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# Syntheses of 3,4-Disubstituted Pyrroles and Furans via Lewis Acid-Promoted Semipinacol Rearrangement/Alkyne-Ketone Metathesis Reaction of (*C*)-2-*N*- or *O*-((3-Arylpropargyl)methyl)-Tethered 3,5,5-Trimethyl-2,3-epoxycyclohexan-1-ones

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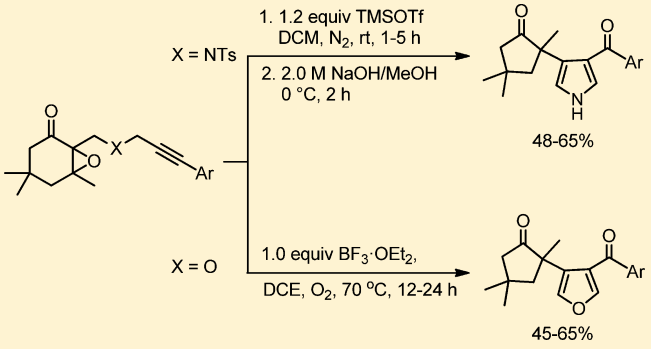
Supporting Information

**ABSTRACT:** The synthesis of 2,3-disubstituted pyrroles via TMSOTf-assisted cyclization reaction of 3,5,5-trimethyl-2,3-epoxycyclohexan-1-ones incorporating a (3-arylpropargyltosylamino)methyl tether at the C-2 position is described. The reaction starts with an acid-promoted semipinacol rearrangement to give a ring contraction cyclopentanone moiety bearing an arylpropargylaminoacetyl side chain. A subsequent alkyne-ketone metathesis affords the pyrrole derivatives in good yields. The 3,4-disubstituted furan analogues can also be available from 3,5,5-trimethyl-2,3-epoxycyclohexan-1-ones with a tethered arylpropargyl methyl ether at the C-2 position and $BF_3{\cdot}OEt_2$ under an atmosphere of oxygen.

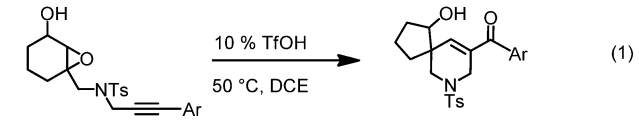


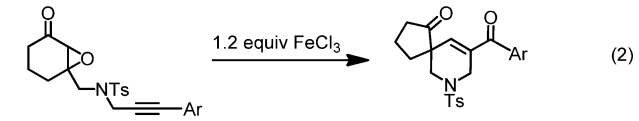

## INTRODUCTION

Furans[1] and pyrroles[2] are important heterocycles that are found in many natural products and pharmaceuticals. Consequently, many efforts have been devoted to the design of expedient and efficient synthetic routes to these five-membered ring heterocycles. Several general methods for the synthesis of pyrroles and furans involve cyclization reactions of 1,4-dicarbonyl derivatives,[3] rhodium(III)-catalyzed additions of alkenes and alkynes across C−N and C−O multiple bonds,[4] metal-catalyzed one-pot multicomponent coupling reactions of alkynes, carbonyl compounds and amines,[5] gold(I)-catalyzed hydroamination or hydration of 1,3-diynes,[6] and the gold-catalyzed dehydrative cyclization of 1-amino-3-alkyn-2-ols and 3-alkyne-1,2-diols.[7] Moreover, a great number of attractive transition-metal-catalyzed cyclization of various of organic substrates have been developed for the construction of the furan and pyrrole rings.[8] Recently, we reported a method for the synthesis of spiropiperidines via TfOH-catalyzed semipinacol rearrangement/alkyne-aldehyde metathesis of (*C*)-3-((3-arylpropargyltosylamino)methyl)-tethered 2,3-epoxycyclohexan-1-ols (Scheme 1, eq 1) and the corresponding epoxycyclohexanone (Scheme 1, eq 2).[9] To further explore this chemistry, we envision that switching the tether to the C-2 position may alter the reaction path and lead to other heterocyclic skeletons. Herein, we report a sequential reaction that provides cyclopentanone-substituted pyrroles and furans from cyclization of (*C*)-2-*N*- or *O*-((3-arylpropargyl)methyl)-tethered 3,5,5-trimethyl-2,3-epoxycyclohexan-1-ones with Lewis acids

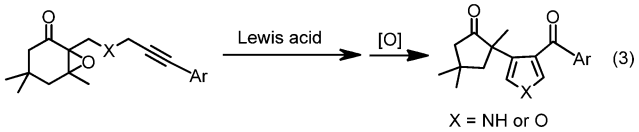
**Scheme 1. Acid-Catalyzed Semipinacol Rearrangement/Alkyne-Ketone Metathesis Reaction**

Our previous work[9]




This work




(Scheme 1, eq 3). In this reaction, an acid-promoted semipinacol rearrangement of the cyclic 2,3-epoxycyclohexa-1-one occurred to give the ring contraction 2,4,4-trimethylcyclopentanone moiety with an *N*- or *O*-3-arylpropargylmethyl side

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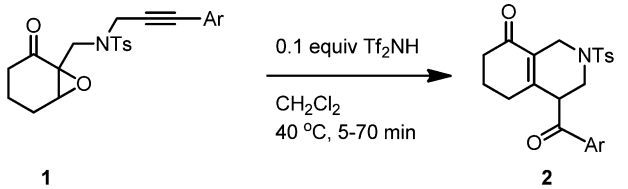
chain at the C-2. A subsequent acid-promoted alkyne-ketone metathesis furnished the five-membered ring heterocycles in moderate to good yields under mild reaction conditions. To the best of our knowledge, this is the first report on the use of the semipinacol rearrangement/alkyne-carbonyl metathesis strategy for the synthesis of pyrroles and furans.[10]

## RESULTS AND DISCUSSION

The initial compound (C)-2-*N*-tosyl-*N*-((3-phenylpropargyl)-methyl)-tethered 2,3-epoxycyclohexan-1-one **1a** was prepared starting from the reaction of cyclohex-2-en-1-one with formaldehyde under the Baylis–Hillmann reaction condition.[11] The resulting 2-hydroxymethylcyclohex-2-en-1-one was treated with *m*-chloroperbenzoic acid followed by replacement of the hydroxyl group with *N*-tosylpropargylamine using the Mitsunobu reaction protocol.[12] The resulting terminal alkyne was transformed to **1a** using the Sonogashira reaction condition.[13] Since 2,3-epoxycyclohexan-1-one derivatives were known to undergo semipinacol rearrangement generating cyclopentanone derivatives under acidic conditions,[14] compound **1a** was subjected to various acid catalysts for the initial study. However, among the acids and the solvents tested, none of the desired ring-contracted products were observed. Instead, isoquinolinone derivative **2a** was isolated in 83% yield when **1a** was treated with 0.1 equiv of $NHTf_2$ under the optimized reaction conditions ($CH_2Cl_2$, 40 °C, 70 min, Scheme 2). Encouraged by the success of $NHTf_2$-catalyzed synthesis of the isoquinolinone derivative **2a**, we next examined the substrate scope of the reaction. As revealed in Scheme 2, substrates with electron-neutral and -donating aryl groups at the terminal position of the acetylene gave the desired isoquinolinones **2a–f** in satisfactory yields (60–85%).[15] Compound **1g**, bearing an electron-withdrawing ester group on the phenyl ring, gave a trace amount of the corresponding isoquinolinone **2g**, and a nitro substituent on the phenyl ring, **1h**, impeded the reaction.

**Scheme 2. Synthesis of Isoquinolinones 2a–h**

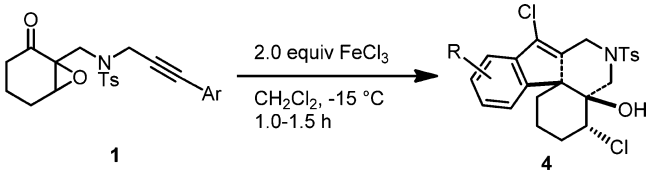



**a** : Ar = phenyl, 83%
**b** : Ar = 3-methylphenyl, 84%
**c** : Ar = 4-methylphenyl, 63%
**d** : Ar = 4-methoxyphenyl, 60%
**e** : Ar = 4-phenylphenyl, 80%
**f** : Ar = 1-naphthyl, 60%
**g** : Ar = 2-carbethoxyphenyl, 5%
**h** : Ar = 4-nitrophenyl, 0%

A possible mechanistic explanation for the formation of isoquinolinone **2** from **1** is stated in Scheme 3. The reaction was initiated by the $HNTf_2$-promoted semipinacol rearrangement of **1a**, which incorporated a hydride transfer to generate the oxonium species **3a**. A transfer of hydride in the semipinacol rearrangement of 2,3-epoxy alcohols promoted by TBSOTf was known in the literature.[16] Intermediate **3a** underwent [2 + 2] cycloaddition and generated the oxete **3b**. The intermediate **3b** proceeded [2 + 2] cycloreversion followed by deprotonation and double bond migration to afford **2a**. Several Lewis- or Brønsted-acid-catalyzed transfers of the oxygen atom from a carbonyl to an alkyne (a formal alkyne–carbonyl metathesis) producing conjugated enones have been reported in the literature.[17]

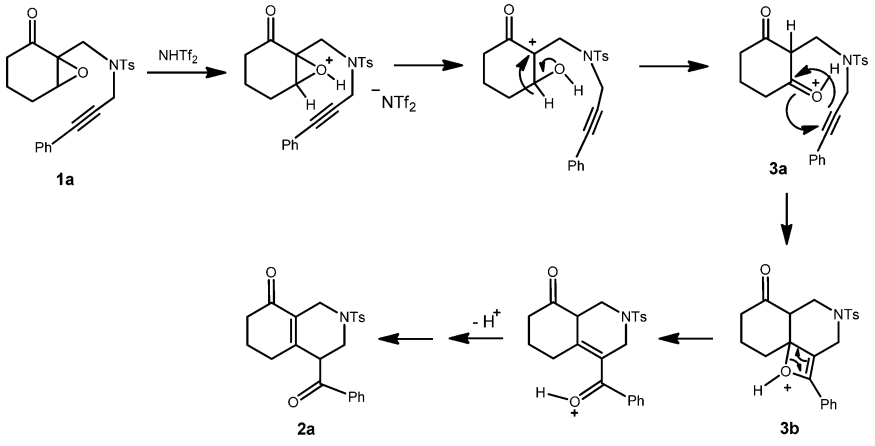
Surprisingly, when subjected to 2.0 equiv of $FeCl_3$ at −15 °C in $CH_2Cl_2$ for 1 h, compound **1a** provided a major product, identified as the heterotetracyclic compound **4a**, as the only stereoisomer isolated in 77% yield (Scheme 4). It is important to mention that three stereogenic centers of **4a** are created; however, only the single diastereomer shown was isolated. The relative stereochemistry of **4a** was accomplished by X-ray diffraction analysis.[15] The formation of **4a** may start with activation of both the carbonyl group and the oxirane by $FeCl_3$

**Scheme 4. $FeCl_3$-Promoted Synthesis of Compounds 4a, 4c, 4f, and 4i**




**a** : Ar = phenyl 77%
**c** : Ar = 4-methylphenyl 76%
**f** : Ar = 1-naphthyl 46%
**i** : Ar = 3-methoxyphenyl 69%

**Scheme 3. Suggested Reaction Path for the Formation of 2a from 1a**





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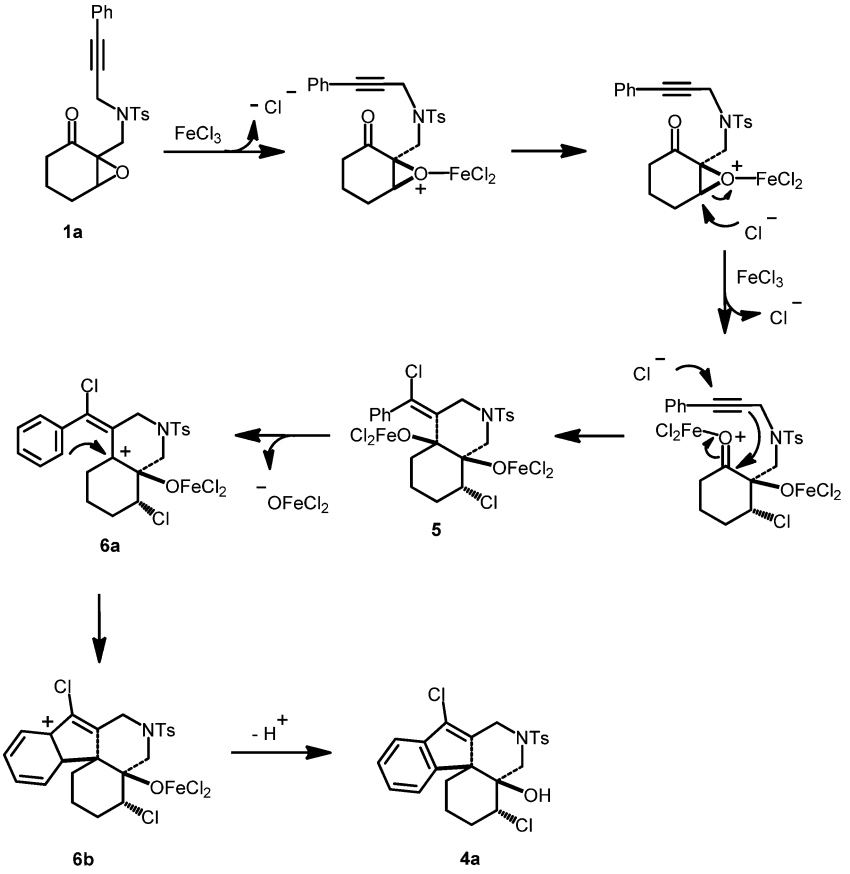
**Scheme 5. Postulated Reaction Path for the Formation of 4a from 1a**




followed by a regioselective $S_N2$-type ring-opening of the oxirane with a chloride ion and an *anti*-addition of the activated carbonyl moiety and a chloride ion across the acetylene resulting in the formation of the intermediate **5** (Scheme 5). Detachment of the $OFeCl_2$ anion from the quaternary carbon center formed the postulated tertiary carbonium ion **6a**, which underwent a Friedel–Crafts type alkylation to give **6b**. Intermediate **6b** led to heterotetracycle **4a** after rearomatization. Moreover, substrates **1c** and **1f**, bearing an electron-neutral group and **1i**, with an electron-donating methoxy substituent at the *meta* position on the phenyl ring, also delivered heterotetracycles **4c**, **4f**, and **4i** in diastereoselective fashion and in 46–76% yields (Scheme 4). Similarly, reaction of **1a** with 2.0 equiv of $FeBr_3$ at −15 °C in $CH_2Cl_2$ for 1 h furnished the corresponding heterotetracyclic dibromide **7** (Figure 1) in 67% isolated yield.[15]

Next, substrate **8** with an additional methyl group at the C-3 position was investigated. When compound **8** was subjected to a variety of acids ($HNTf_2$, TBSOTf, $Sn(OTf)_2$, and $Fe(OTf)_3$ in DCM or DCE, reactions gave a complex mixture in each case. However, the use of TMSOTf with **8** in $CH_3CN$ has proven most efficacious for the semipinacol rearrangement. Thus, subjection of **8** to 0.1 equiv of TMSOTf in $CH_3CN$ at 40 °C for 1 h gave the cyclopentanone derivative **9** with a propargylaminomethyl tether in 79% isolated yield. Unfortunately, compound **9** failed to undergo alkyne-ketone metathesis reaction upon treatment with a variety of acids. Compound **9** was recovered quantitatively in most cases (Scheme 6).

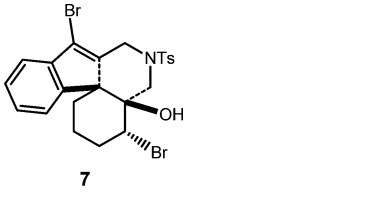
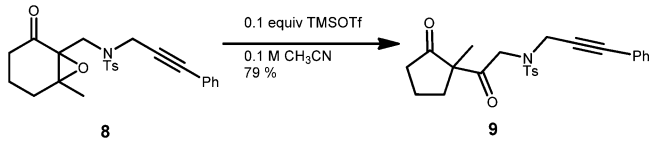



**Figure 1.** Structure of 7.

**Scheme 6. TMSOTf-Promoted Semipinacol Rearrangement of 8 to 9**




We further studied substrates **10** with an additional geminal dimethyl group at the C-5 position of the six-membered ring. As shown in Table 1, a series of reaction conditions was screened using different acids and solvents. Treating of the parent compound **10a** with 0.5 equiv of $BF_3{\cdot}OEt_2$ at 30 °C in $CH_2Cl_2$ (DCM) for 24 h gave the semipinacol rearrangement product **11a** in 29% isolated yield, as well as the *N*-tosylpyrrole derivative **12a** and the pyrrole derivative **13a**[15] in 22 and 8% yield, respectively (Table 1, entry 1). When **1a** was subjected to AgOTf (0.1 equiv) in dichloroethane (DCE) at 70 °C for 48 h, **11a** (29%) and **12a** (37%) were isolated (Table 1, entry 2). By using $In(OTf)_3$ (0.1 equiv) or $Sn(OTf)_3$ in xylene as catalysts, **10a** failed to increase the yield of the *N*-tosylpyrrole **12a**, albeit required an elevated temperature in each case (Table 1, entries


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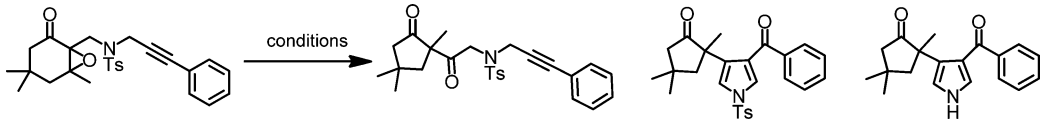
**Table 1. Optimizing of the Reaction Conditions in the Cycloisomerization of 10a with Lewis Acids**

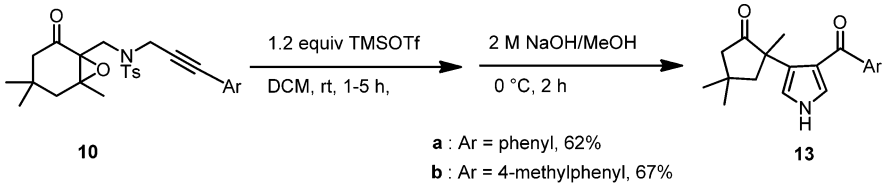



**10a** **11a** **12a** **13a**

| entry | acid (equiv) | conditions[a] | **11a** (%)[b] | **12a** (%)[b] | **13a** (%)[b] |
|---|---|---|---|---|---|
| 1 | $BF_3$·$OEt_2$ (0.5) | DCM, 30 °C, 24 h | 29 | 22 | 8 |
| 2 | AgOTf (0.1) | DCE, 70 °C, 48 h | 29 | 37 | 0 |
| 3 | $In(OTf)_3$ (0.1) | xylene, 135 °C, 24 h | 23 | 19 | 0 |
| 4 | $Sn(OTf)_3$ (0.1) | xylene, 135 °C, 24 h | 3 | 15 | 0 |
| 5 | $FeCl_3$ (1.2) | DCM, 26 °C, 24 h | 0 | 0 | 0 |
| 6 | TMSCl (0.1) | DCE, 70 °C, 24 h | 25 | 0 | 0 |
| 7 | TfOH (0.1) | DCE, 70 °C, 16 h | 0 | 36 | 0 |
| 8 | $Fe(OTf)_3$ (0.1) | DCE, 70 °C, 24 h | 0 | 34 | 0 |
| 9 | TMSOTf (0.1) | $CH_3CN$, 40 °C, 0.2 h | 92 | 0 | 0 |
| 10 | TMSOTf (0.1) | DCE, 75 °C, 26 h | 3 | 42 | 0 |
| 11 | TMSOTf (0.1) | xylene, 135 °C, 2 h | 4 | 45 | 0 |
| 12 | TMSOTf (0.5) | DCM, 29 °C, 24 h | 29 | 22 | 28 |
| 13 | TMSOTf (1.0) | DCM, 30 °C, 6 h | 0 | 18 | 32 |
| 14 | TMSOTf (1.2) | DCM, 30 °C, 4 h | 0 | 18 | 36 |
| 15 | TMSOTf (2.0) | DCM, 30 °C, 3 h | 0 | 18 | 38 |

[a]All reactions were conducted using 0.1 M of **10a**. [b]Isolated yields by column chromatography.

**Scheme 7. Synthesis of Pyrrole 13 from 10**




**10** **13**

**a** : Ar = phenyl, 62%
**b** : Ar = 4-methylphenyl, 67%
**c** : Ar = 3-methylphenyl, 49%
**d** : Ar = 4-phenylphenyl, 53%
**e** : Ar = naphthyl, 62%
**f** : Ar = phenanthryl, 56%
**g** : Ar = 3-methoxyphenyl, 65%
**h** : Ar = 4-bromophenyl, 48%
**i** : Ar = 2-thiophenyl, 52%

3−4). While 1.2 equiv of $FeCl_3$ in DCM at 26 °C failed to give any cyclized product (Table 1, entry 5), a catalytic amount of TMSCl (0.1 equiv) in DCE at 70 °C afforded only **11a** in 25% yield (Table 1, entry 6). Although 0.1 equiv of TfOH and $Fe(OTf)_3$ in DCE at 70 °C proved capable for the full transformation of **10a** to the *N*-tosylpyrrole **12a**, low yields of 36 and 34% were obtained (Table 1, entries 7 and 8). Employing TMSOTf (0.1 molar equiv) in $CH_3CN$ at 29 °C for 10 min produced **11a** as the sole product in 92% yield (Table 1, entry 9). The yield of the pyrrole **12a** can be increased to 42 and 45%, respectively, when **10a** was treated with 0.1 equiv of TMSOTf in DCE at 75 °C or xylene at 135 °C (Table 1, entries 10 and 11). Increasing the TMSOTf loading from 0.1 to 0.5 equiv in DCM at 28 °C for 24 h provided **11a** (29%), **12a** (22%), and **13a** (28%) (Table 1, entry 12). To our delight, the treatment of **10a** with 1.0 equiv of TMSOTf in DCM at 29 °C for 6 h gave complete conversion to pyrrole derivatives **12a** and **13a**, which was isolated in 18 and 32% yield, respectively (Table 1, entry 13). The use of 1.2 equiv of TMSOTf in DCM at 29 °C for 4 h gave pyrrole derivatives **12a** and **13a** in 18 and 36% yield, respectively (Table 1, entry 14). Running the reaction with 2.0 equiv of TMSOTf loading in DCM at 30 °C for 3 h, however, did not significantly improve yields of pyrroles **12a** and **13a** (Table 1, entry 15). Since *N*-tosylpyrroles can be easily transformed into pyrroles under basic conditions, it would be practical to obtain pyrrole **13a** from the starting substrate **10a** in a one-pot two-step process. Thus, **10a** was subjected to 1.2 equiv of TMSOTf in DCM at room temperature for 4 h until the starting material **1a** was not detected by thin layer chromatography. A solution of 2.0 M NaOH in methanol was then added to the reaction mixture at 0 °C, and the resultant mixture was stirred at this temperature for 2 h to provide the pyrrole derivative **13a** as the major product in 62% isolated yield. Thus, the use of 1.2 equiv of TMSOTf in $CH_2Cl_2$ at ambient temperature followed by the basic treatment (NaOH/MeOH) at 0 °C was employed as the standard reaction conditions for the synthesis of pyrrole **13** from the starting substrate **10**.

As can be seen in Scheme 7, substrates **10b−g**, bearing electron-neutral and -rich arenes at the alkyne terminus, gave clean conversion to pyrroles **13b−g**[15] in 49−67% yields under the standard reaction conditions. A bromine atom on the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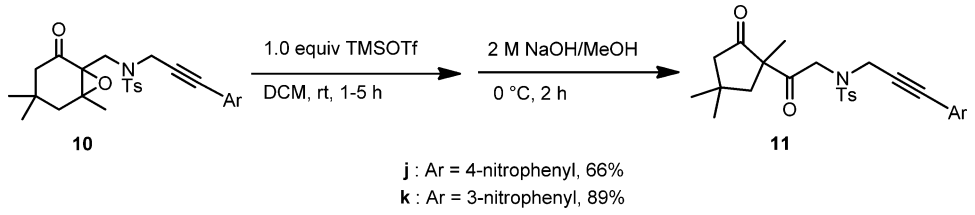
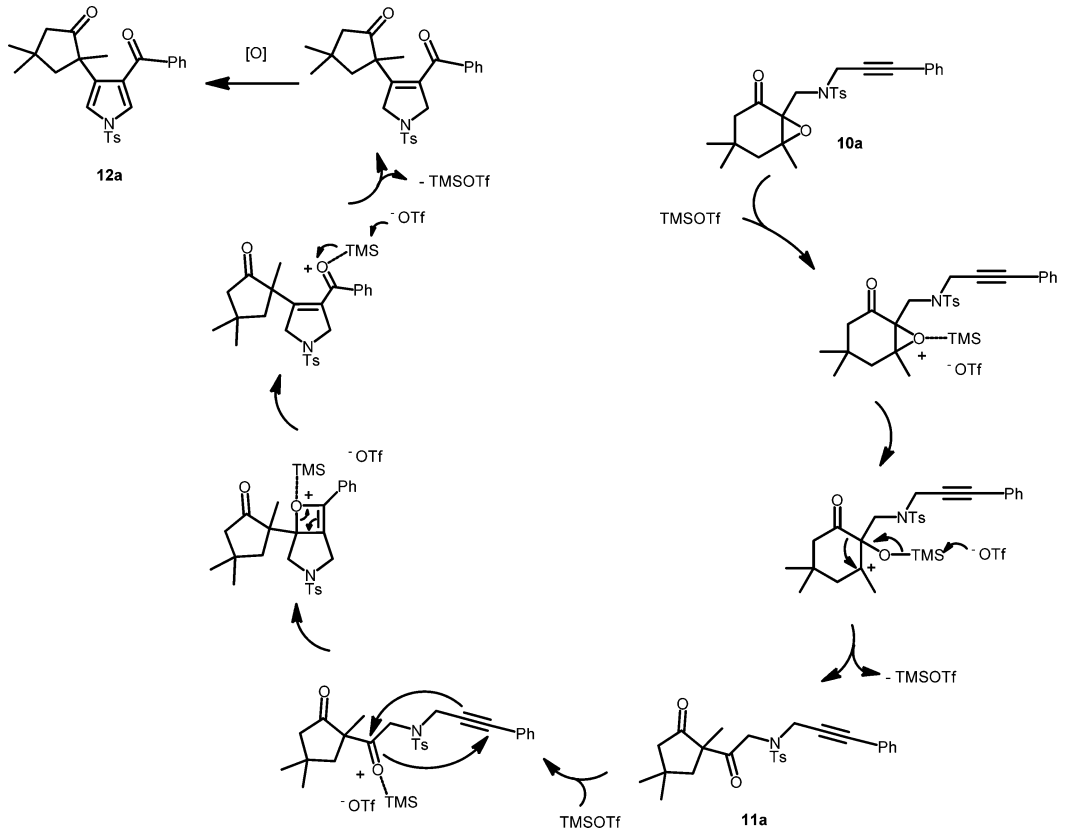
**Scheme 8. Conversion of 10j,k to 11j,k**




**Scheme 9. Suggested Reaction Path for the Formation of 11a and 12a from 10a**



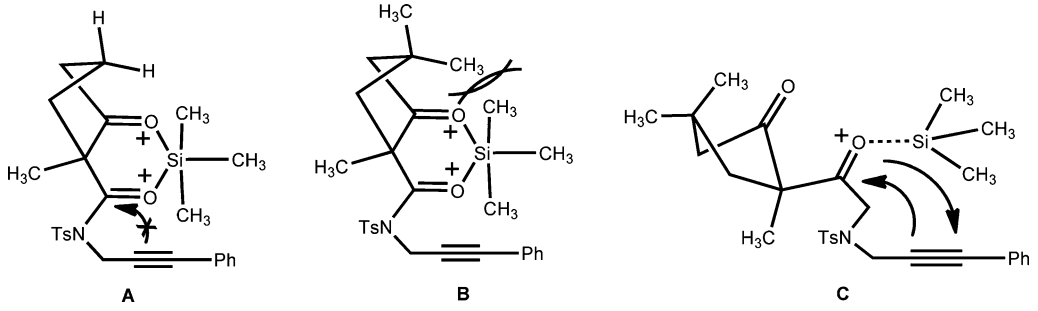




**Figure 2.** Intermediates **A**, **B**, and **C**.

phenyl ring, for example, **10h**, did not impede the cyclization and afforded the desired pyrrole **13h** in 48% yield. Interestingly, a thiophenyl group at the alkyne terminus, **10i**, also delivered the corresponding pyrrole **13i**[15] in 52% yield. However, it must be mentioned that substrates with the electron-withdrawing nitro group, for example, compounds **10j** and **10k**, gave only the semipinacol rearrangement products **11j** and **11k** in 66 and 89% isolated yield, respectively (Scheme 8). None of pyrrole derivatives were observed.

A possible reaction path for the formation of *N*-tosylpyrrole **12a** from the starting substrate **10a** was that initial activation of the oxirane by TMSOTf occurred to give the semipinacol rearrangement product **11a** (Scheme 9). A subsequent TMSOTf-assisted intramolecular [2 + 2] cycloaddition followed by [2 +2] cycloreversion (alkyne-ketone metathesis) occurred to generate an *N*-tosyldihydropyrrole derivative. Oxidation of the *N*-tosyldihydropyrrole during aqueous workup and column chromatography furnished *N*-tosylpyrrole **12a**.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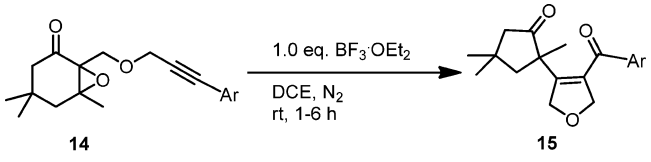
Moreover, in order to provide the evidence for the formation of the pyrrole from the key alkyne−carbonyl metathesis of **11a**, compound **11a** was subjected to the one-pot two-step process. Thus, treatment of **11a** with 1.2 equiv of TMSOTf in DCM at 30 °C for 4 h followed by basic treatments (1.0 M NaOH/MeOH, 0 °C, 2 h) afforded pyrrole **13a** in 67% isolated yield. This result further suggested that pyrrole **13** is generated from an acid-promoted alkyne-ketone metathesis of **11**.

It is important to mention that the alkyne−ketone metathesis did not proceed with compound **8** lacking of a geminal dimethyl group at the C-5 position of the ring. It is speculated that the trimethylsilyl group may coordinate to both carbonyl groups of **8** to form a bicyclic intermediate **A** (Figure 2). The bulky trimethylsilyl and the adjacent methyl groups may inhibit the alkyne from attacking the carbonyl carbon for further cyclization. However, the presence of the geminal dimethyl and the trimethylsilyl moieties causes a large amount of steric congestion in **B**, and intermediate **B** would lead to **C**. Intermediate **C** underwent an acid-promoted alkyne−ketone metathesis to generate pyrrole derivatives.

This method can be applied to the synthesis of 3,4-disubstituted-dihydrofurans and -furans. The starting 2,3-epoxycyclohexan-1-one with a tethered 3-arylpropargyl methyl ether at the C-2 position of the ring, **14a**, is prepared from 3,5,5-trimethylcyclohex-2-en-1-one in the similar fashion as that of **1a**. Among various acids and solvents screened, it was found that $BF_3{\cdot}OEt_2$ in DCE is most effective for the formation of furan derivatives from **14a**. Thus, reaction of **14a** with 1.0 equiv of $BF_3{\cdot}OEt_2$ in DCE (0.025 M) at room temperature for 3 h produced dihydrofuran **15a** as the major products in 71% isolated yields. Several examples for the synthesis of the dihydrofuran derivatives are listed in Scheme 10. It must be

**Scheme 10. $BF_3{\cdot}OEt_2$-Mediated Synthesis of Dihydrofurans 15a−f**



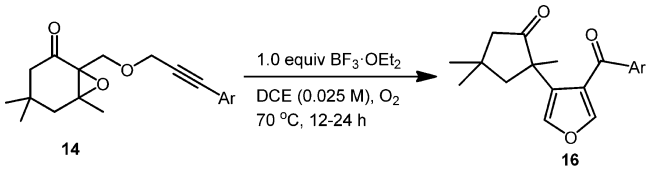

**a** = phenyl, 71%
**b** = 4-methylphenyl, 70%
**c** = 9-phenanthryl, 69%
**d** = 4-bromophenyl, 75%
**e** = 3-methylpheny, 76%
**f** = 1-naphthyl, 72%

mentioned that a trace amount of furan **16**, presumably arising from oxidation of dihydrofuran **15** during aqueous workup and purification process, was detected by thin layer chromatography of the crude mixture in each case.

To our delight, furan **16a**[15] was isolated as the sole product in 56% isolated yield when the $BF_3{\cdot}OEt_2$-promoted cyclization of **14a** was carried out under an atmosphere of oxygen in DCE at 70 °C for 4 h. Further investigations had revealed that substrates lacking strongly electron-withdrawing substituents on the phenyl ring reacted smoothly with $BF_3{\cdot}OEt_2$ under the reaction conditions. As seen in Scheme 11, substrates with an electron-neutral or -rich aryl groups at the alkyne gave furans **16** in 45−65% isolated yields.

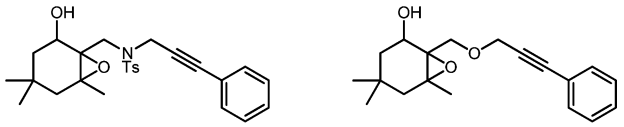
It must be mentioned that reaction of the corresponding (C)-2-*N*- and *O*-3-((phenylpropargyl)methyl)-tethered 3,5,5-trimethyl-2,3-epoxycyclohexan-1-ols, for example, **17** and **18**

**Scheme 11. Synthesis of Furan 16 from 14**




**a** = phenyl, 56%
**b** = 4-methylphenyl, 52%
**c** = 9-phenanthryl, 53%
**d** = 4-bromophenyl, 45%
**e** = 3-methylpheny, 65%
**f** = 1-naphthyl, 62%
**g** = 3-methoxyphenyl, 47%
**h** = 4-phenylphenyl, 50%

(Figure 3), with TMSOTf or $BF_3{\cdot}OEt_2$ resulted in decomposition of the starting substrates, and none of the cyclized products were obtained.




17 18

**Figure 3.** Structures of **17** and **18**.

In conclusion, a simple transformation for the synthesis of 3,4-disubstituted pyrroles and furans has been developed. The reaction is initiated by TMSOTf or $BF_3{\cdot}OEt_2$-promoted tandem semipinacol rearrangement/alkyne-ketone metathesis of 2,3-epoxycyclohexa-1-ones with an *N*- or *O*-(3-arylpropargyl)methyl tether at the C-2 position of the six-membered ring followed by oxidation. The advantages of this process are the mild and metal-free reaction conditions, providing an alternative route to the 3,4-disubstituted pyrroles and furans.

## EXPERIMENTAL SECTION

**General Considerations.** All reactions were performed in oven-dried glassware under nitrogen atmosphere unless otherwise indicated. Anhydrous solvents or reaction mixtures were transferred via an oven-dried syringe or cannula. Solvents were predried by molecular sieves and then by passing through an $Al_2O_3$ column. Melting points were determined in open capillaries with an electronic apparatus and are uncorrected. Chromatographic purification was performed with flash column chromatography on silica P60, 40−63 m (230−400 mesh). $^1H$ nuclear magnetic resonance (NMR) spectra were recorded with 400 and 500 MHz spectrometers. The chemical shifts are reported in parts per million with either $Me_4Si$ (0.00 ppm) or $CDCl_3$ (7.26 ppm) as internal standard. $^{13}C$ NMR spectra were recorded with 100 and 125 MHz spectrometers using $CDCl_3$ (77.0 ppm) as internal standard. Mass spectra were determined by using a spectrometer with 70-eV ionizing voltage and were reported as mass/charge (*m*/*e*) with percent relative abundance. High-resolution mass spectra were obtained with a double-focusing mass spectrometer.

**Representative Procedure for Synthesis of Starting Compound 1.** To a stirring solution of cyclohex-2-en-1-one (28.84 g, 0.30 mol) in MeOH (100 mL) and $H_2O$ (500 mL) at 0 °C under nitrogen were added formaldehyde (37 wt % solution in water, 11.26 g, 0.38 mol), $Ba(OH)_2$ (0.77 g, 4.5 mmol), and *N*-methyl-2-pyrrolidone (NMP, 1.27 g, 15.00 mmol). The reaction mixture was stirred at 29 °C for 4 h. The reaction was then quenched with 20 mL of $HCl_{(aq)}$ at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was neutralized with saturated $NaHCO_{3(aq)}$. The reaction mixture was extracted with $CH_2Cl_2$ (300 mL × 3). The combined extracts were washed with water (300 mL × 3), and brine (300 mL × 3), dried over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anhydrous $MgSO_4$ (20 g), and concentrated under reduced pressure to give a crude oil. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to afford 2-(hydroxymethyl)cyclohex-2-en-1-ol (22.35 g, 0.18 mol, 59%). To a 10 mL round-bottom flask equipped with a stirrer bar and capped with a rubber septum were added 2-(hydroxymethyl)cyclohex-2-en-1-one (22.35 g, 0.18 mol), 226 mL of MeOH and 8.9 mL of 2.0 M of NaOH in MeOH. The reaction mixture was cooled to 0 °C, and to it was added $H_2O_2$ (35% in $H_2O$, 24.10 g, 0.71 mol). The reaction mixture was stirred at 0 °C for 3 h. The mixture was treated with 20 mL of saturated $Na_2S_2O_{3(aq)}$ solution. The resulting mixture was extracted with methylene chloride (200 mL × 3), and the combined extracts were washed with brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (ethyl acetate/hexanes 1:1) to give 2,3-epoxy-2-(hydroxymethyl)cyclohex-2-en-1-one (17.23 g, 0.12 mol, 67%). To a solution of *p*-TsCl (6.29 g, 0.033 mol) in 100 mL of $CH_2Cl_2$ at 0 °C were added propargylamine (1.65 g, 0.030 mol) and $Et_3N$ (3.6 g, 0.036 mol). The reaction was stirred at ambient temperature for 12 h until no propargylamine was detected by TLC. The reaction was quenched with 50 mL of saturated $NH_4Cl_{(aq)}$, and the resulting solution was extracted with $CH_2Cl_2$ (50 mL × 3), and the combined extracts were washed with brine and dried ($MgSO_4$). The filtrate was concentrated under reduced to give the *p*-tosyl propargylamine (5.58 g, 0.027 mol, 90%). To a solution of $PPh_3$ (11.89 g, 0.045 mol) in 200 mL of THF under nitrogen at 0 °C was added diisopropyl azodicarboxylate (DIAD, 9.17 g, 0.045 mol). The reaction was allowed to stir at 0 °C for 20 min and to it was added *p*-tosyl propargylamine (5.58 g, 0.027 mol). The mixture was allowed to stir at 0 °C for 20 min and was treated with 2,3-epoxy-2-(hydroxymethyl)cyclohex-2-en-1-one (5.58 g, 0.027 mol). The reaction was allowed to stir at 0 °C for 30 min and at ambient temperature for 4 h before being quenched with 100 mL of saturated $NH_4Cl_{(aq)}$. The resulting solution was extracted with $CH_2Cl_2$ (40 mL × 3), and the combined extracts were washed with brine and dried ($MgSO_4$). The filtrate was concentrated under reduced pressure to give a crude oil. The oil was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:4) to produce 4-methyl-*N*-((2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-*N*-(prop-2-yn-1-yl)benzenesulfonamide (6.62 g, 0.020 mol, 74%). In a 50-mL round-bottom flask equipped with a stirring bar were added $Pd(PPh_3)_4$ (0.065 g, 0.056 mmol), CuI (0.021 g, 0.11 mmol) and PhI (0.69 g, 3.39 mmol). The system was purged with $N_2$, and $Et_3N$ (2.8 mL) was added. The reaction was allowed to stir at ambient temperature for 20 min followed by addition of 4-methyl-*N*-((2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-*N*-(prop-2-yn-1-yl)benz-enesulfonamide (0.94 g, 2.82 mmol). The reaction was left at ambient temperature for 3 h. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$. The mixture was extracted with $CH_2Cl_2$ (20 mL × 3). The $CH_2Cl_2$ solution was washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash column chromatography on silica gel, eluting with ethyl acetate/hexanes 1:4) to obtain 4-methyl-*N*-((2-oxo-7-oxabicyclo-[4.1.0]heptan-1-yl)methyl)-*N*-(3-phenyl-prop-2-yn-1-yl)-benzenesulfonamide (**1a**) as a white solid (0.90 g, 2.2 mmol, 78%): mp 141−142 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (d, $J$ = 8.2 Hz, 2H), 7.29−7.21 (m, 5H), 7.05 (d, $J$ = 7.0 Hz, 2H), 4.52 (d, $J$ = 18.6 Hz, 1H), 4.25 (d, $J$ = 18.6 Hz, 1H), 4.02 (d, $J$ = 15.8 Hz, 1H), 3.93 (s, 1H), 3.44 (d, $J$ = 15.8 Hz, 1H), 2.56 (dt, $J$ = 17.2 Hz, 4.8 Hz, 1H), 2.32 (s, 3H), 2.31−2.24 (m, 1H), 2.17−2.01 (m, 2H), 1.95−1.84 (m, 1H), 1.74−1.65 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 205.8, 143.8, 135.5, 131.5 (2C), 129.6 (2C), 128.4, 128.0 (2C), 127.9 (2C), 122.1, 85.7, 82.0, 60.3, 60.2, 44.3, 40.3, 37.0, 23.0, 21.4, 17.3; IR ($CH_2Cl_2$) 2944, 1708, 1598, 1349, 1163, 1091 cm$^{-1}$; MS (ESI) $m/e$ (%) 432.1 ([M + Na]$^+$, 100), 286.1 (8), 243.1 (23), 143 (15), 122.54 (17) ; HRMS (ESI) calcd for $C_{23}H_{23}NO_4NaS$ [M + Na]$^+$ 432.1245, found 432.1250.

**General Experimental Procedure for Synthesis of Substrate 10.** Compounds **10a−i** were prepared in the similar fashion as those of substrates **1a−h** starting from treatment of 3,5,5-trimethylcyclohex-2-en-1-one with formaldehyde under Baylis−Hillman reaction conditions. The resulting 3,5,5-trimethyl-2-(hydroxymethyl)cyclohex-2-en-1-ol was oxidized with $H_2O_2$, amidation with *N*-tosylpropargylamide and arylation with aryliodide as those described in the experimental procedure previously.

*Data for 4-Methyl-N-(3-phenylprop-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10a**).* (0.82 g, 1.81 mmol, 85%) A white solid: mp 112−113 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.0 Hz, 2H), 7.29−7.20 (m, 5H), 7.07 (dd, $J$ = 8.0, 4.0 Hz, 2H), 4.46 (d, $J$ = 17.6 Hz, 1H), 4.39 (d, $J$ = 17.6 Hz, 1H), 3.77 (d, $J$ = 16.0 Hz, 1H), 3.74 (d, $J$ = 16.0 Hz, 1H), 2.65 (d, $J$ = 17.6 Hz, 1H), 2.32 (s, 3H), 2.08 (d, $J$ = 17.6 Hz, 1H), 1.99 (dd, $J$ = 17.6, 4.0 Hz, 1H), 1.80 (dd, $J$ = 17.6, 4.0 Hz, 1H), 1.62 (s, 3H), 1.01 (s, 3H), 0.95 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.5, 143.7, 135.3, 131.5, 129.5, 128.3, 128.1, 128.0, 122.3, 85.7, 82.3, 68.9, 63.9, 49.1, 43.9, 42.3, 39.9, 33.8, 30.4, 29.1, 21.5, 21.4; IR ($CH_2Cl_2$) 2959, 1714, 1642, 1351, 1163 cm$^{-1}$; MS (ESI) $m/e$ 474.1 ([M + Na]$^+$, 100), 452.2 (15), 339.1 (15), 323.1 (4), 259.0 (3), 238.0 (3), 171.0 (6); HRMS (ESI) calcd for $C_{26}H_{29}NO_4NaS$ [M + Na] 474.1715, found 474.1711.

*Data for 4-Methyl-N-(3-(p-tolyl)prop-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10b**).* (0.68 g, 1.47 mmol, 69%) A white solid: mp 107−108 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.78 (d, $J$ = 8.2 Hz, 2H), 7.25 (d, $J$ = 8.1 Hz, 2H), 7.03 (d, $J$ = 8.0 Hz, 2H), 6.97 (d, $J$ = 8.1 Hz, 2H), 4.44 (d, $J$ = 18.6 Hz, 1H), 4.38 (d, $J$ = 18.6 Hz, 1H), 3.79 (d, $J$ = 14.8 Hz, 1H), 3.73 (d, $J$ = 14.8 Hz, 1H), 2.07 (d, $J$ = 13.6 Hz, 1H), 2.31 (s, 3H), 2.29 (s, 3H), 2.07 (d, $J$ = 13.6 Hz, 1H), 1.98 (dd, $J$ = 13.6, 1.2 Hz, 1H), 1.82 (d, $J$ = 15.1 Hz, 1H), 1.61 (s, 3H), 1.01 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.4, 143.6, 138.4, 135.4, 131.4 (2C), 129.5 (2C), 127.8 (2C), 128.1 (2C), 119.2, 85.8, 81.6, 68.9, 63.9, 49.2, 43.9, 42.4, 40.0, 33.8, 30.4, 29.1, 21.4 (3C); IR ($CH_2Cl_2$) 2957, 1713, 1599, 1510, 1451, 1351, 1164 cm$^{-1}$; MS (ESI) $m/e$ 488.2 ([M + Na]$^+$, 100), 477.3 (7), 467.2 (21), 466.2 (85); HRMS (ESI) calcd for $C_{27}H_{31}NO_4NaS$ [M + Na]$^+$ 488.1872, found 488.1868.

*Data for 4-Methyl-N-(3-(m-tolyl)prop-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10c**).* (0.91 g, 1.95 mmol, 92%) A white solid: mp 105−106 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.2 Hz, 2H), 7.26 (d, $J$ = 8.2 Hz, 2H), 7.13−7.06 (m, 2H), 6.89 (m, 2H), 4.45 (d, $J$ = 18.6 Hz, 1H), 4.38 (d, $J$ = 18.6 Hz, 1H), 3.79 (d, $J$ = 14.8 Hz, 1H), 3.73 (d, $J$ = 14.8 Hz, 1H), 2.65 (d, $J$ = 13.6 Hz, 1H), 2.34 (s, 3H), 2.29 (s, 3H), 2.08 (d, $J$ = 15.2 Hz, 1H), 1.98 (dd, $J$ = 13.6, 1.2 Hz, 1H), 1.82 (dd, $J$ = 15.1, 1.0 Hz, 1H), 1.62 (s, 3H), 0.94 (s, 3H), 0.88 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.2, 143.5, 137.5, 135.2, 131.9, 129.4 (2C), 129.0, 128.5, 127.9 (2C), 127.8, 121.9, 85.8, 81.8, 68.7, 63.8, 49.0, 43.7, 42.2, 39.8, 33.6, 30.3, 28.9, 21.3 (2C), 21.0; IR ($CH_2Cl_2$) 2958, 2929, 2228, 1714, 1600, 1351 cm$^{-1}$; MS (ESI) $m/e$ 466.2 ([M + H]$^+$, 100), 429.2 (8), 440.2 (3), 353.1 (4); HRMS (ESI) calcd for $C_{27}H_{32}NO_4S$ [M + H]$^+$ 466.2052, found 466.2048.

*Data for N-(3-([1,1′-Biphenyl]-4-yl)prop-2-yn-1-yl)-4-methyl-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10d**).* (0.79 g, 1.07 mmol, 50%) A white solid: mp 102−103 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 8.2 Hz, 2H), 7.55 (d, $J$ = 7.5 Hz, 2H), 7.47−7.42 (m, 4H), 7.37 (d, $J$ = 7.4 Hz, 1H), 7.27 (d, $J$ = 8.4 Hz, 2H), 7.15 (d, $J$ = 8.4 Hz, 2H), 4.48 (d, $J$ = 18.6 Hz, 1H), 4.47 (d, $J$ = 18.6 Hz, 1H), 3.81 (d, $J$ = 14.8 Hz, 1H), 3.76 (d, $J$ = 14.8 Hz, 1H), 2.66 (d, $J$ = 13.6 Hz, 1H), 2.33 (s, 3H), 2.09 (d, $J$ = 15.1 Hz, 1H), 1.99 (d, $J$ = 13.6 Hz, 1H), 1.83 (d, $J$ = 15.1 Hz, 1H), 1.63 (s, 3H), 1.02 (s, 3H), 0.95 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.5, 143.6, 141.0, 140.1, 135.3, 131.9 (2C), 129.5 (2C), 128.8 (2C), 128.0 (2C), 127.6, 126.9 (2C), 126.7 (2C), 121.1, 85.6, 83.0, 68.9, 63.9, 49.1, 43.9, 42.3, 39.9, 33.8, 30.4, 29.0, 21.4 (2C); IR ($CH_2Cl_2$) 2960, 1714, 1599, 1487, 1350, 1261, 1163 cm$^{-1}$; MS (ESI) $m/e$ 550.2 ([M + Na]$^+$, 100), 545.2 (9), 528.2 (3), 200.1 (4); HRMS (ESI) calcd for $C_{32}H_{33}NO_4SNa$ [M + Na]$^+$ 550.2028, found 550.2017.

*Data for 4-Methyl-N-(3-(naphthalen-1-yl)pro-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10e**).* (0.77 g, 1.66 mmol, 78%) A white solid: mp 130−131 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.89−7.92 (m, 1H), 7.75−7.81 (m, 4H), 7.35−7.49 (m, 2H), 7.12−7.35 (m, 2H), 7.11 (d, $J$

= 8.0 Hz, 2H), 4.62 (d, *J* = 18.6 Hz, 1H), 4.55 (d, *J* = 18.6 Hz, 1H), 3.87 (s, 2H), 2.66 (d, *J* = 13.6 Hz, 1H), 2.14 (s, 1H), 2.07 (s, 3H), 1.98 (d, *J* = 13.6 Hz, 1H), 1.80 (d, *J* = 14.8 Hz, 1H), 1.63 (s, 3H), 0.99 (s, 3H), 0.93 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.6, 143.8, 135.3, 133.0 (2C), 130.6 (2C), 129.5, 128.8, 128.1, 128.0 (2C), 126.7, 126.3, 126.1, 124.9, 120.0, 87.2, 84.0, 69.0, 64.0, 49.1, 44.0, 42.4, 40.1, 33.9, 30.4, 29.0, 21.5, 21.2; IR ($CH_2Cl_2$) 2956, 1712, 1598, 1350, 1164 cm$^{-1}$; MS (ESI) *m*/*e* 524.2 ([M + Na]$^+$, 100), 503.2 (12), 502.2 (39), 389.1 (5); HRMS (ESI) calcd for $C_{30}H_{31}NO_4SNa$ [M + Na]$^+$ 524.1872, found 524.1863.

*Data for 4-Methyl-N-(3-(phenanthren-9-yl)prop-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10f**).* (1.04 g, 1.89 mmol, 63%) A white solid: mp 137−138 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.62 (d, *J* = 7.3 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.68−7.56 (m, 5H), 7.14 (d, *J* = 8.2 Hz, 2H), 4.65 (d, *J* = 18.6 Hz, 1H), 4.59 (d, *J* = 18.6 Hz, 1H), 3.90 (s, 2H), 2.68 (d, *J* = 13.6 Hz, 1H), 2.09 (d, *J* = 15.2 Hz, 1H), 2.06 (s, 3H), 2.00 (d, *J* = 13.6 Hz, 1H), 1.83 (d, *J* = 15.2 Hz, 1H), 1.65 (s, 3H), 1.01 (s, 3H), 0.95 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.7, 143.8, 135.4, 132.1, 130.9, 130.8, 130.2, 129.9, 129.5 (2C), 128.3, 128.0 (2C), 127.5, 127.0, 126.9, 126.8, 122.6, 118.8, 86.9, 84.1, 69.1, 64.1, 49.1, 44.0, 42.5, 40.1, 33.9, 30.5, 29.0, 21.5, 21.3; IR ($CH_2Cl_2$) 2957, 1712, 1600, 1598, 1451, 1350, 1163 cm$^{-1}$; MS (ESI) *m*/*e* 574.2 ([M + Na]$^+$, 100), 553.2 (4), 425.2 (2), 352.6 (3); HRMS (ESI) calcd for $C_{34}H_{33}NO_4SNa$ [M + Na]$^+$ 574.2028, found 574.2034.

*Data for N-(3-(3-Methoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10g**).* (0.46 g, 0.96 mmol, 45%) A yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.78 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 8.2 Hz, 1H), 6.82 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 4.45 (d, *J* = 18.6 Hz, 1H), 4.39 (d, *J* = 18.6 Hz, 1H), 3.80−3.72 (m, 5H), 2.65 (d, *J* = 13.6 Hz, 1H), 2.33 (s, 3H), 2.08 (d, *J* = 15.1 Hz, 1H), 1.98 (d, *J* = 13.6 Hz, 1H), 1.82 (d, *J* = 15.1 Hz, 1H), 1.62 (s, 3H), 1.01 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.3, 159.0, 143.6, 135.2, 129.4 (2C), 129.0, 127.9 (2C), 123.9, 123.1, 116.8, 114.3, 85.5, 82.1, 68.8, 63.8, 55.1, 49.0, 43.7, 42.2, 39.7, 33.7, 30.3, 28.9, 21.3, 21.2; IR ($CH_2Cl_2$) 3277, 2959, 2868, 1728, 1628, 1580 cm$^{-1}$; MS (ESI) *m*/*e* 504.2 ([M + Na]$^+$, 100), 483.2 (5), 482.2 (20), 380.2 (8); HRMS (ESI) calcd for $C_{27}H_{31}NO_5SNa$ [M + Na]$^+$ 504.1821, found 504.1816.

*Data for N-(3-(4-Bromophenyl)prop-2-yn-1-yl)-4-methyl-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10h**).* (0.60 g, 1.12 mmol, 53%) A white powder: mp 105−106 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 4.43 (d, *J* = 18.6 Hz, 1H), 4.36 (d, *J* = 18.6 Hz, 1H), 3.77 (br s, 2H), 2.65 (d, *J* = 13.6 Hz, 1H), 2.32 (s, 3H), 2.08 (d, *J* = 15.2 Hz, 1H), 1.96 (d, *J* = 13.6 Hz, 1H), 1.81 (d, *J* = 15.2 Hz, 1H), 1.62 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.5, 143.6, 135.2, 132.8 (2C), 131.2 (2C), 129.4 (2C), 127.9 (2C), 122.4, 121.1, 84.5, 83.6, 68.9, 63.8, 48.9, 43.8, 42.1, 39.6, 33.9, 30.4, 28.8, 21.3 (2C); IR ($CH_2Cl_2$) 2957, 2930, 2871, 2246, 1915, 1713, 1598, cm$^{-1}$; MS (ESI) *m*/*e* 552.1 ([M + Na]$^+$, 100), 547.2 (1),530.1 (1), 440.2 (2); HRMS (ESI) calcd for $C_{26}H_{28}NO_4NaSBr$ [M + Na]$^+$ 552.0820, found 552.0815.

*Data for 4-Methyl-N-(3-(thiophen-2-yl)prop-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10i**).* (1.12 g, 2.45 mmol, 82%) A yellow solid: mp 96−97 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 4.9 Hz, 1H), 6.93 (d, *J* = 2.5 Hz, 1H), 6.87−6.90 (m, 1H), 4.47 (d, *J* = 18.7 Hz, 1H), 4.41 (d, *J* = 18.8 Hz, 1H), 3.73 (s, 2H), 2.65 (d, *J* = 13.6 Hz, 1H), 2.35 (s, 3H), 2.07 (d, *J* = 15.1 Hz, 1H), 1.97 (d, *J* = 13.6 Hz, 1H), 1.86 (d, *J* = 15.1 Hz, 1H), 1.60 (s, 3H), 1.00 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.4, 143.7, 135.0, 132.2, 129.5 (2C), 127.8 (2C), 127.1, 126.6, 122.0, 86.3, 78.8, 68.8, 63.8, 49.0, 43.8, 42.3, 40.0, 33.7, 30.3, 28.9, 21.4, 21.3; IR ($CH_2Cl_2$) 3107, 3070, 2958, 1714, 1598, 1428, 1348, 1163 cm$^{-1}$; MS (ESI) *m*/*e* 458.1 ([M + H]$^+$, 100), 435.2 (10), 424.1 (10), 398.1 (6); HRMS (ESI) calcd for $C_{24}H_{28}NO_4S_2$ [M + H]$^+$ 458.1460, found 458.1453.

*Data for 4-Methyl-N-(3-(4-nitrophenyl)prop-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10j**).* (0.93 g, 1.88 mmol, 88%) A white solid: mp 126−127 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.09 (d, *J* = 8.7 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.7 Hz, 2H), 4.47 (d, *J* = 18.8 Hz, 1H), 4.40 (d, *J* = 18.8 Hz, 1H), 3.82 (d, *J* = 14.7 Hz, 1H), 3.75 (d, *J* = 14.7 Hz, 1H), 2.65 (d, *J* = 13.6 Hz, 1H), 2.32 (s, 3H), 2.09 (d, *J* = 15.2 Hz, 1H), 1.93 (d, *J* = 13.6 Hz, 1H), 1.80 (d, *J* = 15.2 Hz, 1H) 1.52 (s, 3H), 1.00 (s, 3H), 0.92 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.9, 147.1, 143.8, 135.5, 132.3 (2C), 129.6 (2C), 129.2, 128.1 (2C), 123.3 (2C), 88.3, 83.9, 69.3, 63.9, 48.9, 44.0, 42.2, 39.6, 34.2, 30.6, 28.8, 21.5 (2C); IR ($CH_2Cl_2$) 2954, 2359, 1710, 1592, 1516, 1345, 1162 cm$^{-1}$; MS (ESI) *m*/*e* 519.2 ([M + Na]$^+$, 100), 514.2 (3); HRMS (ESI) calcd for $C_{26}H_{28}N_2O_6SNa$ [M + Na]$^+$ 519.1566, found 519.1556.

*Data for 4-Methyl-N-(3-(3-nitrophenyl)prop-2-yn-1-yl)-N-((4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl)-benzenesulfonamide (**10k**).* (0.94 g, 1.89 mmol, 89%) A white solid: mp 131−132 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.10 (dt, *J* = 6.9, 2.2 Hz, 1H), 7.82−7.83 (m, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.45−7.39 (m, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 4.47 (d, *J* = 18.8 Hz, 1H), 4.40 (d, *J* = 18.8 Hz, 1H), 3.80 (d, *J* = 14.8 Hz, 1H), 3.74 (d, *J* = 14.8 Hz, 1H), 2.65 (d, *J* = 13.6 Hz, 1H), 2.32 (s, 3H), 2.09 (d, *J* = 15.2 Hz, 1H), 1.94 (dd, *J* = 13.6, 1.4 Hz, 1H), 1.81 (dd, *J* = 15.2, 1.4 Hz, 1H) 1.62 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.9, 147.9, 144.1, 137.2, 135.4, 129.5 (2C), 129.2, 128.1 (2C), 126.2, 124.0, 123.0, 85.4, 83.2, 69.2, 63.9, 48.9, 44.0, 42.1, 39.5, 34.1, 30.5, 28.8, 21.4 (2C); IR ($CH_2Cl_2$) 3086, 2958, 2873, 1714, 1532, 1351 cm$^{-1}$; MS (ESI) *m*/*e* 519.2 ([M + Na]$^+$, 100), 497.2 (43), 402.1 (5), 351.2 (5) 290.1 (5), 263.1 (8); HRMS (ESI) calcd for $C_{26}H_{28}N_2O_6SNa$ [M + Na]$^+$ 519.1566, found 519.1555.

**Representative Experimental Procedure for Synthesis of Compound 14.** To a solution of 1-(hydroxymethyl)-4,4,6-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one (1.84 g, 10.0 mmol) in 20.0 mL of DCM at 0 °C under nitrogen was added 4-dimethylaminopyridine (0.12 g, 1.0 mmol), $NEt_3$ (1.39 g, 13.0 mmol) and 4-toluenesulfonyl chloride (2.29 g, 12.0 mmol). The reaction mixture was stirred at room temperature for 5 h before quenching with 50 mL of saturated aqueous sodium hydrogen carbonate. The resulting solution was extracted with $CH_2Cl_2$ (50 mL × 3). The combined organic solution was washed with water (100 mL × 3) and brine 100 mL × 3) and dried over $MgSO_4$ (15 g) and concentrated to give a crude solid. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to afford (4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl 4-methylbenzenesulfonate (7.45 g, 2.24 mmol, 75%). To the solution of (4,4,6-trimethyl-2-oxo-7-oxabicyclo[4.1.0]heptan-1-yl)methyl 4-methylbenzenesulfonate (1.02 g, 3.0 mmol) in 6.0 mL of THF at 0 °C under nitrogen was added sodium hydride (0.10 g, 4.5 mmol) and 3-phenylprop-2-yn-1-ol (0.60 g, 4.5 mmol). The reaction mixture was stirred at 55 °C for 5 h before quenching with 50 mL of saturated aqueous sodium hydrogen carbonate. The resulting solution was extracted with $CH_2Cl_2$ (50 mL × 3). The combined organic solution was washed with water (100 mL × 3) and brine (100 mL × 3), dried over $MgSO_4$ (15 g), and concentrated to give a crude liquid.

*Data for 4,4,6-Trimethyl-1-(((3-phenylprop-2-yn-1-yl)oxy)-methyl)-7-oxabicyclo-[4.1.0]heptan-2-one (**14a**).* The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to afford **14a** (0.54 g, 1.79 mmol, 60%) as a yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 (dd, *J* = 5.9, 2.2 Hz, 2H), 7.32−7.26 (m, 3H), 4.49 (d, *J* = 15.9 Hz, 1H), 4.39 (d, *J* = 15.9 Hz, 1H), 4.27 (d, *J* = 10.1 Hz, 1H), 3.68 (d, *J* = 10.1 Hz, 1H), 2.65 (d, *J* = 13.8 Hz, 1H), 2.11 (d, *J* = 15.9 Hz, 1H), 1.95 (dd, *J* = 13.8, 2.0 Hz, 1H), 1.75 (dd, *J* = 15.0, 2.0 Hz, 1H), 0.99 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.5, 131.7 (2C), 128.4, 128.3 (2C), 122.6, 86.5, 84.9, 67.5, 65.1, 63.7, 59.6, 48.6, 44.2, 34.4, 30.7, 27.7, 21.4; IR ($CH_2Cl_2$) 2959, 1712, 1088 cm$^{-1}$; MS (ESI) *m*/*e* (%) 321.1 [M + Na]$^+$, 66), 298.2 (3), 223.1 (100), 202.2 (1); HRMS (ESI) calcd for $C_{19}H_{22}O_3Na$ [M + Na]$^+$ 321.1467, found 321.1474.

*Data for 4,4,6-Trimethyl-1-(((3-(p-tolyl)prop-2-yn-1-yl)oxy)-methyl)-7-oxa-bicyclo[4.1.0]heptan-2-one (**14b**).* (0.65 g, 2.09 mmol, 70%) A yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.32 (d, $J$ = 8.0 Hz, 2H), 7.10 (d, $J$ = 8.0 Hz, 2H), 4.47 (d, $J$ = 14.6 Hz, 1H), 4.38 (d, $J$ = 14.6 Hz, 1H), 4.26 (d, $J$ = 10.0 Hz, 1H), 3.68 (d, $J$ = 10.0 Hz, 1H), 2.64 (d, $J$ = 14.0 Hz, 1H), 2.34 (s, 3H), 2.10 (d, $J$ = 14.8 Hz, 1H), 1.93 (dd, $J$ = 14.0, 1.6 Hz, 1H), 1.74 (dd, $J$ = 14.8, 1.6 Hz, 1H), 1.53 (s, 3H), 0.99 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.4, 138.5, 131.6 (2C), 129.0 (2C), 119.5, 86.6, 84.1, 67.5, 64.9, 63.7, 59.6, 48.6, 44.3, 34.4, 30.6, 27.7, 21.5, 21.4; IR ($CH_2Cl_2$) 2957, 1716, 1509, 1465, 1447, 1357, 1089 cm$^{-1}$; MS (ESI) $m/e$ 335.2 [M + Na]$^+$, 100), 199.0 (7), 143.1 (4); HRMS (ESI) calcd for $C_{20}H_{24}O_3Na$ [M + Na]$^+$ 335.1623, found 335.1631.

*Data for 4,4,6-Trimethyl-1-(((3-(phenanthren-9-yl)prop-2-yn-1-yl)oxy)-methyl)-7-oxabicyclo[4.1.0]heptan-2-one (**14c**).* (0.72 g, 1.81 mmol, 60%) A white solid: mp 96−97 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.67−8.66 (m, 2H), 8.44−8.42 (m, 1H), 7.98 (s, 1H), 7.83 (d, $J$ = 8.0 Hz, 1H), 7.68−7.56 (m, 4H), 4.66 (d, $J$ = 16.0 Hz, 1H), 4.58 (d, $J$ = 16.0 Hz, 1H), 4.39 (d, $J$ = 10.0 Hz, 1H), 3.80 (d, $J$ = 10.0 Hz, 1H), 2.67 (d, $J$ = 14.6 Hz, 1H), 2.11 (d, $J$ = 14.8 Hz, 1H), 1.96 (dd, $J$ = 14.6, 1.6 Hz, 1H), 1.74 (dd, $J$ = 14.8, 1.6 Hz, 1H), 1.56 (s, 3H), 0.99 (s, 3H), 0.96 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.4, 132.2, 131.0, 130.3, 130.0, 128.5, 127.5, 127.1, 126.9, 126.8, 122.7, 122.6, 118.9, 89.4, 84.7, 67.5, 65.3, 63.7, 59.9, 48.6, 44.3, 34.5, 30.7, 27.7, 21.5; IR ($CH_2Cl_2$) 2915, 1712, 1384, 1354, 1084 cm$^{-1}$; MS (ESI) $m/e$ 421.2 [M + Na]$^+$ (35), 292.1 (22), 291.1 (100); HRMS (ESI) calcd for $C_{27}H_{26}O_3Na$ [M + Na]$^+$ 421.1780, found 421.1771.

*Data for 1-(((3-(4-Bromophenyl)prop-2-yn-1-yl)oxy)methyl)-4,4,6-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one (**14d**).* (0.81 g, 2.28 mmol, 75%) A white solid: mp 58−59 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44 (d, $J$ = 8.8 Hz, 2H), 7.29 (d, $J$ = 8.8 Hz, 2H), 4.45 (d, $J$ = 16.0 Hz, 1H), 4.38 (d, $J$ = 16.0 Hz, 1H), 4.25 (d, $J$ = 10.0 Hz, 1H), 3.67 (d, $J$ = 10.0 Hz, 1H), 2.65 (d, $J$ = 13.6 Hz, 1H), 2.10 (d, $J$ = 14.8 Hz, 1H), 1.93 (dd, $J$ = 13.6, 2.0 Hz, 1H), 1.74 (dd, $J$ = 14.8, 2.0 Hz, 1H), 1.53 (s, 3H), 1.00 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.4, 133.1 (2C), 131.6 (2C), 122.7, 121.6, 86.1, 85.4, 67.5, 65.2, 63.7, 59.6, 48.6, 44.3, 34.4, 30.6, 27.7, 21.4; IR ($CH_2Cl_2$) 2958, 1714, 1634, 1486, 1089 cm$^{-1}$; MS (ESI) $m/e$ 379.1, 377.1, 359.1, 321.2, 199.1; HRMS (ESI) calcd for $C_{19}H_{22}BrO_3$ [M + H]$^+$ 377.0752, found 377.0745.

*Data for 4,4,6-Trimethyl-1-(((3-(m-tolyl)prop-2-yn-1-yl)oxy)-methyl)-7-oxabicyclo-[4.1.0]heptan-2-one (**14e**).* (0.72 g, 2.30 mmol, 77%) A yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.26 (s, 1H), 7.25 (d, $J$ = 10.0 Hz, 1H), 7.18 (t, $J$ = 7.2 Hz, 1H), 7.12 (d, $J$ = 7.2 Hz, 1H), 4.47 (d, $J$ = 16.0 Hz, 1H), 4.38 (d, $J$ = 16.0 Hz, 1H), 4.26 (d, $J$ = 10.0 Hz, 1H), 3.67 (d, $J$ = 10.0 Hz, 1H), 2.65 (d, $J$ = 13.6 Hz, 1H), 2.31 (s, 3H), 2.10 (d, $J$ = 15.2 Hz, 1H), 1.93 (dd, $J$ = 13.6, 2.0 Hz, 1H), 1.74 (dd, $J$ = 14.8, 2.0 Hz, 1H), 1.53 (s, 3H), 0.99 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.4, 137.9, 132.3, 129.3, 128.8, 128.2, 122.4, 86.7, 84.5, 67.5, 65.1, 63.7, 59.6, 48.6, 44.3, 34.5, 30.7, 27.8, 21.5, 21.2; IR ($CH_2Cl_2$) 2956, 1716, 1602, 1576, 1471, 1357, 1090 cm$^{-1}$; MS (ESI) $m/e$ 335.2, 291.1, 248.1, 199.0; HRMS (ESI) calcd for $C_{20}H_{24}O_3Na$ [M + Na]$^+$ 335.1623, found 335.1628.

*Data for 4,4,6-Trimethyl-1-(((3-(naphthalene-1-yl)prop-2-yn-1-yl)oxy)methyl)-7-oxabicyclo[4.1.0]heptan-2-one (**14f**).* (0.58 g, 1.68 mmol, 56%) A yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.33 (d, $J$ = 8.0 Hz, 1H), 7.81 (d, $J$ = 7.6 Hz, 2H), 7.66 (d, $J$ = 6.8 Hz, 1H), 7.55 (dd, $J$ = 7.6, 1.2 Hz, 1H), 7.50 (dd, $J$ = 7.2, 0.8 Hz, 1H), 7.39 (d, $J$ = 7.6 Hz, 1H),4.63 (d, $J$ = 16.0 Hz, 1H), 4.55 (d, $J$ = 16.0 Hz, 1H), 4.36 (d, $J$ = 10.0 Hz, 1H), 3.76 (d, $J$ = 10.0 Hz, 1H), 2.65 (d, $J$ = 13.6 Hz, 1H), 2.09 (d, $J$ = 14.8 Hz, 1H), 1.93 (dd, $J$ = 13.6, 2.0 Hz, 1H), 1.74 (dd, $J$ = 14.8, 2.0 Hz, 1H), 1.53 (s, 3H), 0.98 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.3, 133.2, 133.0, 130.6, 128.8, 128.2, 126.7, 126.3, 126.0, 125.1, 120.2, 89.7, 84.6, 67.5, 65.2, 63.7, 59.7, 48.5, 44.2, 34.4, 30.6, 27.7, 21.4; IR ($CH_2Cl_2$) 2956, 1714, 1644, 1395, 1085 cm$^{-1}$; MS (ESI) $m/e$ 371.2, 366.2, 337.2; HRMS (ESI) calcd for $C_{23}H_{24}O_3Na$ [M + Na]$^+$ 371.1623, found 371.1615.

*Data for 1-(((3-(3-Methoxyphenyl)prop-2-yn-1-yl)oxy)methyl)-4,4,6-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one (**14g**).* (0.67 g, 2.05 mmol, 68%) A yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.23−7.19 (m, 1H), 7.03 (d, $J$ = 7.6 Hz, 1H), 6.97−6.96 (m, 1H), 6.87 (dd, $J$ = 8.4, 2.6 Hz, 1H), 4.48 (d, $J$ = 16.0 Hz, 1H), 4.39 (d, $J$ = 16.0 Hz, 1H), 4.27 (d, $J$ = 10.0 Hz, 1H), 3.79 (s, 3H), 3.68 (d, $J$ = 10.0 Hz, 1H), 2.65 (d, $J$ = 13.8 Hz, 1H), 2.11 (d, $J$ = 14.8 Hz, 1H), 1.93 (dd, $J$ = 13.8, 2.0 Hz, 1H), 1.74 (dd, $J$ = 14.8, 2.0 Hz, 1H), 1.54 (s, 3H), 1.00 (s, 3H), 0.94 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.2, 159.1, 129.2, 124.1, 123.4, 116.5, 114.8, 86.3, 84.6, 67.4, 65.0, 63.5, 59.4, 55.1, 48.4, 44.1, 34.3, 30.5, 27.6, 21.3; IR ($CH_2Cl_2$) 2957, 2366, 1717, 1604, 1468, 1290 cm$^{-1}$; MS (ESI) $m/e$ 351.2 [M $^+$ Na]$^+$, 100), 346.2 (11), 291.1 (14), 268.1 (5); HRMS (ESI) calcd for $C_{20}H_{24}O_4Na$ [M + Na]$^+$ 351.1572, found 351.1574.

*Data for 1-(((3-([1,1′-Biphenyl]-4-yl)prop-2-yn-1-yl)oxy)methyl)-4,4,6-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one (**14h**).* (0.73 g, 1.96 mmol, 65%) A white solid: mp 67−68 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.58−7.49 (m, 6H), 7.43 (d, $J$ = 7.5 Hz, 2H), 7.34 (t, $J$ = 7.5 Hz, 1H), 4.51 (d, $J$ = 16.0 Hz, 1H), 4.42 (d, $J$ = 16.0 Hz, 1H), 4.31 (d, $J$ = 10.0 Hz, 1H), 3.71 (d, $J$ = 10.0 Hz, 1H), 2.65 (d, $J$ = 14.8 Hz, 1H); 2.10 (d, $J$ = 14.8 Hz, 1H), 1.94 (dd, $J$ = 14.9, 2.0 Hz, 1H), 1.73 (dd, $J$ = 14.8, 2.0 Hz, 1H), 1.55 (s, 3H), 1.00 (s, 3H), 0.95 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.2, 141.0, 140.0, 132.0 (2C), 128.7 (2C), 127.5, 126.8 (4C), 121.4, 86.3, 85.5, 67.3, 65.0, 63.5, 59.5, 48.4, 44.1, 34.3, 30.5, 27.6, 21.3 cm$^{-1}$; IR ($CH_2Cl_2$) 2957, 1716, 1487, 1358, 1224, 1088 cm$^{-1}$; MS (ESI) $m/e$ 375.2, 303.2, 276.1, 265.1, 121.1; HRMS (ESI) calcd for $C_{25}H_{27}O_3$ [M + H]$^+$ 375.1960, found 375.1951.

**General Experimental Procedure for Synthesis of Isoquinolinone 2.** To a solution of **1a** (0.05 g, 0.12 mmol) in 1.2 mL of $CH_2Cl_2$ at room temperature under nitrogen, $NHTf_2$ (3 mg, 0.01 mmol) was added. The reaction mixture was heated to 40 °C for 70 min until no starting material was detected by TLC. The reaction mixture was cooled to room temperature and was quenched with saturated aqueous $NaHCO_3$ (20 mL). The organic phase was separated, and the aqueous phase was extracted with $CH_2Cl_2$ (20 mL × 3). The combined organic layers were washed with brine (50 mL × 3), dried over anhydrous $MgSO_4$ (5.0 g), and filtered. The filtrate was concentrated under reduced pressure to give the crude mixture.

*Data for 4-Benzoyl-2-tosyl-1,2,3,4,6,7-hexahydroisoquinolin-8(5H)-one (**2a**).* In the typical procedure, to a solution of **1a** (0.05 g, 0.12 mmol) in 1.2 mL of $CH_2Cl_2$ at 40 °C was added $HNTf_2$ (3.0 mg, 0.01 mmol). The reaction mixture was stirred for 70 min. The crude mixture was purified by silica gel column chromatography (ethyl acetate/hexanes 1:2) to give **2a** (0.041 g, 0.10 mmol, 83%) as colorless crystals: mp 210−211 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.98 (d, $J$ = 7.6 Hz, 2H), 7.69−7.61 (m, 3H), 7.54 (d, $J$ = 6.0 Hz, 2H), 7.29 (d, $J$ = 8.0 Hz, 2H), 4.59 (dd, $J$ = 7.3, 5.5 Hz, 1H), 4.09 (d, $J$ = 16.5 Hz, 1H), 3.76 (ddd, $J$ = 12.3, 5.5, 1.0 Hz, 1H), 3.56 (ddd, $J$ = 16.4, 4.9, 2.5 Hz, 1H), 3.09 (dd, $J$ = 12.0, 7.6 Hz, 1H), 2.46−2.39 (m, 2H), 2.41 (s, 3H), 2.30 (m, 1H), 2.12−1.84 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.6, 196.5, 152.2, 144.0, 136.0, 134.2, 133.1, 131.2, 129.8 (2C), 129.2 (2C), 128.6 (2C), 127.8 (2C), 48.7, 46.1, 43.1, 37.6, 29.3, 22.2, 21.5; IR ($CH_2Cl_2$) 2961, 1670, 1646, 1594, 1346, 1164 cm$^{-1}$; MS (ESI) $m/e$ 432.1 ([M + Na]$^+$, 100), 410.1 (6), 380.6 (3), 341.6 (6); HRMS (ESI) calcd for $C_{23}H_{23}NO_4NaS$ [M + Na]$^+$ 432.1245, found 432.1236. Crystals suitable for X-ray diffraction analysis were grown from a solution of $CH_2Cl_2$/hexanes.

*Data for 4-(3-Methylbenzoyl)-2-tosyl-1,2,3,4,6,7-hexahydroisoquinolin-8(5H)-one (**2b**).* In the typical procedure, to a solution of **1b** (0.11 g, 0.25 mmol) in 2.5 mL of $CH_2Cl_2$ was added $HNTf_2$ (9.0 mg, 0.03 mmol). The reaction mixture was stirred for 60 min at 40 °C. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to give **2b** (90 mg, 0.21 mmol, 84%) as a white solid: mp 106−107 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 7.5 Hz, 2H), 7.64 (d, $J$ = 8.1 Hz, 2H), 7.47 (d, $J$ = 7.4 Hz, 1H), 7.42 (t, $J$ = 7.4 Hz, 1H), 7.29 (d, $J$ = 7.9 Hz, 2H), 4.58 (br s, 1H), 4.06 (d, $J$ = 16.3 Hz, 1H), 3.74 (m, 1H), 3.58 (d, $J$ = 16.4 Hz, 1H), 3.12 (m, 1H), 2.44−2.25 (m, 9H), 2.09−1.87 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.7, 196.5, 152.3, 143.9, 139.0, 135.9, 134.9, 132.9, 130.9, 129.7, 128.9, 128.9, 127.6, 125.7, 48.4, 45.9, 42.9, 37.4, 29.2, 22.0, 21.4, 21.3; IR ($CH_2Cl_2$) 2926, 2359, 1671, 1390, 1349, 1165 cm$^{-1}$; MS (ESI) $m/e$ 446.1 ([M + Na]$^+$, 100), 441.2, 384.1,

309.1; HRMS (ESI) calcd for $C_{24}H_{25}NO_4S$ $[M + Na]^+$ 446.1402, found 446.1396.

*Data for 4-(4-Methylbenzoyl)-2-tosyl-1,2,3,4,6,7-hexahydroisoquinolin-8(5H)-one (**2c**).* In the typical procedure, to a solution of **1c** (0.05 g, 0.12 mmol) in 1.2 mL of $CH_2Cl_2$ was added $HNTf_2$ (3.0 mg, 0.01 mmol). The reaction mixture was stirred for 10 min at 40 °C. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to give **2c** (32 mg, 0.076 mmol, 63%) as colorless crystals: mp 207−208 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.89 (d, $J$ = 8.2 Hz, 2H), 7.65 (d, $J$ = 8.2 Hz, 2H), 7.34 (d, $J$ = 8.0 Hz, 2H), 7.29 (d, $J$ = 8.0 Hz, 2H), 4.60 (m, 1H), 4.14 (d, $J$ = 16.4 Hz, 1H), 3.80 (dd, $J$ = 12.1 Hz, 5.5 Hz, 1H), 3.50 (d, $J$ = 17.9 Hz, 1H), 3.01 (dd, $J$ = 12.1 Hz, 8.2 Hz, 1H), 2.46 (s, 3H), 2.45−2.39 (m, 2H), 2.41 (s, 3H), 2.39−2.26 (m, 1H), 2.11−1.86 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.2, 196.6, 152.4, 145.4, 143.9, 135.5, 131.0, 130.1, 129.8, 129.7, 128.7, 127.8, 48.6, 46.2, 43.1, 37.5, 29.2, 22.1, 21.7, 21.5; IR ($CH_2Cl_2$) 2925, 1672, 1606, 1350, 1165 cm$^{-1}$; MS (ESI) $m/e$ (%) 446.1 ($[M + Na]^+$, 100), 314.1 (12), 313.6 (25), 309 (22); HRMS (ESI) $[M + Na]^+$ $C_{24}H_{25}NO_4NaS$ calcd 446.1402, found 446.1401. Crystals suitable for X-ray diffraction analysis were grown from $CH_2Cl_2$ and hexanes.

*Data for 4-(4-Methoxybenzoyl)-2-tosyl-1,2,3,4,6,7-hexahydroisoquinolin-8(5H)-one (**2d**).* In the typical procedure, to a solution of **1d** (0.05 g, 0.11 mmol) in 1.1 mL of $CH_2Cl_2$ was added $HNTf_2$ (3.0 mg, 0.01 mmol). The reaction mixture was stirred at 40 °C for 5 min. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to give **2d** (30 mg, 0.069 mmol, 60%) as a white solid: mp 77−78 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.89 (d, $J$ = 8.8 Hz, 2 H), 7.65 (d, $J$ = 8.1 Hz, 2 H), 7.30 (d, $J$ = 8.1 Hz, 2 H), 7.00 (d, $J$ = 8.8 Hz, 2 H), 4.59 (m, 1H), 4.18 (d, $J$ = 16.4 Hz, 1 H), 3.92 (s, 3H), 3.84 (m, 1H), 3.46 (d, $J$ = 16.4 Hz, 1H), 2.96 (dd, $J$ = 12.0, 8.5 Hz, 1H), 2.45−2.38 (m, 2H), 2.41 (s, 3H), 2.32 (m, 1H), 2.10−1.84 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 196.6, 195.9, 164.4, 152.6, 143.9, 133.0, 131.1, 130.0, 129.8, 129.0, 127.7, 114.3, 55.6, 48.2, 46.3, 43.1, 37.5, 29.1, 22.1, 21.5; IR ($CH_2Cl_2$) 2926, 2852, 1668, 1600, 1348, 1260 cm$^{-1}$; MS (ESI) $m/e$ (%) 462.1 ($[M + Na]^+$, 100), 440.2 (8), 398.2 (14), 398.1 (100), 388.2 (12), 319.2 (10); HRMS (ESI) $[M + Na]^+$ $C_{24}H_{25}NO_5NaS$ calcd 462.1351, found 462.1361.

*Data for 4-([1,1′-Biphenyl]-4-carbonyl)-2-tosyl-1,2,3,4,6,7-hexahydroisoquinolin8(5H)-one (**2e**).* In the typical procedure, to a solution of **1e** (0.05 g, 0.10 mmol) in 1.0 mL of $CH_2Cl_2$ was added $HNTf_2$ (3.0 mg, 0.01 mmol). The reaction mixture was stirred at 40 °C for 25 min. The crude mixture was purified by flash column chromatography (silica gel, 1:2 ethyl acetate/hexanes) to give **2e** (0.04 g, 0.08 mmol, 80%) as a white solid: mp 182−183 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.05 (d, $J$ = 8.3 Hz, 2H), 7.76 (d, $J$ = 8.3 Hz, 2H), 7.66 (d, $J$ = 7.9 Hz, 4H), 7.50 (d, $J$ = 7.3 Hz, 2H), 7.44 (t, $J$ = 7.3 Hz, 1H), 7.29 (d, $J$ = 7.9 Hz, 2H), 4.64 (m, 1H), 4.12 (d, $J$ = 16.1 Hz, 1H), 3.81 (dd, $J$ = 12.0, 5.6 Hz, 1H), 3.57 (d, $J$ = 16.1 Hz, 1H), 3.11 (dd, $J$ = 12.0 Hz, 7.8 Hz, 1H), 2.47−2.30 (m, 3H), 2.40 (s, 3H), 2.15−1.85 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.1, 196.5, 152.2, 146.9, 143.9, 139.3, 134.5, 133.0, 131.1, 129.8, 129.2, 129.0, 128.6, 127.7, 127.7, 127.3, 48.6, 46.1, 43.0, 37.5, 29.2, 22.1, 21.5; IR ($CH_2Cl_2$) 2923, 2853, 1674, 1601, 1349, 1165 cm$^{-1}$; MS (ESI) $m/e$ (%) 508.2 ($[M + Na]^+$, 100), 507.3 (17), 490.4 (12), 463.3 (8), 457.3 (12), 454.3 (27), 449.4 (28), 443.2 (8), 433.2 (8), 432.2 (32); HRMS (ESI) $[M + Na]^+$ $C_{29}H_{27}NO_4NaS$ calcd 508.1559, found 508.1552.

*Data for 4-(1-Naphthoyl)-2-tosyl-1,2,3,4,6,7-hexahydroisoquinolin-8(5H)-one (**2f**).* In the typical procedure, to a solution of **1f** (0.05 g, 0.11 mmol) in 1.1 mL of $CH_2Cl_2$ was added $HNTf_2$ (3.0 mg, 0.01 mmol). The reaction mixture was stirred at 40 °C for 15 min. The crude mixture was purified by flash column chromatography (silica gel, 1:3 ethyl acetate/hexanes) to give **2f** (0.03 g, 0.065 mmol, 60%) as a pale yellow liquid: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.50 (d, $J$ = 8.4 Hz, 1H), 8.08 (d, $J$ = 8.2 Hz, 1H), 7.94 (t, $J$ = 8.2 Hz, 2H), 7.67−7.55 (m, 5H), 7.30−7.25 (m, 2H), 4.53 (m, 1H), 3.91 (d, $J$ = 16.3 Hz, 1H), 3.76 (d, $J$ = 16.3 Hz, 1H), 3.55 (dd, $J$ = 12.8, 5.3 Hz, 1H), 3.37 (dd, $J$ = 12.8, 6.6 Hz, 1H), 2.52−2.42 (m, 3H), 2.31 (s, 3H), 2.23−2.13 (m, 1H), 2.08−1.88 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 200.9, 196.6, 152.1, 143.9, 134.9, 134.1, 133.8, 132.8, 131.0, 130.4, 129.8, 128.6, 128.5, 127.9, 127.8, 127.0, 125.6, 124.3, 52.1, 45.9, 43.2, 37.6, 29.7, 22.2, 21.5; IR ($CH_2Cl_2$) 2925, 1670, 1596, 1349, 1166, 1091 cm$^{-1}$; MS (FAB) $m/e$ (%) 460.2 ($[M + H]^+$, 100), 443.2 (15), 427.4 (21), 424.1 (8), 419.3 (4); HRMS (FAB) $[M + H]^+$ $C_{27}H_{26}NO_4S$ calcd 460.1583, found 460.1579.

*Data for Ethyl 2-(8-Oxo-2-tosyl-1,2,3,4,5,6,7,8-octahydroisoquinoline-4-carbonyl)benzoate (**2g**).* In the typical procedure, to a solution of **1g** (0.10 g, 0.21 mmol) in 2.1 mL of $CH_2Cl_2$ was added $HNTf_2$ (6.0 mg, 0.02 mmol). The reaction mixture was stirred at 40 °C for 30 min. The crude mixture was purified by flash column chromatography (silica gel, 1:5 ethyl acetate/hexanes) to give **2g** (5.0 mg, 0.01 mmol, 5%) as a white solid: mp 206−207 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.01 (d, $J$ = 7.6 Hz, 1H), 7.92 (d, $J$ = 7.9 Hz, 1H), 7.84 (t, $J$ = 7.9 Hz, 1H), 7.70 (d, $J$ = 8.2 Hz, 2H), 7.63 (t, $J$ = 7.6 Hz, 1H), 7.34 (d, $J$ = 8.2 Hz, 2H), 5.01 (d, $J$ = 14.5 Hz, 1H), 4.49 (dd, $J$ = 8.5, 5.0 Hz, 1H), 4.21 (d, $J$ = 17.0 Hz, 1H), 3.89 (d, $J$ = 14.5 Hz, 1H), 3.53 (d, $J$ = 17.0 Hz, 1H), 3.50−3.41 (m, 2H), 2.43 (s, 3H), 2.42−2.35 (m, 1H), 2.14−2.03 (m, 2H), 2.03−1.95 (m, 1H), 1.91−1.81 (m, 1H), 1.77−1.66 (m, 1H), 1.11 (t, $J$ = 7.0 Hz, 3H) ; $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 204.3, 165.6, 144.5, 141.5, 138.2, 135.1, 133.0, 130.1, 130.0, 127.8, 126.3, 125.0, 123.6, 122.6, 91.9, 66.5, 62.7, 56.7, 45.9, 33.7, 31.5, 22.3, 21.6, 15.2; IR ($CH_2Cl_2$) 2925, 1783, 1726, 1598, 1351, 1164, 1092 cm$^{-1}$; MS (ESI) $m/e$ (%) 504.1 ($[M + Na]^+$, 100), 433.1 (20); HRMS (ESI) $C_{26}H_{27}NO_6NaS$ $[M + Na]^+$ calcd 504.1457, found 504.1448.

**General Experimental Procedure for Synthesis of Heterotetracyclic Compound 4.** To a solution of **1a** (0.10 g, 0.25 mmol) in 2.5 mL of $CH_2Cl_2$ at −15 °C under nitrogen was added $FeCl_3$ (0.082 g, 0.50 mmol). The reaction mixture was stirred for 1.5 h at −15 °C until no **1a** was detected by TLC. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (20 mL). The organic phase was separated, and the aqueous phase was extracted with ethyl ether (20 mL × 3). The combined organic layers were washed with brine (50 mL × 3), dried over anhydrous $MgSO_4$ (5 g), and concentrated to give the crude mixture.

*Data for (4R,4aS,12bS)-4,8-Dichloro-6-tosyl-1,2,3,4,4a,5,6,7-octahydroindeno-[2,1-d]isoquinolin-4a-ol (**4a**).* In the typical procedure, to a solution of **1a** (0.10 g, 0.25 mmol) in 2.5 mL of $CH_2Cl_2$ at −15 °C under nitrogen was added $FeCl_3$ (0.082 g, 0.50 mmol). The reaction mixture was stirred at −15 °C for 1.5 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to give **4a** (0.089 g, 0.19 mmol, 77%) as colorless crystals: mp 164−165 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.4 Hz, 2H), 7.59 (d, $J$ = 7.6 Hz, 1H), 7.48 (d, $J$ = 7.6 Hz, 1H), 7.40 (d, $J$ = 7.2 Hz, 1H), 7.37 (d, $J$ = 8.4 Hz, 2H),7.29 (td, $J$ = 8.4, 1.2 Hz, 1H), 4.91 (dd, $J$ = 13.2, 1.5 Hz, 1H), 4.81 (dd, $J$ = 13.2, 5.2 Hz, 1H), 4.05 (dd, $J$ = 13.2, 1.6 Hz, 1H), 3.33 (d, $J$ = 12.8 Hz, 1H), 3.12 (d, $J$ = 13.2 Hz, 1H), 2.45−2.40 (m, 4H), 2.19 (br s, 1H, OH), 2.10 (tt, $J$ = 13.2, 4.4 Hz, 1H), 1.98−1.87 (m, 2H), 1.81 (dq, $J$ = 13.6, 2.4 Hz, 1H), 1.09 (dq, $J$ = 14.0, 1.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 145.6, 144.1, 140.9, 135.9, 133.9, 129.9, 128.8, 127.8, 127.7, 126.4, 124.5, 120.5, 75.4, 64.1, 58.9, 46.8, 41.7, 33.7, 30.3, 21.8, 21.6; IR ($CH_2Cl_2$) 3445, 2952, 1642, 1441, 1159 cm$^{-1}$; MS (ESI) $m/e$ (%) 486.0 ($[M + Na]^+$, 100), 468.1 (5), 392.1 (14), 356.1 (6), 313.1 (9), 300.6 (3); HRMS (ESI) calcd for $C_{23}H_{23}NO_3NaSCl_2$ $[M + Na]^+$ 486.0673, found 486.0670. Crystals suitable for X-ray diffraction analysis were grown from $CH_2Cl_2$ and hexanes.

*Data for (4R,4aS,12bS)-4,8-Dichloro-10-methyl-6-tosyl-1,2,3,4,4a,5,6,7-octahydroindeno[2,1-d]isoquinolin-4a-ol (**4c**).* In the typical procedure, to a solution of **1c** (0.21 g, 0.50 mmol) in 5.0 mL of $CH_2Cl_2$ at −15 °C under nitrogen was added $FeCl_3$ (0.163 g, 1.00 mmol). The reaction mixture was stirred at −15 °C for 1.5 h. The crude mixture was purified by flash column chromatography (silica gel, 1:3 ethyl acetate/hexanes) to give **4c** (0.181 g, 0.38 mmol, 76%) as a white solid: mp 246−247 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.0 Hz, 2H), 7.39−7.34 (m, 4H), 7.20 (d, $J$ = 7.6 Hz, 1H), 4.88 (d, $J$ = 13.2 Hz, 1H), 4.82 (dd, $J$ = 13.2, 4.8 Hz, 1H), 4.05 (dd, $J$ = 13.2, 1.6 Hz, 1H), 3.33 (d, $J$ = 12.8 Hz, 1H), 3.12 (d, $J$ = 12.8 Hz, 1H), 2.46 (s, 3H), 2.45 (m, 1H), 2.43 (s, 3H), 2.20 (br s, 1H, OH), 2.10 (tt, $J$ =


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13.2, 4.4 Hz, 1H), 1.98−1.87 (m, 2H), 1.81−1.78 (m, 1H), 1.11−1.08 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 145.8, 144.1, 138.3, 136.4, 134.6, 129.9, 128.8, 128.6, 127.7, 125.7, 120.2, 75.3, 63.9, 58.7, 46.8, 41.8, 33.7, 30.3, 21.8, 21.7, 21.6; IR ($CH_2Cl_2$) 3549, 2943, 1587, 1578, 1351, 1159 cm$^{-1}$; MS (ESI) *m/e* (%) 500.1 ([M + Na]$^+$, 100), 478.1 (30), 293.1 (3), 212.1 (18); HRMS (ESI) calcd for $C_{24}H_{25}NO_3NaSCl_2$ [M + Na]$^+$ 500.0829, found 500.0830.

*Data for (4R,4aS,14bS)-4,8-Dichloro-6-tosyl-1,2,3,4,4a,5,6,7-octahydrobenzo-[4,5]indeno[2,1-d]isoquinolin-4a-ol (**4f**).* In the typical procedure, to a solution of **1f** (0.23 g, 0.50 mmol) in 5.0 mL of $CH_2Cl_2$ at −15 °C under nitrogen was added $FeCl_3$ (0.163 g, 1.00 mmol). The reaction mixture was stirred at −15 °C for 2.0 h. The crude mixture was purified by flash column chromatography (silica gel, 1:3 ethyl acetate/hexanes) to give **4f** (0.119 g, 0.23 mmol, 46%) as a white solid: mp 227−228 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.19 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.81−7.78 (m, 4H), 7.55 (td, *J* = 8.0, 1.2 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 5.05−4.97 (m, 2H), 4.99 (dd, *J* = 12.8, 1.2 Hz, 1H), 3.38 (d, *J* = 13.2 Hz, 1H), 3.17 (d, *J* = 12.8 Hz, 1H), 2.52 (m, 1H), 2.45 (s, 3H), 2.26 (m, 2H), 2.0 (m, 2H), 1.84 (m, 1H), 1.12 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 145.4, 144.1, 137.8, 134.4, 133.9, 133.5, 129.9, 129.1, 128.6, 128.5, 127.7, 127.1, 126.5, 125.9, 123.3, 122.3, 75.9, 64.0, 58.2, 47.1, 41.8, 33.8, 30.6, 21.9, 21.6; IR ($CH_2Cl_2$) 3380, 2988, 1602, 1597, 1340, 1159 cm$^{-1}$; MS (EI) *m/e* (%) 536.0 ([M + Na]$^+$, 100), 516.1 (6), 333.6 (7), 263.1 (18), 174.1 (8), 138.5 (3); HRMS (ESI) calcd for $C_{27}H_{25}NO_3NaSCl_2$ [M + Na]$^+$ 536.0830, found 536.0822.

*Data for (4R,4aS,12bS)-4,8-Dichloro-11-methoxy-6-tosyl-1,2,3,4,4a,5,6,7-octahydroindeno[2,1-d]isoquinolin-4a-ol (**4i**).* In the typical procedure, to a solution of **1i** (0.22 g, 0.50 mmol) in 5.0 mL of $CH_2Cl_2$ at −15 °C under nitrogen was added $FeCl_3$ (0.163 g, 1.00 mmol). The reaction mixture was stirred at −15 °C for 2.5 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to give **4i** (0.171 g, 0.35 mmol, 69%) as a white solid: mp 235−236 °C; 1H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 2.4 Hz, 1H), 6.80 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.89 (dd, *J* = 12.8, 1.6 Hz, 1H), 4.75 (dd, *J* = 12.8, 4.8 Hz, 1H), 4.04 (dd, *J* = 12.8, 1.6 Hz, 1H), 3.85 (s, 3H), 3.33 (d, *J* = 13.2 Hz, 1H), 3.12 (d, *J* = 13.2 Hz, 1H), 2.45 (s, 3H), 2.40 (m, 1H), 2.06 (tt, *J* = 13.6, 4.0 Hz, 1H), 1.98−1.87 (m, 2H), 1.81 (dquin, *J* = 13.6, 2.0 Hz, 1H), 1.11−1.07 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 159.9, 144.1, 142.6, 137.5, 137.2, 130.1, 129.9, 128.5, 127.7, 125.2, 112.2, 106.2, 75.4, 64.2, 58.3, 55.6, 46.7, 41.7, 33.8, 30.8, 21.9, 21.6; IR ($CH_2Cl_2$) 3321, 2915, 1616, 1447, 1162 cm$^{-1}$; MS (ESI) *m/e* (%) 516.0 ([M + Na]$^+$, 100), 494.1 (21), 337.6 (12), 121.1 (13); HRMS (ESI) calcd for $C_{24}H_{25}NO_4NaSCl_2$ [M + Na]$^+$ 516.0779, found 516.0774.

*Data for (4R,4aS,12bS)-4,8-Dibromo-6-tosyl-1,2,3,4,4a,5,6,7-octahydroindeno-[2,1-d]isoquinolin-4a-ol (**7**).* In the typical procedure, to a solution of **1a** (0.10 g, 0.25 mmol) in 2.5 mL of $CH_2Cl_2$ at −15 °C under nitrogen was added $FeBr_3$ (0.15 g, 0.50 mmol). The reaction mixture was stirred at −15 °C for 1 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to give **7** (93 mg, 0.17 mmol, 67%) as a white solid: mp 205−206 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.78 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 6.8 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.26 (td, *J* = 7.2, 1.2 Hz, 1H), 4.95 (dd, *J* = 12.8, 4.8 Hz, 1H), 4.86 (dd, *J* = 13.2, 1.6 Hz, 1H), 4.12 (dd, *J* = 13.2, 1.6 Hz, 1H), 3.37 (d, *J* = 13.2 Hz, 1H), 3.18 (d, *J* = 13.2 Hz, 1H), 2.55−2.45 (m, 4H), 2.18−2.05 (m, 3H), 1.96 (td, *J* = 13.6, 4.0 Hz, 1H), 1.79−1.73 (m, 1H), 1.09 (dd, *J* = 12.4, 1.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 145.5, 144.1, 141.8, 139.7, 133.9, 129.9 (2C), 127.9, 127.7 (2C), 126.4, 124.5, 121.7, 118.9, 74.9, 59.9, 57.6, 48.5, 43.2, 34.7, 30.3, 22.8, 21.6; IR ($CH_2Cl_2$) 3321, 2915, 1623, 1348, 1162 cm$^{-1}$; MS (ESI) *m/e* 577.9, 575.9, 573.9, 504.1, 482.1, 266.0, 263.1, 219.0; HRMS (ESI) calcd for $C_{23}H_{23}NO_3NaSBr_2$ [M + Na]$^+$ 573.9663, found 573.9672. Crystals suitable for X-ray diffraction analysis were grown from $CH_2Cl_2$ and hexanes.

**Procedure for TMSOTf-Promoted Semipinacol Rearrangement of 8 to 9.** To a solution of **8** (0.10 g, 0.24 mmol) in 2.3 mL of $CH_2Cl_2$ at room temperature under nitrogen was added TMSOTf (0.0053 mL, 0.006 mmol). The reaction mixture was stirred at room temperature for 1 h. After cooling to 0 °C, the reaction was added 1.5 mL of 2 M NaOH in MeOH. The mixture was stirred at room temperature for an additional 2 h. The reaction mixture was diluted with 20 mL of water and extracted with ethyl acetate (20 mL × 3). The combined organic layers were washed with brine (50 mL × 3), dried over anhydrous $MgSO_4$ (10 g), and concentrated to give the crude mixture. The crude oil was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:3) to give **9** (0.079 g, 0.19 mmol, 79%) as a white solid: mp 94−95 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74 (d, *J* = 8.2 Hz, 2H), 7.28−7.22 (m, 5H), 7.16−7.14 (m, 2H), 4.38 (s, 4H), 2.70 (q, *J* = 6.7 Hz, 1H), 2.36 (s, 3H), 2.34−2.29 (m, 2H), 1.97−1.84 (m, 2H), 1.73−1.66 (m, 1H), 1.35 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 216.2, 201.2, 143.7, 136.0, 131.5 (2C), 129.6 (2C), 128.5, 128.1 (2C), 127.5 (2C), 121.9, 86.0, 81.5, 62.7, 51.1, 38.2, 38.0, 33.8, 21.4, 20.6, 19.2; IR ($CH_2Cl_2$) 3053, 2970, 1715, 1440, 1349, 1162 cm$^{-1}$; MS (MALDI) *m/e* (%) 446.1 ([M + Na]$^+$, 73), 406.1 (10); HRMS (MALDI) calcd for $C_{24}H_{25}NO_4SNa$ [M + Na]$^+$ 446.1420, found 446.1414.

**Experimental Procedure for TMSOTf-Promoted Cycloisomerization Reaction of 10a. Formation of 11a, 12a, and 13a.** To a solution of **10a** (0.10 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under nitrogen was added TMSOTf (0.019 mL, 0.11 mmol). The reaction mixture was stirred at room temperature for 24 h, after which time to the reaction mixture was added 10 mL of water. The mixture was extracted with ethyl acetate (20 mL × 3). The combined organic layers were washed with brine (50 mL × 3), dried over anhydrous $MgSO_4$ (10 g) and concentrated to give the crude mixture. The residue was purified by flash column chromatography using a mixture of EtOAc/hexanes (1/2) as eluent to afford **11a** (29 mg, 0.064 mmol, 29%), **12a** (22 mg, 0.048 mmol, 22%) and **13a** (24 mg, 0.062 mmol, 28%).

*Data for 4-Methyl-N-(2-oxo-2-(1,4,4-trimethyl-2-oxocyclopentyl)-ethyl)-N-(3-phenyl-prop-2-yn-1-yl)benzenesulfonamide (**11a**).* A white solid: mp 108−109 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.75 (d, *J* = 8.2 Hz, 2H), 7.29−7.23 (m, 5H), 7.16−7.14 (m, 2H), 4.49−4.40 (m, 4H), 2.80 (d, *J* = 13.7 Hz, 1H), 2.36 (s, 3H), 2.23 (d, *J* = 17.6 Hz, 1H), 2.17 (d, *J* = 17.6 Hz, 1H), 1.55 (d, *J* = 13.7 Hz, 1H), 1.43 (s, 3H), 1.11 (s, 3H), 1.00 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 215.9, 200.9, 143.6, 136.0, 131.5 (2C), 129.6 (2C), 128.5, 128.1 (2C), 127.5 (2C), 121.9, 86.1, 81.5, 63.5, 53.0, 50.8, 46.7, 38.1, 33.4, 29.6, 29.0, 24.1, 21.4; IR ($CH_2Cl_2$) 2959, 2872, 1739, 1724, 1598, 1351 cm$^{-1}$; MS (ESI) *m/e* (%) 474.2 ([M + Na]$^+$, 100), 469.2 (10), 452.2 (5); HRMS (ESI) calcd for $C_{26}H_{29}NO_4SNa$ [M + Na]$^+$ 474.1715, found 474.1724. Crystals suitable for X-ray diffraction analysis were slow recrystallization from dichloromethane and hexanes.

*Data for 2-(4-Benzoyl-1-tosyl-1H-pyrrol-3-yl)-2,4,4-trimethylcyclopentanone (**12a**).* A pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.75 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 2H), 7.43 (s, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.07 (s, 1H), 2.68 (d, *J* = 18.8 Hz, 1H), 2.43 (s, 3H), 2.34 (d, *J* = 18.8 Hz, 1H), 2.26 (d, *J* = 13.6 Hz, 1H), 1.91 (d, *J* = 13.6 Hz, 1H), 1.53 (s, 3H), 1.21 (s, 3H), 1.11 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 220.6, 190.9, 145.9, 139.4, 134.9, 133.4, 132.2, 130.3 (2C), 129.1 (2C), 128.4 (2C), 127.3 (2C), 124.6, 119.3, 53.0, 52.0, 50.4, 32.9, 31.8, 31.0, 25.7, 21.6; IR ($CH_2Cl_2$) 2952, 1734, 1649, 1598, 1343, 1174 cm$^{-1}$; MS (ESI) *m/e* 472.1 [M + Na]$^+$, 450.1, 434.1, 383.1, 374.2, 358.1, 306.1, 190.0; HRMS (ESI) calcd for $C_{26}H_{27}NO_4NaS$ [M + Na]$^+$ 472.1559, found 472.1556.

*Data for 2-(4-Benzoyl-1H-pyrrol-3-yl)-2,4,4-trimethylcyclopentanone (**13a**).* A white solid: mp 195−196 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.00 (br s, 1H), 7.63 (d, *J* = 7.3 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.38 (dd, *J* = 7.5, 7.3 Hz, 2H), 6.95 (s, 1H), 6.57 (s, 1H), 2.82 (d, *J* = 18.8 Hz, 1H), 2.42 (d, *J* = 13.4 Hz, 1H), 2.40 (d, *J* = 19.1 Hz, 1H), 1.94 (d, *J* = 13.4 Hz, 1H), 1.55 (s, 3H), 1.25 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.9, 191.2, 140.9, 131.0, 129.8, 129.6, 128.7 (2C), 128.0 (2C), 120.6, 118.3, 53.6, 52.2, 50.8, 32.7, 32.2, 31.2, 25.6; IR ($CH_2Cl_2$) 3272, 2955, 1725, 1629, 1384 cm$^{-1}$; MS (ESI) *m/e* (%) 318.1 ([M + Na]$^+$, 100), 311.2 (3), 296.7 (24); HRMS (ESI) calcd for $C_{19}H_{21}NO_2Na$ [M + Na]$^+$ 318.1470, found 318.1473.


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Crystals suitable for X-ray diffraction analysis were grown from ethyl acetate and hexanes.

**General Procedure for TMSOTf-Promoted Cycloisomerization Reaction of 10 Followed by Basic Treatments. Formation of 13.** To a solution of **10a** (0.10 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under nitrogen was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred at room temperature for 24 h, after which time the reaction mixture was cooled at 0 °C and 1.5 mL of 2 M NaOH in MeOH was added. The reaction was allowed to stir at room temperature for 2 h. The reaction mixture was treated with 10 mL of water. The mixture was extracted with ethyl acetate (20 mL × 3). The combined organic layers were washed with brine (50 mL × 3), dried over anhydrous $MgSO_4$ (10 g), and concentrated to give the crude mixture.

*Data for 2-(4-Benzoyl-1H-pyrrol-3-yl)-2,4,4-trimethylcyclopentanone (**13a**).* In the typical procedure, to a solution of **10a** (0.11 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under nitrogen was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 4 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13a** (40 mg, 0.14 mmol, 62%) as colorless crystals. All analytical data for **13a** are identical to those of the previous experiment.

*Data for 2,4,4-Trimethyl-2-(4-(4-methylbenzoyl)-1H-pyrrol-3-yl)-cyclopentanone (**13b**).* In the typical procedure, to a solution of **10b** (0.10 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under nitrogen was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 2 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13b** (46 mg, 0.15 mmol, 67%) as a white solid: mp 189−190 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.76 (br s, 1H), 7.60 (d, $J$ = 7.5 Hz, 2H), 7.20 (d, $J$ = 7.8 Hz, 2H), 7.02 (d, $J$ = 1.8 Hz, 1H), 6.61 (d, $J$ = 1.9 Hz, 1H), 2.79 (d, $J$ = 18.8 Hz, 1H), 2.42−2.35 (m, 5H), 1.94 (d, $J$ = 13.5 Hz, 1H), 1.56 (s, 3H), 1.24 (s, 3H), 1.15 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.7, 191.1, 141.5, 138.2, 129.7, 129.3, 129.0, 128.7, 120.8, 118.1, 53.6, 52.2, 50.7, 32.8, 32.0, 31.1, 25.7, 21.5; IR ($CH_2Cl_2$) 3270, 2957, 1725, 1606, 1451, 1383 cm$^{-1}$; MS (ESI) $m/z$ 332.2 ([M + Na]$^+$, 100), 311.2 (5), 310.2 (32), 235.0 (5); HRMS (ESI) calcd for $C_{20}H_{23}NO_2Na$ [M + Na]$^+$ 332.1626, found 332.1618.

*Data for 2,4,4-Trimethyl-2-(4-(3-methylbenzoyl)-1H-pyrrol-3-yl)-cyclopentanone (**13c**).* In the typical procedure, to a solution of **10c** (0.10 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 12 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, 1:2 ethyl acetate/hexanes) to give **13c** (34 mg, 0.11 mmol, 49%) as a white solid: mp 187−188 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.60 (br s, 1H), 7.51 (s, 1H), 7.47 (d, $J$ = 6.3 Hz, 1H), 7.30−7.26 (m, 2H), 7.07 (s, 1H), 6.66 (s, 1H), 2.80 (d, $J$ = 18.8 Hz, 1H), 2.42 (d, $J$ = 13.4 Hz, 1H), 2.39 (d, $J$ = 18.4 Hz, 1H), 2.38 (s, 3H), 1.96 (d, $J$ = 13.4 Hz, 1H), 1.57 (s, 3H), 1.25 (s, 3H), 1.18 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.6, 191.4, 141.0, 137.8, 131.8, 129.7, 129.3, 127.8, 126.0, 120.8, 118.2, 53.6, 52.2, 50.7, 32.7, 32.1, 31.2, 25.6, 21.3; IR ($CH_2Cl_2$) 3720, 3258, 2952, 2359, 2343, 1717, 1623 cm$^{-1}$; MS (ESI) $m/e$ (%) 332.2 ([M + Na]$^+$, 100), 310.2 (10), 269.1 (1), 263.1 (2); HRMS (ESI) calcd for $C_{20}H_{23}NO_2Na$ [M + Na]$^+$ 332.1626, found 332.1622.

*Data for 2-(4-([1,1′-Biphenyl]-4-carbonyl)-1H-pyrrol-3-yl)-2,4,4-trimethyl-cyclopentanone (**13d**).* In the typical procedure, to a solution of **10d** (0.12 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 4 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13d** (44 mg, 0.12 mmol, 53%) as a white solid: mp 178−179 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.02 (br s, 1H), 7.76 (d, $J$ = 8.2 Hz, 2H), 7.62−7.60 (m, 4H), 7.45−7.49 (m, 2H), 7.38−7.42 (m, 1H), 7.08−7.09 (m, 1H), 6.64 (s, 1H), 2.86 (d, $J$ = 18.8 Hz, 1H), 2.46−2.41(m, 2H), 1.98 (d, $J$ = 13.4 Hz, 1H), 1.59 (s, 3H), 1.28 (s, 3H), 1.21 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.9, 190.8, 143.9, 140.2, 139.6, 129.6, 129.4, 128.8, 127.9, 127.2, 126.7, 120.7, 118.3, 53.6, 52.2, 50.8, 32.7, 32.2, 31.2, 25.6; IR ($CH_2Cl_2$) 2958, 2356, 1728, 1622, 1258, 1174 cm$^{-1}$; MS (ESI) $m/e$ (%)370.2 ([M − H]$^-$, 100), 368.2 (28), 239.1 (10), 203.1 (32), 87.1 (17); HRMS (ESI) calcd for $C_{25}H_{24}NO_2$ [M − H]$^-$ 370.1807, found 370.1801.

*Data for 2-(4-(1-Naphthoyl)-1H-pyrrol-3-yl)-2,4,4-trimethylcyclopentanone (**13e**).* In the typical procedure, to a solution of **10e** (0.11 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 1 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13e** (47 mg, 0.14 mmol, 62%) as a pale yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.49 (br s, 1H), 7.92 (d, $J$ = 8.0 Hz, 1H), 7.87 (d, $J$ = 8.0 Hz, 1H), 7.84 (dd, $J$ = 7.5, 1.5 Hz, 1H), 7.47−7.39 (m, 4H), 6.72 (dd, $J$ = 2.9, 2.0 Hz, 1H), 6.64 (t, $J$ = 2.2 Hz, 1H), 2.88 (d, $J$ = 19.0 Hz, 1H), 2.59 (d, $J$ = 13.3 Hz, 1H), 2.45 (d, $J$ = 19.0 Hz, 1H), 2.00 (d, $J$ = 13.3 Hz, 1H), 1.60 (s, 3H), 1.30 (s, 3H), 1.26 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.2, 192.2, 139.2, 133.6, 130.8, 130.7, 129.7, 129.6, 128.0, 126.8, 126.2, 125.8, 125.2, 124.3, 122.7, 118.5, 53.6, 52.2, 50.9, 32.8, 32.4, 31.4, 25.2; IR ($CH_2Cl_2$) 3247, 2958, 2347, 1725, 1631, 1380, 1325 cm$^{-1}$; MS (ESI) $m/e$ (%) 368.2 ([M + Na]$^+$, 89), 347.2 (23), 246.2 (100), 293.1 (10), 242.3 (10); HRMS (ESI) calcd for $C_{23}H_{23}NO_2Na$ [M + Na]$^+$ 368.1626, found 368.1620.

*Data for 2,4,4-Trimethyl-2-(4-(phenanthrene-9-carbonyl)-1H-pyrrol-3-yl)-cyclopentanone (**13f**).* In the typical procedure, to a solution of **10f** (0.12 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 5 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13f** (49 mg, 0.12 mmol, 56%) as a pale yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.88 (br s, 1H), 8.59 (d, $J$ = 8.4 Hz, 1H), 8.55 (d, $J$ = 8.2 Hz, 1H), 7.84 (d, $J$ = 8.2 Hz, 1H), 7.73 (d, $J$ = 7.8 Hz, 1H), 7.65 (td, $J$ = 7.2, 1.1 Hz, 1H), 7.59 (s, 1H), 7.52−7.55 (m, 1H), 7.50−7.46 (m, 1H), 7.38−7.42 (m, 1H), 6.53 (s, 1H), 6.50 (s, 1H), 2.88 (d, $J$ = 19.2 Hz, 1H), 2.56 (d, $J$ = 13.3 Hz, 1H), 2.45 (d, $J$ = 19.2 Hz, 1H), 1.95 (d, $J$ = 13.3 Hz, 1H), 1.54 (s, 3H), 1.30 (s, 3H), 1.26 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.8, 192.2, 127.5, 131.3, 130.4, 130.2, 129.2, 129.1, 127.5, 126.9, 126.8, 126.8, 126.3, 125.9, 122.5, 122.4, 121.9, 118.9, 53.6, 52.0, 51.0, 32.6, 31.6, 24.9; IR ($CH_2Cl_2$) 3255, 2956, 2366, 2339, 1730, 1630 cm$^{-1}$; MS (ESI) $m/e$ (%) 394.2 ([M + H]$^-$, 44), 354.2 (3),345.0 (4), 310.1 (3), 295.0 (3); HRMS (ESI) calcd for $C_{27}H_{24}NO_2$ [M − H]$^-$ 394.1807, found 394.1814.

*Data for 2-(4-(3-Methoxybenzoyl)-1H-pyrrol-3-yl)-2,4,4-trimethylcyclopentanone (**13g**).* In the typical procedure, to a solution of **10g** (0.10 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 4 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13g** (47 mg, 0.15 mmol, 65%) as colorless crystals: mp 176−177 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.03 (br s, 1H), 7.27 (d, $J$ = 8.4 Hz, 1H), 7.20 (d, $J$ = 8.4 Hz, 2H), 7.03−7.00 (m, 2H), 6.58 (s, 1H), 3.81 (s, 3H), 2.81 (d, $J$ = 18.9 Hz, 1H), 2.42 (s, 1H), 2.38 (d, $J$ = 3.8 Hz, 1H), 1.94 (d, $J$ = 13.4 Hz, 1H), 1.55 (s, 3H), 1.25 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.8, 190.9, 159.3, 142.2, 129.8, 129.6, 129.0, 121.4, 120.5, 118.3, 117.4, 113.4, 55.4, 53.6, 52.2, 50.7, 32.7, 32.1, 31.2, 25.6; IR ($CH_2Cl_2$) 2957, 1713, 1598, 1576, 1351, 1290 cm$^{-1}$; MS (ESI) $m/e$ (%) 348.2 ([M + Na]$^+$, 100), 327.2 (10),


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326.22 (50), 235.0 (10); HRMS (ESI) calcd for $C_{20}H_{23}NO_3Na$ [M + Na]$^+$ 348.1576, found 348.1582. Crystals suitable for X-ray diffraction analysis were grown from ethyl acetate and hexanes.

*Data for 2-(4-(4-Bromobenzoyl)-1H-pyrrol-3-yl)-2,4,4-trimethylcyclopentanone (**13h**).* In the typical procedure, to a solution of **10h** (0.12 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 23 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13h** (0.040 g, 0.11 mmol, 48%) as a white solid: mp 193−194 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.79 (br s, 1H), 7.54 (s, 4H), 7.01−7.00 (m, 1H), 6.64−6.63 (m, 1H), 2.79 (d, $J$ = 18.8 Hz, 1H), 2.40 (d, $J$ = 18.8 Hz, 1H), 2.37 (d, $J$ = 13.4 Hz, 1H), 1.95 (d, $J$ = 13.4 Hz, 1H), 1.55 (s, 3H), 1.26 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.5, 189.9, 139.6, 131.3, 130.4, 129.9, 129.4, 125.8, 120.5, 118.4, 53.5, 52.2, 50.7, 32.8, 32.1, 31.2, 25.6; IR ($CH_2Cl_2$) 3269, 2958, 1723, 1627, 1453, 1397 cm$^{-1}$; MS (ESI) $m/e$ (%) 374.1 ([M + H]$^+$, 100), 293.1 (2), 288.6 (7), 269.1 (4); HRMS (ESI) $C_{19}H_{21}NO_2Br$ [M + H]$^+$ 374.0756, found 374.0751.

*Data for 2,4,4-Trimethyl-2-(4-(thiophene-2-carbonyl)-1H-pyrrol-3-yl)cyclopentanone (**13i**).* In the typical procedure, to a solution of **10i** (0.10 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 4 h. After cooling to 0 °C, the reaction mixture was treated with 2 M NaOH in MeOH (1.5 mL). The reaction was stirred at room temperature for 2 h. The crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/hexanes 1:2) to give **13i** (35 mg, 0.12 mmol, 52%) as yellow crystals: mp 164−165 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.66 (br s, 1H), 7.60 (d, $J$ = 3.5 Hz, 1H), 7.57 (d, $J$ = 5.0 Hz, 1H), 7.36 (s, 1H), 7.09 (t, $J$ = 4.2 Hz, 1H), 6.65 (s, 1H), 2.72 (d, $J$ = 18.7 Hz, 1H), 2.38 (d, $J$ = 13.3 Hz, 1H), 2.36 (d, $J$ = 18.7 Hz, 1H), 1.98 (d, $J$ = 13.5 Hz 1H), 1.56 (s, 3H), 1.22 (s, 3H), 1.12 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 222.7, 182.3, 145.8, 131.9, 131.8, 129.7, 127.5, 127.4, 120.8, 118.1, 53.5, 52.3, 50.5, 32.9, 31.8, 30.9, 26.1; IR ($CH_2Cl_2$) 2960, 1728, 1608, 1516, 1417, 1381 cm$^{-1}$; MS (ESI) $m/e$ (%) 324.1 ([M + Na]$^+$, 100), 303.1 (5), 302.1 (40), 232.1 (3); HRMS (ESI) calcd for $C_{17}H_{19}NO_2SNa$ [M + Na]$^+$ 324.1034, found 324.1036. Crystals suitable for X-ray diffraction analysis were grown from ethyl acetate and hexanes.

*Data for 4-Methyl-N-(3-(4-nitrophenyl)prop-2-yn-1-yl)-N-(2-oxo-2-(1,4,4-trimethyl-2-oxocyclopentyl)ethyl)benzenesulfonamide (**11j**).* In the typical procedure, to a solution of **10j** (0.11 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 2 h, and the crude mixture was purified by flash column chromatography (silica gel, 1:3 ethyl acetate/hexanes) to give **11j** (0.073 g, 0.15 mmol, 66%) as a white solid: mp 120−121 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.14 (d, $J$ = 8.7 Hz, 2H), 7.75 (d, $J$ = 8.1 Hz, 2H), 7.35−7.21 (m, 4H), 4.56−4.37 (m, 4H), 2.81 (d, $J$ = 13.7 Hz, 1H), 2.38 (s, 3H), 2.21 (s, 2H), 1.56 (d, $J$ = 13.7 Hz, 1H), 1.45 (s, 3H), 1.12 (s, 3H), 1.01 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 215.9, 200.8, 147.3, 143.9, 136.1, 132.4, 129.7, 128.8, 127.6, 123.5, 87.3, 84.1, 63.7, 53.1, 51.0, 46.6, 38.0, 33.5, 29.7, 29.1, 24.1, 21.5; IR ($CH_2Cl_2$) 2959, 2871, 1716, 1596, 1520, 1344, 1267 cm$^{-1}$; MS (ESI) $m/e$ (%) 495.2 ([M − H]$^-$, 70), 388.2 (13), 364.1 (10), 362 (13), 350.1 (38); HRMS (ESI) calcd for $C_{26}H_{27}N_2O_6S$ [M − H]$^-$ calcd 495.1590, found 495.1582.

*Data for 4-Methyl-N-(3-(3-nitrophenyl)prop-2-yn-1-yl)-N-(2-oxo-2-(1,4,4-trimethyl-2-oxocyclopentyl)ethyl)benzenesulfonamide (**11k**).* In the typical procedure, to a solution of **10k** (0.11 g, 0.22 mmol) in 2.2 mL of $CH_2Cl_2$ at room temperature under air was added TMSOTf (0.048 mL, 0.27 mmol). The reaction mixture was stirred for 2 h, and the crude mixture was purified by flash column chromatography (silica gel, 1:3 ethyl acetate/hexanes) to give **11k** (0.098 g, 0.20 mmol, 89%) as a pale yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.15 (dq, $J$ = 8.0, 1.3 Hz, 1H), 7.95 (s, 1H), 7.75 (d, $J$ = 8.2 Hz, 2H), 7.50−7.42 (m, 2H), 7.31 (d, $J$ = 8.0 Hz, 2H), 4.52 (d, $J$ = 20.4 Hz, 1H), 4.48−4.35 (m, 3H), 2.81 (d, $J$ = 13.7 Hz, 1H), 2.37 (s, 3H), 2.20 (s, 2H), 1.55 (d, $J$ = 13.7 Hz, 1H), 1.44 (s, 3H), 1.11 (s, 3H), 1.00 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 215.9, 200.8, 147.9, 144.0, 137.3, 136.0, 129.7, 129.3, 127.6, 126.4, 123.7, 123.3, 84.5, 83.5, 63.6, 53.0, 51.0, 46.6, 37.9, 33.4, 29.6, 29.0, 24.1, 21.4; IR ($CH_2Cl_2$) 2956, 2928, 1716, 1532, 1351, 1264, 1163 cm$^{-1}$; MS (ESI) $m/e$ (%) 519.2 ([M + Na]$^+$, 100), 497.2 (6), 482.3 (4), 320.6 (3), 181.1 (3); HRMS (ESI) calcd for $C_{26}H_{28}N_2O_6SNa$ [M + Na]$^+$ 519.1566, found 519.1569.

**General Experimental Procedure for $BF_3$-Promoted Cycloisomerization of 14 under Nitrogen. Synthesis of Dihydrofuran 15.** To a solution of **14a** (0.08 g, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under an atmosphere of nitrogen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred at room temperature for 3 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ The organic phase was separated, and the aqueous phase was extracted with $CH_2Cl_2$ (20 mL × 3 mL). The combined organic layers were washed with brine (50 mL × 3), dried over anhydrous $MgSO_4$ (10 g), and concentrated to give the crude mixture.

*Data for 2-(4-Benzoyl-2,5-dihydrofuran-3-yl)-2,4,4-trimethylcyclopentanone (**15a**).* In the typical procedure, to a solution of **14a** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under nitrogen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 3 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **15a** (64 mg, 0.20 mmol, 79%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.85 (dd, $J$ = 7.2, 1.2 Hz, 2H), 7.59 (t, $J$ = 7.5 Hz, 1H), 7.49 (t, $J$ = 7.5 Hz, 2H), 4.94−4.89 (m, 2H), 4.82−4.76 (m, 2H), 2.27 (d, $J$ = 18.0 Hz, 1H), 2.21 (d, $J$ = 18.0 Hz, 1H), 2.18 (d, $J$ = 13.5 Hz, 1H), 2.02 (d, $J$ = 13.5 Hz, 1H), 1.36 (s, 3H), 1.11 (s, 3H), 1.09 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 218.9, 194.6, 145.6, 137.1, 133.7, 132.3, 128.9, 128.8, 78.7, 52.6, 51.7, 50.8, 33.6, 30.3, 30.2, 25.8; IR ($CH_2Cl_2$) 2957, 1734, 1653, 1539, 1447, 1265 cm$^{-1}$; MS (ESI) $m/e$ 299.2, 298.2, 251.2, 237.1; HRMS (ESI) calcd for $C_{19}H_{22}O_3Na$ [M + Na]$^+$ 321.1467, found 321.1460.

*Data for 2,4,4-Trimethyl-2-(4-(4-methylbenzoyl)-2,5-dihydrofuran-3-yl)cyclopentanone (**15b**).* In the typical procedure, to a solution of **14b** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under nitrogen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 2 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **15b** (55 mg, 0.18 mmol, 69%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.76 (d, $J$ = 8.0 Hz, 2H), 7.28 (d, $J$ = 8.0 Hz, 2H), 4.93−4.88 (m, 2H), 4.81−4.76 (m, 2H), 2.43 (s, 3H), 2.26 (d, $J$ = 18.0 Hz, 1H), 2.19 (d, $J$ = 18.0 Hz, 1H), 2.18 (d, $J$ = 13.0 Hz, 1H), 2.02 (d, $J$ = 13.0 Hz, 1H), 1.35 (s, 3H), 1.10 (s, 3H), 1.08 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 218.9, 194.6, 144.8, 144.6, 134.5, 132.5, 129.5, 129.1, 78.7, 52.6, 51.6, 50.7, 33.6, 30.2, 30.1, 25.8, 21.7; IR ($CH_2Cl_2$) 2915, 1738, 1655, 1605, 1384, 1266 cm$^{-1}$; MS (ESI) $m/e$ 335.2, 313.2, 311.2, 299.2; HRMS (ESI) calcd for $C_{20}H_{24}O_3Na$ [M + Na]$^+$ 335.1623, found 335.1614.

*Data for 2,4,4-Trimethyl-2-(4-(phenanthrene-9-carbonyl)-2,5-dihydrofuran-3-yl)cyclopentanone (**15c**).* In the typical procedure, to a solution of **14c** (0.10 g, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under nitrogen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 1 h, and the crude mixture was purified by flash column chromatography (silica gel, 1:1:9 ethyl acetate/dichloromethane/hexanes) to give **15c** (69 mg, 0.17 mmol, 69%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.73 (d, $J$ = 8.1 Hz, 1H), 8.69 (d, $J$ = 8.5 Hz, 1H), 8.46 (dd, $J$ = 8.5, 1.5 Hz, 1H), 7.99 (s, 1H), 7.95 (d, $J$ = 7.5 Hz, 1H), 7.76 (t, $J$ = 7.0 Hz, 1H), 7.72−7.63 (m, 3H), 4.98−4.76 (m, 4H), 2.47 (d, $J$ = 18.5 Hz, 1H), 2.41 (d, $J$ = 13.5 Hz, 1H), 2.32 (d, $J$ = 18.5 Hz, 1H), 1.97 (d, $J$ = 13.5 Hz, 1H), 1.44 (s, 3H), 1.22 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 218.9, 194.4, 151.9, 134.9, 132.3, 131.9, 130.7, 130.3, 129.9, 129.8, 129.0, 128.0, 127.7, 127.4, 127.2, 126.0, 122.9, 122.7, 78.1, 77.7, 52.6, 52.5, 51.7, 33.5, 31.1, 30.9, 24.8; IR ($CH_2Cl_2$) 2952, 1738, 1645, 1579, 1447, 1388, 1251 cm$^{-1}$; MS (ESI) $m/e$ 421.2, 400.2, 399.2, 342.2; HRMS (ESI) calcd for $C_{27}H_{26}O_3Na$ [M + Na]$^+$, 421.1780, found 421.1775.


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*Data for 2-(4-(4-Bromobenzoyl)-2,5-dihydrofuran-3-yl)-2,4,4-trimethylcyclopentanone (**15d**).* In the typical procedure, to a solution of **14d** (94 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under nitrogen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 3 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **15d** (71 mg, 0.19 mmol, 75%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.71 (dd, $J$ = 8.5, 2.0 Hz, 2H), 7.49 (dd, $J$ = 8.5, 2.0 Hz, 2H), 4.93−4.86 (m, 2H), 4.82−4.74 (m, 2H), 2.28 (d, $J$ = 18.0 Hz, 1H), 2.22 (d, $J$ = 18.0 Hz, 1H), 2.15 (d, $J$ = 13.5 Hz, 1H), 1.82 (d, $J$ = 13.5 Hz, 1H), 1.34 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 218.9, 193.5, 146.1, 135.8, 132.2, 131.7, 130.4, 128.9, 78.5, 52.6, 51.7, 50.8, 33.6, 30.4, 30.3, 25.7; IR ($CH_2Cl_2$) 2952, 1738, 1660, 1587, 1399, 1263 cm$^{-1}$; MS (ESI) $m/e$ 379.1, 377.1, 375.1, 347.2, 231.1; HRMS (ESI) calcd for $C_{19}H_{22}BrO_3$ $[M + H]^+$, 377.0752, found 377.0749.

*Data for 2,4,4-Trimethyl-2-(4-(3-methylbenzoyl)-2,5-dihydrofuran-3-yl)cyclopentanone (**15e**).* In the typical procedure, to a solution of **14e** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under nitrogen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 3 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **15e** (59 mg, 0.19 mmol, 76%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.66 (s, 1H), 7.64 (d, $J$ = 7.5 Hz, 1H), 7.41 (d, $J$ = 8.0 Hz, 1H), 7.37 (t, $J$ = 7.5 Hz, 1H), 4.94−4.89 (m, 2H), 4.82−4.76 (m, 2H), 2.42 (s, 3H), 2.28 (d, $J$ = 18.0 Hz, 1H), 2.21 (d, $J$ = 18.0 Hz, 1H), 2.18 (d, $J$ = 13.5 Hz, 1H), 1.82 (d, $J$ = 13.5 Hz, 1H), 1.36 (s, 3H), 1.11 (s, 3H), 1.09 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 219.0, 194.8, 145.4, 138.7, 137.1, 134.5, 132.4, 129.2, 128.7, 126.3, 78.7, 52.6, 51.7, 50.8, 33.6, 30.2, 30.1, 25.8, 21.3; IR ($CH_2Cl_2$) 2957, 1738, 1660, 1601, 1583, 1455, 1273 cm$^{-1}$; MS (ESI) $m/e$ 335.2, 313.2, 291.1, 199.0; HRMS (ESI) calcd for $C_{20}H_{24}O_3Na$ $[M + Na]^+$ 335.1623, found 335.1615.

*Data for 2-(4-(1-Naphthoyl)-2,5-dihydrofuran-3-yl)-2,4,4-trimethylcyclopentanone (**15f**).* In the typical procedure, to a solution of **14f** (90 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under nitrogen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 1 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **15f** (62 mg, 0.18 mmol, 76%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.47 (d, $J$ = 8.0 Hz, 1H), 7.99 (d, $J$ = 8.0 Hz, 1H), 7.89 (d, $J$ = 8.0 Hz, 1H), 7.74 (d, $J$ = 7.0 Hz, 1H), 7.61 (t, $J$ = 7.0 Hz, 1H), 7.55 (t, $J$ = 7.5 Hz, 1H), 7.51 (t, $J$ = 7.5 Hz, 1H), 4.98−4.69 (m, 4H), 2.43 (d, $J$ = 18.5 Hz, 1H), 2.36 (d, $J$ = 18.5 Hz, 1H), 2.30 (d, $J$ = 13.5 Hz, 1H), 1.94 (d, $J$ = 13.5 Hz, 1H), 1.42 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 218.9, 194.8, 151.0, 135.7, 133.8, 132.9, 132.5, 129.9, 128.6, 128.5, 128.2, 126.7, 125.2, 124.5, 78.1, 76.7, 52.7, 52.5, 51.6, 33.6, 30.9, 30.8, 24.9; IR ($CH_2Cl_2$) 2952, 1738, 1653, 1590, 1388, 1277 cm$^{-1}$; MS (ESI) $m/e$ 371.2, 349.2, 321.2, 280.2; HRMS (ESI) calcd for $C_{23}H_{24}O_3Na$ $[M + Na]^+$, 371.1623, found 371.1614.

**General Experimental Procedure for $BF_3$-Promoted Cyclization of 14 under Oxygen. Synthesis of Furan 16.** To a solution of **14a** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at room temperature under an oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred at 70 °C for 16 h until no **14a** was detected by TLC. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The organic phase was separated, and the aqueous phase was extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic layers were washed with brine (50 mL × 3), dried over anhydrous $MgSO_4$ (10 g), and concentrated to give the crude mixture.

*Data for 2-(4-Benzoylfuran-3-yl)-2,4,4-trimethylcyclopentanone (**16a**).* In the typical procedure, to a solution of **14a** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 16 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **16a** (41 mg, 0.14 mmol, 56%) as a colorless powder: mp 99−100 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 7.8 Hz, 2H), 7.75 (s, 1H), 7.59 (t, $J$ = 7.3 Hz, 1H), 7.48 (t, $J$ = 7.5 Hz, 2H), 7.39 (s, 1H), 2.71 (d, $J$ = 18.6 Hz, 1H), 2.42 (d, $J$ = 18.7 Hz, 1H), 2.37 (d, $J$ = 13.6 Hz, 1H), 2.02 (d, $J$ = 13.6 Hz, 1H), 1.59 (s, 3H), 1.26 (s, 3H), 1.18 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 220.7, 190.3, 151.7, 141.7, 139.6, 132.4, 129.9, 128.9, 128.5, 123.9, 52.6, 52.1, 49.1, 33.1, 31.7, 30.9, 25.8; IR ($CH_2Cl_2$) 2958, 1730, 1712, 1647, 744 cm$^{-1}$; MS (ESI) $m/e$ 319.1, 297.2, 223.1; HRMS (ESI) calcd for $C_{19}H_{20}O_3Na$ $[M + Na]^+$ 319.1310, found 319.1313. Crystals suitable for X-ray diffraction analysis were grown from ehyl acetate and hexanes.

*Data for 2,4,4-Trimethyl-2-(4-(4-methylbenzoyl)furan-3-yl)-cyclopentanone (**16b**).* In the typical procedure, to a solution of **14b** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 48 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **16b** (41 mg, 0.13 mmol, 53%) as a white solid: mp 84−85 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.72 (d, $J$ = 1.2 Hz, 1H), 7.70 (d, $J$ = 8.0 Hz, 2H), 7.35 (d, $J$ = 1.2 Hz, 1H), 7.26 (d, $J$ = 8.0 Hz, 2H), 2.67 (d, $J$ = 18.4 Hz, 1H), 2.42 (s, 3H), 2.39 (d, $J$ = 18.4 Hz, 1H), 2.34 (d, $J$ = 13.6 Hz, 1H), 2.00 (d, $J$ = 13.6 Hz, 1H), 1.57 (s, 3H), 1.23 (s, 3H), 1.15 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 220.8, 190.0, 151.2, 143.2, 141.5, 136.9, 129.9, 129.2, 129.1, 124.0, 52.6, 52.1, 49.0, 33.1, 31.6, 30.9, 25.8, 21.6; IR ($CH_2Cl_2$) 2958, 1738, 1651, 1609, 1528, 1372 cm$^{-1}$; MS (ESI) $m/e$ 311.2, 308.1, 342.3; HRMS (ESI) calcd for $C_{20}H_{23}O_3$ $[M + H]^+$ 311.1647, found 311.1646.

*Data for 2,4,4-Trimethyl-2-(4-(phenanthrene-9-carbonyl)furan-3-yl)cyclopentanone (**16c**).* In the typical procedure, to a solution of **14c** (0.10 g, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 24 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **16c** (52 mg, 0.13 mmol, 52%) as a pale yellow oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.72 (d, $J$ = 8.4 Hz, 1H), 8.69 (d, $J$ = 8.4 Hz, 1H), 8.10 (dd, $J$ = 8.4, 0.8 Hz, 1H), 7.91 (d, $J$ = 8.4, 0.8 Hz, 1H), 7.89 (s, 1H), 7.74 (ddd, $J$ = 8.0, 6.8, 1.2 Hz, 1H), 7.69 (ddd, $J$ = 8.0, 6.8, 1.2 Hz, 1H), 7.67−7.64 (m, 2H), 7.61 (ddd, $J$ = 8.0, 6.8, 1.2 Hz, 1H), 7.40 (d, $J$ = 2.0 Hz, 1H), 2.83 (d, $J$ = 18.8 Hz, 1H), 2.56 (d, $J$ = 13.6 Hz, 1H), 2.49 (d, $J$ = 18.8 Hz, 1H), 2.09 (d, $J$ = 13.6 Hz, 1H), 1.57 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 220.7, 191.6, 153.7, 142.2, 136.5, 131.2, 130.6, 129.9, 129.7, 129.4, 128.8, 128.3, 127.9, 127.3, 127.2, 127.1, 126.3, 126.0, 122.8, 122.6, 52.7, 51.9, 49.4, 33.0, 32.1, 31.5, 31.3, 25.2; IR ($CH_2Cl_2$) 2944, 1738, 1651, 1612, 1528, 1373 cm$^{-1}$; MS (ESI) $m/e$ 419.2, 397.2, 336.2, 321.2; HRMS (ESI) calcd for $C_{27}H_{24}O_3Na$ $[M + Na]^+$ 419.1623, found 419.1616.

*Data for 2-(4-(4-Bromobenzoyl)furan-3-yl)-2,4,4-trimethylcyclopentanone (**16d**).* In the typical procedure, to a solution of **14d** (90 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 15 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **16d** (42 mg, 0.11 mmol, 45%) as a white solid: mp 80−82 °C (ethyl acetate/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.71 (d, $J$ = 1.2 Hz, 1H), 7.65 (d, $J$ = 8.0 Hz, 2H), 7.61 (d, $J$ = 8.0 Hz, 2H), 7.38 (d, $J$ = 1.2 Hz, 1H), 2.69 (d, $J$ = 18.5 Hz, 1H), 2.41 (d, $J$ = 18.5 Hz, 1H), 2.31 (d, $J$ = 13.5 Hz, 1H), 1.99 (d, $J$ = 13.5 Hz, 1H), 1.56 (s, 3H), 1.25 (s, 3H), 1.16 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 220.6, 189.1, 151.4, 141.9, 138.3, 131.8, 130.5, 129.9, 127.4, 123.8, 52.6, 52.0, 49.1, 33.1, 31.7, 30.9, 25.7; IR ($CH_2Cl_2$) 2952, 1738, 1651, 1583, 1528, 1365 cm$^{-1}$; MS (ESI) $m/e$ 377.1, 375.1, 338.3, 321.2; HRMS (ESI) calcd for $C_{19}H_{20}O_3Br$ $[M + H]^+$ 375.0596, found 375.0600.

*Data for 2,4,4-Trimethyl-2-(4-(3-methylbenzoyl)furan-3-yl)-cyclopentanone (**16e**).* In the typical procedure, to a solution of **14e** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 12 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **16e** (51 mg, 0.16 mmol, 65%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.72 (d, $J$ = 1.2 Hz, 1H), 7.58 (s, 1H), 7.56 (d, $J$ = 7.5 Hz, 1H), 7.38−7.32 (m, 3H), 2.68 (d, $J$ = 18.5


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Hz, 1H), 2.41 (s, 3H), 2.39 (d, $J$ = 18.4 Hz, 1H), 2.35 (d, $J$ = 13.5 Hz, 1H), 2.00 (d, $J$ = 13.5 Hz, 1H), 1.57 (s, 3H), 1.24 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 220.8, 190.6, 151.7, 141.6, 139.7, 138.4, 129.9, 129.4, 128.3, 126.2, 124.0, 52.6, 52.1, 49.0, 33.1, 31.7, 30.9, 25.7, 21.3; IR ($CH_2Cl_2$) 2959, 1738, 1651, 1601, 1524, 1369 cm$^{-1}$; MS (ESI) $m/e$ 311.2, 293.2, 283.2; HRMS (ESI) calcd for $C_{20}H_{23}O_3$ $[M + H]^+$ 311.1647, found 311.1646.

*Data for 2-(4-(1-Naphthoyl)furan-3-yl)-2,4,4-trimethylcyclopentanone (**16f**).* In the typical procedure, to a solution of **14f** (90 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 12 h, and the crude mixture was purified by flash column chromatography (silica gel, 1:1:9 ethyl acetate/dichloromethane/hexanes) to give **16f** (53 mg, 0.15 mmol, 62%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.07 (dd, $J$ = 6.0, 3.5 Hz, 1H), 7.96 (d, $J$ = 8.0 Hz, 1H), 7.88 (dd, $J$ = 6.0, 3.5 Hz, 1H), 7.61 (dd, $J$ = 7.0, 0.5 Hz, 1H), 7.54−7.47 (m, 4H), 7.37 (d, $J$ = 1.5 Hz, 1H), 2.80 (d, $J$ = 18.5 Hz, 1H), 2.52 (d, $J$ = 13.5 Hz, 1H), 2.47 (d, $J$ = 18.5 Hz, 1H), 2.07 (d, $J$ = 13.5 Hz, 1H), 1.63 (s, 3H), 1.31 (s, 3H), 1.26 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 220.7, 191.7, 153.7, 142.1, 137.7, 133.7, 131.1, 130.5, 129.7, 128.3, 127.3, 126.5, 126.4, 126.1, 125.4, 124.2, 52.7, 51.9, 49.4, 33.1, 32.0, 31.3, 25.3; IR ($CH_2Cl_2$) 2959, 1738, 1651, 1530, 1372, 1145 cm$^{-1}$; MS (ESI) $m/e$ 447.2, 321.2, 275.2, 242.1; HRMS (ESI) calcd for $C_{23}H_{23}O_3$ $[M + H]^+$ 347.1647, found 347.1641.

*Data for 2-(4-(3-Methoxybenzoyl)furan-3-yl)-2,4,4-trimethylcyclopentanone (**16g**).* In the typical procedure, to a solution of **14g** (80 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 24 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **16g** (38 mg, 0.12 mmol, 47%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.74 (d, $J$ = 1.4 Hz, 1H), 7.39−7.33 (m, 3H), 7.31−7.30 (m, 1H), 7.12 (dt, $J$ = 7.2, 2.2 Hz, 1H), 3.85 (s, 3H), 2.40 (d, $J$ = 18.6 Hz, 1H), 2.34 (d, $J$ = 13.6 Hz, 1H), 2.01 (d, $J$ = 13.6 Hz, 1H), 2.01 (d, $J$ = 13.7 Hz, 1H), 1.58 (s, 3H), 1.24 (s, 3H), 1.16 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 220.8, 190.0, 159.7, 151.7, 141.6, 140.9, 129.9, 129.4, 123.9, 121.6, 118.9, 113.4, 55.5, 52.6, 52.1, 49.1, 33.1, 31.6, 30.9, 25.8; IR ($CH_2Cl_2$) 2957, 2366, 1739, 1654, 1530, 1372 cm$^{-1}$; MS (ESI) $m/e$ (%) 349.1 ($[M + Na]^+$, 100), 327.2, 307.1, 256.1; HRMS (ESI) calcd for $C_{20}H_{23}O_4$ $[M + H]^+$, 327.1596, found 327.1587.

*Data for 2-(4-([1,1′-Biphenyl]-3-carbonyl)furan-3-yl)-2,4,4-trimethylcyclopentanone (**16h**).* In the typical procedure, to a solution of **14h** (90 mg, 0.25 mmol) in 10.0 mL of $CH_2Cl_2$ at 70 °C under oxygen was added $BF_3{\cdot}OEt_2$ (0.032 mL, 0.25 mmol). The reaction mixture was stirred for 24 h, and the crude mixture was purified by flash column chromatography (silica gel, ethyl acetate/dichloromethane/hexanes 1:1:9) to give **16h** (46 mg, 0.12 mmol, 50%) as a pale yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.86 (d, $J$ = 8.2 Hz, 2H), 7.78 (d, $J$ = 1.4 Hz, 1H), 7.68 (d, $J$ = 8.3 Hz, 2H), 7.62 (d, $J$ = 8.4 Hz, 2H), 7.46 (t, $J$ = 7.4 Hz, 2H), 7.40−7.37 (m, 2H), 2.69 (d, $J$ = 18.6 Hz, 1H), 2.41 (d, $J$ = 18.4 Hz, 1H), 2.37 (d, $J$ = 13.5 Hz, 1H), 2.01 (d, $J$ = 13.6 Hz, 1H), 1.59 (s, 3H), 1.24 (s, 3H), 1.17 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 220.6, 189.8, 151.3, 145.2, 141.6, 139.8, 138.1, 130.0, 129.6, 128.9, 128.1, 127.2, 127.1, 123.9, 52.6, 52.0, 49.0, 33.0., 31.6, 30.9, 25.7; IR ($CH_2Cl_2$) 2952, 1737, 1649, 1603, 1462, 1375 cm$^{-1}$; MS (ESI) $m/e$ 311.2, 373.2, 342.2, 292.2, 222.1; HRMS (ESI) calcd for $C_{25}H_{24}O_3Na$ $[M + Na]^+$ 395.1623, found 395.1622.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

NMR spectra for compounds **1a−i**, **2a−g**, **4a,c,f,i**, **7**, **8**, **9**, **10a−k**, **11a,j,k**, **12a**, **13a−i**, **14a−h**, **15a−f**, and **16a−h** and X-ray crystallographic information files for compounds **2a,c**, **4a**, **7**, **11a**, **13a,g,i**, **16a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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