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# Tunable Diastereoselective Desymmetrization of Cyclohexadienones Triggered by Copper-Catalyzed Three-Component Coupling Reaction

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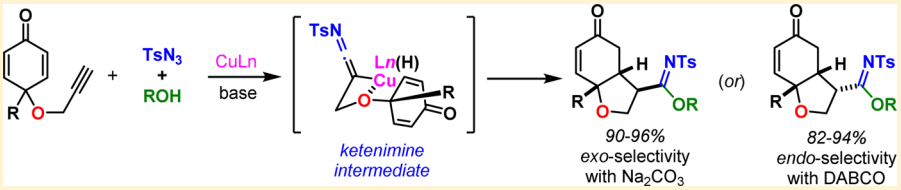
Supporting Information



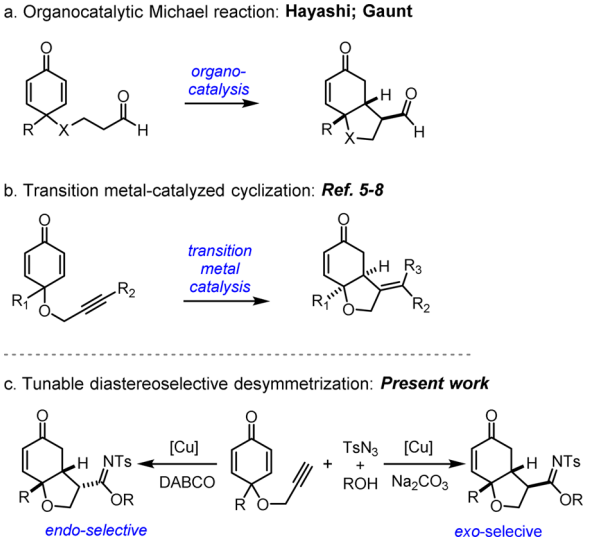

**ABSTRACT:** Catalytic tandem diastereoselective desymmetrization of cyclohexadienone-containing 1,6-enynes has been achieved through copper-catalyzed [3 + 2]-cycloaddition followed by ketenimine formation and subsequent intramolecular conjugate addition. The cascade reaction provides *cis*-hydrobenzofurans in good yields with excellent diastereoselectivity. The *exo*- or *endo*-selectivity of bicyclic scaffolds depends on the selection of the base in the reaction. In addition, *N*-tethered bicyclic products further transformed into tricyclic compounds via intramolecular Michael addition.

## INTRODUCTION

Tether-mediated desymmetrization of symmetric molecules is one of the powerful tools en route to efficient diastereo- and enantioselective syntheses of biologically active complex targets.[1] In this context, a number of efficient synthetic methods have been developed for the desymmetrization of *meso*-cyclohexa-2,5-dienones[2] which are readily prepared from the oxidative dearomatization of the corresponding phenolic precursors.[3] In the past decade, Hayashi et al. and Gaunt et al. developed a highly enantioselective desymmetrization strategy via an organocatalytic intramolecular Michael reaction (Scheme 1a).[4] Recently, many research groups reported transition-metal-catalyzed desymmetrization of cyclohexadienones (Scheme 1b).[5−7] Very recently, our group demonstrated the palladium-catalyzed regioselective domino cyclization of alkyne-tethered cyclohexadienones using boronic acids.[8]

Transition-metal-catalyzed multicomponent reactions (MCR) have been found to be an attractive synthetic strategy and have gained considerable attention in drug discovery due to rapid access to complex molecules in a single operation.[9] In the past decade, Chang et al. developed highly efficient synthesis of *N*-sulfonylimidates by a copper catalyzed three-component coupling of sulfonyl azides, terminal alkynes, and alcohols.[10] In 2010, the same research group extended the scope of the above reaction to four-component coupling by addition of nitrostyrenes via the Michael reaction, which is limited to arylacetylenes.[11] During our continuous efforts in exploring the desymmetrization of $C_2$-symmetric molecules,[8,12] we envisioned that copper-catalyzed three-component coupling/conjugate addition reaction of alkyne-tethered cyclohexadienones would provide a potential route for the synthesis of *cis*-hydrobenzofurans (Scheme 1c).

**Scheme 1. Previous and Present Desymmetrization Approaches**




## RESULTS AND DISCUSSION

The *meso*-1,6-dienyne **1a** was selected as a model substrate and was reacted with tosylazide and methanol in the presence of 10 mol % CuI and $Et_3N$ in $CH_2Cl_2$ (Table 1, entry 1). Gratifyingly, the reaction proceeded to afford the required product as a mixture

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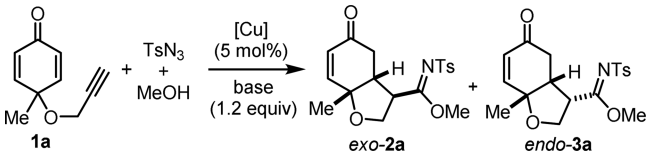
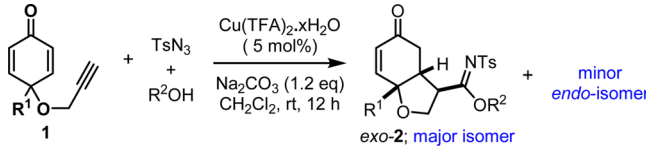
**Table 1. Reaction Optimization**[a−c]

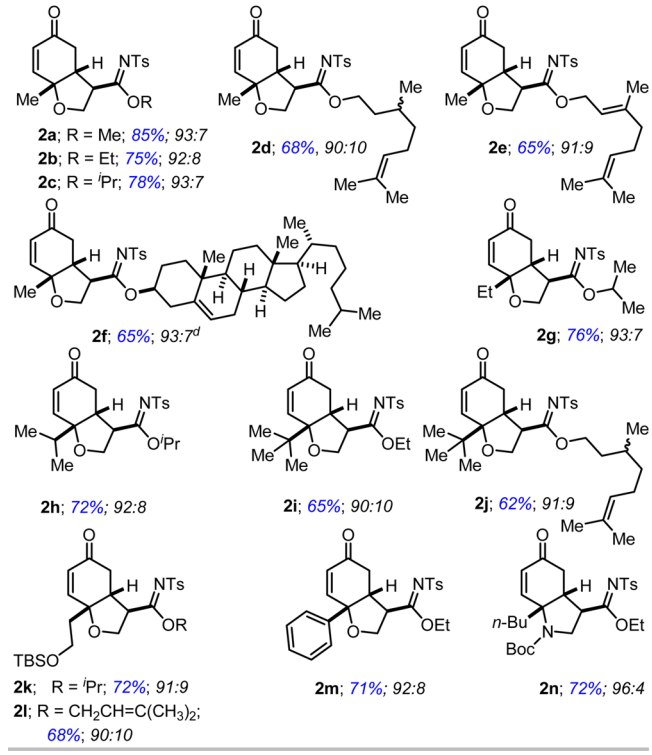



| entry | catalyst | base | solvent | yield (%) | 2a/3a[d] |
|---|---|---|---|---|---|
| 1 | CuI | $Et_3N$ | $CH_2Cl_2$ | 82 | 60:40 |
| 2 | CuCl | $Et_3N$ | $CH_2Cl_2$ | 86 | 61:39 |
| 3 | $[Cu(CH_3CN)]_4PF_6$ | $Et_3N$ | $CH_2Cl_2$ | 71 | 55:45 |
| 4 | CuBr·$Me_2S$ | $Et_3N$ | $CH_2Cl_2$ | 74 | |
| 5 | $Cu(OAc)_2$ | $Et_3N$ | $CH_2Cl_2$ | 80 | 57:43 |
| 6 | $Cu(TFA)_2{\cdot}xH_2O$ | $Et_3N$ | $CH_2Cl_2$ | 91 | 62:38 |
| 7 | $Cu(TFA)_2{\cdot}xH_2O$ | DBU | $CH_2Cl_2$ | <10 | |
| 8 | $Cu(TFA)_2{\cdot}xH_2O$ | $K_2CO_3$ | $CH_2Cl_2$ | 62 | 60:40 |
| **9** | $Cu(TFA)_2{\cdot}xH_2O$ | **$Na_2CO_3$** | **$CH_2Cl_2$** | **85** | **93:7** |
| **10** | $Cu(TFA)_2{\cdot}xH_2O$ | **DABCO** | **$CH_2Cl_2$** | **75** | **13:87** |
| 11 | $Cu(TFA)_2{\cdot}xH_2O$ | quinine | $CH_2CI_2$ | 10 | |
| 12 | $Cu(TFA)_2{\cdot}xH_2O$ | $Na_2CO_3$ | THF | 75 | 90:10 |
| 13 | $Cu(TFA)_2{\cdot}xH_2O$ | $Na_2CO_3$ | $Et_2O$ | 65 | 84:16 |
| 14 | $Cu(TFA)_2{\cdot}xH_2O$ | $Na_2CO_3$ | 1,4-dioxane | <10 | |
| 15 | $Cu(TFA)_2{\cdot}xH_2O$ | $Na_2CO_3$ | $CH_3CN$ | <10 | |
| 16 | $Cu(TFA)_2{\cdot}xH_2O$ | DABCO | THF | <10 | |
| 17 | $Cu(TFA)_2{\cdot}xH_2O$ | DABCO | $Et_2O$ | <10 | |
| 18 | $Cu(TFA)_2{\cdot}xH_2O$ | DABCO | $CH_3CN$ | 71 | 36:63 |

[a]Reactions were carried out with **1a** (0.5 mmol), tosyl azide (1.2 equiv), and MeOH (1.2 equiv) in 1.5 mL of solvent at room temperature. [b]Combined yields of isolated products. [c]Reaction wtih organic bases carried out for 5 h and reaction wtih inorganic bases carried out for 12 h. [d]Ratio was characterized by $^1$H NMR analysis of the crude reaction mixture.

**Table 2. Copper-Catalyzed Three-Component Coupling Reaction with $Na_2CO_3$**[a−c]




[a]Reactions were carried out with 1 (0.5 mmol), tosyl azide (1.2 equiv), and $R^2OH$ (1.2 equiv) in 1.5 mL of $CH_2Cl_2$ at room temperature; [b]Yields of isolated products. [c]Diastereoselectivity was characterized by $^1$H NMR analysis of crude reaction mixture. [d]Asymmetric induction was not observed.

of *exo*-**2a** and *endo*-**3a** isomers in a 3:2 ratio in 82% combined yield. Various copper catalysts were also investigated to further improve the diastereoselectivity (entries 2−6). Unfortunately, they led to poor *exo/endo* selectivity, albeit in good to excellent yields. Among all of the catalysts screened, $Cu(TFA)_2{\cdot}xH_2O$ was found to be superior, which afforded the product in 91% yield (entry 6). Next, we focused on the screening of different organic and inorganic bases in the presence of $Cu(TFA)_2{\cdot}xH_2O$ (entries 7−11). To our delight, the reaction with $Na_2CO_3$ gave *exo*-**2a** as the major isomer, and DABCO afforded *endo*-**3a** as the major isomer with excellent yields (entries 9 and 10). The solvent screening showed that $CH_2Cl_2$ is the best choice when compared to other polar and protic solvents (entries 12−18). Single-crystal X-ray analysis of *exo*-**2a** and *endo*-**3a** unambiguously established its relative stereochemistry (see the Supporting Information).[13]

Having demonstrated the practicality of this three-component coupling/conjugate addition reaction, we investigated the scope of the alkyne-tethered cyclohexadienones **1** with various alcohols in the presence of $Na_2CO_3$ as a base. We began our studies using substrate **1a** with various primary, secondary, allyl, and complex alcohols that gave corresponding *exo*-products **2a−f** as major isomers with excellent diastereoselectivity in good yields (Table 2). The increase in the steric bulk of the $R^1$ substituent (Et, $^i$Pr, and $^t$Bu) on the substrate's prochiral quaternary carbon center resulted in slightly lower yields for **2g−j** with similar *exo*-selectivity. The reaction proceed smoothly with other $R^1$ substituents such as $(CH_2)_2OTBS$ and phenyl, thus providing the corresponding products **2l**,**m** with good yields. In addition, *N*-tethered cyclohexadienone also gave the corresponding *exo*-hydroindole **2n** in 72% yield with excellent diastereoselectivity.

Later, we investigated the scope of the three-component coupling/conjugate addition reaction with DABCO as a base using the above-optimized conditions (Table 3). When **1a** was treated with various alcohols in the presence of DABCO, *endo*-products **3a−h** were obtained as major isomers with 82−87% diastereoselectivity. Alcohol bearing a terminal acetylene group was also compatible under these reaction conditions to give *endo*-**3i** in 51% yield. As for the larger $R^1$ substituents, the reaction proceeded smoothly to give the corresponding products **3j−o** with slightly lower yields and good *endo*-selectivity. In line with previous observations, *N*-tethered cyclohexadienone with DABCO afforded *endo*-hydroindole **3p** in 74% yield with 94:6 diastereoselectivity.

Interestingly, when unsymmetrically substituted cyclohexadienone **1b** was subjected to similar reaction conditions, cyclization was observed exclusively at the unsubstituted olefin to give single regioisomer *exo*-**4a** (68% yield, dr = 87:13) in the presence of $Na_2CO_3$ or *endo*-**4b** (71% yield, dr = 91:9) in the presence of DABCO. The *C*-tethered substrate **5** under the standard reaction conditions gave imidate **6**, and no desired cyclization product **6a** was observed, probably due to the absence of the



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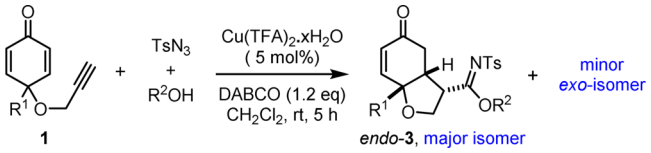
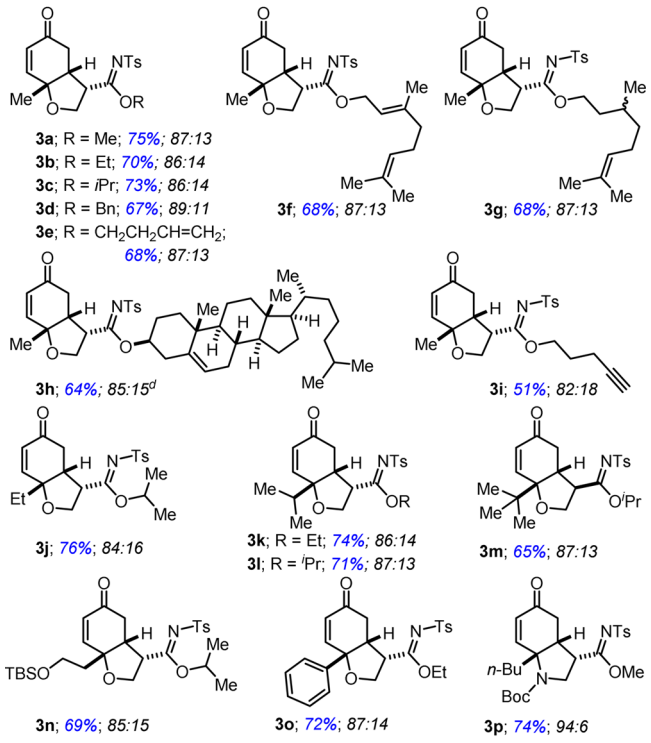
**Table 3. Copper-Catalyzed Three-Component Coupling with DABCO**[a−c]



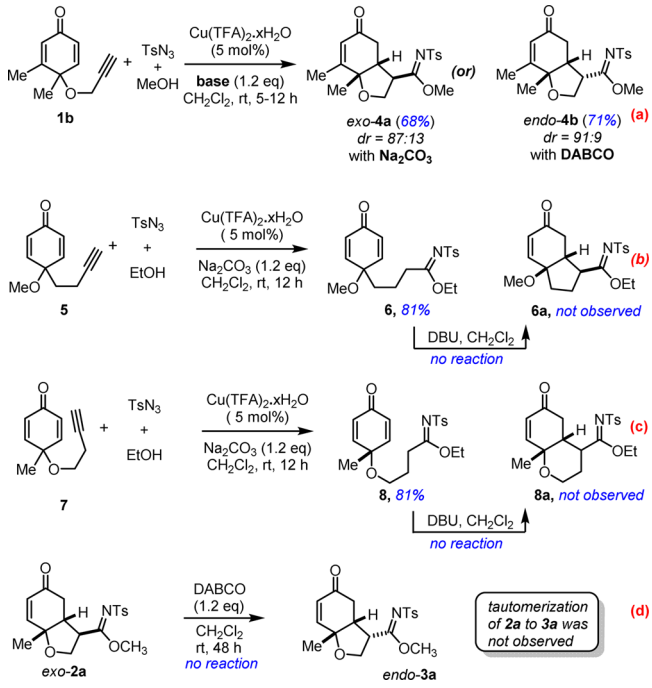

[a]Reactions were carried out with 1 (0.5 mmol), tosyl azide (1.2 equiv), and $R^2OH$ (1.2 equiv) in 1.5 mL of $CH_2Cl_2$ at room temperature. [b]Yields of isolated products. [c]Diastereoselectivity was characterized by $^1H$ NMR analysis of the crude reaction mixture. [d]Asymmetric induction was not observed.

Thorpe−Ingold effect.[14] Similarly, homologated *O*-tethered cyclohexadienone **7** failed to give the six-membered cyclization product **8a** and only afforded uncyclized imidate **8** in 81% yield. Further treatment of compounds **6** and **8** with DBU in $CH_2Cl_2$ did not produce Michael addition products **6a** and **8a**, whereas with strong bases such as NaH or LDA the reaction leads to decomposition. In addition, exposure of *exo*-**2a** to DABCO did not give *endo*-**3a** and recovered the starting material without any tautomerization at the $\alpha$-imidate position (Scheme 2).

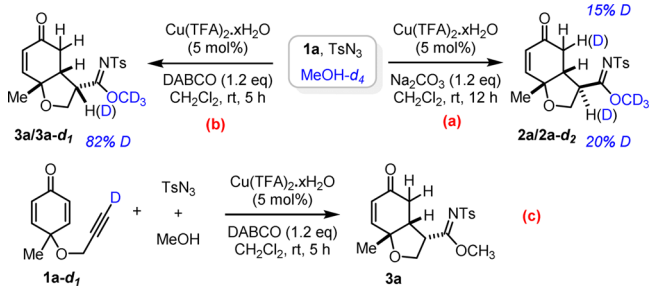
To gain further insight into the mechanism of this multicomponent coupling reaction, the labeling experiments were conducted with MeOH-$d_4$ and isotopically labeled starting materials **1a**-$d_1$. When the reaction of **1a** was conducted with excess MeOH-$d_4$ in the presence of $Na_2CO_3$, 15% and 20% deuterium incorporation was observed at the $\alpha$-keto and $\alpha$-imidate positions, respectively. The same reaction with DABCO afforded 82% of deuterium exchange which was detected at the $\alpha$-imidate position only. The reaction of labeled substrate **1a**-$d_1$ in the presence of DABCO under the standard conditions did not show any deuterium incorporation on **3a** (Scheme 3).

On the basis of our mechanistic studies and previous reports,[8] a plausible reaction mechanism is proposed in Scheme 4. Initially, a highly reactive *N*-sulfonyl triazolyl copper intermediate **A** is

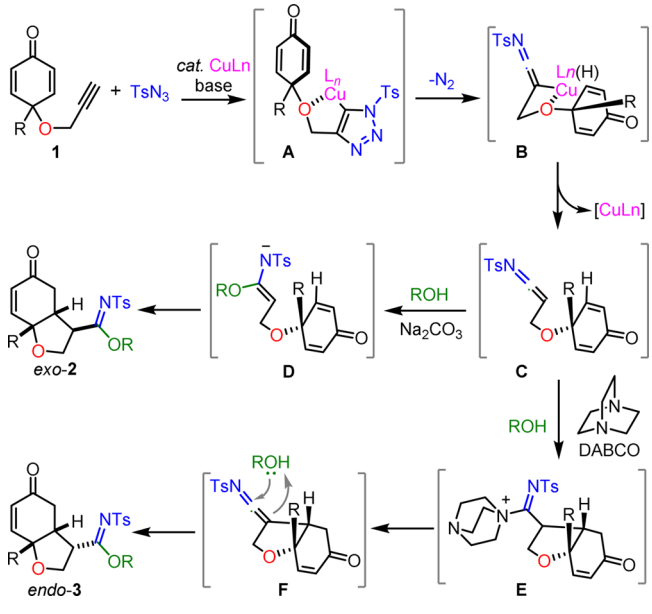
**Scheme 2. Mechanistic Experiments**




**Scheme 3. Studies with $CD_3OD$ and Labeled Substrate 1a-$d_1$**




**Scheme 4. Plausible Reaction Mechanism**



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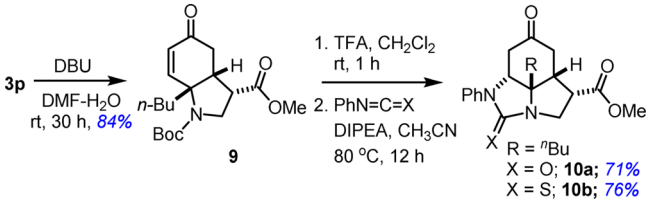
formed form Cu-acetylide and $TsN_3$, which undergo ring opening followed by hetero-Wolff rearrangement to give *N*-sulfonyl ketenimine **C**. In the case of $Na_2CO_3$ as base, a nucleophilic attack of alcohol on the reactive ketenimine **C** led to enamine **D**, which further underwent intramolecular Michael addition to yield the required *exo*-product **2**. In the case of DABCO, base itself attacked the ketenimne **C** followed by Michael addition to give intermediate **E**, and subsequent elimination furnished bicyclic ketenimine **F**. Because of its concave structure, alcohol attacks from the top face of bicyclic intermediate **F**, thus affording *endo*-product **3**.

To demonstrate the utility of *N*-tethered bicyclic products, further transformations were conducted on the enone functionality (Scheme 5). The hydrolysis of sulfonyl imidate **3p**

**Scheme 5. Synthetic Utility**




under mild basic conditions (catalytic DBU) gave the corresponding ester **9** in 84% yield.[15] The deprotection of the Boc group using TFA followed by treatment of amine with phenyl isocyanate or phenyl isothiocyanate afforded the corresponding tricyclic products **10a** or **10b** in good yields, respectively. The relative stereochemistry was confirmed with 2D NMR analysis of compound **10a** (see the Supporting Information).

In summary, we have developed a highly efficient and practical method for the tunable diastereoselective desymmetrization of *meso*-cyclohexa-2,5-dienones using a copper-catalyzed three-component coupling reaction to access *cis*-hydrobenzofurans. In this tandem process, *exo*- or *endo*-selectivity of the bicyclic framework with respect to the imidate group is controlled by the choice of the base. Additionally, mechanistic insights of the reaction revealed that the *endo*-selectivity is due to nucleophilic attack of DABCO on the highly reactive ketenimine intermediate in the reaction pathway. Furthermore, the bicyclic products could be exposed to various transformations to elaborate synthetic utility.

## EXPERIMENTAL SECTION

**General Information.** Unless otherwise noted, all reagents were used as received from commercial suppliers. Copper catalysts were obtained from Sigma-Aldrich and used without further purification. All reactions were performed under nitrogen atmosphere and in a flame-dried or oven-dried glassware with magnetic stirring. All solvents were dried before use following the standard procedures. Reactions were monitored using thin-layer chromatography ($SiO_2$). TLC plates were visualized with UV light (254 nm), iodine treatment, or using ninhydrin stain. Column chromatography was carried out using silica gel (100–200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, and 500 MHz (H) and at 75, 101, and 126 MHz (C), respectively. Chemical shifts ($\delta$) are reported in ppm using the residual solvent peak in $CDCl_3$ (H: $\delta$ = 7.26 and C: $\delta$ = 77.16 ppm) as internal standard, and coupling constants ($J$) are given in Hz. HRMS were recorded using ESI-ToF techniques. All alkyne-tethered cyclohexadienones were prepared according to the procedure described in the literature.[16]

**General Procedure for Copper-Catalyzed Three-Component Coupling Reaction.** To a solution of alkyne-tethered cyclohexa-2,5-dienone 1 (1.0 equiv) and alcohol (1.2 equiv) in $CH_2Cl_2$ (0.5 M) were added $Cu(TFA)_2 \cdot xH_2O$ (5 mol %, amount of the catalyst calculated on the basis of anhydrous molecular weight 289.58), base (1.2 equiv), and $TsN_3$ (1.2 equiv) under inert atmosphere. The reaction mixture was stirred at room temperature for 12 h in the presence of $Na_2CO_3$ or 5 h in the presence of DABCO. The reaction was quenched with saturated $NH_4Cl$ solution and extracted with $CH_2Cl_2$. The combined organic phases were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to give *cis*-hydrobenzofuran *exo*-**2** or *endo*-**3** as a major product. The reaction with $Na_2CO_3$ afforded *exo*-**2** as the major product, and DABCO afforded *endo*-**3** as the major product.

*Methyl 7a-Methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2a**):* white solid; mp = 89–90 °C; $R_f$ = 0.6 (30% EtOAc/hexanes); 190 mg, 85% yield with 93:7 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.3 Hz, 2H), 7.30 (d, $J$ = 8.0 Hz, 2H), 6.61 (dd, $J$ = 10.3, 1.9 Hz, 1H), 6.03 (dd, $J$ = 10.3, 0.7 Hz, 1H), 4.16 (ddd, $J$ = 21.2, 12.7, 7.3 Hz, 2H), 4.00–3.94 (m, 1H), 3.78 (s, 3H), 2.91–2.83 (m, 1H), 2.75 (d, $J$ = 17.8 Hz, 1H), 2.56 (dd, $J$ = 17.8, 5.6 Hz, 1H), 2.43 (s, 3H), 1.52 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.3, 174.0, 152.0, 143.8, 138.7, 129.6, 129.5, 126.9, 80.4, 69.7, 56.2, 48.4, 48.0, 36.4, 23.7, 21.7; IR (thin film) $\nu_{max}$ 3285, 1680, 1601, 1443, 1325, 1158, 1094, 1049, 945, 815, 771, 691 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{18}H_{22}NO_5S$ 364.1219, found 364.1221.

*Ethyl 7a-Methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2b**):* white solid; mp = 92–94 °C; $R_f$ = 0.3 (20% EtOAc/hexanes); 175 mg, 75% yield with 92:8 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.81 (d, $J$ = 8.3 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.53 (dd, $J$ = 10.3, 1.3 Hz, 1H), 6.04 (d, $J$ = 10.3 Hz, 1H), 4.47 (ddd, $J$ = 11.7, 9.6, 8.2 Hz, 1H), 4.12 (t, $J$ = 8.5 Hz, 1H), 4.06 (ddd, $J$ = 14.3, 9.0, 5.5 Hz, 1H), 3.96 (t, $J$ = 9.3 Hz, 1H), 3.87 (dq, $J$ = 10.9, 7.1 Hz, 1H), 3.14–3.07 (m, 1H), 2.59–2.55 (m, 2H), 2.43 (s, 3H), 1.53 (s, 3H), 1.16 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.5, 172.3, 151.1, 143.6, 138.9, 130.7, 129.6, 126.8, 79.5, 68.2, 65.4, 47.6, 46.9, 36.0, 24.8, 21.7, 13.3; IR (thin film) $\nu_{max}$ 3280, 1685, 1601, 1433, 1327, 1158, 1098, 1049, 945, 817, 805, 771, 691 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{19}H_{23}NO_5NaS$ 400.1195, found 400.1219.

*Isopropyl 7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2c**):* yellow oil; $R_f$ = 0.4 (20% EtOAc/hexanes); 187 mg, 78% yield with 93:7 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.75 (d, $J$ = 5.6 Hz, 2H), 7.28 (d, $J$ = 8.1 Hz, 2H), 6.60 (d, $J$ = 10.9 Hz, 1H), 6.00 (d, $J$ = 10.2 Hz, 1H), 5.11–5.00 (m, 1H), 4.18–4.09 (m, 2H), 3.94–3.85 (m, 1H), 2.82 (dd, $J$ = 9.5, 4.5 Hz, 1H), 2.68 (dd, $J$ = 17.8, 0.8 Hz, 1H), 2.55 (dd, $J$ = 17.8, 5.6 Hz, 1H), 2.41 (s, 3H), 1.51 (s, 3H), 1.25 (d, $J$ = 6.3 Hz, 3H), 1.2 (d, $J$ = 6.3 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 195.3, 172.6, 152.2, 143.5, 138.8, 129.6, 129.1, 126.7, 80.2, 72.9, 69.6, 48.5, 47.9, 36.2, 23.8, 21.6, 21.2, 21.1; IR (thin film) $\nu_{max}$ 2927, 1683, 1594, 1376, 1309, 1220, 1156, 1097, 909, 816, 772 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{20}H_{26}NO_5S$ 392.1532, found 392.1529.

*3,7-Dimethyloct-6-enyl-7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2d**):* viscous oil; $R_f$ = 0.4 (20% EtOAc/hexanes); 204 mg, 68% yield with 90:10 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.61 (dd, $J$ = 10.3, 1.8 Hz, 1H), 6.02 (d, $J$ = 10.3 Hz, 1H), 5.04 (t, $J$ = 7.1 Hz, 1H), 4.22–4.07 (m, 4H), 4.00–3.88 (m, 1H), 2.89–2.80 (m, 1H), 2.72 (d, $J$ = 17.7 Hz, 1H), 2.55 (dd, $J$ = 17.8, 5.6 Hz, 1H), 2.42 (s, 3H), 2.03–1.83 (m, 2H), 1.79–1.70 (m, 2H), 1.67 (s, 3H), 1.58 (s, 3H), 1.53–1.45 (m, 1H), 1.51 (s, 3H), 1.38–1.06 (m, 2H), 0.87 (d, $J$ = 5.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.3, 173.4, 152.1, 143.6, 138.8, 131.7, 129.6, 129.3, 126.8, 124.4, 80.3, 69.7, 67.9, 48.6, 48.0, 37.0, 36.4, 35.0, 29.7, 25.8, 25.5, 23.8, 21.7, 19.5, 17.8; IR (thin film) $\nu_{max}$ 2924, 1679, 1598, 1455, 1379, 1160, 879, 772 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{27}H_{37}NO_5NaS$ 510.2290, found 510.2280.

*(E)-3,7-Dimethylocta-2,6-dienyl-7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2e**):* yellow oil; $R_f$ = 0.3 (20% EtOAc/hexanes); 194 mg, 65% yield with 91:9 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.62 (dd, $J$ = 10.3, 1.8 Hz, 1H), 6.01 (d, $J$ = 10.3 Hz, 1H), 5.27 (t, $J$ = 7.1 Hz, 1H), 5.08–5.00 (m, 1H),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4.65 (d, $J$ = 7.2 Hz, 2H), 4.21−4.10 (m, 2H), 4.01−3.90 (m, 1H), 2.93−2.81 (m, 1H), 2.72 (d, $J$ = 17.3 Hz, 1H), 2.55 (dd, $J$ = 17.8, 5.6 Hz, 1H), 2.42 (s, 3H), 2.09−1.98 (m, 4H), 1.68 (s, 3H), 1.59 (s, 6H), 1.51 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 195.4, 173.1, 152.2, 144.3, 143.6, 138.8, 132.1, 129.6, 129.3, 126.9, 123.6, 116.9, 80.3, 69.7, 66.1, 48.5, 47.8, 39.6, 36.4, 26.3, 25.8, 23.8, 21.7, 17.9, 16.8; IR (thin film) $\nu_{max}$ 3292, 2966, 1667, 1597, 1312, 1198, 1157, 1077, 910, 815, 772, 691 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{27}H_{36}NO_5S$ 486.2314, found 486.2317.

*exo-(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl-7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2f**):* white solid; mp = 136−138 °C; $R_f$ = 0.4 (10% EtOAc/hexanes); 287 mg, 65% yield with 93:7 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (d, $J$ = 7.5 Hz, 2H), 7.29 (d, $J$ = 7.4 Hz, 2H), 6.64−6.59 (m, 1H), 6.01 (d, $J$ = 10.3 Hz, 1H), 5.29 (dd, $J$ = 14.6, 4.9 Hz, 1H), 4.68 (dq, $J$ = 16.1, 5.3 Hz, 1H), 4.21−4.09 (m, 2H), 3.98−3.88 (m, 1H), 2.87−2.80 (m, 1H), 2.69 (dd, $J$ = 17.7, 6.2 Hz, 1H), 2.56 (dd, $J$ = 17.8, 5.6 Hz, 1H), 2.43 (s, 3H), 2.39−2.24 (m, 2H), 2.06−1.91 (m, 3H), 1.90−1.76 (m, 3H), 1.68−1.54 (m, 4H), 1.52 (s, 3H), 1.49−1.40 (m, 4H), 1.40−1.27 (m, 4H), 1.19−1.03 (m, 7H), 1.01 (s, 3H), 0.99−0.95 (m, 1H), 0.91 (d, $J$ = 6.5 Hz, 3H), 0.86 (dd, $J$ = 6.6, 1.7 Hz, 6H), 0.67 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.4, 172.6, 172.5, 152.2, 143.5, 139.0, 138.9, 129.6, 129.2, 126.7, 123.5, 80.3, 78.8, 69.8, 56.8, 56.3, 50.0, 48.5, 48.5, 48.0, 42.4, 39.8, 39.7, 37.6, 37.4, 36.8, 36.8, 36.3, 35.9, 32.1, 31.9, 28.3, 28.2, 27.3, 27.1, 24.4, 24.0, 23.8, 23.7, 23.0, 22.7, 21.7, 21.2, 19.4, 18.9, 12.0; IR (thin film) $\nu_{max}$ 2943, 2307, 1687, 1597, 1315, 1158, 901, 771, 690 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{44}H_{63}NO_5NaS$ 740.4325, found 740.4319.

*Isopropyl 7a-ethyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2g**):* yellow solid; mp = 113−115 °C; $R_f$ = 0.4 (30% EtOAc/hexanes); 174 mg, 76% yield with 93:7 diastereoselectivity; $^1$H NMR (500 MHz, $CDCl_3$) 7.76 (d, $J$ = 8.3 Hz, 2H),, 7.29 (d, $J$ = 8.0 Hz, 2H), 6.62 (dd, $J$ = 10.43, 1.8 Hz, 1H), 6.06 (dd, $J$ = 10.4, 0.8 Hz, 1H), 5.06 (hept, $J$ = 6.2 Hz, 1H), 4.17−4.10 (m, 2H), 3.91−3.84 (m, 1H), 2.90 (td, $J$ = 6.4, 1.9 Hz, 1H), 2.68 (ddd, $J$ = 17.9, 1.7, 1.0 Hz, 1H), 2.52 (dd, $J$ = 17.9, 5.9 Hz, 1H), 2.42 (s, 3H), 1.88 (dq, $J$ = 15.0, 7.5 Hz, 1H), 1.77 (dq, $J$ = 14.9, 7.5 Hz, 1H), 1.25 (d, $J$ = 6.0 Hz, 3H), 1.24 (d, $J$ = 6.0 Hz, 3H), 1.04 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.6, 172.8, 151.6, 143.5, 138.9, 129.8, 129.6, 126.7, 82.4, 72.9, 69.7, 48.8, 45.4, 36.5, 30.3, 21.7, 21.3, 21.1, 8.1; IR (thin film) $\nu_{max}$ 2968, 1687, 1595, 1309, 1157, 1097, 910, 772, 693 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{21}H_{28}NO_5S$ 406.1688, found 406.1687.

*Isopropyl 7a-isopropyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2h**):* yellow oil; $R_f$ = 0.4 (30% EtOAc/hexanes); 158 mg, 72% yield with 92:8 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.2 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.60 (dd, $J$ = 10.5, 1.6 Hz, 1H), 6.14 (d, $J$ = 10.5 Hz, 1H), 5.05 (dt, $J$ = 12.4, 6.2 Hz, 1H), 4.14−4.04 (m, 2H), 3.84 (q, $J$ = 10.6 Hz, 1H), 3.00 (t, $J$ = 6.0 Hz, 1H), 2.69 (d, $J$ = 17.7 Hz, 1H), 2.53 (dd, $J$ = 18.1, 6.1 Hz, 1H), 2.42 (s, 3H), 2.06 (dt, $J$ = 13.8, 6.9 Hz, 1H), 1.25 (2d, $J$ = 6.2 Hz, 6H), 1.06 (d, $J$ = 7.0 Hz, 3H), 1.03 (d, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.9, 173.0, 150.8, 143.5, 138.9, 130.6, 129.6, 126.7, 84.3, 72.8, 69.5, 49.9, 43.3, 37.4, 35.5, 21.7, 21.3, 21.2, 17.9, 17.1; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{22}H_{30}NO_5S$ 420.1845, found 420.1841.

*Ethyl 7a-tert-butyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2i**):* viscous oil; $R_f$ = 0.6 (20% EtOAc/hexanes); 133 mg, 65% yield with 90:10 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.2 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.71 (dd, $J$ = 10.6, 1.5 Hz, 1H), 6.16 (d, $J$ = 10.6 Hz, 1H), 4.19 (q, $J$ = 7.1 Hz, 2H), 4.13−4.05 (m, 2H), 3.89−3.78 (m, 1H), 3.21 (t, $J$ = 6.1 Hz, 1H), 2.68 (d, $J$ = 18.0 Hz, 1H), 2.56 (dd, $J$ = 18.5, 6.1 Hz, 1H), 2.42 (s, 3H), 1.29 (t, $J$ = 7.1 Hz, 3H), 1.06 (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.7, 173.6, 150.0, 143.7, 139.0, 130.7, 129.6, 126.8, 85.9, 69.5, 65.2, 50.2, 42.2, 38.3, 37.9, 25.7, 21.7, 13.7; IR (thin film) $\nu_{max}$ 2923, 1686, 1600, 1312, 1156, 1133, 1077, 772, 689 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{22}H_{30}NO_5S$ 420.1845, found 420.1848.

*3,7-Dimethyloct-6-enyl-7a-tert-butyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2j**):* yellow oil; $R_f$ = 0.5 (20% EtOAc/hexanes); 160 mg, 62% yield with 91:9 diastereoselectivity; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.78 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.0 Hz, 2H), 6.71 (dd, $J$ = 10.6, 1.8 Hz, 1H), 6.16 (d, $J$ = 10.6 Hz, 1H), 5.07−5.02 (m, 1H), 4.20−4.08 (m, 4H), 3.84−3.77 (m, 1H), 3.21 (td, $J$ = 6.5, 1.7 Hz, 1H), 2.65 (d, $J$ = 18.5 Hz, 1H), 2.56 (ddd, $J$ = 18.4, 6.2. 0.9 Hz, 1H), 2.42 (s, 3H), 2.05−1.86 (m, 2H), 1.76−1.64 (m, 1H), 1.67 (s, 3H), 1.58 (s, 3H), 1.56−1.38 (m, 2H), 1.35−1.27 (m, 1H), 1.20−1.12 (m, 1H), 1.06 (s, 9H), 0.88 (2d, $J$ = 6.5 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 195.7, 173.6, 173.5, 150.1 (2), 143.6, 138.8, 131.7 (2), 130.5 (2), 129.6, 126.9, 124.3, 85.8, 69.5, 67.8, 50.4, 42.2, 42.1, 38.3, 37.7, 37.1, 37.0, 35.1, 29.6, 25.9, 25.7, 25.5, 25.5, 21.7, 19.5, 19.4, 17.8; IR (thin film) $\nu_{max}$ 3505, 3273, 2922, 2890, 1861, 1686, 1601, 1461, 1385, 1365, 1311, 1225, 1157, 1077, 981, 945, 815, 760, 689 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{30}H_{43}NO_5S$ 530.2935, found 530.2938.

*Isopropyl 7a-(2-(tert-butyldimethylsilyloxy)ethyl)-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2k**).* Light yellow oil; $R_f$ = 0.4 (10% EtOAc/hexanes); 125 mg, 72% yield with 91:9 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.3 Hz, 2H), 6.60 (dd, $J$ = 10.4, 1.8 Hz, 1H), 6.03 (d, $J$ = 10.4 Hz, 1H), 5.05 (hept, $J$ = 6.2 Hz, 1H), 4.20−4.11 (m, 1H), 3.92−3.81 (m, 2H), 3.80−3.73 (m, 2H), 3.15−3.07 (m, 1H), 2.71 (dd, $J$ = 17.9, 5.6 Hz, 1H), 2.60 (d, $J$ = 17.0 Hz, 1H), 2.43 (s, 3H), 2.11−2.03 (m, 1H), 1.93 (ddd, $J$ = 14.4, 6.1, 4.9 Hz, 1H), 1.26 (d, $J$ = 6.2 Hz, 3H), 1.23 (d, $J$ = 6.2 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 195.9, 172.6, 151.8, 143.5, 138.9, 129.6, 129.3, 126.7, 81.7, 72.9, 69.7, 58.4, 48.6, 45.8, 40.6, 36.2, 26.0, 21.7, 21.3, 21.2, 18.3, −5.2; IR (thin film) $\nu_{max}$ 2941, 1687, 1595, 1469, 1381, 1312, 1255, 1157, 1097, 1050, 909, 837, 777, 692 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{27}H_{42}NO_6SSi$ 536.2502, found 536.2493.

*3-Methylbut-2-en-1-yl-7a-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2l**):* yellow solid; mp = 59−61 °C; $R_f$ = 0.5 (20% EtOAc/hexanes); 124 mg, 68% yield with 90:10 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.81 (d, $J$ = 8.3 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.54 (dd, $J$ = 10.4, 1.2 Hz, 1H), 6.04 (d, $J$ = 10.4 Hz, 1H), 5.15 (td, $J$ = 6.9, 1.3 Hz, 1H), 4.59 (dd, $J$ = 12.3, 7.8 Hz, 1H), 4.43 (ddd, $J$ = 11.6, 9.6, 8.1 Hz, 1H), 4.23 (dd, $J$ = 12.2, 6.9 Hz, 1H), 4.08 (t, $J$ = 8.5 Hz, 1H), 3.92 (t, $J$ = 9.3 Hz, 1H), 3.85−3.76 (m, 2H), 3.32−3.24 (m, 1H), 2.71 (dd, $J$ = 18.0, 7.1 Hz, 1H), 2.50 (dd, $J$ = 18.0, 1.9 Hz, 1H), 2.43 (s, 3H), 2.10−1.96 (m, 2H), 1.70 (s, 3H), 1.55 (s, 3H), 0.88 (s, 9H), 0.05 (d, $J$ = 1.9 Hz, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 196.9, 172.3, 150.2, 143.5, 140.6, 139.0, 131.0, 129.5, 126.8, 117.0, 81.1, 67.8, 65.9, 58.8, 47.8, 45.2, 41.6, 36.1, 26.0, 25.9. 21.7, 18.3, 18.2, −5.3, −5.3; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{29}H_{43}NNaO_6SSi$ 584.2473, found 584.2490.

*Ethyl 5-oxo-7a-phenyl-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**2m**):* light yellow oil; $R_f$ = 0.6 (20% EtOAc/hexanes); 139 mg, 71% yield with 92:8 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.1 Hz, 2H), 7.48 (dt, $J$ = 3.2, 1.9 Hz, 2H), 7.44−7.33 (m, 2H), 7.37−7.31 (m, 1H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.62 (dd, $J$ = 10.3, 1.1 Hz, 1H), 6.27 (d, $J$ = 10.3 Hz, 1H), 4.53 (ddd, $J$ = 11.2, 9.5, 8.2 Hz, 1H), 4.35 (t, $J$ = 8.5 Hz, 1H), 4.22 (t, $J$ = 9.2 Hz, 1H), 4.11 (dq, $J$ = 10.9, 7.1 Hz, 1H), 3.93 (dq, $J$ = 10.9, 7.1 Hz, 1H), 3.39−3.31 (m, 1H), 2.65 (dd, $J$ = 17.9, 6.7 Hz, 1H), 2.58 (dd, $J$ = 17.9, 3.8 Hz, 1H), 2.42 (s, 3H), 1.22 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.7, 171.9, 148.7, 143.6, 140.8, 138.8, 131.5, 129.5, 129.0, 128.5, 126.7, 125.0, 83.0, 68.4, 65.5, 48.7, 47.3, 35.7, 21.7, 13.4; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{24}H_{26}NO_5S$ 440.1532, found 440.1519.

*tert-Butyl 7a-butyl-3-(ethoxy(tosylimino)methyl)-5-oxo-2,3,3a,4,5,7a-hexahydro-1H-indole-1-carboxylate (**2n**):* yellow oil; $R_f$ = 0.5 (30% EtOAc/hexanes); 123 mg, 72% yield with 96:4 diastereoselectivity; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.78 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 7.7 Hz, 2H), 7.18 (d, $J$ = 10.2 Hz, 0.7H), 6.96 (d, $J$ = 10.2 Hz, 0.3H), 5.94 (d, $J$ = 10.5 Hz, 1H), 4.23−4.15 (m, 2H), 4.14−3.98 (m, 2H), 3.37 (t, $J$ = 10.1 Hz, 0.3H), 3.30 (t, $J$ = 10.2 Hz, 0.7H), 3.11−3.00 (m, 1H), 2.56 (dd, $J$ = 18.1, 6.3 Hz, 1H), 2.48−2.36 (m, 1H), 2.42 (s, 3H), 1.71−1.58 (m, 2H), 1.52 (s, 3H), 1.47 (s, 6H), 1.43−1.34 (m, 2H), 1.32−1.22 (m, 5H), 0.95 (t, $J$ = 7.1 Hz, 1H), 0.92



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(t, $J$ = 7.1 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 194.9, 194.6, 171.7, 171.6, 153.2, 153.0, 150.1, 143.7, 143.6, 138.6, 138.5, 129.6, 126.9, 126.7, 126.5, 81.1, 80.4, 65.3, 63.4, 62.9, 50.5, 50.4, 44.4, 43.5, 43.4, 42.7, 35.5, 35.3, 34.1, 33.1, 28.7, 28.5, 25.7, 25.7, 23.0, 22.8, 21.7, 14.3, 13.7; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{27}H_{38}N_2NaO_6S$ 541.2343, found 541.2346.

*Methyl 7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3a**):* white solid; mp = 146−148 °C; $R_f$ = 0.5 (30% EtOAc/hexanes); 168 mg, 75% yield with 87:13 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.82 (d, $J$ = 8.2 Hz, 2H), 7.32 (d, $J$ = 8.2 Hz, 2H), 6.51 (d, $J$ = 10.3 Hz, 1H), 6.04 (d, $J$ = 10.3 Hz, 1H), 4.49 (dt, $J$ = 11.5, 8.9 Hz, 1H), 4.12 (t, $J$ = 8.6 Hz, 1H), 3.93 (t, $J$ = 9.3 Hz, 1H), 3.56 (s, 3H), 3.14−3.07 (m, 1H), 2.55 (qd, J = 17.8, 4.8 Hz, 2H), 2.43 (s, 3H), 1.53 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 196.4, 172.9, 151.1, 143.7, 138.7, 130.5, 129.6, 126.8, 79.5, 68.1, 55.2, 47.5, 47.0, 36.1, 24.8, 21.7; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{18}H_{22}NO_5S$ 364.1213, found 364.1238.

*Ethyl 7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3b**):* yellow solid; mp = 98−100 °C; $R_f$ = 0.4 (20% EtOAc/hexanes); 162 mg, 70% yield with 86:14 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.81 (d, $J$ = 8.3 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.53 (dd, $J$ = 10.3, 1.3 Hz, 1H), 6.04 (d, $J$ = 10.3 Hz, 1H), 4.47 (ddd, $J$ = 11.7, 9.6, 8.2 Hz, 1H), 4.13 (t, $J$ = 8.5 Hz, 1H), 4.07 (ddd, $J$ = 14.3, 9.0, 5.5 Hz, 1H), 3.96 (t, $J$ = 9.3 Hz, 1H), 3.87 (dq, $J$ = 10.9, 7.1 Hz, 1H), 3.11 (dt, $J$ = 5.7, 4.2 Hz, 1H), 2.60−2.56 (m, 2H), 2.43 (s, 3H), 1.53 (s, 3H), 1.16 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 196.5, 172.3, 151.1, 143.6, 138.9, 130.7, 129.6, 126.8, 79.5, 68.2, 65.4, 47.6, 46.9, 36.0, 24.8, 21.7, 13.3; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{19}H_{24}NO_5S$ 378.1370, found 378.1390.

*Isopropyl 7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3c**):* yellow oil; $R_f$ = 0.5 (20% EtOAc/hexanes); 175 mg, 73% yield with 86:14 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.54 (dd, $J$ = 10.3, 0.8 Hz, 1H), 6.02 (d, $J$ = 10.3 Hz, 1H), 4.86 (hept, $J$ = 6.2 Hz, 1H), 4.45 (ddd, $J$ = 11.2, 9.6, 8.2 Hz, 1H), 4.10 (t, $J$ = 8.5 Hz, 1H), 3.94 (t, $J$ = 9.3 Hz, 1H), 3.15−3.04 (m, 1H), 2.61 (dd, $J$ = 18.1, 3.9 Hz, 1H), 2.53 (dd, $J$ = 18.1, 6.8 Hz, 1H), 2.41 (s, 3H), 1.50 (s, 3H), 1.16 (d, $J$ = 2.6 Hz, 3H), 1.14 (d, $J$ = 2.5 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.6, 171.4, 151.0, 143.5, 139.0, 130.5 129.5, 126.6, 79.2, 74.4, 68.2, 47.6, 46.2, 35.7, 25.0, 21.6, 21.3, 20.7; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{20}H_{26}NO_5S$ 392.1526, found 392.1539.

*Benzyl 7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3d**):* white solid; mp = 191−193 °C; $R_f$ = 0.6 (30% EtOAc/hexanes); 181 mg, 67% yield with 89:11 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.83 (d, $J$ = 8.3 Hz, 2H), 7.37−7.30 (m, 5H), 7.24−7.20 (m, 2H), 6.45 (dd, $J$ = 10.3, 1.1 Hz, 1H), 5.90 (d, $J$ = 10.2 Hz, 1H), 5.10 (d, $J$ = 12.1 Hz, 1H), 4.68 (d, $J$ = 12.1 Hz, 1H), 4.58−4.44 (m, 1H), 4.10 (t, $J$ = 8.6 Hz, 1H), 3.93 (t, $J$ = 9.3 Hz, 1H), 3.18−3.10 (m, 1H), 2.72−2.54 (m, 2H), 2.45 (s, 3H), 1.52 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.5, 171.9, 151.0, 143.8, 138.8, 133.8, 130.6, 129.6, 129.2, 128.9, 128.7, 126.9, 79.5, 70.8, 68.0, 47.5, 47.1, 36.1, 24.7, 21.7; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{24}H_{26}$ $NO_5S$ 440.1526, found 440.1501.

*But-3-enyl 7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3e**):* red oil; $R_f$ = 0.6 (20% EtOAc/hexanes); 169 mg, 68% yield with 87:13 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.3 Hz, 2H), 7.30 (d, $J$ = 8.1 Hz, 2H), 6.51 (dd, $J$ = 10.4, 1.3 Hz, 1H), 6.03 (d, $J$ = 10.3 Hz, 1H), 5.71−5.53 (m, 1H), 5.05 (dd, $J$ = 3.3, 1.5 Hz, 1H) 5.00 (d, $J$ = 0.9 Hz, 1H), 4.46 (ddd, $J$ = 11.6, 9.6, 8.2 Hz, 1H), 4.11−4.01 (m, 1H), 4.09 (t, $J$ = 8.0 Hz, 1H), 3.93 (t, $J$ = 9.4 Hz, 1H), 3.81 (dt, $J$ = 11.0, 6.2 Hz, 1H), 3.15−3.03 (m, 1H), 2.59−2.53 (m, 2H), 2.42 (s, 3H), 2.27 (q, $J$ = 6.6 Hz, 2H), 1.52 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.4, 172.2, 151.0, 143.6, 138.8, 133.4, 130.6, 129.5, 126.7, 117.8, 79.4, 68.0, 67.9, 47.6, 46.8, 36.0, 32.2, 24.8, 21.6; IR (thin film) $\nu_{max}$ 2975, 1732, 1686, 1599, 1459, 1388, 1310, 1157, 1122, 1096, 1052, 964, 881, 815, 772, 692 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{21}H_{26}NO_5S$ 404.1526, found 404.1545.

*(E)-3,7-Dimethylocta-2,6-dienyl-7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3f**):* yellow oil; $R_f$ = 0.4 (20% EtOAc/hexanes); 203 mg, 68% yield with 87:13 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.81 (d, $J$ = 8.2 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.45 (dd, $J$ = 10.2, 1.1 Hz, 1H), 6.01 (d, $J$ = 10.4 Hz, 1H), 5.16 (t, $J$ = 7.2 Hz, 1H), 5.07−5.00 (m, 1H),), 4.61 (dd, $J$ = 12.2, 7.6 Hz, 1H), 4.55−4.41 (m, 1H), 4.25 (dd, $J$ = 12.2, 7.0 Hz, 1H), 4.12 (t, $J$ = 8.5 Hz, 1H), 3.96 (t, $J$ = 9.3 Hz, 1H), 3.15−3.05 (m, 1H), 2.57 (d, $J$ = 5.0 Hz, 2H), 2.43 (s, 3H), 2.11−1.93 (m, 4H), 1.67 (s, 3H), 1.58 (s, 3H), 1.55 (s, 3H), 1.52 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 196.4, 172.2, 150.8, 144.1, 143.6, 139.0, 132.0, 130.6, 129.6, 126.8, 123.7, 116.6, 79.4, 68.2, 65.9, 47.6, 46.8, 39.6, 36.0, 26.3, 25.8, 25.0, 21.7, 17.8, 16.6; IR (thin film) $\nu_{max}$ 2924, 1686, 1599, 1307, 1156, 1097, 773, 690 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{27}H_{36}NO_5S$ 486.2314, found 486.2311.

*3,7-Dimethyloct-6-enyl-7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3g**):* viscous oil; $R_f$ = 0.5 (20% EtOAc/hexanes); 204 mg, 68% yield with 87:13 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.61 (dd, $J$ = 10.3, 1.8 Hz, 1H), 6.02 (d, $J$ = 10.3 Hz, 1H), 5.04 (t, $J$ = 7.1 Hz, 1H), 4.21−4.09 (m, 4H), 3.99−3.88 (m, 1H), 2.84 (dd, $J$ = 8.7, 5.6 Hz, 1H), 2.72 (d, $J$ = 17.7 Hz, 1H), 2.55 (dd, $J$ = 17.8, 5.6 Hz, 1H), 2.42 (s, 3H), 2.01−1.87 (m, 2H), 1.77−1.63 (m, 2H), 1.67 (s, 3H), 1.58 (s, 3H), 1.54−1.14 (m, 1H), 1.51 (s, 3H), 1.33−1.06 (m, 2H), 0.87 (d, $J$ = 5.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.3, 173.4, 152.1, 143.6, 138.8, 131.7, 129.6, 129.3, 126.8, 124.4, 80.3, 69.7, 67.9, 48.6, 48.0, 37.0, 36.4, 35.0, 29.7, 25.8, 25.5, 23.8, 21.7, 19.6, 19.5, 17.8; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{27}H_{38}NO_5S$ 488.2471, found $C_{27}H_{38}NO_5S$ 488.2464.

*endo-(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl-7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3h**):* white solid; mp = 145−148 °C; $R_f$ = 0.5 (10% EtOAc/hexanes); 283 mg, 64% yield with 85:15 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 8.3 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.55 (d, $J$ = 10.3 Hz, 1H), 6.05 (dd, $J$ = 10.3, 5.5 Hz, 1H), 5.26 (dd, $J$ = 26.0, 5.2 Hz, 1H), 4.57−4.43 (m, 2H), 4.12 (t, $J$ = 9.3 Hz, 1H), 3.97 (t, $J$ = 9.3 Hz, 1H), 3.15−3.08 (m, 1H), 2.61 (ddd, $J$ = 18.1, 6.6, 4.1 Hz, 1H), 2.54 (ddd, $J$ = 18.0, 6.9, 1.8 Hz, 1H), 2.44 (s, 3H), 2.40−2.25 (m, 2H), 2.24−2.12 (m, 1H), 2.03−1.90 (m, 2H), 1.89−1.74 (m, 4H), 1.71−1.56 (m, 2H), 1.60−1.54 (m, 2H), 1.52 (s, 3H), 1.50−1.47 (m, 1H), 1.47−1.38 (m, 4H), 1.38−1.29 (m, 3H), 1.25 (s, 3H),1.17−1.05 (m, 6H), 0.90 (d, $J$ = 6.4 Hz, 3H), 0.87 (d, $J$ = 1.8 Hz, 3H), 0.85 (d, $J$ = 1.8 Hz, 3H), 0.83−0.79 (m, 1H), 0.66 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 185.3, 172.2, 151.7, 143.2, 139.3, 139.2, 130.4, 129.5, 126.7, 123.3, 78.5, 72.7, 61.5, 56.8, 56.3, 50.1, 42.4, 39.8, 39.6, 37.6, 37.0, 36.8, 36.3, 35.9, 35.2, 32.1, 31.9, 28.3, 28.2, 27.3, 26.4, 24.4, 24.0, 23.0, 22.7, 21.7, 21.2, 20.0, 19.4, 18.9, 12.0; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{44}H_{64}NO_5S$ 718.4500, found 718.4526.

*Pent-4-ynyl 7a-methyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3i**):* yellow oil; $R_f$ = 0.5 (25% EtOAc/hexanes); 130 mg, 51% yield with 82:18 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.81 (d, $J$ = 8.3 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.53 (dd, $J$ = 10.3, 1.1 Hz, 1H), 6.04 (d, $J$ = 10.3 Hz, 1H), 4.48 (dt, $J$ = 11.6, 9.5 Hz, 1H), 4.19−4.07 (m, 2H), 3.90 (ddd, $J$ = 17.0, 15.0, 7.6 Hz, 2H), 3.17−3.06 (m, 1H), 2.60−2.55 (m, 2H), 2.43 (s, 3H), 2.18 (td, $J$ = 7.0, 2.4 Hz, 2H), 1.93 (t, $J$ = 2.6 Hz, 1H), 1.76 (dq, $J$ = 10.1, 7.1 Hz, 2H), 1.53 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.5, 172.2, 151.1, 143.7, 138.8, 130.6, 129.6, 126.8, 82.6, 79.5, 69.5, 68.0, 67.7, 47.6, 46.9, 36.1, 26.7, 24.8, 21.7, 15.3; IR (thin film) $\nu_{max}$ 3280, 2967, 1685, 1599, 1458, 1390, 1306, 1253, 1156, 1122, 1091, 1046, 967, 912, 815, 692 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{22}H_{26}NO_5S$ 416.1526, found 416.1510.

*Isopropyl 7a-ethyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3j**):* yellow solid; mp = 122−124 °C; $R_f$ = 0.5 (30% EtOAc/hexanes); 174 mg, 76% yield with 84:16 diastereoselectivity. It was purified by flash chromatography to afford a $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.3 Hz, 2H), 7.30 (d, $J$ = 8.2 Hz, 2H), 6.54 (d, $J$ = 10.4 Hz, 1H), 6.10 (d, $J$ = 10.4 Hz, 1H), 4.86 (dq, $J$ = 12.4, 6.2 Hz, 1H), 4.40 (ddd, $J$ = 11.1, 9.7, 8.0 Hz, 1H), 4.08 (t, $J$ = 8.4 Hz, 1H), 3.93 (t, $J$ = 9.3 Hz, 1H), 3.20−3.10 (m, 1H), 2.52 (dd, $J$ = 18.2, 7.0 Hz, 1H), 2.50 (dd, $J$ = 18.2, 3.6 Hz, 1H), 2.42 (s, 3H), 1.90−1.75



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(m, 2H), 1.17 (d, $J$ = 6.6 Hz, 3H), 1.15 (d, $J$ = 6.6 Hz, 3H), 1.01 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.9, 171.5, 150.2, 143.5, 139.1, 131.4, 129.6, 126.6, 81.9, 74.4, 67.9, 48.0, 43.8, 36.2, 31.7, 21.7, 21.3, 20.7, 8.3; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{21}H_{28}NO_5S$ 406.1683, found 406.1687.

*Ethyl 7a-isopropyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3k**):* yellow oil; $R_f$ = 0.5 (30% EtOAc/hexanes); 157 mg, 74% yield with 86:14 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.81 (d, $J$ = 8.3 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.52 (dd, $J$ = 10.5, 1.2 Hz, 1H), 6.19 (d, $J$ = 10.5 Hz, 1H), 4.36 (ddd, $J$ = 11.5, 10.0, 7.8 Hz, 1H), 4.09 (ddd, $J$ = 12.4, 9.4, 6.2 Hz, 2H), 3.93−3.86 (m, 2H), 3.23−3.16 (m, 1H), 2.56 (dd, $J$ = 18.3, 7.4 Hz, 1H), 2.47 (d, $J$ = 1.6 Hz, 1H), 2.43 (s, 3H), 2.06 (dq, $J$ = 13.8, 6.9 Hz, 1H), 1.17 (t, $J$ = 7.1 Hz, 3H), 1.04 (2d, $J$ = 6.9 Hz, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 197.0, 172.4, 149.1, 143.6, 138.9, 132.3, 129.6, 126.8, 84.2, 67.4, 65.4, 48.6, 42.2, 37.6, 36.3, 21.7, 17.9, 16.8, 13.3; IR (thin film) $\nu_{max}$ 3280, 2967, 1685, 1599, 1306, 1156, 1046, 815, 692 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{21}H_{28}NO_5S$ 406.1683, found 406.1682.

*Isopropyl 7a-isopropyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3l**):* yellow oil; $R_f$ = 0.5 (30% EtOAc/hexanes); 156 mg, 71% yield with 87:13 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 8.2 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.53 (d, $J$ = 10.5 Hz, 1H), 6.18 (d, $J$ = 10.5 Hz, 1H), 4.88 (dt, $J$ = 12.5, 6.2 Hz, 1H), 4.33 (td, $J$ = 10.2, 7.7 Hz, 1H), 4.04 (t, $J$ = 8.3 Hz, 1H), 3.90−3.82 (m, 1H), 3.26−3.17 (m, 1H), 2.54−2.49 (m, 2H), 2.43 (s, 3H), 2.05 (dt, $J$ = 13.7, 6.9 Hz, 1H), 1.18 (d, $J$ = 6.6 Hz, 3H), 1.16 (d, $J$ = 6.5 Hz, 3H), 1.03 (2d, $J$ = 6.9 Hz, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 197.1, 171.5, 149.1, 143.5, 139.1, 132.1, 129.6, 126.6, 84.1, 74.4, 67.4, 48.8, 41.5, 37.2, 36.3, 21.7, 21.3, 20.7, 17.7, 16.8; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{22}H_{29}NNaO_5S$ 442.1659, found 442.1662.

*Isopropyl 7a-tert-butyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3m**):* light red solid; mp = 107−110 °C; $R_f$ = 0.4 (10% EtOAc/hexanes); 137 mg, 65% yield with 87:13 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.71 (dd, $J$ = 10.6, 1.8 Hz, 1H), 6.17 (d, $J$ = 10.6 Hz, 1H), 5.05 (dt, $J$ = 12.4, 6.2 Hz, 1H), 4.12−4.02 (m, 2H), 3.84−3.75 (m, 1H), 3.16 (tt, $J$ = 9.7, 4.9 Hz, 1H), 2.68 (d, $J$ = 18.2 Hz, 1H), 2.56 (dd, $J$ = 18.5, 6.3 Hz, 1H), 2.42 (s, 3H), 1.25 (2d, $J$ = 6.2 Hz, 6H), 1.06 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 197.1, 171.5, 150.4, 143.4, 139.1, 130.9, 129.6, 126.6, 81.0, 74.4, 67.8, 58.8, 47.8, 44.6, 41.7, 35.8, 26.0, 21.7, 21.3, 20.7, 18.3; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{23}H_{31}NO_5SNa$ 456.1815, found 456.1833.

*Isopropyl 7a-(2-(tert-butyldimethylsilyloxy)ethyl)-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3n**):* light yellow oil; $R_f$ = 0.5 (10% EtOAc/hexanes); 120 mg, 69% yield with 85:15 diastereoselectivity. It was purified by flash chromatography to afford a $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 8.3 Hz, 2H), 7.30 (d, $J$ = 8.1 Hz, 2H), 6.58 (dd, $J$ = 10.4, 1.1 Hz, 1H), 6.06 (d, $J$ = 10.4 Hz, 1H), 4.87 (dq, $J$ = 12.4, 6.2 Hz, 1H), 4.42 (ddd, $J$ = 11.5, 9.7, 8.0 Hz, 1H), 4.08 (t, $J$ = 8.4 Hz, 1H), 3.90 (t, $J$ = 9.3 Hz, 1H), 3.84−3.77 (m, 2H), 3.29 (ddd, $J$ = 7.3, 5.0, 1.7 Hz, 1H), 2.69 (dd, $J$ = 18.2, 7.3 Hz, 1H), 2.54 (dd, $J$ = 18.2, 2.5 Hz, 1H), 2.43 (s, 3H), 2.11−1.95 (m, 2H), 1.16 (2d, $J$ = 6.1 Hz, 6H), 0.88 (s, 9H), 0.05 (2s, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 197.1, 171.5, 150.4, 143.4, 139.1, 130.9, 129.6, 126.6, 81.0, 74.4, 67.8, 58.8, 47.8, 44.6, 41.7, 35.8, 26.0, 21.7, 21.3, 20.7, 18.3, −5.3, −5.3; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{27}H_{42}NO_6SSi$ 536.2497, found 536.2509.

*Ethyl 5-oxo-7a-phenyl-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (**3o**):* yellow oil; $R_f$ = 0.3 (10% EtOAc/hexanes); 141 mg, 72% yield with 87:14 diastereoselectivity; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.3 Hz, 2H), 7.51−7.24 (m, 7H), 6.70 (dd, $J$ = 10.3, 1.8 Hz, 1H), 6.32 (d, $J$ = 10.3 Hz, 1H), 4.42−4.14 (m, 5H), 3.12−3.02 (m, 1H), 2.69 (dd, $J$ = 17.8, 1.6 Hz, 1H), 2.56 (dd, $J$ = 17.8, 5.5 Hz, 1H), 2.43 (s, 3H), 1.27 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$. 195.7, 172.9, 149.2, 143.7, 140.1, 138.7, 130.6, 129.6, 129.0, 128.5, 126.8, 125.3, 83.9, 70.4, 65.4, 50.0, 49.0, 35.8, 21.7, 13.7; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{24}H_{26}NO_5S$ 440.1526, found 440.1501.

*tert-Butyl 7a-butyl-3-(methoxy(tosylimino)methyl)-5-oxo-2,3,3a,4,5,7a-hexahydro-1H-indole-1-carboxylate (**3p**):* yellow oil; $R_f$ = 0.6 (30% EtOAc/hexanes); 123 mg, 74% yield with 94:6 diastereoselectivity; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 7.7 Hz, 2H), 7.28 (d, $J$ = 7.0 Hz, 2H), 7.16 (d, $J$ = 10.0 Hz, 0.7H), 6.94 (d, $J$ = 10.1 Hz, 0.3H), 5.92 (d, $J$ = 10.1 Hz, 1H), 4.16−3.95 (m, 2H), 3.75 (s, 3H), 3.39−3.27 (m, 1H), 3.10−3.00 (m, 1H), 2.54 (dd, $J$ = 18.0, 5.8 Hz, 1H), 2.46−2.36 (m, 1H), 2.40 (s, 3H), 2.24−1.80 (m, 1H), 1.66−1.54 (m, 1H), 1.50 (s, 3H), 1.45 (s, 6H), 1.41−1.22 (m, 4H), 0.91 (t, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 194.7, 194.5, 172.3, 172.1, 153.1, 152.9, 150.0, 143.8, 138.4, 138.3, 129.6, 126.9, 126.6, 126.4, 81.0, 80.3, 63.4, 62.9, 56.1, 50.4, 50.7, 44.3, 43.4, 42.6, 35.4, 34.0, 33.0, 28.6, 28.5, 25.6, 25.3, 22.9, 22.7, 21.6, 14.2; IR (thin film) $\nu_{max}$ 3017, 2960, 1684, 1607, 1385, 1152, 1093, 952, 749, 678 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{26}H_{37}N_2O_6S$ 505.2367, found 505.2374.

*Methyl 7,7a-dimethyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3 carbimidate (exo-**4a**):* white solid; mp = 120−122 °C; $R_f$ = 0.4 (20% EtOAc/hexanes); 145 mg, 68% yield with 87:13 diastereoselectivity; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 5.91 (s, 1H), 4.15 (td, $J$ = 9.5, 6.2 Hz, 1H), 4.00 (t, $J$ = 9.2 Hz, 1H), 3.93 (dd, $J$ = 9.1, 6.2 Hz, 1H), 3.77 (s, 3H), 2.85 (ddd, $J$ = 9.8, 5.7, 1.7 Hz, 1H), 2.68 (d, $J$ = 17.9 Hz, 1H), 2.55 (dd, $J$ = 17.8, 5.8 Hz, 1H), 2.42 (s, 3H), 1.95 (d, $J$ = 1.1 Hz, 3H), 1.52 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 194.8, 174.1, 162.4, 143.7, 138.6, 129.6, 128.1, 126.8, 82.3, 69.2 56.1, 48.6, 48.0, 36.3, 22.8, 21.7, 17.8; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{19}H_{24}NO_5S$ 378.1375, found 378.1375.

*Methyl 7,7a-dimethyl-5-oxo-N-tosyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbimidate (endo-**4b**):* white solid; mp = 139−141 °C; $R_f$ = 0.5 (20% EtOAc/hexanes); 151 mg, 71% yield with 91:9 diastereoselectivity; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.83 (d, $J$ = 8.3 Hz, 2H), 7.32 (d, $J$ = 8.0 Hz, 2H), 5.96−5.93 (m, 1H), 4.50 (ddd, $J$ = 11.9, 9.4, 8.3 Hz, 1H), 4.10 (t, $J$ = 8.6 Hz, 1H), 3.75 (t, $J$ = 9.13 Hz, 1H), 3.55 (s, 3H), 3.07 (ddd, $J$ = 11.9, 6.3, 3.0 Hz, 1H), 2.62−2.56 (m, 2H), 2.44 (s, 3H), 1.97 (d, $J$ = 1.3 Hz, 3H), 1.55 (s, 3H); $^{13}$C NMR (101 MHz) $\delta$ 195.9, 173.1, 160.9, 143.7, 138.8, 129.6, 129.5, 126.8, 81.7, 67.9, 55.2, 48.2, 47.3, 36.0, 23.7, 21.7, 17.9; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{19}H_{24}NO_5S$ 378.1375, found 378.1374.

*Ethyl 4-(1-methoxy-4-oxocyclohexa-2,5-dienyl)-N-tosylbutanimidate (**6**):* light yellow oil; $R_f$ = 0.6 (10% EtOAc/hexanes); 180 mg, 81% yield; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 8.3 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 6.74 (d, $J$ = 10.3 Hz, 2H), 6.38 (d, $J$ = 10.2 Hz, 2H), 4.13 (q, $J$ = 7.1 Hz, 2H), 3.20 (s, 3H), 2.87 (t, $J$ = 7.4 Hz, 2H), 2.42 (s, 3H), 1.82−1.58 (m, 4H), 1.25 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 185.4, 175.1, 150.8, 143.3, 139.2, 131.9, 129.5, 126.7, 75.5, 64.8, 53.2, 38.9, 33.9, 21.7, 20.3, 13.8; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{20}H_{26}NO_5S$ 392.1526, found 392.1518.

*Ethyl 4-(1-methyl-4-oxocyclohexa-2,5-dienyloxy)-N-tosylbutanimidate (**8**):* light yellow oil; $R_f$ = 0.6 (10% EtOAc/hexanes); 179 mg, 81% yield; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.82 (d, $J$ = 8.3 Hz, 2H), 7.30 (d, $J$ = 8.0 Hz, 2H), 6.82 (d, $J$ = 10.3 Hz, 2H), 10.28 (d, $J$ = 6.28 Hz, 2H), 4.14 (q, $J$ = 7.1 Hz, 2H), 3.36 (t, $J$ = 6.0 Hz, 2H), 2.98 (t, $J$ = 6.6 Hz, 2H), 2.43 (s, 3H), 1.97−1.91 (m, 2H), 1.42 (s, 3H), 1.28 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 185.3, 175.6, 152.2, 143.2, 139.3, 130.1, 129.4, 126.6, 72.4, 64.6, 64.5, 30.9, 26.4, 26.4, 21.6, 13.7; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{20}H_{25}NO_5SNa$ 414.1346, found 414.1336.

*1-tert-Butyl 3-methyl 7a-butyl-5-oxo-3,3a,4,5-tetrahydro-1H-indole-1,3(2H,7aH)-dicarboxylate (**9**).* To a well-stirred solution of sulfonylimidate **3p** (200 mg, 0.396 mmol) in DMF and $H_2O$ (95/5, 2 mL) was added DBU in DMF (10 mol %, 5.6 $\mu$L). The reaction mixture was stirred at room temperature for 30 h and then diluted by addition of $Et_2O$ (10 mL × 3). The mixture was washed with water three times, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (20% ethyl acetate in hexanes; $R_f$ = 0.3) to afford the ester **9** (116 mg, 84% yield) as yellow oil: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.14 (d, $J$ = 10.1 Hz, 0.6H), 6.90 (d, $J$ = 10.1 Hz, 0.4H), 5.86 (d, $J$ = 10.4 Hz, 1H), 3.89−3.73 (m, 1H), 3.69 (s, 3H), 3.37 (t, $J$ = 10.6 Hz, 1H), 2.97−2.82 (m, 1H), 2.82−2.74 (m, 1H), 2.67−2.52 (m, 2H), 2.37 (t, $J$ = 10.6 Hz, 0.6H), 2.12 (t, $J$ = 10.6 Hz, 0.4H), 1.67−1.56 (m, 1H), 1.49 (s, 3H), 1.43 (s, 6H), 1.39−1.21 (m, 4H), 0.96−0.82 (m, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 196.4, 196.2, 172.3, 153.3, 153.0, 150.3, 126.5, 126.3, 81.0, 80.2, 64.0, 63.4, 52.3, 49.5, 44.3, 43.9, 43.5, 43.2, 36.3,



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33.8, 32.8, 28.5, 25.6, 25.3, 22.9, 22.7, 14.2; HRMS (ESI) $m/z$ calcd for $[M + Na]^+$ $C_{19}H_{29}NNaO_5$ 374.1938, found 374.1935.

*Methyl 3¹-Butyl-2,7-dioxo-1-phenyldecahydroimidazo[4,5,1-hi]-indole-5-carboxylate (**10a**).* To a solution of bicycle **9** (50 mg, 0.036 mmol) in $CH_2Cl_2$ (2 mL) was added trifluoroacetic acid (TFA, 2 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated $Na_2CO_3$ (15 mL), extracted with EtOAc (15 mL × 3), dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure.

To a well-stirred solution of above crude product in $CH_3CN$ (2 mL) was added 4-phenyl isocyanate (25 mg, 0.213 mmol) and DIPEA (37 μL, 0.213 mmol) under nitrogen atmosphere, and the resulting mixture was stirred at 80 °C for 12 h. The reaction was quenched with water (10 mL), extracted with EtOAc (10 mL × 3), and purified by flash column chromatography (40% ethyl acetate in hexanes; $R_f$ = 0.4) to afford tricycle **10a** (36 mg, 71%) as a light yellow liquid: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36 (t, $J$ = 7.9 Hz, 2H), 7.25 (d, $J$ = 7.9 Hz, 2H), 7.18 (t, $J$ = 7.4 Hz, 1H), 4.47 (t, $J$ = 3.1 Hz, 1H), 4.34 (dd, $J$ = 12.9, 9.8 Hz, 1H), 3.76 (s, 3H), 3.50 (dd, $J$ = 12.9, 6.1 Hz, 1H), 2.88−2.76 (m, 2H), 2.76 (dd, $J$ = 18.6, 2.8 Hz, 1H), 2.56 (dd, $J$ = 17.1, 5.4 Hz, 1H), 2.41 (dd, $J$ = 18.6, 3.5 Hz, 1H), 2.20 (dd, $J$ = 17.2, 13.4 Hz, 1H), 1.76−1.63 (m, 2H), 1.51−1.31 (m, 4H), 0.95 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 206.8, 173.6, 160.3, 136.88, 129.4, 125.8, 123.2, 66.7, 55.6, 52.7, 49.7, 46.0, 44.5, 43.1, 38.0, 36.1, 26.1, 22.9, 14.1; IR (thin film) $\nu_{max}$ 2955, 1697, 1596, 1497, 1391, 1206, 1024, 754, 696 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{21}H_{27}N_2O_4$ 371.1965, found 371.1964.

*Methyl 3¹-butyl-7-oxo-1-phenyl-2-thioxodecahydroimidazo-[4,5,1-hi]indole-5-carboxylate (**10b**):* light yellow oil; $R_f$ = 0.6 (40% EtOAc/hexanes); 41 mg, 76% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45−7.38 (m, 2H), 7.36−7.32 (m, 1H), 7.17 (t, $J$ = 1.7 Hz, 1H), 7.17−7.14 (m, 1H), 4.84 (dd, $J$ = 12.9, 9.9 Hz, 1H), 4.44 (t, $J$ = 3.2 Hz, 1H), 3.77 (s, 3H), 3.74 (dd, $J$ = 13.0, 6.0 Hz, 1H), 2.91−2.85 (m, 1H), 2.83 (dd, $J$ = 5.3, 1.9 Hz, 1H), 2.61 (dd, $J$ = 14.1, 3.4 Hz, 1H), 2.57 (dd, $J$ = 15.7, 3.9 Hz, 1H), 2.37 (dd, $J$ = 18.6, 3.6 Hz, 1H), 2.16 (dd, $J$ = 17.5, 13.6 Hz, 1H), 1.85−1.65 (m, 2H), 1.49−1.31 (m, 4H), 0.94 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 206.5, 186.8, 173.4, 138.3, 129.7, 128.5, 128.0, 71.1, 61.8, 52.8, 48.6, 43.8, 43.3, 38.7, 35.8, 26.0, 22.8, 14.0. IR (thin film) $\nu_{max}$ 2955, 2870, 1723, 1497, 1381, 1297, 1194, 1025, 763,695 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $[M + H]^+$ $C_{21}H_{27}N_2O_3S$ 387.1737, found 387.1724.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00936.

$^1$H and $^{13}$C spectra for all new compounds, deuterium-labeling experiments, X-ray crystallographic data for compounds *exo*-**2a** and *endo*-**3a**, and NOE interaction data for compound **10a** (PDF)

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

X-ray crystallographic data *endo*-**3a**(CIF)

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### Notes

The authors declare no competing financial interest.

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