JOC The Journal of Organic Chemistry

Article

Cite This: J. Org. Chem. 2017, 82, 11543-11557

pubs.acs.org/joc

Synthesis of Spirolactams and Fused Bicyclic Lactams via Acid-Promoted Cyclolactamization of (Ethynyl(tosyl)amino)methyl-Tethered Cyclohex-2-enols

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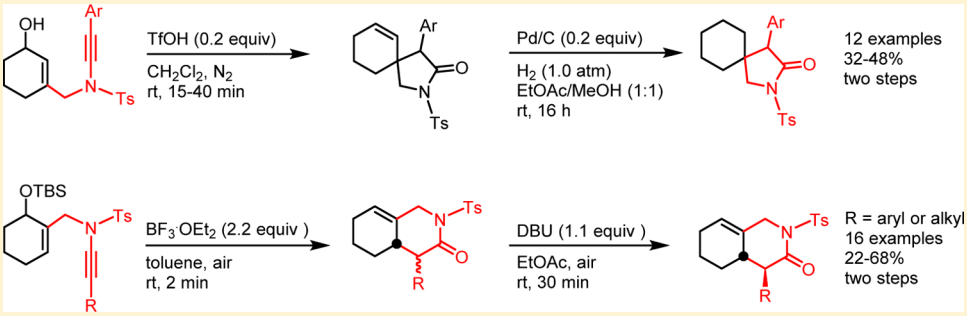
Supporting Information



ABSTRACT: A simple synthetic method to construct the spirolactam framework from TfOH-catalyzed spirolactamization of cyclohex-2-enols bearing a tethered (arylethynyl(tosyl)amino)methyl moiety is described. The reaction proceeded through a keteniminium–allylic carbocation intermediate. Hydration of the keteniminium ion, followed by attack of the resulting enolate onto the tethered allylic carbocation, provided the spirolactam ring skeleton. This strategy could also be employed in the synthesis of fused bicyclic lactams from BF_3·OEt_2-assisted cyclolactamization of TBS-protected 2-(ethynyl(tosyl)amino)-methylcyclohex-2-enols.

INTRODUCTION

Azaspirocyclic frameworks are present in a wide range of bioactive natural products and pharmaceutically important compounds.[1] Many methods have been developed to enable the synthesis of spirolactam ring systems. These include the dearomatizing spirocyclization of *N*-benzylglyoxamide-derived thionium ions,[2] the oxidative radical cyclization of xanthate-tethered *p*-oxygenated *N*-benzylacetamides,[3] the intramolecular spirocyclization of arene ruthenium complexes bearing *β*-amido phosphonate side chains,[4] the samarium(II) iodide-mediated cyclization of unsaturated keto-lactams,[5] the *N*-iodosuccimide-promoted intramolecular electrophilic *ipso*-iodocyclization of *N*-arylpropiolamides,[6] the platinum(II)-catalyzed cyclization of six-membered-ring enamides,[7] the $TiCl_4$-mediated tandem Prins and Friedel–Crafts reaction of 1,1-diarylethylenes with isatin derivatives,[8] the intramolecular *ipso*-halocyclization of *N*-(4-methoxyphenyl)-*N*-(3-aryl-2-propyn-1-yl)triflamide,[9] and the copper(I)- or ruthenium(II)-mediated radical cyclization of unsaturated cyclic haloamides.[10] Considering the versatile and highly reactive potential of ynamides for their facile construction of structurally diverse heterocycles[11] and in continuation of our ongoing interest to develop novel synthetic routes to fused and bridged bicyclic lactams (Scheme 1, eqs 1–3),[12,13] here we describe an efficient method for preparation of spirolactams from TfOH-catalyzed spirolactamization of 3-(arylethynyl(tosyl)amino)methylcyclohex-2-enols (Scheme 1, eq 4). Moreover, this strategy can also be exploited in the synthesis of hexahydroisoquinolin-3(2*H*)-one derivatives from cyclolactamization of TBS-protected 2-(ethynyl(tosyl)amino)-methylcyclohex-2-enols with 2.2 equiv of BF_3·OEt_2 in minutes under air (Scheme 1, eq 5).

RESULTS AND DISCUSSION

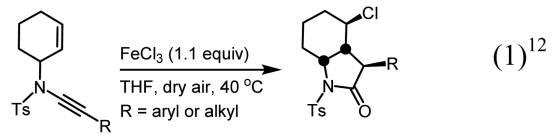
The parent substrate 3-(phenylethynyl(tosyl)amino)-methylcyclohex-2-enol (**1a**) was prepared from substitution of the iodide of 3-(iodomethyl)cyclohex-2-enone[14] with NHTsBoc, followed by a selective removal of the Boc group with trifluoroacetic acid, affording 3-(tosylamino)-methylcyclohex-2-enone.[15] Reduction of the keto group with $NaBH_4$ produced 3-(tosylamino)methylcyclohex-2-enol, which was then coupled with (bromoethynyl)benzene in the presence of $CuSO_4$·$5H_2O$ (0.1 equiv), 1,10-phenanthroline (0.2 equiv), and K_2CO_3 (2.0 equiv) to furnish the parent compound **1a** in 63% overall yield (see the Experimental Section for details).[16] Initially, subjection of **1a** to a catalytic amount of $FeCl_3$ (Table 1, entry 1) or the Ph_3PAuCl/AgOTf cocatalyst system in DCM (Table 1, entry 2) at rt failed to provide any cyclized product. Pleasingly, the use of 0.1 molar equiv of BF_3·OEt_2 in DCM (0.1

Received: August 26, 2017
Published: October 9, 2017

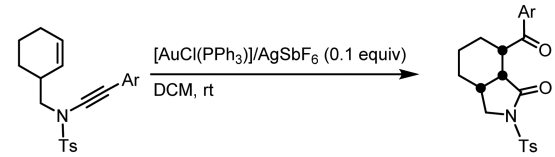
DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543–11557

Scheme 1. Acid-Promoted Cyclolactamization Reactions of Ynamide-Tethered Cyclohexenes and Cyclohex-2-enols

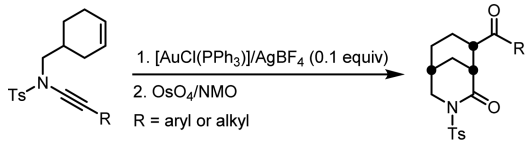
Previous work:



(1)[12]



(2)[13]



(3)[13]

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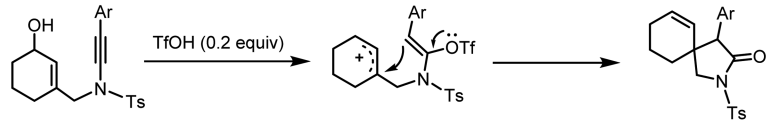
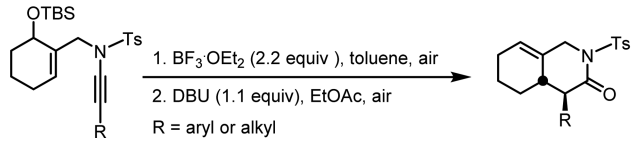


(4)



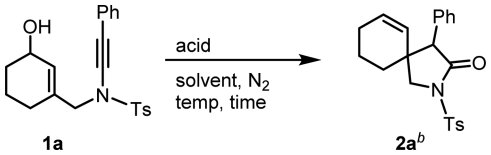
(5)

M concentration) at rt under nitrogen for 40 min gave the unsaturated spirolactam **2a** as a 1:1 ratio of diastereomers in a combined yield of 21% (Table 1, entry 3). Attempts to epimerize the α-carbon stereocenter using bases such as LDA, DBU, KOH, and *t*-BuOK or separate the diastereomeric mixture by column chromatography over silica gel were unsuccessful. Delightfully, the saturated spirolactam **3a** was formed in 82% yield upon treatment of the diastereomeric mixture of **2a** with Pd/C (0.2 equiv) in EtOAc/MeOH under 1 atm of H_2 for 16 h (Table 2). Subsequently, spirolactamization of **1a** with 0.1 equiv of other Brønsted and Lewis acids such as TfOH, Tf_2NH, TMSOTf, $InCl_3$, $InBr_3$, $In(OTf)_3$, and $In(NTf_2)_3$ in DCM (0.1 M concentration) was successful, albeit generating **2a** in low to moderate yields (31−51%, Table 1, entries 4−10). Inspiringly, when the loading of TfOH increased to 0.2 equiv in DCM at 0.1 M concentration, the reaction finished in 1 h and **1a** delivered **2a** in 45% isolated yield (Table 1, entry 11). When the concentration of **1a** in DCM was raised to 0.3 M with 0.2 equiv of TfOH, the spirolactamization was complete within 15 min, producing a 66% yield of **2a** (Table 1, entry 12). Encouraged by the result, we next screened the effects of reaction temperature and solvent using 0.2 equiv of TfOH in DCM at 0.3 M concentration. Running the reaction at 0 °C required a longer reaction time (6 h) and generated the desired spirolactam **2a** in 37% yield (Table 1, entry 13). At an elevated temperature (50 °C), **1a** produced **2a** within 5 min and in 49% yield (Table 1, entry 14). Finally, the influence of different solvents was examined. The use of DCE, toluene, and ether led to **2a** in lower yields (9−43%) and required longer reaction times (40 min−12 h) (Table 1, entries 15−17). Therefore, conducting the spirolactamization of **1a** with 0.2 equiv of TfOH in DCM at 0.3 M concentration at rt under nitrogen was found to be the optimal reaction conditions for the formation of the unsaturated spirolactam **2a** (Table 1, entry 12).

Next, various 3-(arylethynyl(tosyl)amino)methylcyclohex-2-enols were employed with the optimized reaction conditions, and the results of spirolactamization of **1** followed by hydrogenation reaction of the crude mixture are listed in Table 2. The two-step sequence was equally viable with substrates bearing neutral (Me, Ph, **1a−e**, entries 1−5), electron-donating (OMe, **1f,g**, entries 6 and 7), and electron-withdrawing (CO_2Me, **1h,i**, entries 8 and 9) substituents around the phenyl ring, affording the corresponding spirolactams **3a−i** in reasonable yields from 32 to 48% over the two steps (Table 2, entries 1−9). Interestingly,

DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557

Table 1. Optimization of the Spirolactamization Reaction Conditions[a]



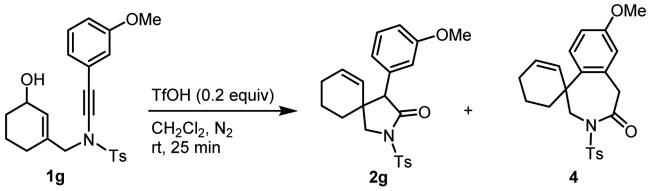
1a 2a[b]

entry	acid (equiv)	solvent	conc (M)	temp (°C)	time	yield (%)
1	$FeCl_3$ (0.1)	DCM	0.1	28	24 h	
2	Au(I)/Ag(I) (0.1)	DCM	0.1	28	24 h	
3	$BF_3{\cdot}OEt_2$ (0.1)	DCM	0.1	28	40 min	21[c]
4	TfOH (0.1)	DCM	0.1	28	12 h	39[c]
5	Tf_2NH (0.1)	DCM	0.1	28	70 min	40[c]
6	TMSOTf (0.1)	DCM	0.1	28	3 h	51[c]
7	$InCl_3$ (0.1)	DCM	0.1	28	35 min	28[c]
8	$InBr_3$ (0.1)	DCM	0.1	28	1 h	32[d]
9	$In(OTf)_3$ (0.1)	DCM	0.1	28	1 h	31[d]
10	$In(NTf_2)_3$ (0.1)	DCM	0.1	28	20 min	32[d]
11	TfOH (0.2)	DCM	0.1	28	1 h	45[c]
12	TfOH (0.2)	DCM	0.3	28	15 min	66[d]
13	TfOH (0.2)	DCM	0.3	0	6 h	37[d]
14	TfOH (0.2)	DCM	0.3	50	5 min	49[d]
15	TfOH (0.2)	DCE	0.3	28	40 min	43[c]
16	TfOH (0.2)	toluene	0.3	28	70 min	34[d]
17	TfOH (0.2)	ether	0.3	28	12 h	9[d]

[a]All reactions were conducted on a 0.3 mmol scale with 0.1 or 0.2 equiv of acid in DCM (3.0 mL), unless otherwise indicated. [b]A 1:1 ratio of diastereomers was obtained. [c]Isolated yields obtained from column chromatography over silica gel. [d]NMR yields.

spirolactamization of **1g**, with a methoxy group at the *m*-position of the phenyl ring, gave a 40% yield of the targeted spirolactam **2g** together with a side product, which was identified as the 8-azaspiro[5.6]dodecen-9-one derivative **4** (Scheme 2), in 23% isolated yield. Spirolactam **2g** was further

Scheme 2. Formation of Spirolactams 2g and 4 from 1g

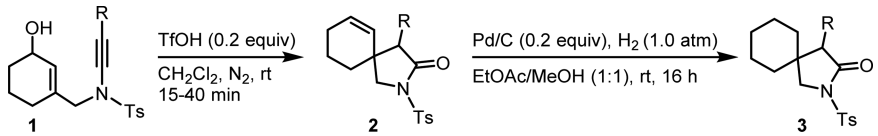


1g 2g 40% 4 23%

hydrogenated with Pd/C (0.2 equiv) in MeOH/EtOAc (1:1) under 1 atm of H_2 to afford the saturated spirolactam **3g** in 32% yield over the two steps (Table 2, entry 7). Moreover, incorporation of halogen atoms on the phenyl ring in **1j** and **1k** did not interfere with the transformation, and the spirolactamization led to the corresponding spirolactams **3j** and **3k** in 33 and 36%, respectively, over the two steps (Table 2, entries 10 and 11). Furthermore, the spirolactamization reaction of substrate **1l**, containing a *m*-trifluoromethyl group which is a popular fluorine-containing functional group in drug molecules, also proceeded smoothly to generate spirolactam **3l** in 38% over the two steps (Table 2, entry 12). Among the unsaturated spirolactams obtained, structures of **3c** and **4** were confirmed by X-ray crystallography.[17] ORTEP plots of spirolactams **3c** (Figure S1), **3j** (Figure S2), **3k** (Figure S3), and **4** (Figure S4) are provided in the Supporting Information. However, attempts to induce spirolactamization reaction of the thienyl- or *n*-hexyl-substituted substrates, **1m** and **1n**, failed. Both starting substrates decomposed after treatment with TfOH (Table 2, entries 13 and 14).

Scheme 3 illustrates a possible reaction pathway for the TfOH-catalyzed spirolactamization of **1** to **2**. The reaction was initiated from electrophilic activation of **1** with TfOH to provide the keteniminium intermediate **5**. Trapping of the

Table 2. TfOH-Catalyzed Spirolactamization of 1 Followed by Hydrogenation[a]



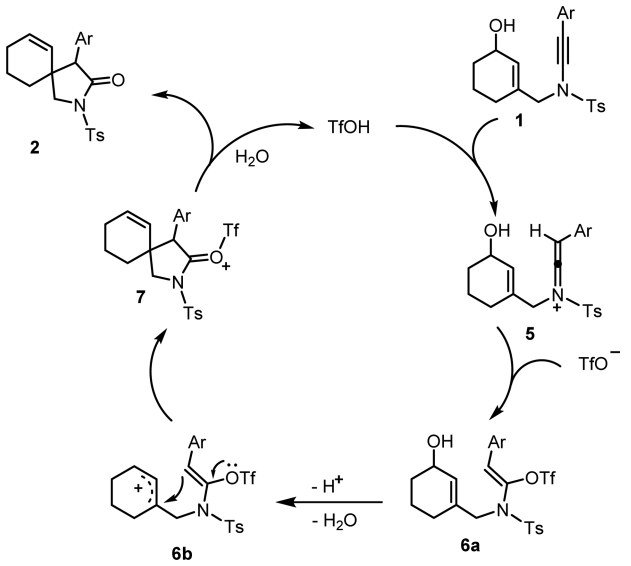
1 2 3

entry	R	substrate	product[b] (%)
1	phenyl	**1a**	**3a** (45%)
2	4-methylphenyl	**1b**	**3b** (40%)
3	2-methylphenyl	**1c**	**3c**[c] (37%)
4	3,4-dimethylphenyl	**1d**	**3d** (43%)
5	4-phenylphenyl	**1e**	**3e** (48%)
6	4-methoxyphenyl	**1f**	**3f** (40%)
7	3-methoxyphenyl	**1g**	**3g**[d] (32%)
8	4-(methoxycarbonyl)phenyl	**1h**	**3h** (41%)
9	3-(methoxycarbonyl)phenyl	**1i**	**3i** (37%)
10	4-fluorophenyl	**1j**	**3j**[c] (33%)
11	4-chlorophenyl	**1k**	**3k**[c] (36%)
12	3-trifluoromethylphenyl	**1l**	**3l** (38%)
13	2-thienyl	**1m**	
14	*n*-hexyl	**1n**	

[a]All reactions were conducted on a 0.4 mmol scale with 0.2 equiv of TfOH in 1.3 mL of DCM at rt. Hydrogenation was performed with 0.2 equiv of Pd/C under 1 atm of H_2 in EtOAc/MeOH. [b]Isolated yield obtained over the two steps. [c]The structure has been confirmed by X-ray crystallography. [d]A side product, 8-azaspiro[5.6]dodecen-9-one derivative **4**, was isolated in 23% yield.

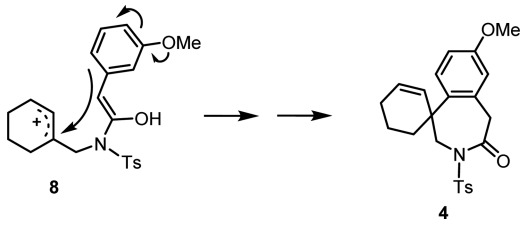
DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557

Scheme 3. Proposed Reaction Path for the TfOH-Catalyzed Spirolactamization of 3-(Arylethynyl(tosyl)amino)methylcyclohex-2-enols



keteniminium ion with triflate anion afforded the ketene *N,O*-acetal intermediate **6a**, which led to **6b** after a protonation/dehydration sequence. Attack of the vinyl triflate onto the pendant allylic carbocation followed by hydrolysis furnished the spirolactam skeleton **7**, which released TfOH in the catalytic cycle to generate the unsaturated spirolactam **2**. However, intermediate **8**, with a methoxy substituent at the *m*-position of the phenyl ring, underwent a Freidel–Crafts reaction to deliver the 8-azaspiro[5.6]dodecen-9-one derivative **4** (Scheme 4). It

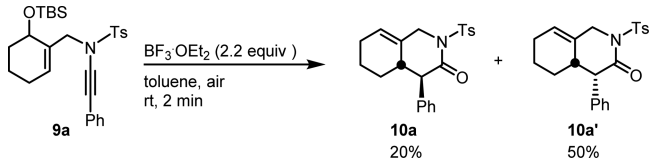
Scheme 4. Formation of Spirolactam 4



must be mentioned that the strategy of electrophilic activation–nucleophilic trapping of ynamides has been explored for the construction of various heterocyclic scaffolds.[18] Moreover, prior to our studies, ynamides were employed in the synthesis of *β*-lactams,[19a] fused bicyclic lactams,[19b,c] and medium-sized lactams.[19d]

This chemistry can be extended to the preparation of hexahydroisoquinolin-3(2*H*)-one derivatives, which are present in many biologically active alkaloids,[20] from cyclolactamization of TBS-protected 2-(ethynyl(tosyl)amino)methylcyclohex-2-enols with $BF_3{\cdot}OEt_2$. It must be noted that the TBS protection of the hydroxyl group is critical for the successful transformation. The unprotected parent substrate, 2-(phenylethynyl(tosyl)amino)methylcyclohex-2-enol, was unstable and slowly decomposed at ambient temperature. The starting substrate **9a** was prepared from Cu(II)-catalyzed coupling of TBS-protected 2-(tosylamino)methylcylohex-2-enol[21] with (bromoethynyl)-benzene following the literature proedure.[16] Following a survey of a series of Lewis and Brønsted acids such as $BF_3{\cdot}OEt_2$, $FeCl_3$, $In(OTf)_3$, $In(NTf_2)_3$, TMSOTf, TsOH, and TfOH and various solvents and temperatures, we were pleased to observed that $BF_3{\cdot}OEt_2$ (2.2 equiv) in toluene exhibited the best activity for the desired cyclolactamization. In a typical experimental procedure, **9a** was treated with 2.2 equiv of $BF_3{\cdot}OEt_2$ in toluene at rt under air for 2 min and a 2:5 ratio of diastereomers **10a** and **10a′** was formed in a combined yield of 70% (Scheme 5). Pleasingly, treatment of the resulting crude

Scheme 5. Reaction of 9a with $BF_3{\cdot}OEt_2$



diastereomeric mixture with 1.1 equiv of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in EtOAc under air at rt for 30 min gave exclusively the *exo*-isomer **10a** (65% yield, over the two steps) with the phenyl substituent at the sterically less hindered convex face. In this process, the thermodynamically unstable *endo*-isomer **10a′** was enolized in the presence of DBU in EtOAc, followed by face-selective protonation during aqueous workup, providing the more stable *exo*-isomer **10a**. The structure and relative stereochemistry of **10a** were confirmed by X-ray diffraction analysis (Figure S5).[17]

The postulated reaction pathway for the transformation of **9a** into **10a** is illustrated in Scheme 6. Activation of the ynamide moiety of **9a** with $BF_3{\cdot}OEt_2$ led to the keteniminium intermediate **11**. Removal of the siloxy group by BF_3 and trapping the keteniminium ion with BF_2O^- formed the intermediate **12**. Attack of the boron enolate onto the pendant allylic carbocation led to the isoquinolinone skeleton **13**. Hydrolysis of **13** upon aqueous workup, followed by epimerization of *endo*-isomer **10a′** with DBU in EtOAc, gave exclusively the thermodynamically more stable *exo*-isomer **10a**.

Several TBS-protected 2-(ethynyl(tosyl)amino)methylcyclohex-2-enols **9** were subjected to $BF_3{\cdot}OEt_2$-assisted cyclolactamization followed by epimerization with DBU, and results are summarized in Table 3. Compounds **9a–f** bearing a neutral aryl group on the ynamide moiety proved effective, as the targeted bicyclic lactams **10a–f** were isolated in good yields (55–68%) over the two-step sequence (Table 3, entries 1–6). Substrates **9g** and **9h** with an electron-withdrawing ester group on the phenyl ring were also efficient, affording the corresponding bicyclic lactams **10g** and **10h** in 63 and 57% yield, respectively (Table 3, entries 7 and 8). Substrates containing a halogen atom on the phenyl ring were tolerated and provided the halogenated bicyclic lactams **10i** (61%) and **10j**[17] (60%) (Table 3, entries 9 and 10). The structure and relative stereochemistry of **10j** was confirmed by X-ray diffraction analysis (Figure S6).[17] Cyclolactamization of **9k**, with a *p*-methoxy group on the phenyl ring, was also observed to provide the desired bicyclic lactam **10k**, albeit in only 22% yield (Table 3, entry 11). The low yield obtained for **10k** may be due to the electron flow from the *p*-methoxy group of the intermediate **14** to form **15** (Figure 1), which resulted in a partial decomposition of the starting ynamide **9k**.

The alkyl-substituted substrates **9l–n** and the terminal alkyne **9o** were also reactive, delivering the corresponding hexahydroisoquinolin-3(2*H*)-one derivatives **10l–o** in yields ranging from 37 to 40% (Table 3, entries 12–15).

DOI: 10.1021/acs.joc.7b02158
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Scheme 6. Proposed Mechanism for Formation of 10a from 9a

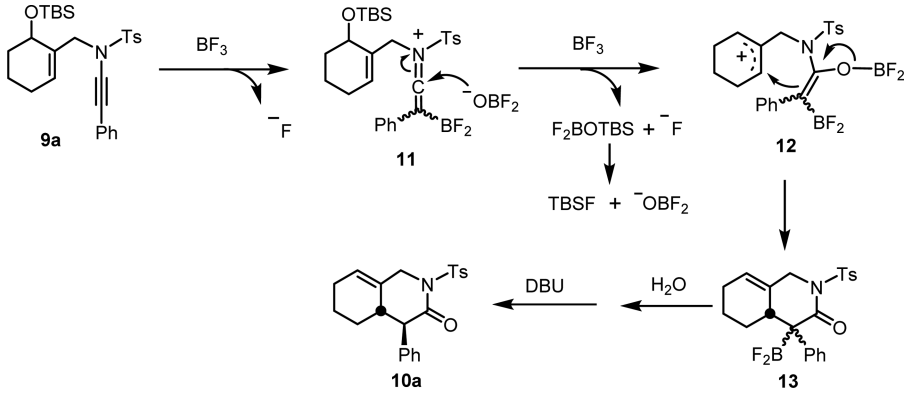
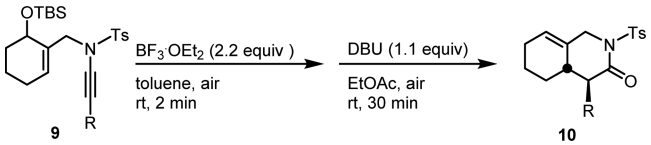


Table 3. Cyclolactamization/Epimerization Sequence to 10[a]



entry	R	substrate	product[c]	yield[b] (%)
1	phenyl	**9a**	**10a**[d]	65
2	2-methylphenyl	**9b**	**10b**	65
3	3-methylphenyl	**9c**	**10c**	59
4	4-methylphenyl	**9d**	**10d**	57
5	4-phenylphenyl	**9e**	**10e**	68
6	1-naphthyl	**9f**	**10f**	55
7	3-(methoxycarbonyl)phenyl	**9g**	**10g**	63
8	4-(methoxycarbonyl)phenyl	**9h**	**10h**	57
9	4-fluorophenyl	**9i**	**10i**	61
10	4-chloropheny	**9j**	**10j**[d]	60
11	4-methoxyphenyl	**9k**	**10k**	22
12[b]	*n*-hexyl	**9l**	**10l**	37
13[b]	methyl	**9m**	**10m**	40
14[b]	ethyl	**9n**	**10n**	39
15	hydrogen	**9o**	**10o**	38
16	3-thienyl	**9p**		

[a]Reaction conditions: all reactions were carried out on a 0.20 mmol scale with 2.2 equiv of $BF_3{\cdot}OEt_2$ in toluene under air. The epimerization step was carried out with DBU in DMF at 60 °C under air for 2 h. [b]Isolated yield. [c]Only the diastereomer depicted was isolated in each case. [d]The structure and relative stereochemistry was confirmed by X-ray crystallography.

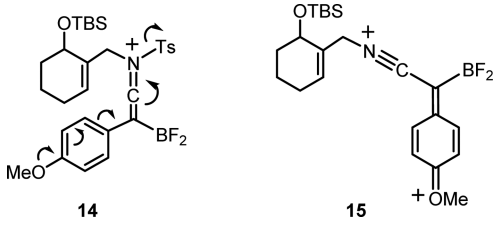


Figure 1. Structures of **14** and **15**.

Unfortunately, substrate **9p**, which contained a thienyl group at the alkyne, decomposed under the optimized reaction conditions (Table 3, entry 16).

In conclusion, we have described an efficient method for the construction of spirolactam and hexahydroisoquinolin-3(2*H*)-one ring frameworks through acid-promoted cyclolactamization of cyclohex-2-enols bearing an (ethynyl(tosyl)amino)methyl tether at the C-3 and C-2 positions of the ring, respectively. Efforts are underway to evaluate the biological activity of the spirolactams and fused bicyclic lactams.

EXPERIMENTAL SECTION

General Considerations. All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with dry solvents, unless otherwise noted. The addition of anhydrous solvents or liquid (reagents) was performed with an oven-dried syringe or cannula through a septum. Solids were added under gentle stream of nitrogen. Solvents were predried by molecular sieves and then by passing through activated Al_2O_3 columns. All commercially available chemicals were used as received without further purification. All reactions were monitored by analytical thin-layer chromatography (TLC) and visualized with UV light (254−360 nm). Melting points were measured in open glass capillaries with an electronic apparatus and are uncorrected. Flash column chromatography was performed with silica gel P60, 40−63 μm (230−400 mesh). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a 400 or 500 MHz spectrometer. Chemical shifts (δ) were expressed in parts per million (ppm) and referenced to Me_4Si (δ 0.00) as an internal standard or calibrated using the residual protic solvent for $CDCl_3$ ($CHCl_3$, δ 7.26) as an internal standard. Data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and b = broad), and coupling constants (J) are reported in hertz (Hz). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on the same spectrometers at 100 or 125 MHz. Carbon chemical shifts (δ) are also quoted in ppm and are referenced to the central carbon resonances of the solvents ($CDCl_3$, δ 77.00). Infrared (IR) spectra were recorded as a solid or a thin film on an FT-IR spectrophotometer, and data are represented as frequency of absorption (cm^{-1}). Mass spectra (MS) were recorded on spectrometers using electrospray ionization (ESI) with ion-trap analyzers. Peaks are listed according to their mass/charge (m/e) value with percent relative abundance. High-resolution mass spectra (HRMS) were recorded in positive mode on spectrometers using ESI equipped with time-of-flight (TOF) analyzers.

General Experimental Procedure for the Synthesis of 3-(Arylethynyl(tosyl) amino)methyl-Tethered Cyclohex-2-enols 1a−n. To a solution of 1,3-cyclohexanedione (3.36 g, 30.0 mmol) and isobutanol (10.0 mL, 108.2 mmol) in toluene (20.0 mL) was added *p*-toluenesulfonic acid (0.26 g, 1.51 mmol). The reaction mixture was heated to reflux with a Dean−Stark apparatus to remove water. After 10 h, the mixture was cooled to room temperature, followed by addition of triethylamine (0.20 mL, 1.43 mmol). The reaction mixture was concentrated under reduced pressure. The crude mixture was purified via flash column chromatography over silica gel (1:2 ethyl acetate/hexanes) to give 3-isobutoxycyclohex-2-enone (4.45 g, 26.40 mmol, 88%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (s, 1H), 3.45 (d, J = 5.5 Hz, 2H), 2.27 (t, J = 6.4 Hz, 2H), 2.21 (t, J = 6.4 Hz, 2H), 1.85 (m, 3H), 0.83 (d, J = 6.7 Hz, 6H); ^{13}C NMR (100

DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557

MHz, $CDCl_3$) δ 199.2, 177.7, 102.3, 74.2, 36.4, 28.6, 27.3, 20.9, 18.7; MS m/z 169 ($[M + H]^+$, 100), 141 (54), 113 (88), calcd for $C_{10}H_{17}O_2$ 169.1228, found 169.1221. To a solution of tetramethylethylenediamine (9.1 mL, 60.0 mmol) in THF (30.0 mL) at 0 °C was added *n*-BuLi (1.6 M, 37.5 mL, 60.0 mmol) dropwise, and the mixture was allowed to stir at 0 °C for 0.5 h, followed by addition of dimethyl sulfide (4.4 mL, 60.0 mmol). The resulting mixture was stirred at room temperature for 4 h. To the reaction mixture at −78 °C was added a solution of 3-isobutoxycyclohex-2-enone (5.04 g, 30.0 mmol) in THF (30.0 mL). The reaction mixture was further stirred for 2 h at room temperature, followed by addition of 2.5 N $HCl_{(aq)}$ (40.0 mL) at 0 °C. The reaction mixture was extracted with ether (30 mL × 4), and the combined organic layers were washed with water (200 mL × 3) and saturated aqueous NaCl solution (200 mL × 3), dried over anhydrous $MgSO_4$ (10.00 g), and concentrated. The crude mixture was purified via flash column chromatography over silica gel (1:10 ethyl acetate/hexanes) to give 3-((methylthio)methyl)cyclohex-2-enone (3.84 g, 24.60 mmol, 82%). The crude product was used for the following step without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (s, 1H), 3.20 (s, 2H), 2.46 (t, J = 5.9 Hz, 2H), 2.39 (t, J = 6.6 Hz, 2H), 2.07−2.01 (m, 2H), 2.00 (s, 3H). To a stirred solution of 3-((methylthio)methyl)cyclohex-2-enone (3.50 g, 22.40 mmol) in CH_2Cl_2 (25.0 mL) was added methyl iodide (12.71 g, 89.60 mmol) at room temperature. The mixture was heated at 45 °C for 3 d in a sealed tube. The reaction mixture was poured into $Na_2S_2O_{3(aq)}$ (20 mL) and extracted with CH_2Cl_2 (20 mL × 3). The combined organic extracts were washed with saturated aqueous NaCl solution (60 mL × 3), dried over anhydrous $MgSO_4$, and concentrated to give the crude 3-(iodomethyl)cyclohex-2-enone (0.98 g, 4.15 mmol). The crude product was used for the following step without additional purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (s, 1H), 4.00 (s, 2H), 2.55 (t, J = 6.6 Hz, 2H), 2.40 (t, J = 6.7 Hz, 2H), 2.07 (m, J = 6.4 Hz, 2H). To the crude 3-(iodomethyl)cyclohex-2-enone (3.02 g, 12.80 mmol) and K_2CO_3 (2.12 g, 15.36 mmol) in 6.0 mL of acetone was added via syringe a solution of *N*-(*tert*-butoxycarbonyl)-4-methylbenzenesulfonamide (0.91 g, 3.19 mmol) in 6.0 mL of acetone. The mixture was stirred at room temperature for 10 h. The reaction mixture was concentrated, poured into saturated $NH_4Cl_{(aq)}$, and extracted with CH_2Cl_2 (10 mL × 3). The combined organic solution was washed with water (200 mL × 3) and saturated aqueous NaCl solution (200 mL × 3), dried over anhydrous $MgSO_4$ (10.00 g), and concentrated. The crude mixture was purified via flash column chromatography over silica gel (1:3 ethyl acetate/hexanes) to give *tert*-butyl ((3-oxocyclohex-1-en-1-yl)methyl)(tosyl)carbamate (4.37 g, 11.53 mmol, 90%) as a pale yellow powder: mp 121−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 5.94 (s, 1H), 4.57 (s, 2H), 2.45 (s, 3H), 2.41 (t, J = 6.2 Hz, 2H), 2.33 (t, J = 5.8 Hz, 2H), 2.04 (quin, J = 6.0 Hz, 2H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.9, 160.0, 150.5, 144.7, 136.4, 129.3 (2C), 128.1 (2C), 124.7, 85.0, 50.7, 37.4, 27.8 (3C), 26.9, 22.2, 21.6; IR (CH_2Cl_2) 1732, 1674, 1356, 1282, 1255, 1167, 1149 cm^{-1}; MS (ESI) m/e 402.1 ($[M + Na]^+$, 100), 122.5 (20); HRMS (ESI) m/e calcd for $C_{19}H_{25}O_5SNa$ $[M + Na]^+$ 402.1351, found 402.1344. To a solution of *tert*-butyl ((3-oxocyclohex-1-en-1-yl)methyl)(tosyl)carbamate (1.23 g, 3.25 mmol) in CH_2Cl_2 (32.0 mL) was added trifluoroacetic acid (TFA, 1.85 g, 16.26 mmol). After the reaction misture was stirred at room temperature for 12 h, 10 wt % $Na_2CO_{3(aq)}$ was added (it is important to keep the pH value of the aqueous layer over pH 10). The water layer was extracted with CH_2Cl_2 (100 mL × 3). The combined organic phases were washed with saturated aqueous NaCl solution (100 mL × 3), dried over anhydrous $MgSO_4$ (10.00 g), and evaporated under reduced pressure to give the crude product. The crude mixture was purified via flash column chromatography over silica gel (1:3 ethyl acetate/hexanes) to give 4-methyl-*N*-((3-oxocyclohex-1-en-1-yl)methyl)benzenesulfonamide (0.88 g, 3.15 mmol, 97%) as a white powder: mp 125−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 5.96 (s, 1H), 5.86 (t, J = 6.5 Hz, 1H), 3.67 (d, J = 6.4 Hz, 2H), 2.42 (s, 3H), 2.31 (t, J = 6.7 Hz, 2H), 2.23 (t, J = 5.7 Hz, 2H), 1.91 (quin, J = 6.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 160.1, 143.6, 136.6, 129.7 (2C), 126.9 (2C), 125.6, 47.7, 37.3, 27.0, 22.1, 21.4; IR (CH_2Cl_2) 1660, 1328, 1192 cm^{-1}; MS (ESI) m/e 302.1 ($[M + Na]^+$, 100), 122.5 (20); HRMS (ESI) m/e calcd for $C_{14}H_{17}NO_3SNa$ $[M + Na]^+$ 302.0827, found 302.0822. To a solution of 4-methyl-*N*-((3-oxocyclohex-1-en-1-yl)methyl)benzenesulfonamide (0.88 g, 3.15 mmol) and $CeCl_3 \cdot 7H_2O$ (1.33 g, 3.58 mmol) in MeOH (15.0 mL) at 0 °C was added $NaBH_4$ (0.25 g, 6.50 mmol), and the mixture was stirred for 1 h. The mixture was poured into 100.0 mL of saturated ammonium chloride solution. The resulting aqueous phase was extracted with CH_2Cl_2 (100 mL × 3). The combined extracts were washed with water (100 mL × 3) and saturated aqueous NaCl solution (100 mL × 3), dried over anhydrous $MgSO_4$ (10.00 g), and concentrated in vacuo to give a crude oil. The crude mixture was purified by flash column chromatography over silica gel (1:3 ethyl acetate/hexanes) to produce *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)4-methylbenzenesulfonamide (0.86 g, 3.04 mmol, 93%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 5.63 (br s, 1H), 5.55 (t, J = 6.3 Hz, 1H), 4.09 (br s, 1H), 3.41 (d, J = 6.2 Hz, 2H), 2.57 (br s, 1H), 2.41 (s, 3H), 1.98−1.85 (m, 1H), 1.85−1.59 (m, 3H), 1.54−1.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 136.9, 136.7, 129.5 (2C), 127.0 (2C), 126.8, 65.2, 48.5, 31.4, 26.2, 21.4, 18.7; IR (CH_2Cl_2) 3283, 1599, 1323, 1158 cm^{-1}; MS (ESI) m/e 304.1 ($[M + Na]^+$, 100), 122.5 (35); HRMS (ESI) m/e calcd for $C_{14}H_{19}O_3NSNa$ $[M + Na]^+$ 304.0983, found 304.0987. To a dry and nitrogen-flushed two-neck flask, equipped with a magnetic stirring bar and a septum, were charged with (bromoethynyl)benzene (0.60 g, 3.30 mmol), toluene (3.0 mL), *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol), and K_2CO_3 (0.83 g, 6.00 mmol). After the reaction mixture was stirred for 5 min at room temperature, $CuSO_4 \cdot 5H_2O$ (0.075 g, 0.30 mmol) and 1,10-phenanthroline (0.11 g, 0.60 mmol) were added. The reaction mixture was allowed to stir at 70 °C until no trace of starting material could be detected (TLC). Upon cooling to room temperature, the reaction mixture was filtered through a plug of Celite and concentrated in vacuo to give a crude oil. The crude mixture was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to afford *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**) (0.89 g, 2.340 mmol, 78%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.82 (m, 2H), 7.38−7.30 (m, 4H), 7.29−7.25 (m, 3H), 5.78−5.74 (m, 1H), 4.20 (br, 1H), 3.98−3.88 (m, 2H), 2.46 (s, 3H), 2.09−1.91 (m, 2H), 1.86−1.78 (m, 1H), 1.77−1.68 (m, 1H), 1.62−1.49 (m, 2H), 1.40−1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 135.3, 134.6 131.1, 130.2, 129.7, 128.2, 127.7, 127.7, 122.8, 82.4, 70.9, 65.6, 57.7, 31.5, 26.0, 21.6, 18.8; IR (CH_2Cl_2) 3382, 2237, 1598, 1364, 1169 cm^{-1}; MS (ESI) m/e 404.1 ($[M + Na]^+$, 100); HRMS (ESI) m/e calcd for $C_{22}H_{24}NO_3S$ $[M + H]^+$ 382.1477, found 382.1482.

*N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-4-methyl-N-(p-tolylethynyl)benzenesulfonamide (**1b**).* The crude mixture obtained from the coupling reaction of 1-(bromoethynyl)-4-methylbenzene (0.64 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1b** (0.94 g, 2.38 mmol, 79%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.81 (m, 2H), 7.37−7.33 (m, 2H), 7.25−7.20 (m, 2H), 7.11−7.06 (m, 2H), 5.77−5.72 (m, 1H), 4.23−4.14 (m, 1H), 3.97−3.86 (m, 2H), 2.45 (s, 3H), 2.33 (s, 3H), 2.07−1.91 (m, 2H), 1.86−1.77 (m, 1H), 1.76−1.66 (m, 1H), 1.60−1.48 (m, 2H), 1.47−1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 137.9, 135.4, 134.6, 131.3, 130.1, 129.7, 129.0, 127.7, 119.6, 81.6, 70.8, 65.6, 57.7, 31.5, 26.0, 21.6, 21.4, 18.2; IR (CH_2Cl_2) 3374, 2237, 1597, 1364, 1169 cm^{-1}; MS (ESI) m/e 418.0 ($[M + Na]^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_3S$ $[M + H]^+$ 396.1633, found 396.1637.

*N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-4-methyl-N-(o-tolylethynyl)benzenesulfonamide (**1c**).* The crude mixture obtained from the coupling reaction of 1-(bromoethynyl)-2-methylbenzene (0.64 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1c** (0.81 g, 2.05 mmol, 68%) as a colorless oil: ^{1}H NMR (400 MHz,

DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557

$CDCl_3$) δ 7.86−7.82 (m, 2H), 7.37−7.33 (m, 2H), 7.30−7.26 (m, 1H), 7.18−7.14 (m, 2H), 7.14−7.07 (m, 1H), 5.78−5.74 (m, 1H), 4.23−4.16 (m, 1H), 3.99 (d, J = 13.8 Hz, 1H), 3.91 (d, J = 13.7 Hz, 1H), 2.45 (s, 3H), 2.43 (s, 3H), 2.09−1.93 (m, 2H), 1.87−1.78 (m, 1H), 1.78−1.68 (m, 1H), 1.62−1.49 (m, 2H), 1.45−1.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 139.4, 135.4, 134.7, 131.2, 130.2, 129.7, 129.3, 127.7, 127.6, 125.5, 122.6, 86.1, 69.9, 65.6, 57.7, 31.6, 26.0, 21.6, 20.8, 18.9; IR (CH_2Cl_2) 3379, 2235, 1598, 1364, 1169 cm^{-1}; MS (ESI) m/e 418.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_3S$ [M + H]$^+$ 396.1633, found 396.1636.

*N-((3,4-Dimethylphenyl)ethynyl)-N-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (**1d**).* The crude mixture obtained from the coupling reaction of 4-(bromoethynyl)-1,2-dimethylbenzene (0.69 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1d** (0.92 g, 2.25 mmol, 75%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.81 (m, 2H), 7.37−7.33 (m, 2H), 7.14−7.11 (m, 1H), 7.09−7.02 (m, 2H), 5.77−5.73 (m, 1H), 4.22−4.15 (m, 1H), 3.96−3.86 (m, 2H), 2.45 (s, 3H), 2.24 (s, 3H), 2.22 (s, 3H), 2.07−1.91 (m, 2H), 1.85−1.77 (m, 1H), 1.76−1.66 (m, 1H), 1.58−1.48 (m, 2H), 1.41−1.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 1367., 136.6, 135.4, 134.7, 132.4, 130.1, 129.7, 129.6, 128.8, 127.8, 119.9, 81.4, 70.9, 65.6, 57.7, 31.5, 26.0, 21.6, 19.7, 19.5; IR (CH_2Cl_2) 3375, 2236, 1597, 1363, 1165 cm^{-1}; MS (ESI) m/e 432.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{27}NO_3NaS$ [M + Na]$^+$ 432.1609, found 432.1607.

*N-([1,1′-Biphenyl]-4-ylethynyl)-N-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (**1e**).* The crude mixture obtained from the coupling reaction of 4-(bromoethynyl)-1,1′-biphenyl (0.85 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1e** (0.95 g, 2.07 mmol, 69%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.83 (m, 2H), 7.59−7.55 (m, 2H), 7.54−7.50 (m, 2H), 7.47−7.32 (m, 7H), 5.80−5.75 (m, 1H), 4.25−4.17 (m, 1H), 4.00−3.89 (m, 2H), 2.46 (s, 3H), 2.10−1.92 (m, 2H), 1.89−1.79 (m, 1H), 1.78−1.68 (m, 1H), 1.63−1.50 (m, 2H), 1.46−1.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 140.5, 140.3, 135.3, 134.7, 131.6, 130.3, 129.8, 128.8, 127.8, 127.6, 126.9, 121.7, 83.0, 70.8, 65.6, 57.7, 31.5, 26.0, 21.7, 18.9; IR (CH_2Cl_2) 3372, 2235, 1597, 1365, 1169 cm^{-1}; MS (ESI) m/e 480.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{28}H_{27}NO_3NaS$ [M + Na]$^+$ 480.1609, found 480.1612.

*N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-N-((4-methoxyphenyl)ethynyl)-4-methylbenzenesulfonamide (**1f**).* The crude mixture obtained from the coupling reaction of 1-(bromoethynyl)-4-methoxybenzene (0.70 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1f** (1.01 g, 2.46 mmol, 82%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.81 (m, 2H), 7.38−7.33 (m, 2H), 7.30−7.25 (m, 2H), 6.84−6.79 (m, 2H), 5.76−5.72 (m, 1H), 4.23−4.14 (m, 1H), 3.96−3.87 (m, 2H), 3.80 (s, 3H), 2.46 (s, 3H), 2.08−1.91 (m, 2H), 1.85−1.77 (m, 1H), 1.76−1.67 (m, 1H), 1.57−1.51 (m, 2H), 1.38−1.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 144.6, 135.5, 134.7, 133.2, 133.0, 129.7, 127.8, 114.7, 113.9, 80.9, 70.5, 65.6, 57.5, 55.3, 31.5, 26.1, 21.6, 18.8; IR (CH_2Cl_2) 3396, 2238, 1606, 1364, 1248, 1169 cm^{-1}; MS (ESI) m/e 434.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_4S$ [M + H]$^+$ 412.1583, found 412.1585.

*N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-N-((3-methoxyphenyl)ethynyl)-4-methylbenzenesulfonamide (**1g**).* The crude mixture obtained from the coupling reaction of 1-(bromoethynyl)-3-methoxybenzene (0.70 g, 3.32 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1g** (1.03 g, 2.50 mmol, 83%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.81 (m, 2H), 7.38−7.33 (m, 2H), 7.21−7.16 (m, 1H), 6.94−6.90 (m, 1H), 6.88−6.80 (m, 2H), 5.78−5.74 (m, 1H), 4.24−4.17 (m, 1H), 3.98−3.88 (m, 2H), 3.79 (s, 3H), 2.46 (s, 3H), 2.07−1.91 (m, 2H), 1.86−1.78 (m, 1H), 1.76−1.67 (m, 1H), 1.58−1.51 (m, 2H), 1.41−1.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 144.7, 135.3, 134.7, 130.3, 129.8, 129.3, 127.8, 123.9, 123.6, 116.2, 114.1, 82.3, 70.9, 65.6, 57.6, 55.3, 31.5, 26.0, 21.6, 18.8; IR (CH_2Cl_2) 3393, 2238, 1591, 1440, 1364 cm^{-1}; MS (ESI) m/e 434.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_4S$ [M + H]$^+$ 412.1583, found 412.1584.

*Methyl 4-((N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-4-methylphenylsulfonamido)ethynyl)benzoate (**1h**).* The crude mixture obtained from the coupling reaction of methyl 4-(bromoethynyl)-benzoate (0.79 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1h** (0.78 g, 1.77 mmol, 59%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.93 (m, 2H), 7.86−7.82 (m, 2H), 7.39−7.34 (m, 4H), 5.79−5.76 (m, 1H), 4.26−4.18 (m, 1H), 4.00−3.93 (m, 2H), 3.91 (s, 3H), 2.46 (s, 3H), 2.07−1.90 (m, 2H), 1.87−1.79 (m, 1H), 1.78−1.68 (m, 1H), 1.60−1.52 (m, 2H), 1.44−1.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 145.0, 135.1, 134.6, 130.5, 130.4, 129.8, 129.5, 128.7, 127.8, 127.8, 85.7, 71.0, 65.6, 57.6, 52.2, 31.5, 26.0, 21.7, 18.9; IR (CH_2Cl_2) 3525, 2233, 1722, 1605, 1368, 1276, 1170 cm^{-1}; MS (ESI) m/e 462.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{26}NO_5S$ [M + H]$^+$ 440.1532, found 440.1534.

*Methyl 3-((N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-4-methylphenylsulfonamido)ethynyl)benzoate (**1i**).* The crude mixture obtained from the coupling reaction of methyl 3-(bromoethynyl)-benzoate (0.79 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1i** (0.69 g, 1.56 mmol, 52%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.97 (m, 2H), 7.94−7.92 (m, 1H), 7.86−7.82 (m, 2H), 7.53−7.49 (m, 1H), 7.39−7.35 (m, 2H), 5.80−5.75 (m, 1H), 4.25−4.17 (m, 1H), 3.99−3.90 (m, 2H), 3.92 (s, 3H), 2.46 (s, 3H), 2.07−1.90 (m, 2H), 1.87−1.79 (m, 1H), 1.78−1.68 (m, 1H), 1.61−1.49 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 144.8, 135.1, 134.6, 132.1, 130.4, 130.3, 129.8, 128.6, 128.4, 127.7, 123.4, 83.4, 70.2, 65.6, 57.7, 52.3, 31.5, 26.0, 21.6, 18.9; IR (CH_2Cl_2) 3427, 2237, 1716, 1599, 1436, 1368, 1168 cm^{-1}; MS (ESI) m/e 462.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{26}NO_5S$ [M + H]$^+$ 440.1532, found 440.1531.

*N-((4-Fluorophenyl)ethynyl)-N-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (**1j**).* The crude mixture obtained from the coupling reaction of 1-(bromoethynyl)-4-fluorobenzene (0.66 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1j** (0.80 g, 2.00 mmol, 66%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.80 (m, 2H), 7.39−7.34 (m, 2H), 7.34−7.28 (m, 2H), 7.01−6.94 (m, 2H), 5.77−5.73 (m, 1H), 4.24−4.16 (m, 1H), 3.97−3.87 (m, 2H), 2.46 (s, 3H), 2.07−1.91 (m, 2H), 1.86−1.78 (m, 1H), 1.78−1.68 (m, 1H), 1.62−1.50 (m, 2H), 1.39−1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 ($^1J_{C-F}$ = 247.5 Hz, d), 144.7, 135.3, 133.2 ($^3J_{C-F}$ = 8.2 Hz, d), 130.2, 129.8, 127.7, 118.8 ($^4J_{C-F}$ = 3.3 Hz, d), 115.5 ($^2J_{C-F}$ = 21.9 Hz, d), 82.0, 69.8, 65.6, 57.6, 31.6, 26.0, 21.7, 18.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.5; IR (CH_2Cl_2) 3379, 2240, 1599, 1364, 1170 cm^{-1}; MS (ESI) m/e 422.1 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{22}H_{23}NO_3SF$ [M + H]$^+$ 400.1383, found 400.1386.

*N-((4-Chlorophenyl)ethynyl)-N-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (**1k**).* The crude mixture obtained from the coupling reaction of 1-(bromoethynyl)-4-chlorobenzene (0.71 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1k** (0.94 g, 2.26 mmol, 75%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.80 (m, 2H), 7.39−7.33 (m, 2H), 7.28−7.22 (m, 4H), 5.78−5.72 (m, 1H), 4.25−4.16 (m, 1H), 3.98−3.87 (m, 2H), 2.46 (s, 3H), 2.06−1.90 (m, 2H), 1.86−1.78 (m,

DOI: 10.1021/acs.joc.7b02158
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1H), 1.77−1.68 (m, 1H), 1.58−1.49 (m, 2H), 1.42−1.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 135.2, 134.6, 133.7, 132.3, 130.3, 129.8, 128.6, 127.7, 121.3, 83.3, 70.0, 65.6, 57.6, 31.5, 26.0, 21.7, 18.8; IR (CH_2Cl_2) 3569, 2234, 1364, 1167, 658 cm^{-1}; MS (ESI) *m/e* 440.1 ([M+Na+2]$^+$, 37), 438.1 ([M + Na]$^+$, 100). HRMS (ESI) *m/e* calcd for $C_{22}H_{23}NO_3SCl$ [M + H]$^+$ 416.1087, found 416.1084.

*N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-4-methyl-N-((3-(trifluoromethyl)phenyl)ethynyl)benzenesulfonamide (**1l**).* The crude mixture obtained from the coupling reaction of 1-(bromoethynyl)-3-(trifluoromethyl)benzene (0.82 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:3) to give **1l** (0.86 g, 1.91 mmol, 64%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.81 (m, 2H), 7.57−7.54 (s, 1H), 7.53−7.47 (m, 2H), 7.43−7.35 (m, 3H), 5.79−5.75 (m, 1H), 4.25−4.18 (m, 1H), 4.00−3.90 (m, 2H), 2.46 (s, 3H), 2.06−1.91 (m, 2H), 1.87−1.79 (m, 1H), 1.79−1.69 (m, 1H), 1.58−1.50 (m, 2H), 1.44−1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 135.1, 134.6, 134.0, 130.9 ($^2J_{C-F}$ = 32.3 Hz, q), 130.4, 129.9, 128.8, 127.8, 127.7 ($^3J_{C-F}$ = 3.9 Hz, q), 125.1, 124.1 ($^3J_{C-F}$ = 3.9 Hz, q), 123.7 ($^1J_{C-F}$ = 270.1 Hz, q), 84.0, 69.9, 65.6, 57.6, 31.5, 26.0, 21.7, 18.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.0; IR (CH_2Cl_2) 3391, 2239, 1598, 1368, 1168 cm^{-1}; MS (ESI) *m/e* 472.1 ([M + Na]$^+$, 100); HRMS (ESI) *m/e* calcd for $C_{23}H_{23}NO_3SF_3$ [M + H]$^+$ 450.1351, found 450.1351.

*N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-4-methyl-N-(thiophene-2-ylethynyl)benzenesulfonamide (**1m**).* The crude mixture obtained from the coupling reaction of 2-(bromoethynyl)thiophene (0.62 g, 3.30 mmol) and *N*-((3-hydroxycyclohex-1-en-1- yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1/1) to give **1m** (0.71 g, 1.83 mmol, 61%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.80 (m, 2H), 7.39−7.35 (m, 2H), 7.27−7.24 (m, 1H), 7.16−7.13 (m, 1H), 6.97−6.94 (m, 1H), 5.75−5.71 (m, 1H), 4.22−4.14 (m, 1H), 3.98−3.89 (m, 1H), 2.47 (s, 3H), 2.05−1.89 (m, 2H), 1.85−1.77 (m, 1H), 1.77−1.67 (m, 1H), 1.57−1.50 (m, 2H), 1.38−1.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 135.2, 134.6, 132.7, 130.3, 129.8, 127.8, 127.6, 127.0, 122.8, 86.0, 65.6, 64.2, 57.7, 31.5, 26.0, 21.7, 18.8; IR (CH_2Cl_2) 3373, 2231, 1598, 1367, 1169 cm^{-1}; MS (ESI) *m/e* 410.0 ([M + Na]$^+$, 100); HRMS (ESI) *m/e* calcd for $C_{20}H_{22}NO_3S_2$ [M + H]$^+$ 388.1041, found 388.1041.

*N-((3-Hydroxycyclohex-1-en-1-yl)methyl)-4-methyl-N-(oct-1-yn-1-yl)benzenesulfonamide (**1n**).* The crude mixture obtained from the coupling reaction of 1-bromooct-1-yne (0.62 g, 3.30 mmol), and *N*-((3-hydroxycyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.84 g, 3.00 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1/3) to give **1n** (1.05 g, 2.70 mmol, 90%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.75 (m, 2H), 7.36−7.31 (m, 2H), 5.70−5.66 (m, 1H), 4.21−4.14 (m, 1H), 3.83 (d, *J* = 13.8 Hz, 1H), 3.75 (d, *J* = 13.8 Hz, 1H), 2.45 (s, 3H), 2.23 (t, *J* = 12.1, 7.0 Hz, 2H), 2.03−1.89 (m, 2H), 1.85−1.77 (m, 1H), 1.76−1.66 (m, 1H), 1.56−1.51 (m, 2H), 1.48−1.40 (m, 2H), 1.37−1.22 (m, 7H), 0.88 (t, *J* = 7.1, 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 135.4, 134.6, 129.5, 129.5, 127.6, 73.0, 70.1, 65.4, 57.5, 31.4, 31.2, 28.7, 28.3, 25.8, 22.5, 21.5, 18.7, 18.3, 13.9; IR (CH_2Cl_2) 1363, 1170 cm^{-1}; MS (ESI) *m/e* 412.2 ([M + Na]$^+$, 100); HRMS (ESI) *m/e* calcd for $C_{22}H_{32}NO_3S$ [M + H]$^+$ 390.2103, found 390.2107.

General Experimental Procedure for the Spirolactamization/Hydrogenation of *N*-((3-Hydroxycyclohex-1-en-1-yl)-methyl)-4-methyl-*N*-(arylethynyl)benzenesulfonamides: Synthesis of Spiro-γ-lactams 3a−o. *Example for the Synthesis of **3a**.* To a stirred solution of **1a** (0.15 g, 0.40 mmol) in CH_2Cl_2 (1.3 mL) at room temperature under an atmosphere of nitrogen was added TfOH (7.0 μL, 0.080 mmol, 20 mol %). After the reaction mixture was stirred for 20 min, saturated aqueous sodium bicarbonate (20 mL) and CH_2Cl_2 (20 mL) were added. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (30.0 mL × 3). The combined organic layers were washed with saturated aqueous NaCl solution (30.0 mL × 3), dried over anhydrous $MgSO_4$, and concentrated in vacuo to give the crude mixture **2a**. To an oven-dried 10 mL round-bottom flask equipped with a stirrer bar and capped with a rubber septum was added **2a** in MeOH/EtOAc = 1:1 (4.0 mL) at room temperature, followed by addition of Pd/C (8.5 mg, 0.080 mmol). The flask was evacuated and backfilled with a balloon of hydrogen twice. The reaction was vigorously stirred under 1 atm of hydrogen for 16 h. The crude mixture was filtered through a bed of Celite and eluted with dichloromethane (30.0 mL). The filtrate was concentrated in vacuo to give the crude mixture. The crude mixture was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give 4-phenyl-2-tosyl-2-azaspiro[4.5]decan-3-one (**3a**) (0.069 g, 0.180 mmol, 45% over the two steps) as a white solid: mp 120−121 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99−7.95 (m, 2H), 7.37−7.33 (m, 2H), 7.26−7.23 (m, 3H), 6.94−6.89 (m, 2H), 3.99 (d, *J* = 10.2 Hz, 1H), 3.60 (dd, *J* = 10.2, 0.8 Hz, 1H), 3.37 (s, 1H), 2.45 (s, 3H), 1.64−1.53 (m, 3H), 1.51−1.43 (m, 2H), 1.40−1.27 (m, 2H), 1.22−1.16 (m, 1H), 1.09−0.99 (m, 1H), 0.80 (td, *J* = 12.9, 5.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 145.2, 135.2, 133.1, 129.7, 129.7, 128.3, 128.1, 127.5, 61.6, 54.1, 41.5, 35.9, 29.6, 25.1, 22.5, 22.0, 21.7; IR (CH_2Cl_2) 1739, 1362, 1170 cm^{-1}; MS (ESI) *m/e* 406.2 ([M + Na]$^+$, 100); HRMS (ESI) *m/e* calcd for $C_{22}H_{26}NO_3S$ [M + H]$^+$ 384.1633, found 384.1635.

*4-(p-Tolyl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3b**).* The crude mixture obtained from spirolactamization/hydrogenation of **1b** (0.16 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3b** (0.064 g, 0.160 mmol, 40% over the two steps) as a white solid: mp 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.94 (m, 2H), 7.37−7.33 (m, 2H), 7.08−7.03 (m, 2H), 6.82−6.78 (m, 2H), 3.97 (d, *J* = 10.1 Hz, 1H), 3.57 (d, *J* = 10.2 Hz, 1H), 3.34 (s, 1H), 2.45 (s, 3H), 2.30 (s, 3H), 1.64−1.52 (m, 3H), 1.51−1.40 (m, 2H), 1.40−1.24 (m, 2H), 1.22−1.15 (m, 1H), 1.10−0.98 (m, 1H), 0.81 (td, *J* = 12.7, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 145.1, 137.2, 135.1, 130.0, 129.6, 129.6, 129.0, 128.0, 61.2, 54.1, 41.4, 35.8, 29.8, 25.1, 22.5, 22.0, 21.7, 21.0; IR (CH_2Cl_2) 1740, 1361, 1173 cm^{-1}; MS (ESI) *m/e* 420.2 ([M + Na]$^+$, 100); HRMS (ESI) *m/e* calcd for $C_{23}H_{28}NO_3S$ [M + H]$^+$ 398.1790, found 398.1789.

*4-(o-Tolyl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3c**).* The crude mixture obtained from spirolactamization/hydrogenation of **1c** (0.16 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3c** (0.059 g, 0.15 mmol, 37% over the two steps) as a white solid: mp 121−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.95 (m, 2H), 7.38−7.33 (m, 2H), 7.15−7.09 (m, 2H), 7.02−6.96 (m, 1H), 6.60−6.55 (m, 1H), 3.90 (d, *J* = 10.1 Hz, 1H), 3.76 (d, *J* = 10.2 Hz, 1H), 3.67 (s, 1H), 2.46 (s, 3H), 2.27 (s, 3H), 1.73−1.67 (m, 1H), 1.66−1.55 (m, 2H), 1.50−1.34 (m, 3H), 1.33−1.15 (m, 2H), 1.13−1.00 (m, 1H), 0.94 (td, *J* = 12.9, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 145.2, 137.1, 135.1, 132.4, 130.7, 129.6, 128.9, 128.1, 127.4, 125.8, 57.3, 53.9, 41.9, 36.7, 30.5, 25.2, 22.6, 22.1, 21.7, 20.3; IR (CH_2Cl_2) 1736, 1362, 1171 cm^{-1}; MS (ESI) *m/e* 420.2 ([M + Na]$^+$, 100); HRMS (ESI) *m/e* calcd for $C_{23}H_{28}NO_3S$ [M + H]$^+$ 398.1790, found 398.1790. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.[17]

*4-(3,4-Dimethylphenyl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3d**).* The crude mixture obtained from spirolactamization/hydrogenation of **1d** (0.16 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3d** (0.071 g, 0.17 mmol, 43% over the two steps) as a white solid: mp 110−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.95 (m, 2H), 7.37−7.32 (m, 2H), 7.00−6.96 (m, 1H), 6.65−6.61 (m, 1H), 6.61−6.69 (m, 1H), 3.93 (d, *J* = 10.1 Hz, 1H), 3.60 (d, *J* = 10.1 Hz, 1H), 3.29 (s, 1H), 2.44 (s, 3H), 2.19 (s, 3H), 2.14 (s, 3H), 1.65−1.51 (m, 3H), 1.50−1.23 (m, 4H), 1.22−1.14 (m, 1H), 1.13−1.00 (m, 1H), 0.85 (td, *J* = 12.6, 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 145.1, 136.4, 135.8, 135.2, 130.6, 130.6, 129.6, 129.5, 128.0, 127.1, 61.2, 54.2, 41.2, 35.9, 30.1, 25.1, 22.5, 22.0, 21.6, 19.7, 19.3; IR (CH_2Cl_2) 1739, 1362, 1171 cm^{-1}; MS (ESI) *m/e* 434.2 ([M + Na]$^+$, 100); HRMS (ESI) *m/e* calcd for $C_{24}H_{30}NO_3S$ [M + H]$^+$ 412.1946, found 412.1949.

*4-([1,1′-Biphenyl]-4-yl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3e**).* The crude mixture obtained from spirolactamization/hydrogenation of **1e** (0.18 g, 0.40 mmol) was purified by flash column

DOI: 10.1021/acs.joc.7b02158
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chromatography (EtOAc/hexanes = 1:10) to give **3e** (0.088 g, 0.19 mmol, 48% over the two steps) as a white solid: mp 189−190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.96 (m, 2H), 7.57−7.52 (m, 2H), 7.50−7.46 (m, 2H), 7.45−7.39 (m, 2H), 7.38−7.32 (m, 3H), 7.02−6.98 (m, 2H), 4.03 (d, J = 10.2 Hz, 1H), 3.60 (d, J = 10.2 Hz, 1H), 3.43 (s, 1H), 2.46 (s, 3H), 1.67−1.45 (m, 5H), 1.42−1.31 (m, 2H), 1.30−1.21 (m, 1H), 1.13−0.99 (m, 1H), 0.85 (td, J = 12.8, 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 145.2, 140.5, 140.5, 135.1, 132.1, 130.1, 129.7, 128.8, 128.1, 127.4, 127.0, 61.3, 54.1, 41.7, 35.9, 29.8, 25.1, 22.6, 22.0, 21.7; IR (CH_2Cl_2) 1736, 1358, 1171, 1120 cm^{-1}; MS (ESI) m/e 482.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{28}H_{30}NO_3S$ [M + H]$^+$ 460.1946, found 460.1947.

*4-(4-Methoxyphenyl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3f**).* The crude mixture obtained from spirolactamization/hydrogenation of **1f** (0.16 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3f** (0.066 g, 0.16 mmol, 40% over the two steps) as a white solid: mp 119−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.93 (m, 2H), 7.38−7.32 (m, 2H), 6.87−6.76 (m, 4H), 3.99 (d, J = 10.2 Hz, 1H), 3.77 (s, 3H), 3.55 (d, J = 10.2 Hz, 1H), 3.33 (s, 1H), 2.45 (s, 3H), 1.66−1.53 (m, 3H), 1.52−1.39 (m, 2H), 1.39−1.24 (m, 2H), 1.19 (d, J = 6.0 Hz, 1H), 1.10−1.00 (m, 1H), 0.80 (td, J = 12.9, 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 159.0, 145.1, 135.1, 130.8, 129.6, 128.0, 125.0, 113.7, 60.8, 55.2, 54.0, 41.5, 35.7, 29.7, 25.1, 22.5, 22.0, 21.7; IR (CH_2Cl_2) 1736, 1363, 1172, 1123 cm^{-1}; MS (ESI) m/e 436.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{28}NO_4S$ [M + H]$^+$ 414.1739, found 414.1741.

*4-(3-Methoxyphenyl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3g**).* The crude mixture obtained from spirolactamization of **1g** (0.16 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give a crude product **2g** (0.064 g) and **4** (0.037 g, 0.09 mmol, 23%). The crude **2g** was subjected to hydrogenation to give **3g** (0.053 g, 0.13 mmol, 32% over the two steps) as a white solid: mp 99−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.95 (m, 2H), 7.37−7.33 (m, 2H), 7.16 (t, J = 7.9 Hz, 1H), 6.81−6.77 (m, 1H), 6.51−6.47 (m, 1H), 6.47−6.44 (m, 1H), 3.96 (d, J = 10.2 Hz, 1H), 3.73 (s, 1H), 3.60 (d, J = 10.2 Hz, 1H), 3.34 (s, 3H), 2.45 (s, 3H), 1.65−1.52 (m, 3H), 1.52−1.43 (m, 2H), 1.42−1.25 (m, 2H), 1.23−1.13 (m, 1H), 1.12−1.00 (m, 1H), 0.85 (td, J = 12.7, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 145.2, 135.1, 134.7, 129.7, 129.3, 128.1, 122.0, 115.8, 112.7, 61.5, 55.2, 54.1, 41.4, 35.9, 30.0, 25.1, 22.5, 22.0, 21.7; IR (CH_2Cl_2) 1736, 1364, 1170, 1125 cm^{-1}; MS (ESI) m/e 436.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{28}NO_4S$ [M + H]$^+$ 414.1739, found 414.1741.

*7-Methoxy-3-tosyl-2,3-dihydrospiro[benzo[d]azepine-1,1′-cyclohex[2]en]-4-(5H)-one (**4**).* White solid: mp 147−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92−7.89 (m, 2H), 7.30−7.27 (m, 2H), 7.26−7.24 (m, 1H), 6.79 (dd, J = 7.1, 2.2 Hz, 1H), 6.50 (d, J = 2.8 Hz, 1H), 5.95 (dt, J = 10.0, 4.0, 3.7 Hz, 1H), 5.59−5.55 (m, 1H), 4.38 (d, J = 15.9 Hz, 1H), 4.24 (d, J = 15.8 Hz, 1H), 3.92 (d, J = 14.8 Hz, 1H), 3.75 (s, 3H), 3.70 (d, J = 14.9 Hz, 1H), 2.41 (s, 3H), 2.22−2.17 (m, 2H), 2.09−2.03 (m, 1H), 1.99−1.89 (m, 1H), 1.84−1.74 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 158.0, 144.8, 136.1, 135.4, 132.6, 132.6, 129.5, 129.2, 129.1, 128.1, 115.7, 114.0, 55.3, 52.2, 45.7, 43.7, 35.8, 24.8, 21.6, 18.5; IR (CH_2Cl_2) 1707, 1492, 1350, 1167, 1086 cm^{-1}; MS (ESI) m/e 434.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_4S$ [M + H]$^+$ 412.1583, found 412.1584. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.[17]

*Methyl 4-(3-Oxo-2-tosyl-2-azaspiro[4.5]decan-4-yl)benzoate (**3h**).* The crude mixture obtained from spirolactamization/hydrogenation of **1h** (0.17 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3h** (0.072 g, 0.16 mmol, 41% over the two steps) as a white solid: mp 147−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.95 (m, 2H), 7.95−7.91 (m, 2H), 7.39−7.34 (m, 2H), 7.03−6.99 (m, 2H), 4.02 (d, J = 10.2 Hz, 1H), 3.90 (s, 3H), 3.60 (d, J = 10.2 Hz, 1H), 3.45 (s, 1H), 2.46 (s, 3H), 1.67−1.57 (m, 3H), 1.52−1.25 (m, 4H), 1.24−1.17 (m, 1H), 1.07−0.94 (m, 1H), 0.74 (td, J = 12.7, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 166.7, 145.4, 138.3, 135.0, 129.9, 129.7, 129.5, 128.1, 61.5, 54.0, 52.1, 41.8, 35.9, 29.8, 25.1, 22.5, 22.0, 21.7; IR (CH_2Cl_2) 1724, 1284, 1172, 1117 cm^{-1}; MS (ESI) m/e 464.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{28}NO_5S$ [M + H]$^+$ 442.1688, found 442.1686.

*Methyl 3-(3-Oxo-2-tosyl-2-azaspiro[4.5]decan-4-yl)benzoate (**3i**).* The crude mixture obtained from spirolactamization/hydrogenation of **1i** (0.17 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3i** (0.066 g, 0.15 mmol, 37% over the two steps) as a white solid: mp 116−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.93 (m, 3H), 7.68−7.65 (m, 1H), 7.38−7.33 (m, 3H), 7.16−7.11 (m, 1H), 4.07 (d, J = 10.2 Hz, 1H), 3.90 (s, 3H), 3.57 (d, J = 10.2 Hz, 1H), 3.46 (s, 1H), 2.45 (s, 3H), 1.68−1.54 (m, 3H), 1.53−1.22 (m, 5H), 1.05−0.92 (m, 1H), 0.72 (td, J = 12.7, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 166.6, 145.3, 135.0, 134.2, 133.3, 131.1, 130.3, 129.7, 128.8, 128.4, 128.0, 61.4, 53.9, 52.1, 41.6, 35.7, 29.5, 25.0, 22.5, 21.9, 21.7; IR (CH_2Cl_2) 1725, 1363, 1291, 1172, 1114 cm^{-1}; MS (ESI) m/e 464.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{28}NO_5S$ [M + H]$^+$ 442.1688, found 442.1691.

*4-(4-Fluorophenyl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3j**).* The crude mixture obtained from spirolactamization/hydrogenation of **1j** (0.16 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3j** (0.053 g, 0.13 mmol, 33% over the two steps) as a white solid: mp 123−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.93 (m, 2H), 7.39−7.33 (m, 2H), 7.00−6.88 (m, 4H), 4.02 (d, J = 10.2 Hz, 1H), 3.55 (d, J = 10.2 Hz, 1H), 3.38 (s, 1H), 2.46 (s, 3H), 1.66−1.54 (m, 3H), 1.54−1.27 (m, 4H), 1.24−1.16 (m, 1H), 1.08−0.94 (m, 1H), 0.75 (td, J = 12.7, 4.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 162.2 ($^1J_{C-F}$ = 245.4 Hz, d), 145.3, 135.1, 131.4 ($^3J_{C-F}$ = 8.0 Hz, d), 129.7, 128.7 ($^4J_{C-F}$ = 3.4 Hz, d), 128.1, 115.3 ($^2J_{C-F}$ = 21.3 Hz, d), 60.9, 53.9, 41.6, 35.7, 29.6, 25.1, 22.5, 22.0, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.5; IR (CH_2Cl_2) 1736, 1364, 1173, 1167 cm^{-1}; MS (ESI) m/e 424.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{22}H_{25}NO_3FS$ [M + H]$^+$ 402.1539, found 402.1540. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.[17]

*4-(4-Chlorophenyl)-2-tosyl-2-azaspiro[4.5]decan-3-one (**3k**).* The crude mixture obtained from spirolactamization/hydrogenation of **1k** (0.17 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3k** (0.060 g, 0.14 mmol, 36% over the two steps) as a white solid: mp 132−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.93 (m, 2H), 7.38−7.33 (m, 2H), 7.27−7.22 (m, 2H), 6.90−6.85 (m, 2H), 4.02 (d, J = 10.2 Hz, 1H), 3.56 (d, J = 10.2 Hz, 1H), 3.37 (s, 1H), 2.46 (s, 3H), 1.66−1.54 (m, 3H), 1.53−1.26 (m, 4H), 1.24−1.15 (m, 1H), 1.08−0.94 (m, 1H), 0.74 (td, J = 12.8, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 145.3, 135.0, 133.6, 131.4, 131.1, 129.7, 128.5, 128.0, 60.9, 53.9, 41.6, 35.7, 29.6, 25.1, 22.5, 21.9, 21.7; IR (CH_2Cl_2) 1738, 1362, 1172, 1124, 664 cm^{-1}; MS (ESI) m/e 442.2 ([M + 2 + Na]$^+$, 35), 440.3 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{22}H_{25}NO_3ClS$ [M + H]$^+$ 418.1244, found 418.1247. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.[17]

*2-Tosyl-4-(3-(trifluoromethyl)phenyl)-2-azaspiro[4.5]decan-3-one (**3l**).* The crude mixture obtained from spirolactamization/hydrogenation of **1l** (0.18 g, 0.40 mmol) was purified by flash column chromatography (EtOAc/hexanes = 1:10) to give **3l** (0.069 g, 0.15 mmol, 38% over the two steps) as a white solid: mp 107−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.94 (m, 2H), 7.56−7.51 (m, 1H), 7.43−7.34 (m, 3H), 7.17−7.13 (m, 2H), 4.03 (d, J = 10.2 Hz, 1H), 3.60 (d, J = 10.2 Hz, 1H), 3.45 (s, 1H), 2.46 (s, 3H), 1.70−1.55 (m, 3H), 1.54−1.31 (m, 4H), 1.27−1.19 (m, 1H), 1.09−0.96 (m, 1H), 0.72 (td, J = 12.7, 4.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 145.5, 134.9, 134.1, 133.2, 130.8 ($^2J_{C-F}$ = 32.3 Hz, q), 129.8, 128.8, 128.0, 126.5 ($^3J_{C-F}$ = 3.6 Hz, q), 124.6 ($^3J_{C-F}$ = 3.6 Hz, q), 123.8 ($^1J_{C-F}$ = 270.8 Hz, q), 61.5, 53.9, 41.7, 35.8, 29.7, 25.0, 22.5, 21.9, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −61.6; IR (CH_2Cl_2) 1738, 1329, 1170, 1124 cm^{-1}; MS (ESI) m/e 474.2 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{25}NO_3F_3S$ [M + H]$^+$ 452.1503, found 452.1507.

DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557

Representative Experimental Procedure for the Synthesis of TBS-Protected *N*-Tosyl-2-((arylethynyl)amino)methyl)-cyclohex-2-enols 9a–l,p. *Example for the Synthesis of **9a**.* To a dry and nitrogen-flushedtwo-neck flask, equipped with a magnetic stirring bar and a septum, were charged with (bromoethynyl)benzene (0.40 g, 2.20 mmol), toluene (2.0 mL), *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide[20] (0.79, 2.00 mmol), and K_2CO_3 (0.55 g, 4.00 mmol). After the reaction mixture was stirred at room temperature for 5 min, $CuSO_4 \cdot 5H_2O$ (0.050 g, 0.20 mmol), and 1,10-phenanthroline (0.072 g, 0.400 mmol) were added. The reaction was stirred at 70 °C until no trace of starting material could be detected on TLC. Upon cooling to room temperature, the reaction mixture was filtered through a pad of Celite and concentrated in vacuo. The crude mixture was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)-methyl)-4-methyl-*N*-(phenylethynyl)benzenesulfonamide (**9a**) (0.65 g, 1.31 mmol, 65%) as a white solid: mp 96–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.33–7.24 (m, 5H), 5.80 (t, J = 3.5 Hz, 1H), 4.28–4.19 (m, 2H), 3.66 (d, J = 13.3 Hz, 1H), 2.45 (s, 3H), 2.12–2.02 (m, 1H), 2.01–1.90 (m, 1H), 1.79–1.59 (m, 3H), 1.55–1.45 (m, 1H), 0.90 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 134.4, 133.3, 131.1, 131.1, 129.6, 128.2, 127.9, 127.5, 123.1, 83.1, 70.8, 65.3, 54.7, 32.2, 25.9, 25.5, 21.6, 18.0, 17.7, −4.3, −4.6; IR (CH_2Cl_2) 2237, 1369, 1171 cm^{-1}; MS (ESI) m/e 518.4 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{28}H_{38}NO_3SSi$ [M + H]$^+$ 496.2342, found 496.2345.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methyl-N-(o-tolylethynyl)benzenesulfonamide (**9b**).* The crude mixture was obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-(bromoethynyl)-2-methylbenzene (0.43 g, 2.20 mmol) purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:70) to give **9b** (0.66 g, 1.30 mmol, 65%) as a white solid: mp 99–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.83 (m, 2H), 7.35–7.33 (m, 2H), 7.26–7.25 (m, 1H), 7.16–7.15 (m, 2H), 7.11–7.07 (m, 1H), 5.79 (t, J = 3.6 Hz, 1H), 4.30–4.27 (m, 2H), 3.64 (d, J = 13.2 Hz, 1H), 2.45 (s, 3H), 2.33 (s, 3H), 2.09–2.04 (m, 1H), 1.97–1.92 (m, 1H), 1.76–1.64 (m, 3H), 1.53–1.47 (m, 1H), 0.90 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 139.4, 134.4, 133.3, 131.2, 131.0, 129.7, 129.3, 127.8, 127.5, 125.4, 122.9, 86.7, 69.9, 65.3, 54.8, 32.2, 25.9, 25.5, 21.6, 20.7, 18.0, 17.7, −4.3, −4.6; IR (CH_2Cl_2) 2235, 1370, 1172 cm^{-1}; MS (ESI) m/e 532.35 ([M + Na]$^+$, 100), 510.53 ([M + H]$^+$, 40); HRMS (ESI) m/e calcd for $C_{29}H_{40}NO_3SSi$ [M + H]$^+$ 510.2498, found 510.2500.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methyl-N-(m-tolylethynyl)benzenesulfonamide (**9c**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-(bromoethynyl)-3-methylbenzene (0.43 g, 2.20 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give **9c** (0.67 g, 1.30 mmol, 65%) as a white solid: mp 51–52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 7.19–7.04 (m, 4H), 5.79 (t, J = 3.6 Hz, 1H), 4.28–4.20 (m, 2H), 3.66 (d, J = 13.3 Hz, 1H), 2.44 (s, 3H), 2.30 (s, 3H), 2.13–1.89 (m, 2H), 1.79–1.59 (m, 3H), 1.56–1.45 (m, 1H), 0.90 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 137.8, 134.4, 133.3, 131.6, 131.0, 129.6, 128.4, 128.1, 128.1, 127.8, 122.8, 82.7, 70.9, 65.3, 54.7, 32.2, 25.9, 25.5, 21.6, 21.2, 18.0, 17.7 (2C), −4.3, −4.7; IR (CH_2Cl_2) 2236, 1369, 1171 cm^{-1}; MS (ESI) m/e 532.3 ([M + Na]$^+$, 100), 510.5 (20); HRMS (ESI) m/e calcd for $C_{29}H_{40}NO_3SSi$ [M + H]$^+$ 510.2498, found 510.2498.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methyl-N-(p-tolylethynyl)benzenesulfonamide (**9d**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-(bromoethynyl)-3-methylbenzene (0.43 g, 2.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:70) to give **9d** (0.61 g, 1.20 mmol, 60%) as a white solid: mp 82–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.82 (m, 2H), 7.35–7.33 (m, 2H), 7.21–7.19 (m, 2H), 7.09–7.07 (m, 2H), 5.79 (t, J = 3.6 Hz, 1H), 4.26–4.20 (m, 2H), 3.66 (d, J = 13.3 Hz, 1H), 2.45 (s, 3H), 2.33 (s, 3H), 2.09–2.03 (m, 1H), 1.96–1.92 (m, 1H), 1.73–1.59 (m, 3H), 1.53–1.45 (m, 1H), 0.89 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 137.7, 134.4, 133.4, 131.2, 131.1, 129.6, 129.0, 127.9, 119.9, 82.4, 70.8, 65.4, 54.8, 32.2, 25.9, 25.5, 21.6, 21.4, 18.0, 17.7, −4.3, −4.6; IR (CH_2Cl_2) 2237, 1369, 1171 cm^{-1}; MS (ESI) m/e 532.3 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{29}H_{40}NO_3SSi$ [M + H]$^+$ 510.2498, found 510.2498.

*N-([1,1′-Biphenyl]-4-ylethynyl)-N-((6-((tert-butyldimethylsilyl)-oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (**9e**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)- 4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 4-(bromoethynyl)-1,1′- biphenyl (0.57 g, 2.20 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give **9e** (0.73 g, 1.28 mmol, 64%) as a white solid: mp 147–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.83 (m, 2H), 7.60–7.55 (m, 2H), 7.54–7.50 (m, 2H), 7.47–7.41 (m, 2H), 7.40–7.34 (m, 5H), 5.81 (t, J = 3.6 Hz, 1H), 4.29–4.22 (m, 2H), 3.69 (d, J = 13.3 Hz, 1H), 2.46 (s, 3H), 2.14–1.91 (m, 2H), 1.80–1.60 (m, 3H), 1.59–1.46 (m, 1H), 0.91 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 140.4, 140.3, 134.4, 133.3, 131.5, 131.1, 129.7, 128.8, 127.9, 127.5, 126.9, 126.9, 122.0, 83.8, 70.8, 65.4, 54.8, 32.2, 25.9, 25.5, 21.6, 18.0, 17.7, −4.3, −4.6; IR (CH_2Cl_2) 2235, 1369, 1171 cm^{-1}; MS (ESI) m/e 594.3 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{34}H_{42}NO_3SSi$ [M + H]$^+$ 572.2655, found 572.2656.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methyl-N-(naphthalen-1-ylethynyl)benzenesulfonamide (**9f**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-(bromoethynyl)naphthalene (0.51 g, 2.20 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give **9f** (0.33 g, 0.60 mmol, 30%) as a yellow solid: mp 105–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20–8.15 (m, 1H), 7.91–7.87 (m, 2H), 7.84–7.80 (m, 1H), 7.78–7.74 (m, 1H), 7.54–7.46 (m, 3H), 7.41–7.32 (m, 3H), 5.89 (t, J = 3.7 Hz, 1H), 4.39–4.31 (m, 2H), 3.73 (d, J = 13.2 Hz, 1H), 2.44 (s, 3H), 2.15–1.95 (m, 2H), 1.82–1.64 (m, 3H), 1.59–1.49 (m, 1H), 0.91 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 134.4, 133.5, 133.2, 133.1, 131.3, 129.8, 129.1, 128.2, 127.9, 127.8, 126.5, 126.3 (2C), 125.2, 120.9, 87.6, 69.5, 65.4, 54.8, 32.3, 25.9, 25.5, 21.6, 18.1, 17.8, −4.3, −4.6; IR (CH_2Cl_2) 2232, 1369, 1171 cm^{-1}; MS (ESI) m/e 568.3 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{32}H_{40}NO_3SSi$ [M + H]$^+$ 546.2498, found 546.2501.

*Methyl 3-((N-((6-((tert-Btyldimethylsilyl)oxy)cyclohex-1-en-1-yl)-methyl)-4-methylphenylsulfonamido)ethynyl)benzoate (**9g**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with methyl 3-(bromoethynyl)-benzoate (0.53 g, 2.20 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give **9g** (0.44 g, 0.80 mmol, 40%) as a white solid: mp = 61–62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.95 (m, 1H), 7.93–7.90 (m, 1H), 7.86–7.82 (m, 2H), 7.50–7.46 (m, 1H), 7.39–7.33 (m, 3H), 5.80 (t, J = 3.7 Hz, 1H), 4.28–4.21 (m, 2H), 3.92 (s, 3H), 3.70 (d, J = 13.4 Hz, 1H), 2.46 (s, 3H), 2.14–1.91 (m, 2H), 1.80–1.59 (m, 3H), 1.57–1.46 (m, 1H), 0.90 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 144.7, 135.0, 134.3, 133.2, 132.1, 131.1, 130.3, 129.7, 128.4, 128.4, 127.8, 123.6, 84.1, 70.1, 65.4, 54.7, 52.2, 32.2, 25.9, 25.5, 21.6, 18.0, 17.7, −4.3, −4.7; IR (CH_2Cl_2) 1727, 1370, 1255, 1171 cm^{-1}; MS (ESI) m/e 576.3 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{30}H_{40}NO_5SSi$ [M + H]$^+$ 554.2396, found 554.2398.

*Methyl 4-(((N-((6-((tert-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4- methylphenyl)sulfonamido)ethynyl)benzoate (**9h**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en- 1-yl)methyl)-4-methyl-

DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543–11557

benzenesulfonamide (0.79 g, 2.00 mmol) with methyl 4-(bromoethynyl)benzoate (0.53 g, 2.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:70) to give **9h** (0.39 g, 0.70 mmol, 35%) as a white solid: mp 113−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.93 (m, 2H), 7.84−7.82 (m, 2H), 7.37−7.32 (m, 4H), 5.80 (t, J = 3.6 Hz, 1H), 4.27−4.22 (m, 2H), 3.91 (s, 3H), 3.70 (d, J = 13.4 Hz, 1H), 2.45 (s, 3H), 2.11−2.05 (m, 1H), 1.98−1.94 (m, 1H), 1.76−1.61 (m, 3H), 1.53−1.48 (m, 1H), 0.90 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 134.3, 133.2, 131.2, 130.5, 130.3, 129.7, 129.4, 128.6, 128.1, 127.8, 86.5, 71.0, 65.3, 54.7, 52.1, 32.2, 25.9, 25.5, 21.6, 18.0, 17.7, −4.3, −4.7; IR (CH_2Cl_2) 2232, 1724, 1372, 1275, 1172 cm^{-1}; MS (ESI) m/e 576.32 ([M + Na]$^+$, 100), 554.46 ([M + H]$^+$, 60); HRMS (ESI) m/e calcd for $C_{30}H_{40}NO_5SSi$ [M + H]$^+$ 554.2396, found 554.2394.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-N-((4-fluorophenyl)ethynyl)-4-methylbenzenesulfonamide (**9i**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-(bromoethynyl)-4-fluorobenzene (0.44 g, 2.20 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give **9i** (0.47 g, 0.92 mmol, 46%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.80 (m, 2H), 7.38−7.33 (m, 2H), 7.31−7.25 (m, 2H), 7.01−6.94 (m, 2H), 5.78 (t, J = 3.6 Hz, 1H), 4.27−4.18 (m, 2H), 3.68 (d, J = 13.4 Hz, 1H), 2.46 (s, 3H), 2.12−1.88 (m, 2H), 1.78−1.56 (m, 3H), 1.54−1.45 (m, 1H), 0.89 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1 ($^1J_{C-F}$ = 247.2 Hz, d), 144.5, 134.4, 133.3, 133.1 ($^3J_{C-F}$ = 8.2 Hz, d), 130.9, 130.0, 129.7, 129.2, 127.8, 119.1, 119.1, 115.5 ($^2J_{C-F}$ = 21.9 Hz, d), 82.7, 65.4, 54.7, 32.2, 25.9, 25.5, 21.6, 18.0, 17.7, −4.3, −4.7; ^{19}F NMR (375 MHz, $CDCl_3$) δ −112.8; IR (CH_2Cl_2) 2239, 1368, 1171, 1091 cm^{-1}; MS (ESI) m/e 536.4 ([M + Na]$^+$, 100), 400.4 (10); HRMS (ESI) m/e calcd for $C_{28}H_{37}NO_3SFSi$ [M + H]$^+$ 514.2247, found 514.2248.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-N-((4-chlorophenyl)ethynyl)-4-methylbenzenesulfonamide (**9j**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex- 1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-(bromoethynyl)-4-chlorobenzene (0.47 g, 2.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:70) to give **9j** (0.42 g, 0.80 mmol, 40%) as a white solid: mp 85−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.81 (m, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.26−7.21 (m, 4H), 5.78 (t, J = 3.6 Hz, 1H), 4.24−4.21 (m, 2H), 3.68 (d, J = 13.4 Hz, 1H), 2.46 (s, 3H), 2.10−2.04 (m, 1H), 1.96−1.91 (m, 1H), 1.73−1.61 (m, 3H), 1.53−1.49 (m, 1H), 0.90 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 134.4, 133.5, 133.3, 132.3, 131.1, 129.7, 128.6, 127.8, 121.6, 84.1, 69.9, 65.4, 54.7, 32.2, 25.9, 25.5, 21.6, 18.0, 17.7, −4.3, −4.6; IR (CH_2Cl_2) 2236, 1370, 1171, 775 cm^{-1}; MS (ESI) m/e 552.23 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{28}H_{37}ClNO_3SSi$ [M + H]$^+$ 530.1952, found 530.1951.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-N-((4-methoxyphenyl)ethynyl)-4-methylbenzenesulfonamide (**9k**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-(bromoethynyl)-4-methoxybenzene (0.46 g, 2.20 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give **9k** (0.31 g, 0.60 mmol, 30%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.28−7.23 (m, 2H), 6.84−6.78 (m, 2H), 5.78 (t, J = 3.7 Hz, 1H), 4.28−4.17 (m, 2H), 3.79 (s, 3H), 3.67 (d, J = 13.4 Hz, 1H), 2.45 (s, 3H), 2.13−1.87 (m, 2H), 1.78−1.57 (m, 3H), 1.54−1.44 (m, 1H), 0.89 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 144.4, 134.4, 133.4, 133.1, 130.9, 129.6, 127.8, 115.0, 113.8, 81.6, 70.3, 65.4, 55.3, 54.8, 32.2, 25.9, 25.8, 25.4, 21.6, 18.0, 17.7, −4.3, −4.7; IR (CH_2Cl_2) 2246, 1360, 1251, 1169 cm^{-1}; MS (ESI) m/e 548.4 ([M + Na]$^+$, 65), 526.4 ([M + H]$^+$, 43), 426.4 (65), 412.4 (100); HRMS (ESI) m/e calcd for $C_{29}H_{40}NO_4SSi$ [M + H]$^+$ 526.2447, found 526.2449.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methyl-N-(oct-1-yn-1-yl)benzenesulfonamide (**9l**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 1-bromooct-1-yne (0.42 g, 2.20 mmol) was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:35) to give **9l** (0.78 g, 1.55 mmol, 78%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.75 (m, 2H), 7.35−7.30 (m, 2H), 5.71 (t, J = 3.7 Hz, 1H), 4.20 (t, J = 4.3 Hz, 1H), 4.09 (dd, J = 13.5, 1.3 Hz, 1H), 3.53 (d, J = 13.5 Hz, 1H), 2.44 (s, 3H), 2.21 (t, J = 6.9 Hz, 2H), 2.10−1.86 (m, 2H), 1.77−1.56 (m, 3H), 1.54−1.38 (m, 3H), 1.36−1.19 (m, 7H), 0.91−088 (m, 11H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 134.5, 133.5, 130.4, 129.4, 127.8, 73.7, 70.1, 65.3, 54.6, 32.2, 31.3, 28.9, 28.4, 25.9, 25.4, 22.6, 21.6, 18.4, 18.0, 17.7, 14.0, −4.4, −4.7; IR (CH_2Cl_2) 2254, 1367, 1170 cm^{-1}; MS (ESI) m/e 526.5 ([M + Na]$^+$, 100), 504.6 ([M + H]$^+$, 75), 390.5 (30); HRMS (ESI) m/e calcd for $C_{28}H_{46}NO_3SSi$ [M + H]$^+$ 504.2968, found 504.2969.

*N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methyl-N-(thiophene-3-ylethynyl)benzenesulfonamide (**9p**).* The crude mixture obtained from the coupling reaction of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4-methylbenzenesulfonamide (0.79 g, 2.00 mmol) with 3-(bromoethynyl)thiophene (0.41 g, 2.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:50) to give **9p** (0.46 g, 0.92 mmol, 46%) as a white solid: mp 89−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.81 (m, 2H), 7.36−7.34 (m, 2H), 7.31−7.30 (m, 1H), 7.26−7.23 (m, 1H), 7.01−7.00 (m, 1H), 5.78 (t, J = 3.6 Hz, 1H), 4.24−4.17 (m, 2H), 3.70 (d, J = 13.5 Hz, 1H), 2.45 (s, 3H), 2.08−1.91 (m, 2H), 1.71−1.61 (m, 3H), 1.52−1.46 (m, 1H), 0.89 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 134.5, 133.3, 130.8, 130.1, 129.6, 128.1, 127.8, 125.0, 121.8, 82.4, 65.7, 65.4, 54.8, 32.2, 25.9, 25.4, 21.6, 18.0, 17.7, −4.3, −4.7; IR (CH_2Cl_2) 2136, 1370, 1187 cm^{-1}; MS (ESI) m/e 524.28 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{26}H_{36}NO_3S_2Si$ [M + H]$^+$ 502.1906, found 502.1907.

*Synthesis of N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-4- methyl-N-(prop-1-yn-1-yl)benzenesulfonamide (**9m**).* To a solution of **9o** (0.42 g, 1.00 mmol) in THF (5.0 mL) at −78 °C was added *n*-BuLi (0.7 mL, 1.6 M in hexanes) via syringe. The mixture was slowly warmed to −30 °C over 1 h, followed by addition of methyl iodide (0.07 mL). The mixture was slowly warmed to room temperature over 30 min. The crude mixture was diluted with EtOAc (30.0 mL). The solution washed with saturated $NaHCO_{3(aq)}$ (30.0 mL). The water layer was extracted with EtOAc (50.0 mL × 3). The combined organic layers were washed with water (100.0 mL ×3) and saturated aqueous NaCl solution (100.0 mL × 3), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the crude product. The crude mixture was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:50) to give **9m** (0.22 g, 0.50 mmol, 50%) as a white solid: mp 70−71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.76 (m, 2H), 7.34−7.32 (m, 2H), 5.72 (t, J = 3.6, 1H), 4.19−4.17 (m, 1H), 4.06−4.02 (m, 1H), 3.62 (d, J = 13.9 Hz, 1H), 2.45 (s, 3H), 2.05−1.94 (m, 2H) 1.86 (s, 3H), 1.73−1.65 (m, 2H), 1.52−1.45 (m, 1H), 1.32−1.25 (m, 1H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 134.7, 133.5, 130.0, 129.5, 127.7, 72.8, 65.4, 65.2, 54.7, 32.2, 25.9, 25.4, 21.6, 18.0, 17.7, 3.3, −4.3, −4.7; IR (CH_2Cl_2) 2261, 1366, 1171 cm^{-1}; MS (ESI) m/e 456.35 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{36}NO_3SSi$ [M + H]$^+$434.2185, found 434.2186.

*Synthesis of N-(But-1-yn-1-yl)-N-((6-((tert-butyldimethylsilyl)oxy)-cyclohex-1- en-1-yl)methyl)-4-methylbenzenesulfonamide (**9n**).* To a solution of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)-methyl)-4-methylbenzenesulfonamide (4.35 g, 11.0 mmol) in THF (50.0 mL) at 0 °C was added *n*-BuLi (7.6 mL, 1.6 M in hexanes). After 5 min of stirring, a solution of formylbenzotriazole (1.94 g, 13.20 mmol) in THF (17.0 mL) was added. The reaction mixture was allowed to stir for 4 h at room temperature. The crude mixture was diluted with EtOAc (50.0 mL) and washed with a saturated aqueous

DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557

solution of $NaHCO_3$ (50.0 mL). The water layer was extracted with EtOAc (50.0 mL × 3). The combined organic layers were washed with water (100.0 mL × 3) and saturated aqueous NaCl solution (100.0 mL × 3), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the crude product, which was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:50) to give *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-*N*-tosylformamide as a white solid (3.73 g, 8.80 mmol, 80%). To a solution of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-*N*-tosylformamide (4.93 g, 11.64 mmol) and PPh_3 (9.16 g, 34.91 mmol) in THF (116.0 mL) was added CCl_4 (9.4 mL) via syringe over a period of 5 h at 70 °C. After being stirred for an additional 1 h, the mixture was diluted with EtOAc (100.0 mL). The solution was washed with water (100.0 mL × 3) and saturated aqueous NaCl solution (100.0 mL × 3), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the crude product. The crude mixture was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:50) to give *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)-methyl)-*N*-(2,2-dichlorovinyl)-4-methylbenzenesulfonamide as a white solid (4.57 g, 9.31 mmol, 80%). To a solution of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-*N*-(2,2-dichlorovinyl)-4-methylbenzenesulfonamide (0.74 g, 1.50 mmol) in THF (7.5 mL) at −78 °C was added *n*-BuLi (2.1 mL, 1.6 M in hexanes) via syringe. The mixture was slowly warmed to −30 °C over 1 h, followed by addition of ethyl iodide (0.14 mL). The mixture was slowly warmed to room temperature over 4 h. The crude mixture was diluted with EtOAc (30.0 mL) and then washed with a saturated aqueous solution of $NaHCO_{3(aq)}$. The water layer was extracted with EtOAc (50.0 mL × 3). The combined organic layers were washed with water (50.0 mL × 3) and saturated aqueous NaCl solution (50.0 mL × 3), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the crude product, which was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:50) to give **9n** (0.27 g, 0.60 mmol, 40%) as a white solid: mp 55−56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.76 (m, 2H), 7.34−7.32 (m, 2H), 5.72 (t, J = 3.6 Hz, 1H), 4.21−4.19 (m, 1H), 4.10−4.07 (m, 1H), 3.54 (d, J = 13.4 Hz, 1H), 2.45 (s, 3H), 2.26−2.20 (q, 2H), 2.07−2.02 (m, 1H), 1.95−1.93 (m, 1H), 1.74−1.66 (m, 2H), 1.64−1.58 (m, 1H), 1.51−1.47 (m, 1H), 1.09 (d, J = 7.5 Hz, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 134.5, 133.5, 130.5, 129.4, 127.8, 73.3, 71.4, 65.3, 54.6, 32.2, 25.9, 25.4, 21.6, 18.0, 17.7, 14.2, 12.2, −4.4, −4.7; IR (CH_2Cl_2) 2256, 1367, 1171 cm^{-1}; MS (ESI) m/e 470.53 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{38}NO_3SSi$ [M + H]$^+$ 448.2342, found 448.2341.

*Synthesis of N-((6-((tert-Butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)methyl)-N-ethynyl-4-methylbenzenesulfonamide (**9o**).* To a solution of *N*-((6-((*tert*-butyldimethylsilyl)oxy)cyclohex-1-en-1-yl)-methyl)-*N*-(2,2-dichlorovinyl)-4-methylbenzenesulfonamide (1.47 g, 3.00 mmol) in THF (15.0 mL) at −78 °C was added *n*-BuLi (4.1 mL, 1.6 M in hexanes) via syringe. The mixture was slowly warmed to −30 °C over 1 h, followed by addition of a saturated aqueous solution of $NaHCO_{3(aq)}$. The mixture was slowly warmed to room temperature over 30 min. The crude mixture was diluted with EtOAc (30.0 mL). The resulting solution was washed with a saturated aqueous solution of $NaHCO_{3(aq)}$ (30.0 mL). The water layer was extracted with EtOAc (50.0 mL × 3). The combined organic layers were washed with water (100.0 mL × 3) and saturated aqueous NaCl solution (100.0 mL × 3), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the crude product, which was purified via flash column chromatography over silica gel (EtOAc/hexanes = 1:50) to give **9o** (0.57 g, 1.36 mmol, 46%) as a white solid: mp 89−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.78 (m, 2H), 7.36−7.33 (m, 2H), 5.73 (t, J = 3.6 Hz, 1H), 4.19−4.17 (m, 1H), 4.12−4.08 (m, 1H), 3.66 (d, J = 13.8 Hz, 1H), 2.67 (s, 1H), 2.45 (s, 3H), 2.07−2.01 (m, 1H), 1.95−1.90 (m, 1H), 1.73−1.58 (m, 3H), 1.52−1.45 (m, 1H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 134.5, 133.1, 130.6, 129.6, 127.8, 65.4, 58.9, 54.3, 32.1, 25.9, 25.3, 21.6, 18.0, 17.7, −4.3, −4.7; IR (CH_2Cl_2) 2136, 1370, 1172 cm^{-1}; MS (ESI) m/e 442.46 ([M + Na]$^+$, 100), 420.53 ([M + H]$^+$, 30); HRMS (ESI) m/e calcd for $C_{22}H_{34}NO_3SSi$ [M + H]$^+$ 420.2029, found 420.2031

Representative Experimental Procedure for the Cyclolactamization/Epimerization of TBS-Protected *N*-Tosyl-2-((arylethynyl)amino)methyl)cyclohex-2-enols. Synthesis of Aryl-Substituted Hexahydroisoquinolin-3-(*2H*)-one Derivatives 10a−k. *Example for the Synthesis of **10a**.* To a solution of **9a** (0.10 g, 0.20 mmol) in toluene (2.0 mL) at room temperature under air was added $BF_3{\cdot}OEt_2$ (54.0 μL, 0.44 mmol). The reaction mixture was stirred for 2 min until no **9a** could be detected by TLC. The reaction mixture was quenched with 5 mL of saturated $NaHCO_{3(aq)}$ and 5 mL of EtOAc. The organic phase was separated, and the aqueous phase was extracted with EtOAc (15.0 mL × 3). The combined organic solution was washed with water (50 mL × 3) and saturated aqueous NaCl solution (50 mL × 3), dried over anhydrous $MgSO_4$, and concentrated in vacuo to give the crude mixture **10a** and **10a′**. To a solution of the crude mixture **10a** and **10a′** in EtOAc (2.0 mL) at room temperature under air was added DBU (33.0 μL, 0.22 mmol). The reaction mixture was stirred for 30 min until no **10a′** could be detected by TLC. The reaction mixture was concentrated and purified by flash column chromatography (EA/hexanes = 1:7) to give (4*R**,4a*S**)-4-phenyl-2-tosyl-1,2,4a,5,6,7-hexahydroisoquinolin-3(4*H*)-one (**10a**) (0.050 g, 0.13 mmol, 65% over the two steps) as a white solid: mp 187−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.88 (m, 2H), 7.31−7.20 (m, 5H), 7.05−7.01 (m, 2H), 5.91−5.85 (m, 1H), 4.73−4.66 (m, 1H), 4.49−4.42 (m, 1H), 3.24 (d, J = 12.1 Hz, 1H), 2.67−2.56 (m, 1H), 2.41 (s, 3H), 2.15−2.00 (m, 2H), 1.68−1.56 (m, 1H), 1.52−1.38 (m, 2H), 1.17−1.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 144.6, 137.1, 135.9, 130.2, 129.3, 129.0 128.7, 128.5, 127.3, 125.3, 57.0, 51.2, 38.4, 27.0, 25.0, 21.6, 19.9; IR (CH_2Cl_2) 1697, 1355, 1169 cm^{-1}; MS (ESI) m/e 404.4 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{22}H_{24}NO_3S$ [M + H]$^+$ 382.1477, found 382.1478. Crystals suitable for X-ray diffraction analysis were grown from acetone and hexanes.[17]

(4R,4aS*)-4-(o-Tolyl)-2-tosyl-1,4,4a,5,6,7-hexahydroisoquinolin-3(2H)-one (**10b**).* The crude mixture obtained from cyclolactamization/epimerization of **9b** (0.10 g, 0.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:10) to give **10b** (0.051 g, 0.13 mmol, 65% over the two steps) as a white solid: mp 199−200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.90 (m, 2H), 7.28−7.26 (m, 2H), 7.12−7.07 (m, 3H), 6.93−6.91 (m, 1H), 5.93−5.92 (m, 1H), 4.63−4.50 (m, 2H), 3.49−3.46 (d, J = 12.0 Hz, 1H), 2.66−2.64 (m, 1H), 2.41 (s, 3H), 2.10−2.08 (m, 5H), 1.64−1.58 (m, 1H), 1.55−1.43 (m, 2H), 1.19−1.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 144.6, 136.2, 136.1, 135.9, 130.9, 130.1, 129.5, 129.2, 128.8, 127.3, 126.1, 125.8, 54.3, 51.7, 37.6, 26.7, 25.1, 21.6, 20.0, 19.8; IR (CH_2Cl_2) 1688, 1353, 1186 cm^{-1}; MS (ESI) m/e 418.38 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_3S$ [M + H]$^+$ 396.1633, found 396.1637.

(4R,4aS*)-4-(m-Tolyl)-2-tosyl-1,2,4a,5,6,7-hexahydroisoquinolin-3(4H)-one (**10c**).* The crude mixture obtained from cyclolactamization/epimerization of **9c** (0.10 g, 0.20 mmol) was purified via flash column chromatography over silica gel (EA/hexanes = 1:7) to give **10c** (0.047 g, 0.12 mmol, 59% over the two steps) as a white solid: mp 134−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.89 (m, 2H), 7.30−7.25 (m, 2H), 7.18−7.13 (m, 1H), 7.06−7.01 (m, 1H), 6.85−6.79 (m, 2H), 5.90−5.86 (m, 1H), 4.71−4.64 (m, 1H), 4.48−4.42 (m, 1H), 3.19 (d, J = 12.1 Hz, 1H), 2.65−2.55 (m, 1H), 2.41 (s, 3H), 2.28 (s, 3H), 2.13−2.02 (m, 2H), 1.67−1.56 (m, 1H), 1.53−1.39 (m, 2H), 1.18−1.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 144.6, 138.1, 137.2, 135.9, 130.3, 129.6, 129.3, 128.8, 128.4, 128.2, 126.0, 125.3, 57.0, 51.3, 38.4, 27.0, 25.0, 21.6, 21.4, 19.9; IR (CH_2Cl_2) 1694, 1354, 1169 cm^{-1}; MS (ESI) m/e 418.3 ([M + Na]$^+$, 100), 197.3 (10); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_3S$ [M + H]$^+$ 396.1633, found 396.1636.

(4R,4aS*)-4-(p-Tolyl)-2-tosyl-1,4,4a,5,6,7-hexahydroisoquinolin-3(2H)-one (**10d**).* The crude mixture obtained from cyclolactamization/epimerization of **9d** (0.10 g, 0.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:10) to give **10d** as a white solid (0.045 g, 0.11 mmol, 57% over the two steps): mp 182−183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.89 (m, 2H), 7.28−7.26 (m, 2H), 7.09−7.07 (m, 2H), 6.93−6.91 (m, 2H),

DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557

5.87−5.86 (m, 1H), 4.70−4.66 (m, 1H), 4.46−4.42 (m, 1H), 3.21−3.18 (d, J = 12.1 Hz, 1H), 2.60−2.59 (m, 1H), 2.40 (s, 3H), 2.29 (s, 3H), 2.07 (m, 2H), 1.64−1.59 (m, 1H), 1.52−1.41 (m, 2H), 1.16−1.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 144.6, 137.0, 136.0, 134.1, 130.4, 129.3, 129.3, 128.8, 125.2, 56.6, 51.2, 38.3, 27.1, 25.0, 21.6, 21.1, 20.0; IR (CH_2Cl_2) 1696, 1355, 1186 cm^{-1}; MS (ESI) m/e 418.4 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_3S$ [M + H]$^+$ 396.1633, found 396.1634.

(4R,4aS*)-4-([1,1′-Biphenyl]-4-yl)-2-tosyl-1,2,4a,5,6,7-hexahydroisoquinolin-3(4H)-one (**10e**).* The crude mixture obtained from cyclolactamization/epimerization of **9e** (0.11 g, 0.20 mmol) was purified via flash column chromatography over silica gel (EA/hexanes = 1:7) to give **10e** (0.062 g, 0.14 mmol, 68% over the two steps) as a white solid: mp 162−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.90 (m, 2H), 7.56−7.48 (m, 4H), 7.44−7.38 (m, 2H), 7.35−7.26 (m, 3H), 7.13−7.08 (m, 2H), 5.92−5.87 (m, 1H), 4.75−4.68 (m, 1H), 4.50−4.44 (m, 1H), 3.29 (d, J = 12.1 Hz, 1H), 2.71−2.60 (m, 1H), 2.41 (s, 3H), 2.14−2.04 (m, 2H), 1.70−1.60 (m, 1H), 1.58−1.41 (m, 2H), 1.23−1.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 144.7, 140.8, 140.3, 136.2, 135.9, 130.2, 129.4, 129.3, 128.8, 128.7, 127.4, 127.2, 127.1, 125.4, 56.7, 51.2, 38.4, 27.1, 25.0, 21.6, 20.0; IR (CH_2Cl_2) 1695, 1355, 1170 cm^{-1}; MS (ESI) m/e 480.3 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{28}H_{28}NO_3S$ [M + H]$^+$ 458.1790, found 458.1790.

(4R,4aS*)-4-(Naphthalen-1-yl)-2-tosyl-1,2,4a,5,6,7-hexahydroisoquinolin-3(4H)-one (**10f**).* The crude mixture obtained from cyclolactamization/epimerization of **9f** (0.10 g, 0.20 mmol) was purified via flash column chromatography over silica gel (EA/hexanes = 1:7) to give **10f** (0.048 g, 0.11 mmol, 55% over the two steps) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.3 Hz, 2H), 7.81 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.46−7.32 (m, 3H), 7.28−7.19 (m, 4H), 6.01−5.96 (m, 1H), 4.77−4.69 (m, 1H), 4.66−4.59 (m, 1H), 3.82 (d, J = 11.2 Hz, 1H), 2.96−2.84 (m, 1H), 2.39 (s, 3H), 2.14−2.03 (m, 2H), 1.65−1.53 (m, 1H), 1.44−1.31 (m, 2H), 1.18−1.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 144.7, 135.7, 134.3, 133.8, 130.1, 129.3, 129.2, 128.9, 128.4 (2C), 126.2, 125.8, 125.3, 125.2, 123.5, 52.0, 37.5, 27.2, 25.1, 21.6, 19.6; IR (CH_2Cl_2) 1692, 1355, 1187 cm^{-1}; MS (ESI) m/e 454.4 ([M + Na]$^+$, 100), 233.4 (10); HRMS (ESI) m/e calcd for $C_{26}H_{26}NO_3S$ [M + H]$^+$ 432.1633, found 432.1632.

Methyl 3-((4R,4aS*)-3-Oxo-2-tosyl-1,2,3,4,4a,5,6,7-octahydroisoquinolin-4-yl)benzoate (**10g**).* The crude mixture obtained from cyclolactamization/epimerization of **9g** (0.11 g, 0.20 mmol) was purified via flash column chromatography over silica gel (EA/hexanes = 1:7) to give **10g** (0.055 g, 0.13 mmol, 63% over the two steps) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.87 (m, 3H), 7.72 (t, J = 1.6 Hz, 1H), 7.37 (t, J = 7.7 Hz, 1H), 7.31−7.23 (m, 3H), 5.93−5.88 (m, 1H), 4.75−4.68 (m, 1H), 4.51−4.44 (m, 1H), 3.89 (s, 3H), 3.31 (d, J = 12.3 Hz, 1H), 2.72−2.62 (m, 1H), 2.41 (s, 3H), 2.14−2.04 (m, 2H), 1.69−1.58 (m, 1H), 1.50−1.38 (m, 2H), 1.15−1.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 166.8, 144.8, 137.4, 135.8, 133.7, 130.5, 130.2, 129.9, 129.4, 128.7 (3C), 125.6, 56.8, 52.1, 51.0, 38.2, 27.1, 25.0, 21.6, 20.0; IR (CH_2Cl_2) 1719, 1356, 1288, 1170 cm^{-1}; MS (ESI) m/e 462.3 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{26}NO_5S$ [M + H]$^+$ 440.1532, found 440.1532.

Methyl 4-((4R,4aS*)-3-Oxo-2-tosyl-1,2,3,4,4a,5,6,7-octahydroisoquinolin-4-yl)benzoate (**10h**).* The crude mixture obtained from cyclolactamization/epimerization of **9h** (0.11 g, 0.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:10) to give **10h** (0.050 g, 0.11 mmol, 57% over the two steps) as a white solid: mp 175−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.94 (m, 2H), 7.91−7.89 (m, 2H), 7.29−7.27 (m, 2H), 7.12−7.10 (m, 2H), 5.91−5.90 (m, 1H), 4.72−4.68 (m, 1H), 4.48−4.45 (m, 1H), 3.89 (s, 3H), 3.33−3.30 (d, J = 12.2 Hz, 1H), 2.63−2.62 (m, 1H), 2.42 (s, 3H), 2.09 (m, 2H), 1.65−1.59 (m, 1H), 1.48−1.41 (m, 2H), 1.13−1.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 166.7, 144.8 142.3, 135.7, 129.8, 129.8, 129.3, 129.3, 129.1, 128.7, 125.6, 56.9, 52.1, 51.1, 38.3, 26.9, 24.9, 21.6, 19.9; IR (CH_2Cl_2) 1719, 1356, 1282, 1170 cm^{-1}; MS (ESI) m/e 462.4 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{24}H_{26}NO_5S$ [M + H]$^+$ 440.1532, found 440.1528.

(4R,4aS*)-4-(4-Fluorophenyl)-2-tosyl-1,2,4a,5,6,7-hexahydroisoquinolin-3(4H)-one (**10i**).* The crude mixture obtained from cyclolactamization/epimerization of **9i** (0.10 g, 0.20 mmol) was purified via flash column chromatography over silica gel (EA/hexanes = 1:7) to give **10i** (0.049 g, 0.12 mmol, 61% over the two steps) as a white solid: mp 173−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.88 (m, 2H), 7.30−7.26 (m, 2H), 7.03−6.94 (m, 4H), 5.91−5.86 (m, 1H), 4.74−4.67 (m, 1H), 4.48−4.41 (m, 1H), 3.23 (d, J = 12.2 Hz, 1H), 2.63−2.52 (m, 1H), 2.41 (s, 3H), 2.14−2.03 (m, 2H), 1.68−1.58 (m, 1H), 1.51−1.41 (m, 2H), 1.15−1.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 162.0 ($^1J_{C-F}$ = 247.2 Hz, d), 144.8, 135.8, 132.8 ($^4J_{C-F}$ = 3.2 Hz, d), 130.6 ($^3J_{C-F}$ = 8.0 Hz, d), 130.0, 129.3, 128.7, 125.4, 115.5 ($^2J_{C-F}$ = 21.4 Hz, d), 56.2, 51.0, 38.4, 27.0, 25.0, 21.6, 20.0; ^{19}F NMR (375 MHz, $CDCl_3$) δ −116.1; IR (CH_2Cl_2) 1711, 1358, 1221, 1187 cm^{-1}; MS (ESI) m/e 422.3 ([M + Na]$^+$, 100), 400.5 (43), 201.5 (15); HRMS (ESI) m/e calcd for $C_{22}H_{23}NO_3SF$ [M + H]$^+$ 400.1383, found 400.1385.

(4R,4aS*)-4-(4-Chlorophenyl)-2-tosyl-1,4,4a,5,6,7-hexahydroisoquinolin-3(2H)-one (**10j**).* The crude mixture obtained from cyclolactamization/epimeriation of **9j** (0.11 g, 0.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:10) to give **10j** (0.050 g, 0.12 mmol, 60% over the two steps) as a white solid: mp 185−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.89 (m, 2H), 7.29−7.24 (m, 4H), 6.98−6.96 (m, 2H), 5.90−5.89 (m, 1H), 4.71−4.67 (m, 1H), 4.46−4.43 (m, 1H), 3.24−3.21 (d, J = 12.3 Hz, 1H), 2.57 (m, 1H), 2.42 (s, 3H), 2.09 (m, 2H), 1.65−1.61 (m, 1H), 1.51−1.42 (m, 2H), 1.13−1.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 144.8, 135.8, 135.5, 133.3, 130.4, 129.9, 129.3, 128.8, 125.5, 56.4, 51.0, 38.3, 27.0, 25.0, 21.7, 20.0; IR (CH_2Cl_2) 1692, 1356, 1187, 816 cm^{-1}; MS (ESI) m/e 438.4 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{22}H_{23}ClNO_3S$ [M + H]$^+$ 416.1087, found 416.1087. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.[17]

(4R,4aS*)-4-(4-Methoxyphenyl)-2-tosyl-1,2,4a,5,6,7-hexahydroisoquinolin-3(4H)-one (**10k**).* The crude mixture obtained from spirolactamization/epimerization of **9k** (0.10 g, 0.20 mmol) was purified via flash column chromatography over silica gel (EA/hexanes = 1:7) to give **10k** as a white solid (0.018 g, 0.043 mmol, 22% over the two steps): mp 187−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.88 (m, 2H), 7.30−7.24 (m, 2H), 6.98−6.93 (m, 2H), 6.85−6.79 (m, 2H), 5.89−5.84 (m, 1H), 4.73−4.65 (m, 1H), 4.47−4.40 (m, 1H), 3.77 (s, 3H), 3.18 (d, J = 12.2 Hz, 1H), 2.62−2.52 (m, 1H), 2.41 (s, 3H), 2.14−2.02 (m, 2H), 1.68−1.54 (m, 1H), 1.54−1.39 (m, 2H), 1.17−1.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 158.8, 144.6, 135.9, 130.4, 130.0, 129.3, 129.1, 128.8, 125.1, 114.1, 56.2, 55.2, 51.1, 38.4, 27.1, 25.0, 21.6, 20.0; IR (CH_2Cl_2) 1702, 1354, 1249, 1169 cm^{-1}; MS (ESI) m/e 434.4 ([M + Na]$^+$, 100), 213.3 (10); HRMS (ESI) m/e calcd for $C_{23}H_{26}NO_4S$ [M + H]$^+$ 412.1583, found 412.1581.

Representative Experimental Procedure for the Cyclolactamization/Epimerization of TBS-Protected *N*-Tosyl-2-((alkylethynyl)amino)methyl)cyclohex-2-enols. Synthesis of Alkyl-Substituted Hexahydroisoquinolin-3-(*2H*)-one Derivatives 10l−o. *Example for the Synthesis of **10l**.* To a solution of **9l** (0.10 g, 0.20 mmol) in toluene (2.0 mL) at room temperature under air was added $BF_3{\cdot}OEt_2$ (54.0 μL, 0.44 mmol). The reaction mixture was stirred for 2 min until no **9l** could be detected by TLC. The reaction mixture was quenched with 5 mL of saturated $NaHCO_{3(aq)}$ and 5 mL of EtOAc. The organic phase was separated, and the aqueous phase was extracted with EtOAc (15.0 mL × 3). The combined organic solution was washed with water (50 mL × 3) and saturated aqueous NaCl solution (50 mL × 3), dried over anhydrous $MgSO_4$, and concentrated in vacuo to give a crude mixture. To a solution of the crude mixture in DMF (2.0 mL) at 60 °C under air was added DBU (33.0 μL, 0.22 mmol). The reaction mixture was stirred for 2 h. The reaction mixture was concentrated and purified by flash column chromatography (EtOAc/hexanes = 1:10) to give (4S*,4aS*)-4-hexyl-2-tosyl-1,2,4a,5,6,7-hexahydroisoquinolin-3(4*H*)-one (**10l**)

DOI: 10.1021/acs.joc.7b02158
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(0.029 g, 0.074 mmol, 37% over the two steps) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.86 (m, 2H), 7.33−7.28 (m, 2H), 5.82−5.77 (m, 1H), 4.49−4.33 (m, 2H), 2.42 (s, 3H), 2.27−2.18 (m, 1H), 2.15−2.01 (m, 3H), 1.94−1.85 (m, 1H), 1.79−1.64 (m, 2H), 1.60−1.42 (m, 2H), 1.32−1.11 (m, 9H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 144.5, 136.3, 131.1, 129.3, 128.5, 124.8, 51.1, 49.5, 35.3, 31.7, 29.5, 28.4, 27.5, 25.6, 24.9, 22.6, 21.6, 20.5, 14.1; IR (CH_2Cl_2) 1694, 1359, 1186 cm^{-1}; MS (ESI) m/e 412.4 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{22}H_{32}NO_3S$ [M + H]$^+$ 390.2103, found 390.2105.

(4S,4aS*)-4-Methyl-2-tosyl-1,4,4a,5,6,7-hexahydroisoquinolin-3(2H)-one (**10m**).* The crude mixture obtained from cyclolactamization/epimerization of **9m** (0.086 g, 0.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:10) to give **10m** as a white solid (0.026 g, 0.081 mmol, 40% over the two steps): mp 98−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.88 (m, 2H), 7.31−7.30 (m, 2H), 5.77 (m, 1H), 4.64−4.60 (m, 1H), 4.35−4.32 (m, 1H), 2.42 (s, 3H), 2.13−2.04 (m, 4H), 2.01−1.93 (m, 1H), 1.77−1.72 (m, 1H), 1.52−1.46 (m, 1H), 1.26−1.20 (m, 1H), 1.15−1.14 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 144.6, 136.2, 130.9, 129.3, 128.5, 124.0, 50.2, 44.1, 38.0, 27.3, 24.9, 21.6, 20.7, 12.9; IR (CH_2Cl_2) 1708, 1355, 1169 cm^{-1}; MS (ESI) m/e 342.4 ([M + Na]$^+$, 100); HRMS (ESI) m/e calcd for $C_{17}H_{22}NO_3S$ [M + H]$^+$ 320.1320, found 320.1321.

(4S,4aS*)-4-Ethyl-2-tosyl-1,4,4a,5,6,7-hexahydroisoquinolin-3(2H)-one (**10n**).* The crude mixture obtained from cyclolactamization/epimerization of **9n** (0.089 g, 0.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:10) to give **10n** (0.026 g, 0.078 mmol, 39% over the two steps) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.88 (m, 2H), 7.31−7.29 (m, 2H), 5.80 (m, 1H), 4.50−4.46 (m, 1H), 4.37−4.34 (m, 1H), 2.42 (s, 3H), 2.13−2.05 (m, 3H), 1.94−1.83 (m, 2H), 1.92−1.83 (m, 2H), 1.72−1.66 (m, 1H), 1.54−1.46 (m, 1H), 1.30−1.22 (m, 1H), 0.81−0.77 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 144.5, 136.3, 130.9, 129.3, 128.5, 124.8, 51.0, 50.1, 34.5, 27.3, 24.9, 21.6, 20.9, 20.5, 9.8; IR (CH_2Cl_2) 1699, 1356, 1169 cm^{-1}; MS (ESI) m/e 356.4 ([M + Na]$^+$, 100), 334.6 ([M + H]$^+$, 50); HRMS (ESI) m/e calcd for $C_{18}H_{24}NO_3S$ [M + H]$^+$ 334.1477, found 334.1479.

*2-Tosyl-1,4,4a,5,6,7-hexahydroisoquinolin-3(2H)-one (**10o**).* The crude mixture obtained from cyclolactamization/epimerization of **9o** (0.084 g, 0.20 mmol) was purified by flash column chromatography over silica gel (EtOAc/hexanes = 1:10) to give **10o** (0.023 g, 0.075 mmol, 38% over the two steps) as a white solid: mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.89 (m, 2H), 7.32−7.30 (m, 2H), 5.82 (m, 1H), 4.49−4.39 (m, 2H), 2.56−2.50 (m, 1H), 2.42 (m, 4H), 2.19−2.12 (s, 1H), 2.09−2.07 (m, 2H), 1.90−1.83 (m, 1H), 1.70−1.63 (m, 1H), 1.55−1.49 (m, 1H), 1.27−1.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ170.3, 144.7, 136.0, 130.6, 129.3, 128.6, 124.8, 51.3, 40.9, 31.5, 28.5, 24.9, 21.6, 20.1; IR (CH_2Cl_2) 1697, 1354, 1169 cm^{-1}; MS (ESI) m/e 328.3 ([M + Na]$^+$, 100),; HRMS (ESI) m/e calcd for $C_{16}H_{20}NO_3S$ [M + H]$^+$ 306.1164, found 306.1165.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02158.

NMR spectra for compounds **1a−n**, **2**, **3a−l**, **4**, **9a−p**, and **10a−o** (PDF)

X-ray crystallographic data for compounds **3c**, **3j**, **3k**, **4**, **10a**, and **10j** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work has been supported by the Ministry of Science and Technology (MOST 105-2113-M-003-001) and National Taiwan Normal University.

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DOI: 10.1021/acs.joc.7b02158
J. Org. Chem. 2017, 82, 11543−11557