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Atom-Economic Synthesis of Pentaleno[2,1-*b*]indoles via Tandem Cyclization of Alkynones Initiated by Aminopalladation

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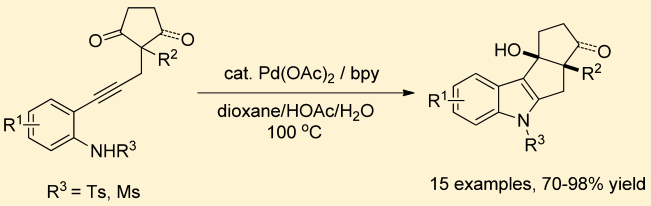
Supporting Information

ABSTRACT: An atom-economic $Pd(OAc)_2$-catalyzed tandem cyclization of alkynones to synthesize pentaleno[2,1-*b*]indoles was developed efficiently. In the formed tetracyclic indole framework, two neighboring stereocenters, one being all-carbon quaternary, are being constructed in a single process with excellent diastereoselectivity. This reaction was initiated by aminopalladation of alkynes and quenched by addition to the intramolecular carbonyl groups.



INTRODUCTION

As an important structural unit widely found in heterocyclic compounds with biological and medicinal applications, indoles, including cyclopenta[*b*]indoles, have attracted much attention from organic as well as pharmaceutical chemists.[1,2] As a result, various synthetic protocols have been developed to prepare this heterocyclic skeletons.[3,4] Among which, transition-metal-catalyzed intramolecular cyclization of 2-alkynylanilines is an established synthetic strategy due to the availability of starting materials, tolerance for functional groups, and mild reaction conditions.[3d,5] The success for these reactions lies in that the alkyne in 2-alkynylanilines can be activated by transition metals and then attacked by an intramolecular amino group easily. Among the transition metals, palladium is one of the most often used metal and has proven to be powerful for the synthesis of indoles.[6] However, for all of these methods established in the literature, examples to cyclopenta[*b*]indoles catalyzed by palladium from 2-alkynylanilines have not been reported.[7]

Cascade cyclization sequences offer efficient routes for the expeditious assembly of polycyclic products.[8] The advantages for which include atom and synthetic step economy, reduction of workup and purification, as well as minimization of wastes. Especially, palladium-catalyzed cascade cyclization reactions have proven to be much effective for construction of such compounds.[9] In addition, our group has been devoted to palladium(II)-catalyzed redox-neutral reactions initiated by nucleopalladation of alkynes for years.[10] Recently, we developed palladium(II)-catalyzed tandem cyclizations of alkynones or alkynenitriles initiated by oxypalladation or aminopalladation and quenched by addition to carbonyl or cyano group which provided convenient ways for the preparation of annulated isocoumarins, naphthylamines, and indoles, respectively (Scheme 1, equations a–c).[11] As a continuation of the work focused on Pd(II)-catalyzed tandem cyclization reactions, we report here a $Pd(OAc)_2$-catalyzed cyclization of alkynones to synthesize cyclopenta[*b*]indoles initiated by aminopalladation of alkynes (Scheme 1, equation d).

RESULTS AND DISCUSSION

In our previous study on aminopalladation initiated tandem cyclization of alkynenitriles, it was found when a substrate bearing a cyclopentanone unit was subjected to the reaction conditions, an addition to the carbonyl group occurred preferentially to give a special cyclopenta[*b*]indole, pentaleno-[2,1-*b*]indole (Scheme 2).[11c] In the formed compound, two neighboring stereocenters, one being all-carbon quaternary, is being constructed in a single process with excellent diastereoselectivity. Comparing to lots of methods for the synthesis of functionalized cyclopenta[*b*]indoles, there are few examples for the synthesis of pentaleno[2,1-*b*]indoles.[12] Therefore, we decided to use 2-alkynylanilines which contain a cyclopentanone unit as substrates to synthesize functionalized pentaleno[2,1-*b*]indoles.

First, a similar substrate **1a** was chosen as the model to screen the reaction conditions (Table 1). The reaction did not occur under the catalysis of $Pd(OAc)_2$/bipyridine at 100 °C without additives (entry 1). When sodium phosphate was added, only indole **3a** was formed (entry 2). Subsequent screening showed that the addition of acids was beneficial to the tandem cyclization, especially acetic acid, giving the expected product pentaleno[2,1-*b*]indole **2a** successfully (entries 3–6).[13] Then the effect of ligand was surveyed. Both 4,4′-dinitro-bpy and 4,4′-dimethoxy-bpy gave lower yields in contrast to bpy, and 1,10-phenanthroline did not improve the reaction either (entries 7–9). The reaction became complicated under the catalysis of $Pd(COOCF_3)_2$ or $PdCl_2$ (entries 10 and 11). The catalyst $Pd(CH_3CN)_4(BF_4)_2$ was also inferior to $Pd(OAc)_2$, affording the product in a low yield (entry 12).

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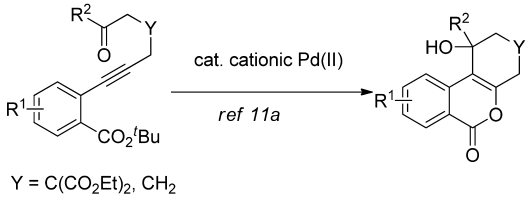
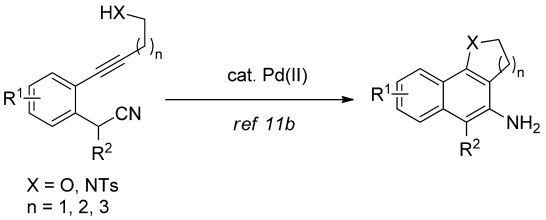
Scheme 1. Nucleopalladation Initiated Tandem Cyclization Developed in Our Group

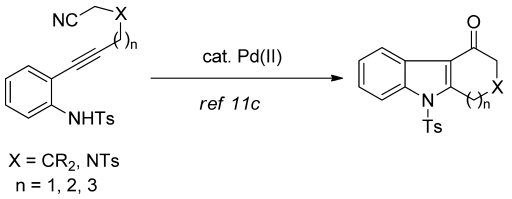
a) Oxypalladation initiated tandem cyclization of alkynones for the synthesis of annulated coumarins



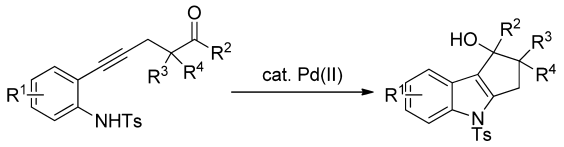
b) Amino-or oxy-palladation initiated tandem cyclization of alkynenitriles for the synthesis of annulated naphthylamines



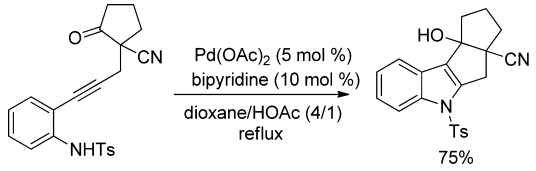
c) Aminopalladation initiated tandem cyclization of alkynenitriles for the synthesis of annulated indoles



d) This work: aminopalladation initiated tandem cyclization of alkynones for the synthesis of cyclopenta[*b*]indoles



Scheme 2. Initial Finding



Performing the reaction at a lower or higher temperature resulted in slightly lower yields of **2a** (entries 13 and 14). The investigation of the solvents revealed that THF gave a same yield as dioxane, and others, such as DCE, toluene, DME, DMF, and CH_3CN, were less effective (entries 15−20). Without the catalyst, no reaction occurred (entry 21). Finally, it was found that the addition of water can improve this transformation to 80% yield (entry 22). It was worth noting that more or less byproduct **3a** was observed in above screened reactions and it cannot be completely inhibited. $AuPPh_3Cl$ and $PtCl_2$ were also used as the catalyst in the reaction. For the catalyst $AuPPh_3Cl$, only byproduct **3a** was formed; When $PtCl_2$ was used as the catalyst, no reaction occurred.

With the optimized conditions (Table 1, entry 22) in hand, substrate generality was examined for the synthesis of functionalized pentaleno[2,1-*b*]indoles (Table 2). To our delight, the reaction showed broad substrate scope and furnished the desired products **2b**−**2o** in good yields. Substrates with electron-donating group, such as methyl or methoxyl, reacted smoothly to give the corresponding products successfully (**2b**, **2c**, **2g**, and **2j**). When the benzene ring was substituted with an electron-withdrawing group, such as an ester or trifluoromethyl, the reaction also conducted well, albeit in slightly lower yields (**2f** and **2h**). In addition, fluorine or chlorine atom can also be well tolerated in the transformation (**2d** and **2e**). Changing the substituent on the nitrogen atom from Ts to Ms did not influence the cyclization (**2m**). Similarly, the substrate bearing two carbonyl groups worked efficiently to provide **2n** in a good yield. However, when substrate **1o** was tried under the standard conditions, only indole **3o** was obtained. This experiment indicates the important role of substituent effect (R^2 in Table 2) for the addition to carbonyl group (Scheme 3, equation a), and which may be due to the Thorpe-Ingold effect.[14] Then, substrate **1p** was used to synthesize polycyclic indole. We were pleased to find that the reaction occurred effectively to give the desired product **2p** in excellent yield (Scheme 3, equation b). It is worth noting that only one diastereomer is formed in our new reaction. Besides Ts and Ms, we also tested the reaction of substrate with acetyl (Ac) or benzoyl (Bz) group substituted on the nitrogen atom. When the substituent was an Ac group, no reaction occurred. When Bz was substituted, only an unidentified product was formed. We also tried to increase the size of the ring annulated to the indole from 5 to 6, however, the according substrate could not be prepared at present.

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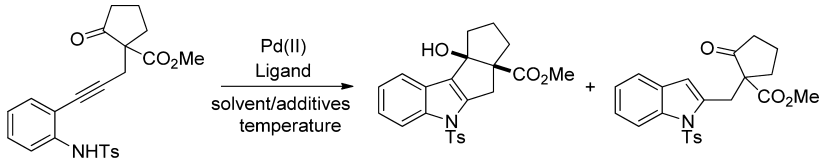
Table 1. Screening the Conditions for the Synthesis of 2a[a]

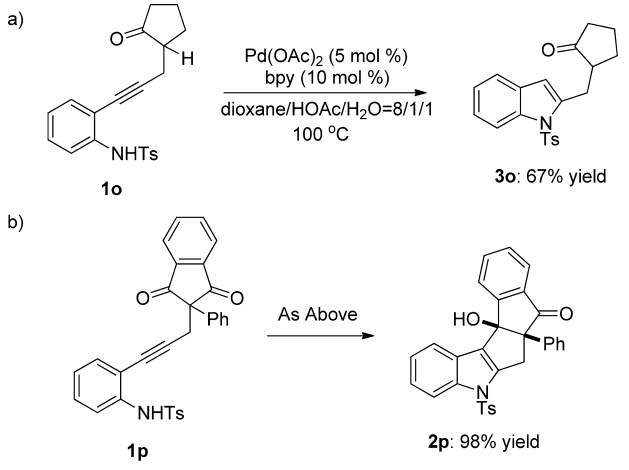


1a **2a** **3a**

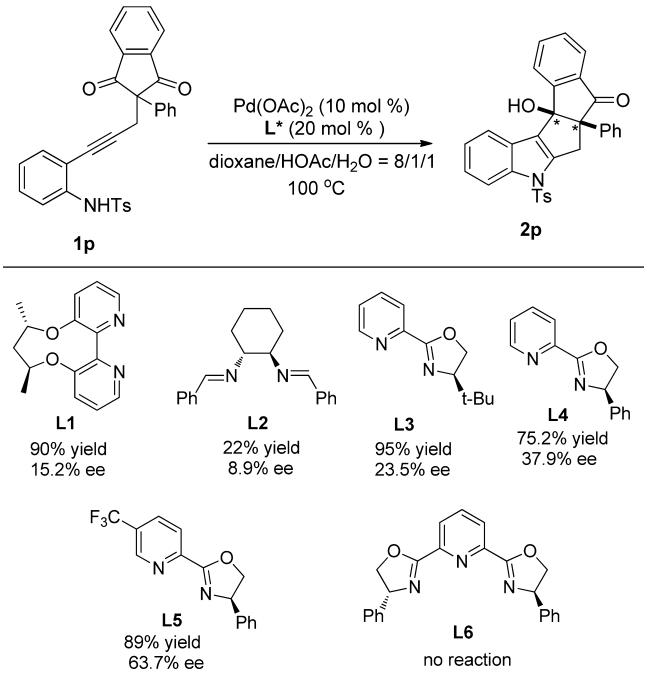
entry	catalyst	ligand	solvent	T (°C)/t (h)	additives	**2a** (%)
1	$Pd(OAc)_2$	bpy	dioxane	100 (10)		trace
2	$Pd(OAc)_2$	bpy	dioxane	100 (4.0)	Na_3PO_4	67 (**3a**)
3	$Pd(OAc)_2$	bpy	dioxane	100 (1.5)	TsOH	56
4	$Pd(OAc)_2$	bpy	dioxane	100 (6.5)	$PhCO_2H$	67
5	$Pd(OAc)_2$	bpy	dioxane	100 (1.0)	TFA	29
6	$Pd(OAc)_2$	bpy	dioxane	100 (1.5)	HOAc	72
7	$Pd(OAc)_2$	4-NO_2-bpy	dioxane	100 (20)	HOAc	27
8	$Pd(OAc)_2$	4-OMe-bpy	dioxane	100 (3.5)	HOAc	66
9	$Pd(OAc)_2$	1,10-Phen[b]	dioxane	100 (15)	HOAc	55
10	$Pd(COOCF_3)_2$	bpy	dioxane	100 (1.5)	HOAc	complicated
11	$PdCl_2$	bpy	dioxane	100 (1.5)	HOAc	complicated
12	$Pd(CH_3CN)_4(BF_4)_2$	bpy	dioxane	100 (4.0)	HOAc	35
13	$Pd(OAc)_2$	bpy	dioxane	80 (6.5)	HOAc	65
14	$Pd(OAc)_2$	bpy	dioxane	120 (1.0)	HOAc	67
15	$Pd(OAc)_2$	bpy	DCE	100 (4.0)	HOAc	35
16	$Pd(OAc)_2$	bpy	toluene	100 (4.0)	HOAc	47
17	$Pd(OAc)_2$	bpy	THF	100 (2.0)	HOAc	73
18	$Pd(OAc)_2$	bpy	DME	100 (2.0)	HOAc	45
19	$Pd(OAc)_2$	bpy	DMF	100 (1.0)	HOAc	66
20	$Pd(OAc)_2$	bpy	CH_3CN	100 (3.5)	HOAc	49
21	-	bpy	dioxane	100 (10)	HOAc	no reaction
22	$Pd(OAc)_2$	bpy	dioxane	100 (1.5)	HOAc+H_2O	80

[a]Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), catalyst (5 mol%), ligand (10 mol%), and additives (for entries 2−5, 2 equiv of the additive was added; for entries 6−21, 0.25 mL of HOAc was added; for entry 22, 0.25 mL of HOAc and 0.25 mL of H_2O were added) were dissolved in solvent (2 mL) as shown in the table, the mixture was stirred at 100 °C until the consumption of **1a** as monitored by TLC. [b]1,10-phen = 1,10-phenanthroline.

Scheme 3. Reactions of Substrates 1o and 1p



Scheme 4. Asymmetric Tandem Cyclization of 1p



Next, the asymmetric version of the reaction was studied. Compound **1p** was chosen as the substrate (Scheme 4). Our preliminary results showed that the reaction of **1p** in the presence of $Pd(OAc)_2$ and chiral pyridine oxazoline ligand **L5**[15] at 100 °C can give the product **2p** in a good yield with moderate ee value (Scheme 4).

In order to understand the mechanism, we conducted the reaction of **3a** in the same reaction conditions as Table 2 and it

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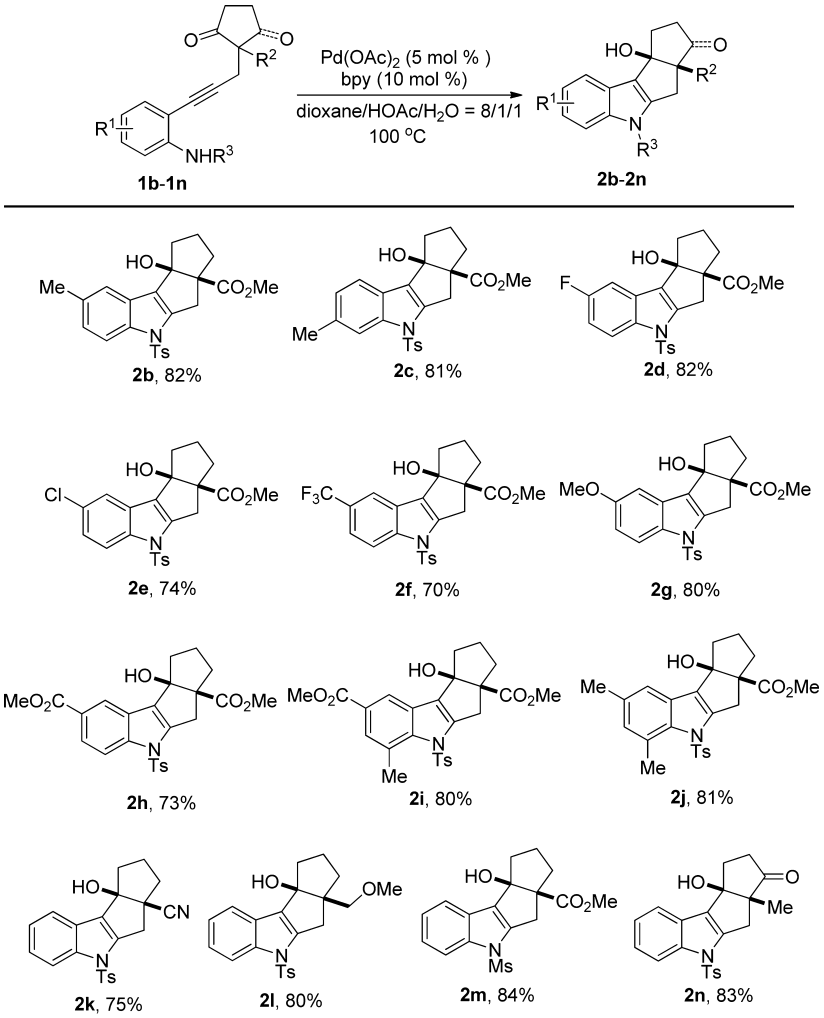
Table 2. Tandem Cyclization of Substrates 1b−1n[a]



[a]Reaction conditions: **1** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (5 mol%), and bpy (10 mol%) were dissolved in dioxane/HOAc/H_2O (2 mL/0.25 mL/0.25 mL), the mixture was stirred at 100 °C until the consumption of **1** as monitored by TLC.

was found that no reaction occurred. This result excludes that compound **3a** is the actual precursor of product **2a** upon acidic catalysis, which indicates that our reaction is a tandem process, not a one-pot, two-step reaction. Based on the above result and our previous work,[11] a proposed mechanism is outlined in Scheme 5. Taking substrate **1a** as an example, the palladium(II) catalyst coordinates with the carbon−carbon triple bond in the substrate at the first step of the reaction, then *trans*-aminopalladation occurs to generate the intermediate **B**. The nucleophilic addition of the C−Pd bond to the intramolecular carbonyl group generates **C** and the protonolysis of **C** results in the formation of product **2a**. Meanwhile, the protonolysis of **B** gives rise to the byproduct **3a**.

CONCLUSIONS

In conclusion, we have developed a palladium(II)-catalyzed tandem cyclization of 2-alkynylanilines substituted with a cyclopentanone, which is initiated by aminopalladation of alkynes and quenched by addition to the intramolecular carbonyl group. In the formed compounds, two neighboring stereocenters, one being all-carbon quaternary, are being constructed in a single process with excellent diastereoselectivity. This reaction provides an efficient and atom-economic way for the synthesis of pentaleno[2,1-*b*]indoles. Studies are ongoing to expand the scope and application of the present methodology.

EXPERIMENTAL SECTION

General Information. All solvents were dried and distilled using standard procedures. Unless otherwise noted, reagents were obtained from commercial sources and used without further purification. ^1H NMR, ^{13}C NMR, and ^{19}F NMR were recorded in deuterated chloroform ($CDCl_3$). For ^1H NMR spectroscopic analysis, trimethylsilane (TMS) ($\delta = 0$) in $CDCl_3$ served as an internal standard. For ^{13}C NMR spectroscopic analysis, $CDCl_3$ ($\delta = 77.0$) served as an internal standard. For ^{19}F NMR spectroscopic analysis, $PhOCF_3$ ($\delta = -57.8$) served as an external standard. Coupling constants are recorded in hertz, and chemical shifts are recorded as δ values in ppm. The following abbreviations are used to describe multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. High-resolution mass spectra were carried out on a mass spectrometer with a TOF analyzer (ESI). Infrared spectra were recorded on a FT-IR spectrometer. Melting points were determined by using a local hot-stage melting point apparatus and were uncorrected. For column chromatography, silica gel of 200−300 mesh size was used.

General Procedure for Preparation of Substrates 1a−1p.[16] 2-(Prop-2-yn1-yl)cyclopentanones[17] (2 mmol) was added to a solution of $PdCl_2(Ph_3P)_2$ (28 mg, 0.04 mmol), CuI (11 mg, 0.06 mmol), and 2-

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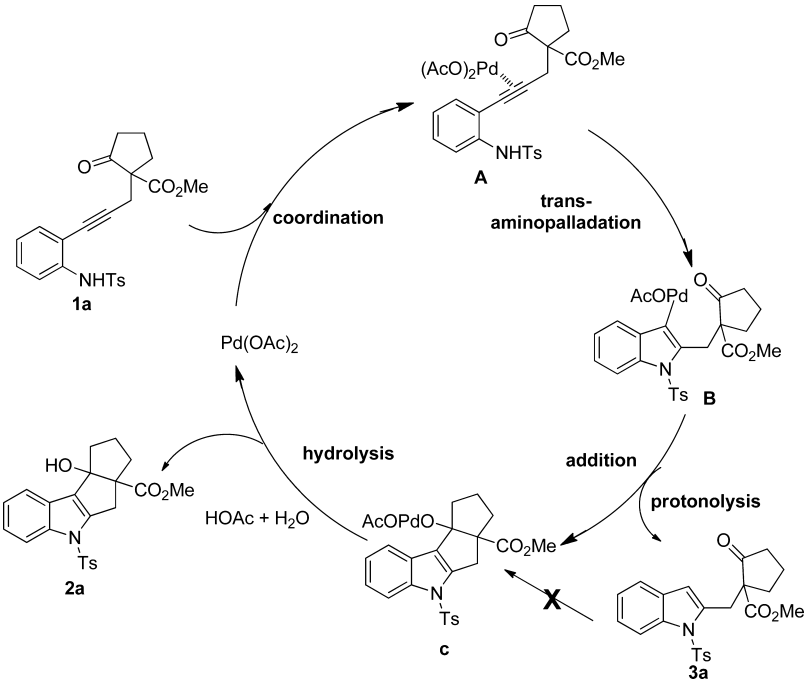
Scheme 5. Proposed Mechanism



iodoanilines (2.2 mmol) in 10 mL of triethylamine and the mixture was stirred at 50 °C until the consumption of 2-(prop-2-yn1-yl)cyclopentanones as monitored by TLC. The resulting mixture was quenched with water (10 mL), extracted with ethyl acetate (3 × 15 mL). The organic layer was dried over anhydrous Na_2SO_4, and then evaporated under reduced pressure. The residue was purified by flash chromatography (petroleum ether:ethyl acetate = 4:1) to give the coupling products which are used for the next step directly.

The above Sonogashira coupling product was dissolved in CH_2Cl_2 (10 mL) in a 50 mL flask, then pyridine (4 mmol) and TsCl (2.4 mmol) were added to the solution. The resulting mixture was stirred at room temperature for 15 h. The organic phase was washed with 20 mL of 1 M HCl solution and the aqueous phase was extracted with 20 mL of CH_2Cl_2 for 2 times. The combined organic phase was dried with anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (petroleum ether:ethyl acetate = 4:1) to give the products **1a−1p**.

*Methyl 1-(3-(2-(4-Methylphenylsulfonamido)phenyl)prop-2-yn-1-yl)-2-oxo-cyclopentanecarboxylate (**1a**).* Yellow oil; (544 mg; 64% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 8 Hz, 1H), 7.51 (s, 1H), 7.29−7.19 (m, 4H), 6.95 (t, J = 7.6 Hz, 1H), 3.79 (s, 3H), 2.95 (d, J = 16.8 Hz, 1H), 2.84 (d, J = 17.2 Hz, 1H), 2.61−2.51 (m, 2H), 2.39−2.30 (m, 4H), 2.21−2.08 (m, 2H), 2.05−1.97 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 212.9, 170.5, 143.4, 137.8, 135.7, 131.4, 129.0, 128.7, 126.7, 123.4, 118.4, 113.2, 92.5, 76.8, 58.3, 52.4, 37.5, 32.9, 23.6, 20.8, 19.1; IR (neat, cm^{-1}): ν 3248, 2959, 1724, 1589, 1488, 1399, 1332, 1379, 1156, 1097, 903, 814, 758, 670; HRMS (ESI) calcd for $C_{23}H_{27}N_2O_5S$ $(M+NH_4)^+$: 443.1635; Found: 443.1629.

*Methyl 1-(3-(5-Methyl-2-(4-methylphenylsulfonamido)phenyl)-prop-2-yn-1-yl)-2-oxo-cyclopentanecarboxylate (**1b**).* Yellow oil; (641 mg; 73% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 9.2 Hz, 1H), 7.29 (s, 1H), 7.21 (d, J = 8 Hz, 2H), 7.01 (d, J = 7.2 Hz, 2H), 3.78 (s, 3H), 2.92 (d, J = 16.8 Hz, 1H), 2.81 (d, J = 17.2 Hz, 1H), 2.59−2.50 (m, 2H), 2.37−2.28 (m, 4H), 2.19−2.07 (m, 5H), 2.05−1.99 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 213.2, 170.8, 143.6, 136.2, 135.6, 133.6, 132.1, 130.0, 129.4, 127.1, 119.3, 113.6, 92.0, 76.6, 58.8, 52.9, 38.0, 33.2, 24.1, 21.4, 20.3, 19.5; IR (neat, cm^{-1}): ν 3263, 2955, 2922, 1749, 1724, 1597, 1495, 1435, 1399, 1228, 1160, 1090, 1013, 905, 866, 814, 663; HRMS (ESI) calcd for $C_{24}H_{29}N_2O_5S$ $(M+NH_4)^+$: 457.1792; Found: 457.1791.

*Methyl 1-(3-(4-Methyl-2-(4-methylphenylsulfonamido)phenyl)-prop-2-yn-1-yl)-2-oxo-cyclopentanecarboxylate (**1c**).* Yellow oil; (598 mg; 68% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 7.6 Hz, 2H), 7.40 (d, J = 10.0 Hz, 2H), 7.22 (d, J = 8 Hz, 2H), 7.08 (d, J = 7.6 Hz, 1H), 6.76 (d, J = 7.6 Hz, 1H), 3.77 (s, 3H), 2.93 (d, J = 16.8 Hz, 1H), 2.82 (d, J = 17.2 Hz, 1H), 2.59−2.49 (m, 2H), 2.35−2.33 (m, 4H), 2.28 (s, 3H), 2.19−2.09 (m, 2H), 2.04−1.98 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 213.3, 170.8, 143.6, 139.6, 137.9, 136.1, 131.4, 129.3, 127.0, 124.6, 119.4, 110.5, 91.7, 76.6, 58.8, 52.8, 37.9, 33.2, 24.0, 21.5, 21.3, 19.4; IR (neat, cm^{-1}): ν 3264, 2956, 2921, 1749, 1725, 1611, 1564, 1398, 1335, 1228, 1152, 1090, 1015, 955, 890, 813, 731, 661; HRMS (ESI) calcd for $C_{24}H_{29}N_2O_5S$ $(M+NH_4)^+$: 457.1792; Found: 457.1792.

*Methyl 1-(3-(5-Fluoro-2-(4-methylphenylsulfonamido)phenyl)-prop-2-yn-1-yl)-2-oxo-cyclopentanecarboxylate (**1d**).* Yellow oil; (648 mg; 73% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8 Hz, 2H), 7.56−7.53 (m, 1H), 7.36 (br, 1H), 7.22 (d, J = 8 Hz, 2H), 6.96−6.88 (m, 2H), 3.79 (s, 3H), 2.91 (d, J = 17.2 Hz, 1H), 3.80 (d, J = 16.8 Hz, 1H), 2.56−2.52 (m, 2H), 2.37−2.30 (m, 4H), 2.15−2.09 (m, 2H), 2.04−1.98 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 213.1, 170.8, 158.0 (d, J = 243.2 Hz), 143.8, 136.0, 134.5, 129.4, 127.2, 121.1 (d, J = 8.2 Hz), 118.1 (d, J = 24.5 Hz), 116.3 (d, J = 22.4 Hz), 115.7 (d, J = 9.7 Hz), 93.5, 76.6, 58.7, 53.0, 37.9, 33.4, 24.0, 21.4, 19.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ −117.94; IR (neat, cm^{-1}): ν 3260, 2957, 1749, 1725, 1597, 1491, 1436, 1399, 1337, 1229, 1157, 1090, 1040, 908, 873, 813, 755, 701, 663; HRMS (ESI) calcd for $C_{23}H_{26}FN_2O_5S$ $(M+NH_4)^+$: 461.1541; Found: 461.1540.

*Methyl 1-(3-(5-Chloro-2-(4-methylphenylsulfonamido)phenyl)-prop-2-yn-1-yl)-2-oxo-cyclopentanecarboxylate (**1e**).* Yellow oil; (643 mg; 70% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 8.4 Hz, 2H), 7.56 (s, 1H), 7.52 (dd, J_1 = 6 Hz, J_2 = 4 Hz, 1H), 7.24 (d, J = 8 Hz, 2H), 7.17 (t, J = 2.8 Hz, 2H), 3.79 (s, 3H), 2.93 (d, J = 16.8 Hz, 1H), 2.82 (d, J = 17.2 Hz, 1H), 2.60−2.52 (m, 2H), 2.39−2.31 (m, 4H), 2.17−2.08 (m, 2H), 2.04−1.98 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 213.1, 170.8, 143.9, 136.9, 135.8, 131.2, 129.5, 129.1, 128.8, 127.1, 120.0, 115.0, 93.9, 76.3, 58.6, 52.9, 37.9, 33.4, 24.0, 21.3, 19.4; IR (neat, cm^{-1}): ν 3257, 2957, 2891, 1748, 1724, 1596, 1483, 1395, 1338, 1229, 1161, 1089, 902, 813, 755,

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704, 662; HRMS (ESI) calcd for $C_{23}H_{26}ClN_2O_5S$ $(M+NH_4)^+$: 477.1245; Found: 477.1246.

*Methyl 1-(3-(2-(4-Methylphenylsulfonamido)-5-(trifluoromethyl)-phenyl)prop-2-yn-1 -yl)-2-oxocyclopentanecarboxylate (**1f**).* Colorless oil; (592 mg; 60% yield for two steps); ^{1}H NMR(400 MHz, $CDCl_3$): δ 8.00 (br, 1H), 7.84 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 1H), 7.48 (s, 1H), 7.43 (d, J = 8.8 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 2.97 (d, J = 16.8 Hz, 1H), 2.89 (d, J = 17.2 Hz, 1H), 2.64−2.54 (m, 2H), 2.43−2.35 (m, 4H), 2.19−2.11 (m, 2H), 2.07−2.02 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 213.2, 170.9, 144.1, 141.4, 135.9, 129.6, 128.7, 127.1, 125.7, 125.1 (q, J = 32.8 Hz), 123.3 (q, J = 270 Hz), 117.2, 112.9, 94.5, 76.0, 58.5, 52.8, 37.8, 33.6, 23.9, 21.2, 19.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.40; IR (neat, cm^{-1}): ν 3259, 2960, 1748, 1725, 1615, 1595, 1500, 1435, 1332, 1254, 1163, 1119, 1087, 900, 846, 814, 734, 658; HRMS (ESI) calcd for $C_{24}H_{26}F_3N_2O_5S$ $(M+NH_4)^+$: 511.1509; Found: 511.1512.

*Methyl 1-(3-(5-Methoxy-2-(4-methylphenylsulfonamido)phenyl)-prop-2-yn-1-yl)-2-oxocyclopentanecarboxylate (**1g**).* Colorless oil; (547 mg; 60% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 8 Hz, 2H), 7.49 (d, J = 9.2 Hz, 1H), 7.20 (d, J = 8.4 Hz, 2H), 7.12 (s, 1H), 6.80 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1H), 6.71 (d, J = 2.8 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 2.89 (d, J = 17.2 Hz, 1H), 2.78 (d, J = 17.2 Hz, 1H), 2.57−2.49 (m, 2H), 2.36−2.27 (m, 4H), 2.18−2.03 (m, 2H), 2.02−1.97 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 213.2, 170.8, 156.1, 143.5, 136.1, 131.2, 129.3, 127.1, 122.4, 116.2, 115.9, 115.3, 92.0, 77.6, 58.7, 55.3, 52.9, 38.0, 33.2, 24.0, 21.4, 19.5; IR (neat, cm^{-1}): ν 3263, 2958, 1748, 1724, 1602, 1575, 1495, 1450, 1399, 1334, 1288, 1261, 1158, 1090, 904, 864, 833, 703, 664; HRMS calcd (ESI) for $C_{24}H_{29}N_2O_6S$ $(M+NH_4)^+$: 473.1741; Found: 473.1741.

*Methyl 3-(3-(1-(Methoxycarbonyl)-2-oxocyclopentyl)prop-1-yn-1-yl)-4-(4-methyl-phenylsulfonamido)benzoate (**1h**).* Colorless oil; (590 mg; 61% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.89 (d, J = 2 Hz, 1H), 7.85 (dd, J_1 = 8.8 Hz, J_2 = 2 Hz, 1H), 7.82 (d, J = 8 Hz, 2H), 7.63 (d, J = 8.4 Hz, 1H), 7.25 (d, J = 8 Hz, 2H), 3.84 (s, 3H), 3.80 (s, 3H), 2.98 (d, J = 17.2 Hz, 1H), 2.89 (d, J = 17.2 Hz, 1H), 2.61−2.53 (m, 2H), 2.43−2.36 (m, 1H), 2.34 (s, 3H), 2.23−2.10 (m, 2H), 2.07−2.03 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 213.0, 170.7, 165.3, 143.9, 142.0, 135.7, 132.9, 130.1, 129.4, 126.9, 124.6, 116.4, 112.3, 93.7, 76.2, 58.4, 52.7, 51.7, 37.7, 33.3, 23.8, 21.1, 19.2; IR (neat, cm^{-1}): ν 3251, 2954, 1748, 1718, 1602, 1577, 1494, 1437, 1341, 1299, 1234, 1162, 1089, 901, 814, 764, 704, 660; HRMS (ESI) calcd for $C_{25}H_{29}N_2O_7S$ $(M+NH_4)^+$: 501.1690; Found: 501.1690.

*Methyl 3-(3-(1-(Methoxycarbonyl)-2-oxocyclopentyl)prop-1-yn-1-yl)-5-methyl-4-(4-methylphenylsulfonamido)benzoate (**1i**).* Yellow oil; (587 mg; 59% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 1.6 Hz, 1H), 7.71 (d, J = 2 Hz, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 3.90 (s, 3H), 3.76 (s, 3H), 2.65 (d, J = 16.8 Hz, 1H), 2.57 (d, J = 17.2 Hz, 1H), 2.55−2.46 (m, 5H), 2.42 (s, 3H), 2.33−2.24 (m, 1H), 2.13−2.08 (m, 2H), 2.08−1.99 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 213.3, 170.8, 165.8, 143.9, 139.7, 137.8, 136.6, 132.6, 130.8, 129.3, 128.2, 127.4, 121.2, 91.6, 77.9, 58.6, 52.9, 52.2, 38.1, 33.1, 24.0, 21.5, 19.7, 19.5; IR (neat, cm^{-1}): ν 3247, 2954, 2924, 1750, 1721, 1595, 1434,1400, 1333, 1282, 1232, 1158, 1087, 1001, 886, 839, 814, 768, 750, 706, 669, 628; HRMS (ESI) calcd for $C_{26}H_{31}N_2O_7S$ $(M+NH_4)^+$: 515.1846; Found: 515.1848.

*Methyl 1-(3-(3,5-Dimethyl-2-(4-methylphenylsulfonamido)-phenyl)prop-2-yn-1-yl)-2-oxocyclopentanecarboxylate (**1j**).* Yellow solid; (472 mg; 52% yield for two steps); m.p.: 105−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8 Hz, 2H), 7.21 (d, J = 8 Hz, 2H), 6.99 (s, 1H), 6.86 (s, 1H), 6.52 (s, 1H), 3.73 (s, 3H), 2.63 (d, J = 17.2 Hz, 1H), 2.58 (d, J = 16.8 Hz, 1H), 2.50−2.40 (m, 8H), 2.36−2.22 (m, 4H), 2.17−2.10 (m, 1H), 2.08−1.96 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 213.4, 170.7, 143.3, 137.5, 136.9, 136.6, 132.7, 132.3, 130.3, 129.0, 127.3, 121.2, 89.7, 78.9, 58.6, 52.6, 38.0, 32.7, 23.9, 21.3, 20.4, 19.5, 19.1; IR (neat, cm^{-1}): ν 3261, 2955, 2922, 1749, 1724, 1597, 1436, 1398, 1329, 1225, 1157, 1090, 891, 859, 812, 667, 623; HRMS (ESI) calcd for $C_{25}H_{31}N_2O_5S$ $(M+NH_4)^+$: 471.1948; Found: 471.1949.

*N-(2-(3-(1-Cyano-2-oxocyclopentyl)prop-1-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (**1k**).*[11c] Yellow solid; (526 mg; 67% yield for two steps); m.p.: 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 8.4 Hz, 1H), 7.46 (s, 1H), 7.27−7.21 (m, 4H), 6.97 (t, J = 7.6 Hz, 1H), 2.97 (d, J = 17.2 Hz, 1H), 2.86 (d, J = 17.2 Hz, 1H), 2.64−2.55 (m, 2H), 2.47−2.38 (m, 1H), 2.35 (s, 3H), 2.27−2.20 (m, 1H), 2.18−2.07 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 207.5, 143.9, 138.1, 135.9, 132.3, 129.6, 129.5, 127.2, 123.9, 119.0, 117.9, 112.9, 89.5, 79.3, 47.6, 36.6, 34.1, 25.0, 21.4, 19.1; IR (neat, cm^{-1}): ν 3249, 3062, 2975, 2883, 2238, 1754, 1589, 1447, 1399, 1158, 1092, 908, 817, 763, 669; HRMS (ESI) calcd for $C_{22}H_{24}N_3O_3S$ $(M+NH_4)^+$: 410.1533; Found: 410.1532.

*N-(2-(3-(1-(Methoxymethyl)-2-oxocyclopentyl)prop-1-yn-1-yl)-phenyl)-4-methylbenzenesulfonamide (**1l**).* White solid; (428 mg; 52% yield for two steps); m.p.: 80−82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 8 Hz, 2H), 7.63 (br, 1H), 7.57 (d, J = 8 Hz, 1H), 7.22−7.13 (m, 3H), 6.95 (t, J = 7.6 Hz, 1H), 3.48 (d, J = 8.8 Hz, 1H), 3.41 (d, J = 8.8 Hz, 1H), 3.33 (s, 3H), 2.58 (d, J = 17.2 Hz, 1H), 2.52 (d, J = 17.2 Hz, 1H), 2.36−2.31 (m, 5H), 2.27−2.23 (m, 1H), 2.01−1.90 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 219.5, 143.6, 138.1, 136.3, 131.7, 129.4, 128.9, 127.1, 123.6, 118.6, 113.6, 93.1, 77.3, 75.2, 59.3, 52.0, 38.5, 31.5, 23.9, 21.3, 18.9; IR (neat, cm^{-1}): ν 3247, 2954, 2923, 2887, 1733, 1597, 1572, 1488, 1427, 1399, 1333, 1285, 1263, 1163, 1095, 1039, 959, 878, 813, 772, 742, 710, 634; HRMS (ESI) calcd for $C_{23}H_{29}N_2O_4S$ $(M+NH_4)^+$: 429.1843; Found: 429.1844.

*Methyl 1-(3-(2-(Methylsulfonamido)phenyl)prop-2-yn-1-yl)-2-oxocyclopentane-carboxylate (**1m**).* Colorless oil; (461 mg; 66% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 7.6 Hz, 1H), 7.36 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 2H), 7.33−7.29 (m, 1H), 7.10−7.06 (m, 1H), 3.77 (s, 3H), 3.02 (s, 3H), 2.96 (d, J = 17.2 Hz, 1H), 2.89 (d, J = 17.2 Hz, 1H), 2.62−2.50 (m, 2H), 2.41−2.34 (m, 1H), 2.21−2.01 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 213.2, 170.8, 138.3, 131.8, 129.4, 124.2, 119.4, 113.9, 92.8, 77.4, 58.7, 52.8, 39.2, 37.9, 33.5, 24.0, 19.4; IR (neat, cm^{-1}): ν 3264, 2956, 2891, 1747, 1732, 1600, 1574, 1490, 1423, 1397, 1333, 1277, 1228, 1151, 1103, 1042, 1024, 998, 965, 869, 819, 755, 734, 631; HRMS (ESI) calcd for $C_{17}H_{23}N_2O_5S$ $(M+NH_4)^+$: 367.1322; Found: 367.1324.

*4-Methyl-N-(2-(3-(1-methyl-2,5-dioxocyclopentyl)prop-1-yn-1-yl)phenyl)benzene-sulfonamide (**1n**).* Yellow solid; (569 mg; 72% yield for two steps); m.p.: 121−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.4 Hz, 2H), 7.65 (s, 1H), 7.57 (d, J = 8 Hz, 1H), 7.23−7.18 (m, 4H), 6.96 (t, J = 7.6 Hz, 1H), 2.96−2.77 (m, 4H), 2.68 (s, 2H), 2.36 (s, 3H), 1.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 214.5, 143.7, 138.2, 136.3, 131.8, 129.5, 129.4, 127.2, 123.6, 118.6, 112.9, 91.13, 78.1, 54.89, 35.1, 24.4, 21.4, 19.0; IR (neat, cm^{-1}): ν 3237, 2962, 2922, 1722, 1598, 1575, 1489, 1451, 1397, 1338, 1287, 1224, 1165, 1092, 1038, 998, 949, 902, 817, 761, 724, 680, 618; HRMS (ESI) calcd for $C_{22}H_{25}N_2O_4S$ $(M+NH_4)^+$: 413.1530; Found: 413.1531.

*4-Methyl-N-(2-(3-(2-oxocyclopentyl)prop-1-yn-1-yl)phenyl)-benzenesulfonamide (**1o**).* Colorless oil; (500 mg; 68% yield for two steps); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8 Hz, 1H), 7.44 (br, 1H), 7.23−7.20 (m, 4H), 6.98−6.94 (m, 1H), 2.71 (dd, J_1 = 17.2 Hz, J_2 = 5.6 Hz, 1H), 2.61 (dd, J_1 = 17.2 Hz, J_2 = 6.4 Hz, 1H), 2.44−2.31 (m, 6H), 2.23−2.16 (m, 1H), 2.10−2.06 (m, 1H), 1.87−1.86 (m, 1H), 1.77−1.73 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 218.8, 143.9, 138.1, 136.3, 131.9, 129.6, 129.1, 127.3, 124.0, 119.1, 114.2, 94.8, 76.6, 47.7, 38.0, 29.1, 21.6, 20.5, 19.7; IR (neat, cm^{-1}): ν 3249, 2959, 2877, 1730, 1590, 1490, 1450, 1402, 1336, 1278, 1245, 1158, 1093, 1043, 907, 813, 755, 665; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_3S$ $(M+NH_4)^+$: 385.1580; Found: 385.1577.

*N-(2-(3-(1,3-Dioxo-2-phenyl-2,3-dihydro-1H-inden-2-yl)prop-1-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (**1p**).* Yellow solid; (758 mg; 75% yield for two steps); m.p.: 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (dd, J_1 = 5.6 Hz, J_2 = 3.2 Hz, 2H), 7.89 (dd, J_1 = 6 Hz, J_2 = 3.2 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.51−7.48 (m, 3H), 7.37−7.29 (m, 4H), 7.18−7.10 (m, 3H), 6.91−6.89 (m, 1H),

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6.82 (t, J = 7.6 Hz, 1H), 3.31 (s, 2H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 199.6, 143.6, 141.5, 138.0, 136.4, 136.0, 134.9, 131.8, 129.4, 129.1, 129.0, 128.2, 127.2, 126.8, 124.0, 123.5, 118.8, 113.1, 91.5, 78.0, 60.5, 25.6, 21.5; IR (neat, cm^{-1}): ν 3428, 3281, 3062, 1740, 1703,1594, 1491, 1448, 1398, 1329, 1295, 1242, 1160, 1091, 1038, 964, 921, 881, 813, 781, 755, 696, 657; HRMS (ESI) calcd for $C_{31}H_{27}N_2O_4S$ $(M+NH_4)^+$: 523.1686; Found: 523.1686.

General Procedure of the Tandem Cyclization of Alkynones Initiated by Aminopalladation. To an oven-dried Schlenk tube were added alkynone **1** (0.2 mmol), palladium acetate (2.3 mg, 0.01 mmol, 5 mol%), and 2,2′-bipyridine (3.2 mg, 0.02 mmol, 10 mol%), and then 2 mL of dioxane, 0.25 mL of acetic acid, 0.25 mL of H_2O were added sequentially. The resulting mixture was stirred at 100 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvents were evaporated under reduced pressure and the residue was purified by flash column chromatography (petroleum ether:ethyl acetate = 4:1) to give product **2**.

*Methyl 9c-Hydroxy-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]indole-3a-carboxylate (**2a**).* White solid; (68 mg; 80% yield); m.p.: 131−132 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8 Hz, 1H), 7.74 (d, J = 8 Hz, 2H), 7.49 (d, J = 7.6 Hz, 1H), 7.25−7.19 (m, 4H), 4.01 (d, J = 17.6 Hz, 1H), 3.74 (s, 3H), 3.03 (d, J = 17.6 Hz, 1H), 2.74 (s, 1H), 2.63−2.55 (m, 1H), 2.34−2.29 (m, 4H), 2.04−1.97 (m, 1H), 1.87−1.81 (m, 2H), 1.33−1.26 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.9, 145.0, 142.3, 140.4, 135.2, 129.9, 126.8, 126.6, 124.7, 124.0, 123.6, 118.7, 114.3, 90.6, 66.9, 52.2, 39.4, 38.7, 37.5, 23.9, 21.5; IR (neat, cm^{-1}): ν 3477, 2956, 2874, 1701, 1596, 1443, 1406, 1373, 1298, 1210, 1177, 1143, 1097, 1044, 993, 959, 927, 878, 856, 809, 745, 707, 664; HRMS (ESI) calcd for $C_{23}H_{27}N_2O_5S$ $(M+NH_4)^+$: 443.1635; Found: 443.1637.

*Methyl 9c-Hydroxy-8-methyl-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]-indole-3a-carboxylate (**2b**).* White solid; (72 mg; 82% yield); m.p.: 164−166 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.29 (s, 1H), 7.23−7.21 (d, J = 8.4 Hz, 2H), 7.08 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 4.01 (d, J = 18 Hz, 1H), 3.72 (s, 3H), 3.03 (d, J = 18 Hz, 1H), 2.73 (s, 1H), 2.62−2.54 (m, 1H), 2.37 (s, 3H), 2.33 (s, 3H), 2.31−2.28 (m, 1H), 2.03−1.95 (m, 1H), 1.86−1.80 (m, 2H), 1.31−1.25 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.9, 144.9, 142.4, 138.6, 135.2, 133.3, 129.9, 126.7, 126.5, 125.2, 124.8, 118.8, 114.0, 90.5, 66.8, 52.2, 39.4, 38.7, 37.5, 23.8, 21.4, 21.1; IR (neat, cm^{-1}): ν 3486, 2952, 2921,2861, 1697, 1607, 1446, 1396, 1358, 1286, 1212, 1171, 1134, 1095, 1041, 999, 925, 893, 868, 743, 703, 660; HRMS (ESI) calcd for $C_{24}H_{29}N_2O_5S$ $(M+NH_4)^+$: 457.1792; Found: 457.1791.

*Methyl 9c-Hydroxy-7-methyl-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]-indole-3a-carboxylate (**2c**).* Yellow solid; (71.2 mg; 81% yield); m.p.: 120−121 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.72 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 7.6 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 1H), 3.98 (d, J = 17.6 Hz, 1H), 3.71 (s, 3H), 3.00 (d, J = 17.6 Hz, 1H), 2.73 (s, 1H), 2.62−2.54 (m, 1H), 2.45 (s, 3H), 2.33 (s, 3H), 2.30−2.25 (m, 1H), 2.02−1.94 (m, 1H), 1.85−1.79 (m, 2H), 1.31−1.25 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ174.9, 144.9, 141.5, 140.8, 135.3, 134.1, 129.8, 126.8, 126.5, 124.9, 122.3, 118.4, 114.6, 90.6, 66.8, 52.2, 39.5, 38.6, 37.5, 23.8, 21.8, 21.4; IR (neat, cm^{-1}): ν 3483, 2952, 2866, 1718, 1620, 1596, 1490, 1436, 1365, 1295, 1276, 1238, 1170, 1089, 1033, 990, 960, 916, 879, 812, 731, 706, 663, 620; HRMS (ESI) calcd for $C_{24}H_{29}N_2O_5S$ $(M+NH_4)^+$: 457.1792; Found: 457.1792.

*Methyl 8-Fluoro-9c-hydroxy-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]-indole-3a-carboxylate (**2d**).* White solid; (72.7 mg; 82% yield); m.p.: 164−166 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (dd, J_1 = 9.2 Hz, J_2 = 4.4 Hz, 1H), 7.71 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.14 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.97 (td, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 4.00 (d, J = 18 Hz, 1H), 3.72 (s, 3H), 3.02 (d, J = 17.6 Hz, 1H), 2.81 (s, 1H), 2.62−2.54 (m, 1H), 2.34 (s, 3H), 2.28−2.23 (m, 1H), 2.03−1.95 (m, 1H), 1.87−1.80 (m, 2H), 1.32−1.24 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ174.8, 159.7 (d, J = 240 Hz), 145.2, 144.1, 136.6, 135.0, 129.9, 126.6 (d, J = 3.8 Hz), 126.5, 125.7 (d, J = 10.6 Hz), 115.3 (d, J = 9.9 Hz), 111.5 (d, J = 25.1 Hz), 104.7 (d, J = 24.3 Hz), 90.4, 66.8, 52.3, 39.4, 38.7, 37.5, 23.9, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ −118.70; IR (neat, cm^{-1}): ν 3480, 2955, 2926, 1727, 1694, 1615, 1598, 1453, 1438, 1369, 1272, 1206, 1168, 1094, 996, 907, 836, 742, 663; HRMS (ESI) calcd for $C_{23}H_{26}FN_2O_5S$ $(M+NH_4)^+$: 461.1541; Found: 461.1541.

*Methyl 8-Chloro-9c-hydroxy-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]-indole-3a-carboxylate (**2e**).* Yellow solid; (68 mg; 74% yield); m.p.: 163−165 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.8 Hz, 1H), 7.71 (d, J = 8 Hz, 2H), 7.47 (d, J = 1.6 Hz, 1H), 7.25 (d, J = 8.4 Hz, 2H), 7.21 (dd, J_1 = 8.8 Hz, J_2 = 2 Hz, 1H), 4.00 (d, J = 18 Hz, 1H), 3.72 (s, 3H), 3.02 (d, J = 18 Hz, 1H), 2.80 (s, 1H), 2.62−2.54 (m, 1H), 2.35 (s, 3H), 2.96−2.49 (m, 1H), 2.03−1.95 (m, 1H), 1.87−1.81 (m, 2H), 1.32−1.23 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.8, 145.3, 143.8, 138.6, 134.9, 130.0, 129.5, 126.5, 126.2, 125.8, 124.0, 118.5, 115.3, 90.4, 66.8, 52.3, 39.3, 38.8, 37.5, 23.9, 21.5; IR (neat, cm^{-1}): ν 3488, 2952, 2925, 2878, 2847, 1729, 1700, 1598, 1567, 1436, 1396, 1364, 1297, 1279, 1224, 1169, 1143, 1093, 1039, 994, 927, 909, 808, 777, 707, 662; HRMS (ESI) calcd for $C_{23}H_{26}ClN_2O_5S$ $(M+NH_4)^+$: 477.1245; Found: 477.1243.

*Methyl 9c-Hydroxy-5-tosyl-8-(trifluoromethyl)-2,3,3a,4,5,9c-hexahydro-1H-pentaleno-[2,1-b]indole-3a-carboxylate (**2f**).* White solid; (61.5 mg; 70% yield); m.p.: 164−166 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 8.8 Hz, 1H), 7.79 (s, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.51 (dd, J_1 = 8.8 Hz, J_2 = 1.2 Hz, 1H), 7.27 (d, J = 7.6 Hz, 2H), 4.03 (d, J = 17.6 Hz, 1H), 3.73 (s, 3H), 3.07 (d, J = 17.6 Hz, 1H), 2.87 (s, 1H), 2.63−2.55 (m, 1H), 2.36 (s, 3H), 2.33−2.30 (m, 1H), 2.07−1.99 (m, 1H), 1.91−1.84 (m, 2H), 1.33−1.26 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta\delta$ 174.8, 145.7, 144.2, 141.8, 134.8, 130.2, 126.6, 126.0 (q, J = 32 Hz), 124.5, 124.3 (q, J = 270.7 Hz), 120.9 (d, J = 3.4 Hz), 116.3 (d, J = 4.2 Hz), 114.5, 90.4, 67.0, 52.3, 39.3, 39.1, 37.5, 23.9, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ −61.21; IR (neat, cm^{-1}): 3486, 2958, 2883, 1697, 1623, 1597, 1457, 1437, 1399, 1374, 1272, 1227, 1169, 1133, 1110, 1094, 1054, 996, 927, 886, 854, 816, 739, 707, 662, 630; HRMS calcd (ESI) for $C_{24}H_{26}F_3N_2O_5S$ $(M+NH_4)^+$: 511.1509; Found: 511.1509.

*Methyl 9c-Hydroxy-8-methoxy-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno-[2,1-b]-indole-3a-carboxylate (**2g**).* White solid; (72.8 mg; 80% yield); m.p.: 154−156 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 9.2 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8 Hz, 2H), 6.93 (d, J = 2.4 Hz, 1H), 6.85 (dd, J_1 = 9.2 Hz, J_2 = 2.4 Hz, 1H), 3.98 (d, J = 17.6 Hz, 1H), 3.76 (s, 3H), 3.71 (s, 3H), 2.99 (d, J = 17.6 Hz, 1H), 2.82 (s, 1H), 2.62−2.54 (m, 1H), 2.34−2.27 (m, 4H), 2.20−1.95 (m, 1H), 1.86−1.80 (m, 2H), 1.31−1.25 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.9, 156.5, 144.9, 143.0, 135.1, 134.9, 129.8, 126.7, 126.5, 125.6, 115.2, 112.4, 101.5, 90.5, 66.8, 55.5, 52.2, 39.4, 38.6, 37.4, 23.8, 21.4; IR (neat, cm^{-1}): ν 3450, 2950, 2865, 1724, 1622, 1597, 1457, 1441, 1402, 1362, 1338, 1297, 1274, 1237, 1169, 1138, 1090, 1029, 997, 929, 864, 798, 734, 706, 665; HRMS (ESI) calcd for $C_{24}H_{29}N_2O_6S$ $(M+NH_4)^+$: 473.1741; Found: 473.1739.

*Dimethyl 9c-Hydroxy-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]indole-3a,8-dicarboxylate (**2h**).* White solid; (70.6 mg; 73% yield); m.p.: 165−167 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 8.01 (d, J = 8.8 Hz, 1H), 7.95 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 8 Hz, 2H), 7.25 (d, J = 8 Hz, 2H), 4.02 (d, J = 18 Hz, 1H), 3.89 (s, 3H), 3.74 (s, 3H), 3.06 (d, J = 18 Hz, 1H), 2.81 (s, 1H), 2.62−2.56 (m, 1H), 2.36−2.33 (m, 4H), 2.08−2.01 (m, 1H), 1.90−1.82 (m, 2H), 1.35−1.27 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.8, 166.9, 145.4, 143.7, 142.9, 135.0, 130.3, 127.0, 126.6, 125.6, 125.3, 124.4, 120.8, 114.0, 90.5, 67.0, 52.3, 52.0, 39.4, 39.0, 37.6, 23.9, 21.5; IR (neat, cm^{-1}): ν 3469, 2957, 2877, 1717, 1702, 1619, 1594, 1458, 1434, 1397, 1366, 1285, 1254, 1235, 1206, 1170, 1125, 1091, 1043, 998, 970, 923, 898, 856, 836, 815, 707; HRMS (ESI) calcd for $C_{25}H_{29}N_2O_7S$ $(M+NH_4)^+$: 501.1690; Found: 501.1689.

*Dimethyl 9c-Hydroxy-6-methyl-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]-indole-3a,8-dicarboxylate (**2i**).* White solid; (79.6 mg; 80% yield); m.p.: 149−151 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.70 (s, 1H), 7.51 (d, J = 8 Hz, 2H), 7.23 (d, J = 8 Hz, 2H), 4.06 (d, J = 18.4 Hz, 1H), 3.89 (s, 3H), 3.77 (s, 3H), 3.10 (d, J = 18.4 Hz, 1H), 2.83 (s, 1H), 2.62−2.56 (m, 4H), 2.37−2.33 (m, 4H), 2.09−2.01 (m, 1H), 1.88−1.84 (m, 2H), 1.33−1.26 (m, 1H);

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$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.1, 167.0, 146.3, 145.1, 143.6,136.5, 130.1, 129.4, 128.1, 126.8, 126.5, 126.3, 118.4, 90.4, 66.7, 52.5, 52.2, 41.6, 39.1, 37.6, 24.0, 22.2, 21.5; IR (neat, cm^{-1}): ν 3492, 2954, 2871, 1709, 1634, 1594, 1574, 1437, 1365, 1297, 1271, 1234, 1208, 1169, 1117, 1086, 1065, 1038, 923, 894, 814, 730, 701, 668; HRMS (ESI) calcd for $C_{26}H_{31}N_2O_7S$ $(M+NH_4)^+$: 515.1846; Found: 515.1851.

*Methyl 9c-Hydroxy-6,8-dimethyl-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno-[2,1-b]-indole-3a-carboxylate (**2j**).* White solid; (73.5 mg; 81% yield); m.p.: 145−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.14 (s, 1H), 6.83 (s, 1H), 4.01 (d, J = 18 Hz, 1H), 3.75 (s, 3H), 3.03 (d, J = 17.2 Hz, 1H), 2.74 (s, 1H), 2.58−2.52 (m, 4H), 2.34 (s, 3H), 2.32 (s, 3H), 2.31−2.27 (m, 1H), 2.03−1.94 (m, 1H), 1.84−1.79 (m, 2H), 1.28−1.19 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.2, 145.1, 144.6, 139.4, 136.4, 134.1, 129.8, 129.7, 128.3, 127.2, 126.4, 126.3, 116.7, 90.5, 66.6, 52.4, 41.6, 38.7, 37.5, 23.9, 22.0, 21.6, 20.8; IR (neat, cm^{-1}): ν 3499, 3446, 2951, 2925, 2872, 1699, 1635, 1596, 1437, 1364, 1329, 1297, 1234, 1171, 1086, 1035, 991, 900, 844, 816, 733, 702, 668, 617; HRMS (ESI) calcd for $C_{25}H_{31}N_2O_5S$ $(M+NH_4)^+$: 471.1948; Found: 471.1947.

*9c-Hydroxy-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]indole-3a-carbonitrile (**2k**).* Yellow solid; m.p.: 136−137 °C; (58.8 mg; 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 7.2 Hz, 1H), 7.31 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.27−7.23 (m, 3H), 3.85 (d, J = 17.6 Hz, 1H), 3.31 (d, J = 17.6 Hz, 1H), 2.74 (s, 1H), 2.47−2.39 (m, 1H), 2.36 (s, 3H), 2.34−2.29 (m, 1H), 2.13−2.03 (m, 2H), 1.93−1.88 (m, 1H), 1.42−1.36 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 145.5, 140.3, 139.7, 134.9, 130.1, 126.5, 126.4, 124.6, 124.0, 123.8, 121.9, 118.9, 114.3, 89.7, 56.0, 40.5, 39.9, 38.3, 24.3, 21.5; IR (neat, cm^{-1}): ν 3436, 3061, 2959, 2866, 2244, 1602, 1482, 1409, 1366, 1295, 1222, 1172, 1095, 1046, 987, 910, 811, 731, 661; HRMS (ESI) calcd for $C_{22}H_{24}N_3O_3S$ $(M+NH_4)^+$: 410.1533; Found: 410.1531.

*3a-(Methoxymethyl)-5-tosyl-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]indol-9c-ol (**2l**).* Colorless oil; (65.8 mg; 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, J_1 = 6.4 Hz, J_2 = 2 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.52 (dd, J_1 = 6.8 Hz, J_2 = 3.2 Hz, 1H), 7.25−7.18 (m, 4H), 3.66 (d, J = 8.8 Hz, 1H), 3.50 (d, J = 17.6 Hz, 1H), 3.48 (d, J = 8.8 Hz, 1H), 3.34 (s, 4H), 2.93 (d, J = 17.2 Hz, 1H), 2.32 (s, 3H), 2.24−2.19 (m, 1H), 1.93−1.87 (m, 1H), 1.75−1.69 (m, 3H), 1.29−1.25 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 144.7, 142.1, 140.3, 135.4, 129.7, 129.3, 126.5, 125.3, 123.6, 123.5, 118.8, 114.3, 88.1, 77.3, 59.7, 59.0, 39.2, 39.2, 37.5, 23.8, 21.4; IR (neat, cm^{-1}): ν 3517, 3056, 2947, 2860, 1617, 1597, 1475, 1446, 1402, 1366, 1298, 1220, 1171, 1146, 1089, 1042, 1019, 990, 951, 878, 810, 746, 702, 663; HRMS (ESI) calcd for $C_{23}H_{25}NO_4SNa$ $(M+Na)^+$: 434.1397; Found: 434.1397.

*Methyl 9c-Hydroxy-5-(methylsulfonyl)-2,3,3a,4,5,9c-hexahydro-1H-pentaleno[2,1-b]-indole-3a-carboxylate (**2m**).* Colorless oil; (58.7 mg; 84% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89−7.87 (m, 1H), 7.61−7.59 (m, 1H), 7.32−7.30 (m, 2H), 3.89 (d, J = 18 Hz, 1H), 3.75 (s, 3H), 3.09 (s, 3H), 2.94 (d, J = 18 Hz, 1H), 2.90 (s, 1H), 2.63−2.55 (m, 1H), 2.40−2.35 (m, 1H), 2.08−2.01 (m, 1H), 1.92−1.74 (m, 2H), 1.44−1.25 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.2, 142.4, 140.5, 126.6, 124.8, 124.4, 124.0, 119.2, 114.0, 90.8, 67.0, 52.5, 40.9, 39.1, 38.9, 37.8, 24.1; IR (neat, cm^{-1}): ν 3504, 2957, 2869 1718, 1619, 1477, 1446, 1410, 1362, 1325, 1277, 1221, 1168, 1139, 1116, 1092, 1035, 993, 961, 909, 786, 729, 684, 645; HRMS (ESI) calcd for $C_{17}H_{23}N_2O_5S$ $(M+NH_4)^+$: 367.1322; Found: 367.1324.

*9c-Hydroxy-3a-methyl-5-tosyl-3a,4,5,9c-tetrahydro-1H-pentaleno[2,1-b]indol-3(2H)-one (**2n**).* Yellow solid; (65.6 mg; 83% yield); m.p.: 123−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8 Hz, 1H), 7.67 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 6.8 Hz, 1H), 7.28−7.23 (m, 2H), 7.22 (d, J = 8 Hz, 2H), 3.56 (d, J = 17.6 Hz, 1H), 3.10 (d, J = 17.2 Hz, 1H), 2.77 (dd, J_1 = 12.8 Hz, J_2 = 9.2 Hz, 1H), 2.49−2.42 (m, 1H), 2.33 (s, 3H), 2.28−2.19 (m, 1H), 2.09 (s, 1H), 1.93−1.85 (m, 1H), 1.25 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 220.6, 145.2, 144.2, 140.0, 134.8, 130.0, 127.1, 126.6, 124.5, 124.3, 123.7, 118.7, 114.6, 83.9, 62.9, 37.7, 36.3, 29.8, 21.5, 15.5; IR (neat, cm^{-1}): ν 3348, 3054, 2961, 2921, 2862, 1715, 1596, 1485, 1444, 1403, 1364, 1222, 1172, 1122, 1082, 1055, 983, 914, 849, 810, 737, 661; HRMS (ESI) calcd for $C_{22}H_{21}NO_4SNa$ $(M+Na)^+$: 418.1083; Found: 418.1082.

*11b-Hydroxy-6a-phenyl-5-tosyl-6,6a-dihydro-5H-benzo[5,6]-pentaleno[2,1-b]indol-7(11bH)-one (**2p**).* Yellow solid; (99 mg; 98% yield); m.p.: 184−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (t, J = 7.2 Hz, 2H), 7.74−7.65 (m, 4H), 7.59 (d, J = 7.2 Hz, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.27−7.17 (m, 7H), 7.15 (d, J = 8 Hz, 2H), 4.16 (d, J = 18 Hz, 1H), 3.89 (d, J = 18.0 Hz, 1H), 2.45 (br, 1H), 2.24 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 204.6, 154.9, 145.4, 141.4, 139.7, 137.2, 135.9, 135.2, 135.0, 130.1, 129.4, 128.7, 128.2, 127.7, 127.6, 126.7, 124.8, 124.6, 124.4, 124.4, 123.8, 118.9, 114.4, 85.2, 75.0, 37.3, 21.5; IR (neat, cm^{-1}): ν 3501, 2094, 3057, 2960, 2928, 2867, 1698, 1599, 1495, 1470, 1444, 1396, 1360, 1343, 1316, 1282, 1255, 1173, 1148, 1102, 1065, 1026, 975, 933, 902, 853, 835, 811, 748, 727, 704, 665, 639, 619; HRMS (ESI) calcd for $C_{31}H_{27}N_2O_4S$ $(M+NH_4)^+$: 523.1686; Found: 523.1683.

*Methyl 2-oxo-1-((1-Tosyl-1H-indol-2-yl)methyl)-cyclopentanecarboxylate (**3a**).* Yellow solid; m.p.: 125−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 7.6 Hz, 1H), 7.29−7.25 (m, 1H), 7.20 (d, J = 7.6 Hz, 1H), 7.16 (d, J = 8.4 Hz, 2H), 6.36 (s, 1H), 3.93 (d, J = 16 Hz, 1H), 3.70 (s, 3H), 3.48 (d, J = 15.6 Hz, 1H), 2.68−2.62 (m, 1H), 2.47−2.40 (m, 1H), 2.31 (s, 3H), 2.19−2.10 (m, 2H), 2.04−1.96 (m, 1H), 1.84−1.79 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ214.5, 171,1, 144.9, 137.2, 137.0, 135.5, 129.8, 129.8, 126.3, 124.5, 123.9, 120.6, 115.3, 112.1, 61.2, 52.9, 38.7, 32.4, 31.4, 21.6, 19.6; IR (neat, cm^{-1}): ν 2957, 2907, 1720, 1595, 1489, 1444, 1362, 1292, 1210, 1172, 1144, 1096, 1041, 974, 914, 876, 808, 741, 662; HRMS (ESI) calcd for $C_{23}H_{27}N_2O_5S$ $(M+NH_4)^+$: 443.1635; Found:443.1631.

*2-((1-Tosyl-1H-indol-2-yl)methyl)cyclopentanone (**3o**).* Yellow oil; (49.2 mg; 67% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 7.6 Hz, 1H), 7.27 (td, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 7.21 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.17 (d, J = 8.4 Hz, 2H), 6.39 (s, 1H), 3.60 (dd, J_1 = 15.6 Hz, J_2 = 4.0 Hz, 1H), 2.87−2.80 (m, 1H), 2.73−2.69 (m, 1H), 2.42−2.35 (m, 1H), 2.31 (s, 3H), 2.21−2−12 (m, 2H), 2.05−1.96 (m, 1H), 1.82−1.77 (m, 1H), 1.60−1.52 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ219.5, 144.9, 139.8, 137.4, 135.7, 129.9, 129.8, 126.4, 124.2, 123.7, 120.3, 115.1, 110.7, 49.4, 37.9, 29.7, 29.2, 21.6, 20.5; IR (neat, cm^{-1}): ν 2968, 2926, 2254, 1743, 1595, 1447, 1366, 1215, 1162, 1086, 1046, 908, 859, 809, 734, 663; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_3S$ $(M+NH_4)^+$: 385.1580; Found: 385.1581.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02817.

Copies of ^{1}H and ^{13}C NMR spectra data for all compounds and copies of ^{19}F NMR spectra data for compounds **1d**, **1f**, **2d**, and **2f** (PDF)

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

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