allyl)benzenesulfonamide (**1d**).* Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 83% (275 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.7 Hz, 2H), 7.80 (d, J = 8.2 Hz, 2H), 7.39 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 6.56 (d, J = 15.9 Hz, 1H), 6.26 (dd, J = 13.9, 8.0 Hz, 1H), 4.86 (t, J = 6.1 Hz, 1H), 3.83 (t, J = 5.6 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.1, 143.8, 142.6, 137.0, 130.5, 129.8, 129.4, 127.2, 126.9, 123.9, 45.1, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{16}N_2O_4SNa$ 355.0723; found 355.0720.

*(E)-N-(3-(4-Cyanophenyl)allyl)-4-methylbenzenesulfonamide (**1g**).* Purified via flash column chromatography with 45% ethyl acetate/petroleum ether, yielding 43% (148 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 7.33 (dd, J = 7.9, 6.9 Hz, 4H), 6.50 (d, J = 15.9 Hz, 1H), 6.19 (dt, J = 15.9, 6.0 Hz, 1H), 4.84 (s, 1H), 3.81 (t, J = 5.2 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 140.6, 137.0, 132.4, 131.0, 129.8, 128.5, 127.2, 126.9, 118.7, 111.2, 45.1, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{16}N_2O_2SNa$ 335.0825; found 335.0833.

*(E)-N-(3-(4-(Ethylthio)phenyl)allyl)-4-methylbenzenesulfonamide (**1h**).* Purified via flash column chromatography with 33% ethyl acetate/petroleum ether, yielding 73% (253 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 8.3 Hz, 2H), 6.39 (d, J = 15.8 Hz, 1H), 6.05−5.91 (m, 1H), 4.61 (s, 1H), 3.74 (d, J = 5.0 Hz, 2H), 2.93 (q, J = 7.3 Hz, 2H), 2.41 (s, 3H), 1.31 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 137.1, 136.6, 133.6, 132.5, 129.7, 128.7, 127.2, 126.8, 123.7, 45.5, 27.4, 21.5, 14.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{21}NO_2S_2Na$ 370.0906; found 370.0910.

*(E)-N-(3-([1,1′-Biphenyl]-4-yl)allyl)-4-methylbenzenesulfonamide (**1i**).* Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 81% (294 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 7.3 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.36 (dd, J = 16.7, 7.7 Hz, 5H), 6.50 (d, J = 15.8 Hz, 1H), 6.09 (dd, J = 14.3, 7.9 Hz, 1H), 4.71 (s, 1H), 3.81 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 140.7, 140.5, 137.2, 135.1, 132.6, 129.8, 128.8, 127.4, 127.2, 126.9, 126.8, 124.2, 45.5, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{21}NO_2SNa$ 386.1185; found 386.1182.

*(E)-4-Methyl-N-(3-(m-tolyl)allyl)benzenesulfonamide (**1j**).* Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 68% (204 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.15 (t, J = 7.7 Hz, 1H), 7.02 (t, J = 6.5 Hz, 3H), 6.38 (d, J = 15.8 Hz, 1H), 5.97 (dt, J = 15.8, 6.4 Hz, 1H), 4.92 (t, J = 6.0 Hz, 1H), 3.72 (t, J = 5.9 Hz, 2H), 2.39 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 138.1, 137.2, 136.1, 133.1, 129.7, 128.7, 128.4, 127.2, 127.1, 123.9, 123.6, 45.5, 21.5, 21.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{19}NO_2SNa$ 324.1029; found 324.1034.

*(E)-N-(3-(3-Methoxyphenyl)allyl)-4-methylbenzenesulfonamide (**1k**).* Purified via flash column chromatography with 40% ethyl

DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198

acetate/petroleum ether, yielding 55% (174 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.21 (t, J = 7.8 Hz, 1H), 6.89−6.75 (m, 3H), 6.42 (d, J = 15.8 Hz, 1H), 6.01 (dt, J = 15.8, 6.3 Hz, 1H), 4.87 (t, J = 6.1 Hz, 1H), 3.80 (s, 3H), 3.78−3.72 (m, 2H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 143.5, 137.6, 137.1, 132.9, 129.8, 129.5, 127.2, 124.5, 119.1, 113.5, 111.7, 55.2, 45.4, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{19}NO_3SNa$ 340.0978; found 340.0980.

(E)-N-(3-(3-Chlorophenyl)allyl)-4-methylbenzenesulfonamide ***(1l)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 72% (231 mg).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.26−7.18 (m, 3H), 7.15−7.08 (m, 1H), 6.39 (d, J = 15.8 Hz, 1H), 6.02 (dt, J = 15.8, 6.2 Hz, 1H), 4.72 (t, J = 5.9 Hz, 1H), 3.84−3.74 (m, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 138.0, 137.2, 134.5, 131.6, 129.8, 127.8, 127.2, 126.3, 125.8, 124.6, 45.2, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{16}ClNO_2SNa$ 344.0482; found 344.0487.

(E)-N-(3-(3-Acetylphenyl)allyl)-4-methylbenzenesulfonamide ***(1m)***. Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 51% (167 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 11.0, 6.6 Hz, 4H), 7.44 (d, J = 7.8 Hz, 1H), 7.38 (dd, J = 10.5, 5.3 Hz, 1H), 7.32−7.28 (m, 2H), 6.49 (d, J = 15.9 Hz, 1H), 6.11 (dt, J = 15.8, 6.2 Hz, 1H), 5.09 (s, 1H), 3.78 (t, J = 5.7 Hz, 2H), 2.59 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1, 143.6, 137.4, 137.1, 136.7, 131.8, 130.8, 129.7, 128.8, 127.7, 127.2, 126.2, 125.8, 45.2, 26.6, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{19}NO_3SNa$ 352.0978; found 352.0970.

(E)-4-Methyl-N-(3-(o-tolyl)allyl)benzenesulfonamide ***(1n)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 75% (225 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.26−7.19 (m, 1H), 7.12 (dt, J = 11.4, 5.7 Hz, 3H), 6.65 (d, J = 15.7 Hz, 1H), 5.88 (dt, J = 15.6, 6.3 Hz, 1H), 4.85 (t, J = 5.9 Hz, 1H), 3.76 (t, J = 6.2 Hz, 2H), 2.40 (s, 4H), 2.24 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 137.2, 135.4, 135.2, 130.9, 130.3, 129.8, 127.8, 127.2, 126.1, 125.7, 125.5, 45.7, 21.5, 19.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{19}NO_3SNa$ 324.1029; found 324.1033.

(E)-N-(3-(2-Fluorophenyl)allyl)-4-methylbenzenesulfonamide ***(1o)***. Purified via flash column chromatography with 33% ethyl acetate/petroleum ether, yielding 77% (234 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.0 Hz, 2H), 7.27 (t, J = 8.3 Hz, 3H), 7.19 (dd, J = 13.5, 6.7 Hz, 1H), 7.10−6.93 (m, 2H), 6.57 (d, J = 16.0 Hz, 1H), 6.10 (dt, J = 15.9, 6.3 Hz, 1H), 4.91 (s, 1H), 3.76 (t, J = 6.1 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 158.9, 143.6, 137.0, 129.7, 129.2 (d, J = 8.5 Hz), 127.5 (d, J = 3.6 Hz), 127.2, 126.9 (d, J = 4.9 Hz), 125.4 (d, J = 3.5 Hz), 124.1 (d, J = 3.5 Hz), 115.7 (d, J = 22 Hz), 45.7, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{16F}NO_2SNa$ 328.0778; found 328.0775.

(E)-4-Methyl-N-(3-(2-nitrophenyl)allyl)benzenesulfonamide ***(1q)***. Purified via flash column chromatography with 50% ethyl acetate/petroleum ether, yielding 74% (235 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.02 (m, 2H), 7.81 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 7.9 Hz, 1H), 7.33 (d, J = 8.2 Hz, 2H), 6.53 (d, J = 15.9 Hz, 1H), 6.18 (dt, J = 15.9, 6.0 Hz, 1H), 4.91 (s, 1H), 3.93−3.68 (m, 2H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 143.8, 137.9, 137.1, 132.2, 130.4, 129.8, 129.5, 127.8, 127.2, 122.4, 120.9, 45.0, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{16}N_2O_4SNa$ 355.0723; found 355.0721.

(E)-N-(3-(3-Chloro-4-methylphenyl)allyl)-4-methylbenzenesulfonamide ***(1r)***. Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 83% (278 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 1.2 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.03 (dd, J = 7.8, 1.3 Hz, 1H), 6.35 (d, J = 15.8 Hz, 1H), 5.96 (dt, J = 15.8, 6.3 Hz, 1H), 4.87 (s, 1H), 3.76 (t, J = 5.8 Hz, 2H), 2.43 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 137.2, 135.5, 134.5, 131.5, 131.0, 129.7, 127.2, 126.8, 124.7, 124.6, 45.3, 21.5, 19.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{18}ClNO_2SNa$ 358.0639; found 358.0637.

(E)-N-(3-(3,4-Dimethylphenyl)allyl)-4-methylbenzenesulfonamide ***(1s)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 63% (198 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (t, J = 8.7 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.11−6.93 (m, 3H), 6.40 (d, J = 15.8 Hz, 1H), 5.97 (dt, J = 15.7, 6.4 Hz, 1H), 4.61 (s, 1H), 3.75 (t, J = 5.9 Hz, 2H), 2.45 (s, 3H), 2.25 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 137.2, 136.7, 136.6, 133.75, 133.2, 129.8, 129.7, 127.7, 127.2, 123.9, 122.8, 45.6, 21.5, 19.7, 19.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{21}NO_2SNa$ 338.1185; found 338.1191.

(E)-N-(3-(4-Methoxy-3-methylphenyl)allyl)-4-methylbenzenesulfonamide ***(1t)***. Purified via flash column chromatography with 33% ethyl acetate/petroleum ether, yielding 57% (188 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 4.6 Hz, 2H), 6.77−6.72 (m, 1H), 6.37 (d, J = 15.8 Hz, 1H), 5.87 (dt, J = 15.8, 6.5 Hz, 1H), 4.61 (s, 1H), 3.84 (d, J = 2.4 Hz, 3H), 3.74 (td, J = 6.4, 1.2 Hz, 2H), 2.44 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 143.4, 137.2, 132.9, 129.7, 128.5, 128.3, 127.2, 126.7, 125.3, 121.4, 109.8, 55.3, 45.7, 21.5, 16.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{21}NO_3SNa$ 354.1134; found 354.1140.

(E)-N-(3-(5-Fluoro-2-methoxyphenyl)allyl)-4-methylbenzenesulfonamide ***(1u)***. Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 73% (244 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 7.1 Hz, 2H), 6.94−6.85 (m, 2H), 6.80−6.68 (m, 2H), 5.98 (dt, J = 15.8, 6.3 Hz, 1H), 4.87 (dd, J = 20.4, 14.5 Hz, 1H), 3.77 (dd, J = 9.0, 3.7 Hz, 5H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 155.8, 152.8, 143.5, 137.2, 129.7, 127.2, 127.0, 125.9, 114.8 (d, J = 23 Hz), 113.1 (d, J = 24 Hz), 111.91 (d, J = 8.2 Hz), 56.03 (d, J = 4.3 Hz), 45.7, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{18}FNO_3SNa$ 358.0884; found 358.0888.

(E)-N-(3-(3,5-Dichlorophenyl)allyl)-4-methylbenzenesulfonamide ***(1v)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 46% (163 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 7.7 Hz, 2H), 7.20 (s, 1H), 7.05 (s, 2H), 6.30 (d, J = 15.8 Hz, 1H), 5.99 (dt, J = 15.5, 5.9 Hz, 1H), 4.83 (d, J = 49.0 Hz, 1H), 3.76 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 139.2, 137.2, 135.1, 130.2, 129.8, 127.6, 127.5, 127.2, 124.7, 45.0, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{15}Cl_2NO_2SNa$ 378.0093; found 378.0098.

(E)-N-(3-(2,3-Dihydrobenzofuran-5-yl)allyl)-4-methylbenzenesulfonamide ***(1w)***. Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 56% (184 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.11 (s, 1H), 6.97 (d, J = 8.3 Hz, 1H), 6.68 (d, J = 8.2 Hz, 1H), 6.36 (d, J = 15.8 Hz, 1H), 5.84 (dt, J = 15.7, 6.5 Hz, 1H), 4.97 (d, J = 4.5 Hz, 1H), 4.56 (t, J = 8.7 Hz, 2H), 3.71 (dd, J = 9.1, 3.4 Hz, 2H), 3.16 (t, J = 8.7 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 143.4, 137.2, 133.0, 129.7, 129.0, 127.5, 127.2, 126.9, 122.7, 121.2, 109.1, 71.4, 45.6, 29.5, 21.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{19}NO_3SNa$ 352.0978; found 352.0981.

4-Benzyl-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2a)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 85% (27.8 mg) as a white solid: mp = 168−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.9 Hz, 2H), 7.39−7.27 (m, 5H), 7.14 (d, J = 7.2 Hz, 2H), 5.71 (s, 1H), 4.32 (s, 2H), 3.67 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 162.7, 145.0, 135.6, 135.5, 129.7, 129.1, 128.80, 127.9, 127.5, 122.2, 53.5, 36.7, 21.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{17}NO_3SNa$ 350.0821; found 350.0824. IR (KBr): 3489, 2960, 1723, 1264, 1164, 1028, 752 cm^{-1}.

4-(4-Isopropylbenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2b)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 74% (27.3 mg) as a yellow solid: mp = 139−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 7.9 Hz, 2H), 7.05 (d, J = 7.9 Hz, 2H), 5.72 (s, 1H), 4.32 (s, 2H), 3.64 (s, 2H), 2.89 (dd, J = 13.8, 6.9 Hz, 1H), 2.42 (s, 3H), 1.24 (d, J = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 163.1, 148.2, 145.0, 135.5, 132.9, 129.7, 128.7, 127.9,

DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198

127.1, 122.0, 53.5, 36.3, 33.8, 24.0, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{23}NO_3SNa$ 392.1291; found 392.1294. IR (KBr): 2958, 1723, 1357, 1162, 660, 556 cm^{-1}.

4-(4-Methoxybenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2c)***. Purified via flash column chromatography with 44% ethyl acetate/petroleum ether, yielding 71% (25.3 mg) as a white solid: mp = 164−165 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 5.70 (s, 1H), 4.30 (s, 2H), 3.80 (s, 3H), 3.62 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 163.4, 158.9, 145.0, 135.5, 129.8, 129.7, 127.9, 127.5, 121.8, 114.5, 55.3, 53.4, 35.8, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{19}NO_4SNa$ 380.0927; found 380.0934. IR (KBr): 2907, 1718, 1240, 1157, 1024, 657, 555 cm^{-1}.

1-Tosyl-4-(4-(trifluoromethyl)benzyl)-1,5-dihydro-2H-pyrrol-2-one ***(2d)***. Purified via flash column chromatography with 45% ethyl acetate/petroleum ether, yielding 75% (17.5 mg) as a white solid: mp = 183−185 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 7.8 Hz, 2H), 7.92 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 6.8 Hz, 4H), 5.71 (s, 1H), 4.35 (s, 2H), 3.79 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 160.3, 147.5, 145.3, 142.8, 135.3, 129.8, 129.7, 128.0, 124.3, 123.2, 53.4, 36.2, 21.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{16}N_2O_5SNa$ 395.0672; found 395.0675. IR (KBr): 2923, 1721, 1515, 1349, 1164, 661, 552 cm^{-1}.

4-(4-Fluorobenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2e)***. Purified via flash column chromatography with 33% ethyl acetate/petroleum ether, yielding 86% (29.6 mg) as a light yellow solid: mp = 158−159 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.11 (dd, J = 8.3, 5.4 Hz, 2H), 7.03 (t, J = 8.5 Hz, 2H), 5.69 (s, 1H), 4.31 (s, 2H), 3.65 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 162.5, 145.1, 135.5, 131.3, 130.4 (d, J = 8.1 Hz), 129.7, 127.9, 122.2, 116.1, 115.9, 53.4, 35.8, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{16}FNO_3SNa$ 368.0727; found 368.0731. IR (KBr): 2921, 1719, 1603, 1502, 1156, 823, 659, 552 cm^{-1}.

4-(4-Chlorobenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2f)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 68% (24.5 mg) as a White solid: mp = 178−180 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2H), 7.31 (dd, J = 8.1, 4.6 Hz, 4H), 7.08 (d, J = 8.3 Hz, 2H), 5.69 (s, 1H), 4.31 (s, 2H), 3.65 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 162.0, 145.1, 135.4, 134.0, 133.5, 130.2, 129.7, 129.3, 128.0, 122.4, 53.6, 36.0, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{16}ClNO_3SNa$ 384.0432; found 384.0435. IR (KBr): 2926, 1723, 1355, 1162, 817, 662, 555 cm^{-1}.

4-((5-Oxo-1-tosyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)benzamide ***(2g)***. Purified via flash column chromatography with 50% ethyl acetate/petroleum ether, yielding 60% (22.2 mg) as a light yellow solid: mp = 171−172 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 5.70 (s, 1H), 4.33 (s, 2H), 3.74 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 160.5, 145.3, 140.9, 135.3, 132.9, 129.8, 129.7, 128.0, 123.1, 118.3, 111.8, 53.4, 36.5, 21.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{18}N_2O_4SNa$ 393.0879; found 393.0874. IR (KBr): 2923, 2228, 1723, 1355, 1163, 661, 554 cm^{-1}.

4-(4-(Ethylthio)benzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2h)***. Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 62% (23.9 mg) as a white solid: mp = 169−170 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.2 Hz, 2H), 7.21 (dd, J = 13.2, 5.1 Hz, 4H), 6.98 (d, J = 8.1 Hz, 2H), 5.64 (s, 1H), 4.24 (s, 2H), 3.56 (s, 2H), 2.87 (q, J = 7.3 Hz, 2H), 2.35 (s, 3H), 1.25 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 161.5, 144.0, 135.2, 134.4, 131.9, 128.7, 128.4, 128.2, 126.9, 121.2, 52.3, 35.1, 26.5, 20.6, 13.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{21}NO_3S_2Na$ 410.0855; found 410.0857. IR (KBr): 2963, 1717, 1154, 1091, 1024, 753, 656 cm^{-1}.

4-([1,1′-Biphenyl]-4-ylmethyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2i)***. Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 63% (25.3 mg) as a white solid: mp = 193−194 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.3 Hz, 2H), 7.64−7.56 (m, 4H), 7.47 (t, J = 7.5 Hz, 2H), 7.41−7.32 (m, 3H), 7.23 (d, J = 8.2 Hz, 2H), 5.84−5.75 (m, 1H), 4.38 (s, 2H), 3.74 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 162.6, 145.0, 140.5, 140.4, 135.5, 134.5, 129.7, 129.2, 128.8, 128.0,127.8, 127.5, 127.0, 122.2, 53.5, 36.3, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{21}NO_3SNa$ 426.1134; found 426.1137. IR (KBr): 2920, 1718, 1354, 1160, 753, 661, 555 cm^{-1}.

4-(3-Methylbenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2j)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 69% (23.5 mg) as a white solid: mp = 130−131 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.22 (t, J = 7.5 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.93 (d, J = 7.7 Hz, 2H), 5.73 (s, 1H), 4.31 (s, 2H), 3.63 (s, 2H), 2.42 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 162.9, 145.0, 138.8, 135.5, 135.5, 129.7, 129.5, 128.9, 128.2, 127.9, 125.8, 122.0, 53.5, 36.6, 21.6, 21.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{19}NO_3SNa$ 364.0978; found 364.0985. IR (KBr): 2922, 1722, 1355, 1162, 1026, 660, 556 cm^{-1}.

4-(3-Methoxybenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2k)***. Purified via flash column chromatography with 44% ethyl acetate/petroleum ether, yielding 48% (17.1 mg) as a light yellow solid: mp = 159−160 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 6.6 Hz, 1H), 6.82 (dd, J = 8.1, 2.3 Hz, 1H), 6.71 (d, J = 7.5 Hz, 1H), 6.66 (d, J = 1.8 Hz, 1H), 5.81−5.70 (m, 1H), 4.31 (s, 2H), 3.79 (s, 3H), 3.64 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 162.6, 160.1, 145.0, 137.0, 135.5, 130.1, 129.7, 127.9, 122.1, 121.0, 114.7, 112.6, 55.2, 53.4, 36.7, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{19}NO_4SNa$ 380.0927; found 380.0930. IR (KBr):2929, 1724, 1356, 1162, 1032, 662, 564 cm^{-1}.

4-(3-Chlorobenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2l)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 76% (27.4 mg) as a yellow solid: mp = 122−123 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 4.8 Hz, 2H), 7.05 (s, 1H), 6.96 (d, J = 3.5 Hz, 1H), 5.62 (s, 1H), 4.24 (s, 2H), 3.57 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 161.8, 145.1, 137.5, 135.4, 134.8, 130.3, 129.8, 129.0, 127.9, 127.7, 127.1, 122.5, 53.4, 36.1, 21.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{16}ClNO_3SNa$ 384.0432; found, 384.0434. IR (KBr): 2929, 1723, 1355, 1162, 661, 557 cm^{-1}.

4-(3-Acetylbenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2m)***. Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 52% (19.1 mg) as a light yellow solid: mp = 152−153 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 7.7 Hz, 1H), 7.75 (s, 1H), 7.46 (t, J = 7.7 Hz, 1H), 7.34 (t, J = 9.4 Hz, 3H), 5.70 (s, 1H), 4.32 (s, 2H), 3.74 (s, 2H), 2.60 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 168.1, 161.8, 145.1, 137.8, 136.2, 135.4, 133.4, 129.8, 129.4, 128.4, 128.0, 127.7, 122.6, 53.4, 36.4, 26.7, 21.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{19}NO_4SNa$ 392.0927; found 392.0928. IR (KBr): 2920, 1720, 1353, 1161, 662, 554 cm^{-1}.

4-(2-Methylbenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2n)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 79% (26.9 mg) as a light yellow solid: mp = 91−92 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.20−7.14 (m, 3H), 7.06 (d, J = 6.9 Hz, 1H), 5.59 (s, 1H), 4.32 (s, 2H), 3.66 (s, 2H), 2.42 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 162.5, 145.0, 136.2, 135.5, 133.9, 130.8, 129.7, 129.6, 127.9, 127.8, 126.6, 122.1, 53.6, 34.4, 21.6, 19.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{19}NO_3SNa$ 364.0978; found, 364.0980. IR (KBr): 2927, 1725, 1358, 1027, 750, 661, 556 cm^{-1}.

4-(2-Fluorobenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one ***(2o)***. Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 88% (30.3 mg) as a light yellow solid: mp = 142−143 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 3.8 Hz, 1H), 7.02 (dd, J = 15.9, 8.5 Hz, 3H), 5.61 (s, 1H), 4.28 (s, 2H), 3.62 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 161.5, 160.7 (d, J = 45 Hz), 145.1, 135.4, 130.9 (d, J = 3.9 Hz), 129.7, 129.6 (d, J = 8.0 Hz), 127.9, 124.7

DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198

(d, J = 3.7 Hz), 122.8 (d, J = 15.9 Hz), 122.2, 115.8 (d, J = 21 Hz), 53.4, 29.8 (d, J = 3.3 Hz), 21.6. HRMS-ESI (m/z): calcd for $C_{18}H_{16}FNO_3SNa$ 368.0727; found, 368.0731. IR (KBr): 3637, 1725, 1356, 1164, 759, 662, 555 cm^{-1}.

4-(2-Chlorobenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**2p**). Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 83% (29.9 mg) as a light yellow solid: mp = 113−114 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.3 Hz, 2H), 7.41−7.37 (m, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.27−7.23 (m, 2H), 7.19 (dd, J = 5.9, 3.5 Hz, 1H), 5.69−5.61 (m, 1H), 4.36 (s, 2H), 3.80 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 161.3, 145.0, 135.5, 134.1, 133.7, 130.9, 130.0, 129.7, 129.2, 127.9, 127.4, 122.5, 53.5, 34.3, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{16}ClNO_3SNa$ 384.0432; found 384.0433. IR (KBr): 2922, 1722, 1353, 1162, 752, 660, 553 cm^{-1}.

4-(2-Nitrobenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**2q**). Purified via flash column chromatography with 45% ethyl acetate/petroleum ether, yielding 61% (22.6 mg) as a brown solid: mp = 122−123 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.6 Hz, 1H), 8.04 (s, 1H), 7.92 (d, J = 8.2 Hz, 2H), 7.59−7.49 (m, 2H), 7.32 (d, J = 8.2 Hz, 2H), 5.69 (s, 1H), 4.37 (s, 2H), 3.81 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 160.9, 148.6, 145.2, 137.6, 135.3, 135.0, 130.2, 129.8, 127.9, 123.8, 123.0, 122.7, 53.4, 36.0, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{16}N_2O_5SNa$ 395.0672; found 395.0678. IR (KBr): 2924, 1724, 1529, 1351, 1164, 663, 557 cm^{-1}.

4-(3-Chloro-4-methylbenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**2r**). Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 54% (20.2 mg) as a white solid: mp = 181−182 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.19 (d, J = 7.7 Hz, 1H), 7.12 (s, 1H), 6.93 (d, J = 7.7 Hz, 1H), 5.72 (s, 1H), 4.31 (s, 2H), 3.61 (s, 2H), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 162.0, 145.0, 135.5, 135.3, 134.8, 134.6, 131.5, 129.7, 129.3, 127.9, 127.0, 122.4, 53.3, 35.8, 21.6, 19.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{18}ClNO_3SNa$ 398.0588; found 398.0589. IR (KBr): 2924, 1721, 1396, 1158, 756, 659, 558 cm^{-1}.

4-(3,4-Dimethylbenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**2s**). Purified via flash column chromatography with 35% ethyl acetate/petroleum ether, yielding 59% (20.9 mg) as a white solid: mp = 187−189 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 7.9 Hz, 2H), 7.10 (d, J = 7.5 Hz, 1H), 6.91 (s, 1H), 6.88 (d, J = 7.6 Hz, 1H), 5.75 (s, 1H), 4.32 (s, 2H), 3.63 (s, 2H), 2.45 (s, 3H), 2.26 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 163.2, 145.0, 137.4, 135.8, 135.5, 132.9, 130.2, 130.0, 129.7, 127.9, 126.1, 121.9, 53.4, 36.3, 21.7, 19.7, 19.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{21}NO_3SNa$ 378.1134; found 378.1132. IR (KBr): 2925, 1743, 1548, 1369, 1230, 1053, 749, 697 cm^{-1}.

4-(4-Methoxy-3-methylbenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**2t**). Purified via flash column chromatography with 40% ethyl acetate/petroleum ether, yielding 34% (12.6 mg) as a white solid: mp = 149−151 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 7.9 Hz, 2H), 6.94 (d, J = 8.3 Hz, 1H), 6.90 (s, 1H), 6.78 (d, J = 8.2 Hz, 1H), 5.74 (s, 1H), 4.32 (s, 2H), 3.84 (s, 3H), 3.60 (s, 2H), 2.45 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 163.5, 157.1, 145.0, 135.5, 131.0, 129.7, 127.9, 127.4, 127.1, 127.0, 121.7, 110.3, 55.4, 53.4, 35.9, 21.6, 16.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{21}NO_4SNa$ 394.1083; found 394.1085. IR (KBr): 2919, 2851, 1728, 1644, 1261, 1164, 753, 660 cm^{-1}.

4-(5-Fluoro-2-methoxybenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**2u**). Purified via flash column chromatography with 45% ethyl acetate/petroleum ether, yielding 74% (27.7 mg) as a yellow solid: mp = 120−121 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 6.95 (td, J = 8.5, 3.0 Hz, 1H), 6.84−6.78 (m, 2H), 5.66 (m, 1H), 4.33 (s, 2H), 3.78 (s, 3H), 3.64 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 162.3, 157.9, 155.6, 153.3 (d, J = 2 Hz), 145.0, 135.5, 129.7, 127.9, 125.6 (d, J = 7.3 Hz), 121.8, 117.2 (d, J = 23 Hz), 114.7 (d, J = 23 Hz), 111.5 (d, J = 8.3 Hz), 55.9, 53.5, 31.0, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{18}FNO_4SNa$ 398.0833; found 398.0837. IR (KBr): 2935, 1724, 1498, 1356, 1028, 662, 559 cm^{-1}.

4-(3,5-Dichlorobenzyl)-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**2v**). Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 68% (26.8 mg) as a white solid: mp = 134−135 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.2 Hz, 2H), 7.37−7.30 (m, 3H), 7.04 (s, 2H), 5.74 (s, 1H), 4.32 (s, 2H), 3.63 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 160.6, 145.2, 138.7, 135.6, 135.3, 129.8, 128.0, 127.9, 127.4, 123.0, 53.3, 35.8, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{15}Cl_2NO_3SNa$ 418.0042; found 418.0042. IR (KBr): 2925, 1723, 1388, 1160, 755, 662, 561 cm^{-1}.

4-Methyl-1-tosyl-1,5-dihydro-2H-pyrrol-2-one (**4a**).[18] Purified via flash column chromatography with 25% ethyl acetate/petroleum ether, yielding 52% (13.0 mg) as a white solid: mp = 159−160 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 5.77 (s, 1H), 4.35 (s, 2H), 2.44 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 159.7, 145.0, 135.6, 129.7, 127.9, 122.1, 54.8, 21.6, 15.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{13}NO_3SNa$ 274.0508; found 274.0509. IR (KBr): 2923, 1714, 1351, 1163, 661, 556 cm^{-1}.

4-Methyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (**4b**).[19] Purified via flash column chromatography with 25% ethyl acetate/petroleum ether, yielding 68% (18.0 mg) as a white solid: mp = 110−111 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 5.63 (d, J = 1.1 Hz, 1H), 4.03 (t, J = 6.5 Hz, 2H), 2.48−2.41 (m, 5H), 1.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 156.9, 144.6, 136.0, 129.3, 128.4, 120.5, 43.8, 30.3, 22.9, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{15}NO_3SNa$ 288.0665; found 288.0666. IR (KBr): 2924, 1685, 1354, 1168, 952, 753, 661, 555 cm^{-1}.

4-(Prop-1-en-1-yl)-1-tosylpyrrolidin-2-one (**4c**). Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 69% (19.2 mg) as a colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 5.67−5.48 (m, 1H), 5.39−5.20 (m, 1H), 4.17−3.98 (m, 1H), 3.59−3.44 (m, 1H), 3.41−3.26 (m, 0.2 H), 3.05−2.90 (m, 0.8 H), 2.65−2.50 (m, 1H), 2.45 (s, 3H), 2.30−2.18 (m, 1H), 1.66 (d, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 145.1, 135.2, 129.7, 129.2, 128.9, 128.2, 128.1, 128.0, 128.0, 127.9, 52.3, 39.1, 38.7, 35.1, 30.0, 21.6, 17.7, 13.1. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{17}NO_3SNa$ 302.0821; found 302.0828. IR (KBr): 2923, 1740, 1357, 1171, 956, 662, 553 cm^{-1}.

4-(Prop-1-en-2-yl)-1-tosylpyrrolidin-2-one (**4d**). Purified via flash column chromatography with 30% ethyl acetate/petroleum ether, yielding 53% (14.7 mg) as a white solid: mp = 95−97 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 4.85 (s, 1H), 4.75 (s, 1H), 4.11 (dd, J = 9.8, 7.8 Hz, 1H), 3.63 (dd, J = 9.8, 7.9 Hz, 1H), 2.99 (p, J = 8.2 Hz, 1H), 2.58 (dd, J = 17.2, 8.2 Hz, 1H), 2.45 (s, 3H), 2.40 (dd, J = 17.2, 9.3 Hz, 1H), 1.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 145.2, 142.7, 135.2, 129.7, 128.1, 112.0, 51.0, 38.4, 37.1, 21.7, 20.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{17}NO_3SNa$ 302.0821; found 302.0830. IR (KBr): 2920, 1732, 1160, 1118, 750, 656, 547 cm^{-1}.

N-Cinnamyl-N-tosylacetamide (**5**). Purified via flash column chromatography with 20% ethyl acetate/petroleum ether, yielding 70% (23.0 mg) as a white solid: mp = 118−120 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.1 Hz, 2H), 7.40−7.18 (m, 7H), 6.59 (d, J = 15.9 Hz, 1H), 6.21 (dt, J = 15.8, 6.3 Hz, 1H), 4.61 (d, J = 6.3 Hz, 2H), 2.41 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 145.0, 136.7, 136.2, 134.0, 129.8, 128.6, 128.0, 127.9, 126.6, 123.7, 48.4, 24.9, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{19}NO_3SNa$ 352.0978; found 352.0981. IR (KBr): 2923, 1700, 1348, 1160, 727, 576 cm^{-1}.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00804.

Spectra of all new compounds (PDF)

DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198

X-ray crystallographic data for **2a** (CIF)
X-ray crystallographic data for **4a** (CIF)

AUTHOR INFORMATION

Corresponding Authors

*Fax: (+86) 20-87112906; E-mail: cezqma@scut.edu.cn
*Fax: (+86) 20-87112906; E-mail: jianghf@scut.edu.cn

ORCID

Huanfeng Jiang: 0000-0002-4355-0294

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors are grateful to the National Key Research and Development Program of China (2016YFA0602900), the National Natural Science Foundation of China (21420102003), and the Fundamental Research Funds for the Central Universities (2015ZY001) for financial support.

REFERENCES

(1) For selected reviews: (a) McDonald, R.; Liu, G.; Stahl, S. S. *Chem. Rev.* **2011**, *111*, 2981−3019. (b) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147−1169. (c) Wolfe, J. P. *Synlett* **2008**, *2008*, 2913−2937.

(2) (a) Li, W.; Liu, C.; Zhang, H.; Ye, K.; Zhang, G.; Zhang, W.; Duan, Z.; You, S.; Lei, A. *Angew. Chem., Int. Ed.* **2014**, *53*, 2443−2446. (b) Sharma, U.; Kancherla, R.; Naveen, T.; Agasti, S.; Maiti, D. *Angew. Chem., Int. Ed.* **2014**, *53*, 11895−11899. (c) Zhu, C.; Yang, B.; Bäckvall, J. *J. Am. Chem. Soc.* **2015**, *137*, 11868−11871. and references cited therein. (d) Agasti, S.; Sharma, U.; Naveen, T.; Maiti, D. *Chem. Commun.* **2015**, *51*, 5375−5378.

(3) (a) Ackermann, L.; Pospech, J. *Org. Lett.* **2011**, *13*, 4153−4155. (b) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2007**, *9*, 1407−1409. (c) Liang, H.; Ding, W.; Jiang, K.; Shuai, L.; Yuan, Y.; Wei, Y.; Chen, Y. *Org. Lett.* **2015**, *17*, 2764−2767. (d) Huang, L.; Jiang, H.; Qi, C.; Liu, X. *J. Am. Chem. Soc.* **2010**, *132*, 17652−17654. (e) Wu, L.; Zhang, Z.; Liao, J.; Li, J.; Wu, W.; Jiang, H. *Chem. Commun.* **2016**, *52*, 2628−2361.

(4) (a) Huang, L.; Wang, Q.; Liu, X.; Jiang, H. *Angew. Chem., Int. Ed.* **2012**, *51*, 5696−5700. (b) Ji, F.; Li, X.; Guo, W.; Wu, W.; Jiang, H. *J. Org. Chem.* **2015**, *80*, 5713−5718.

(5) (a) Alessandra, O. Glaxo Wellcome S.P.A., Patent WO2001042238A1, 2001. (b) Giuseppe, A.; Romano, D. F.; Riccardo, G.; Alfredo, P.; Maria, T.; Lucia, M. Glaxo Group Limited Patent WO2005049600A1, 2005.

(6) (a) Xie, Y.; Zhao, Y.; Qian, B.; Yang, L.; Xia, C.; Huang, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 5682−5686. (b) Shao, C.; Yu, H.; Wu, N.; Tian, P.; Wang, R.; Feng, C.; Lin, G.-Q. *Org. Lett.* **2011**, *13*, 788−791.

(7) Ran, R.; He, J.; Xiu, S.; Wang, K.; Li, C. *Org. Lett.* **2014**, *16*, 3704−3707.

(8) (a) Link, J. T.; Raghavan, S.; Gallant, M.; Danishefsky, S. J.; Chou, T. C.; Ballas, L. M. *J. Am. Chem. Soc.* **1996**, *118*, 2825−2842. (b) Pace, P.; Spieser, S. A. H.; Summa, V. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3865−3869. (c) Pal, M.; Swamy, N. K.; Hameed, P. S.; Padakanti, S.; Yeleswarapu, K. R. *Tetrahedron* **2004**, *60*, 3987−3997. (d) Grison, C.; Genève, S.; Coutrot, P. *Tetrahedron Lett.* **2001**, *42*, 3831−3834. (e) van Loon, A. A.; Holton, M. K.; Downey, C. R.; White, T. M.; Rolph, C. E.; Bruening, S. R.; Li, G.; Delaney, K. M.; Pelkey, S. J.; Pelkey, E. *J. Org. Chem.* **2014**, *79*, 8049−8058.

(9) (a) Chen, Q.; Huggins, M. T.; Lightner, D. A.; Norona, W.; McDonagh, A. F. *J. Am. Chem. Soc.* **1999**, *121*, 9253−9264. (b) Coffin, A. R.; Roussell, M. A.; Tserlin, E.; Pelkey, E. T. *J. Org. Chem.* **2006**, *71*, 6678−6681. (c) Greger, J. G.; Yoon-Miller, S. J. P.; Bechtold, N. R.; Flewelling, S. A.; MacDonald, J. P.; Downey, C. R.; Cohen, E. A.; Pelkey, E. T. *J. Org. Chem.* **2011**, *76*, 8203−8214. (d) Toyofuku, M.; Murase, E.; Nagai, H.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *Eur. J. Org. Chem.* **2009**, *2009*, 3141−3144. (e) Kang, S.-K.; Kim, K.-J.; Yu, C.-M.; Hwang, J.-W.; Do, Y.-K. *Org. Lett.* **2001**, *3*, 2851−2853. (f) Trost, B. M.; Roth, G. J. *Org. Lett.* **1999**, *1*, 67−70.

(10) (a) Wang, D.; Izawa, Y.; Stahl, S. S. *J. Am. Chem. Soc.* **2014**, *136*, 9914−9917. (b) Hatano, M.; Nishimura, T.; Yorimitsu, H. *Org. Lett.* **2016**, *18*, 3674−3677.

(11) Use of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) or 2-ditert-butyl4-methylphenol (BHT) as a radical quenching agent made a tiny impaction this reaction.

(12) (a) Ney, J. E.; Wolfe, J. P. *Angew. Chem., Int. Ed.* **2004**, *43*, 3605−3608. (b) Zheng, J.; Huang, L.; Li, Z.; Wu, W.; Li, J.; Jiang, H. *Chem. Commun.* **2015**, *51*, 5894−5897.

(13) Splitter, J. S.; Calvin, M. *J. Am. Chem. Soc.* **1979**, *101*, 7329−7332.

(14) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 6328−6335.

(15) Patil, N. T.; Yamamoto, Y. *Top. Organomet. Chem.* **2006**, *19*, 91−113.

(16) (a) Laha, J. K.; Jethava, K. P.; Dayal, N. *J. Org. Chem.* **2014**, *79*, 8010−8019. (b) Zhao, B. *Org. Biomol. Chem.* **2012**, *10*, 7108−7119.

(17) Byproduct **5** was not afforded without $Pd(OAc)_2$, which suggested that a simple *N*-acylation with Ac_2O was impossible.

(18) Ozaki, S.; Matsushita, H.; Ohmori, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2339−2344.

(19) Chou, S. P.; Hung, C. *Synthesis* **2001**, *2001*, 2450−2462.

(20) Xu, H.-D.; Wu, H.; Jiang, C.; Chen, P.; Shen, M.-H. *Tetrahedron Lett.* **2016**, *57*, 2915−2918.

(21) (a) Ghorai, M. K.; Kumar, A.; Das, K. *Org. Lett.* **2007**, *9*, 5441−5444. (b) Chen, C.; Jin, S.; Zhang, Z.; Wei, B.; Wang, H.; Zhang, K.; Lv, H.; Dong, X.-Q.; Zhang, X. *J. Am. Chem. Soc.* **2016**, *138*, 9017−9020.

(22) (a) Scarborough, C. C.; Stahl, S. S. *Org. Lett.* **2006**, *8*, 3251−3254. (b) Tsui, G. C.; Menard, F.; Lautens, M. *Org. Lett.* **2010**, *12*, 2456−2459. (c) Pyne, S. G.; Dong, Z. *J. Org. Chem.* **1996**, *61*, 5517−5522.

DOI: 10.1021/acs.joc.7b00804
J. Org. Chem. 2017, 82, 8191−8198