JOC The Journal of Organic Chemistry

Article

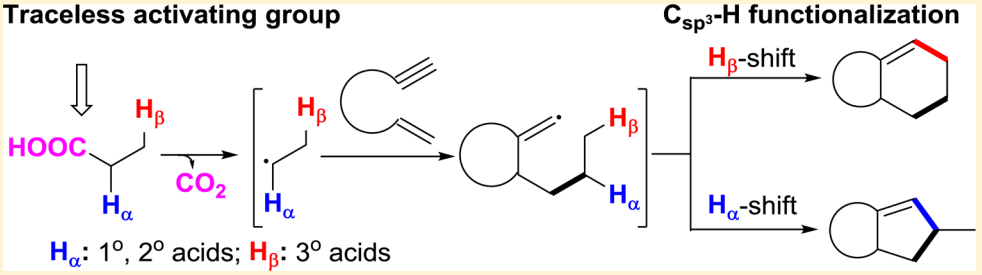
pubs.acs.org/joc

Cycloalkylation of C(sp^3)-H Bond with Neighboring Carboxylic Acid as Traceless Activating Group

Leiyang Lv and Zhiping Li*

Department of Chemistry, Renmin University of China, Beijing 100872, China

Supporting Information

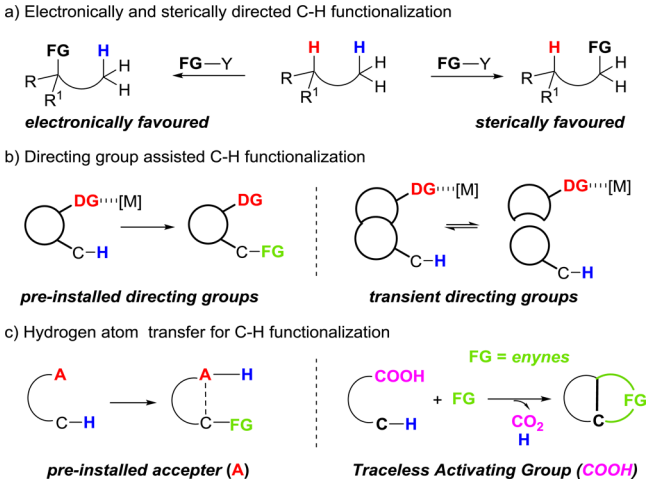


ABSTRACT: Selective functionalization of inert C(sp^3)-H bond is one of cutting-edge challenges in chemical synthesis. A novel strategy for selective C(sp^3)-H bond cycloalkylation is developed with neighboring carboxylic acid as a traceless activating group. Primary and secondary alkyl carboxylic acids undergo decarboxylation/α-C(sp^3)-H cleavage/cycloalkylation to give the five-membered cyclization products, while tertiary acids undergo decarboxylation/β-C(sp^3)-H cleavage/cycloalkylation to generate the six-membered cyclization products.

INTRODUCTION

Alkyl carboxylic acids are ubiquitous in every part of chemical science, and can be readily available from pharmaceuticals, materials, natural products, and large-scale biomass. They are stable, operable, nontoxic and eminently diversifiable in the field of combinatorial chemistry, in which they are considered as the "workhorse" building block.[1] Nowadays, alkyl carboxylic acids have been successfully demonstrated as ideal alternatives to halides or aldehydes to engage in decarboxylative cross couplings, thus delivering various new C−C or C−X bonds.[2,3] However, the simultaneous functionalization of its alkyl C−H bonds remains virtually unexplored. As is well-known, functionalization of inert C−H bonds provides straightforward and worthwhile approaches for synthesis of fine chemicals and complex molecules from simple starting materials.[4] One of the extremely intractable challenges is selective transformation of inert C(sp^3)-H bonds for chemical synthesis. To this end, great efforts have been made and many noteworthy reactions can be classified in Scheme 1. Oxidative transformation and metal carbene insertion have been demonstrated to convert C(sp^3)-H bonds into new chemical entities in an efficient and direct manner (Scheme 1a).[5,6] However, the selectivity of this strategy, to some extent, relies heavily on the electronic and steric characteristics of different C−H bonds. Since the past decades, metal-catalyzed directed C(sp^3)-H bond activation has been extensively exploited to achieve excellent selectivity in C−H bond functionalization, in which the directing group chelates to a metal center and directs the particular nearby C−H activation (Scheme 1b, left).[7] Nevertheless, the covalent installation and removal of directing groups obviously detracts the efficiency of synthetic applications To overcome the limitation, the strategy

Scheme 1. Strategies for C(sp^3)-H Functionalization



with a transient directing group, reversibly linked to the substrate and acts as a temporary directing group, has been demonstrated as an excellent alternative (Scheme 1b, right).[8,9] In addition, intramolecular H-transfer also represents an attractive avenue for selective C(sp^3)-H bond functionalization (Scheme 1c, left).[10] This transformation is initiated by an intramolecular H-shift to form a zwitterionic intermediate, in which a H-acceptor moiety (A), has to be preinstalled in the proximal position to the C−H bond. It is therefore desirable to

Received: December 30, 2016
Published: February 17, 2017

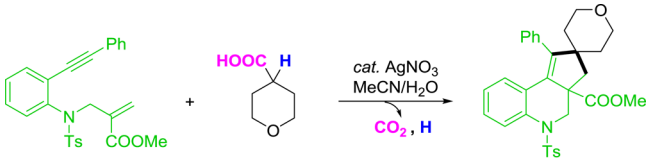
DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

use a simple traceless activating group[11,12] that can react with the other substrate to install a H-acceptor in situ and accomplish C(sp^3)-H bond functionalization (Scheme 1c, right). Toward this idea, we here present a decarboxylative functionalization of alkyl carboxylic acids with enynes that enables regioselective cycloalkylation of its neighboring C(sp^3)-H bonds. To the best of our knowledge, this is the first protocol that combines the advantages of decarboxylative strategy and intramolecular H-transfer, thus allowing the subsequent cycloalkylation of its inert C(sp^3)-H bond.

RESULTS AND DISCUSSION

A variety of templates were examined to react with alkyl carboxylic acids to achieve our tentative idea. After extensive trials, 1,7-enynes were finally identified as the best candidates.[13,14] Then, we commenced our proposal by testing the reaction of 1,7-enyne **1a** with tetrahydro-2*H*-pyran-4-carboxylic acid **2a** for the condition optimization (Table 1). After

Table 1. Optimization of Reaction Conditions[a]



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

entry	[Ag]	solvent	T (°C)	yield of **3aa** (%)[b]
1	$AgNO_3$	MeCN/H_2O	100	65
2	$AgNO_3$	MeCN/H_2O	120	45
3	$AgNO_3$	MeCN/H_2O	80	46
4	Ag_2CO_3	MeCN/H_2O	100	65
5	$AgBF_4$	MeCN/H_2O	100	64
6	AgOTf	MeCN/H_2O	100	51
7	$AgSbF_6$	MeCN/H_2O	100	55
8		MeCN/H_2O	100	0
9	$AgNO_3$	MeCN	100	0
10	$AgNO_3$	acetone/H_2O	100	47
11	$AgNO_3$	DMF/H_2O	100	17
12	$AgNO_3$	THF/H_2O	100	0
13	$AgNO_3$	EtOH/H_2O	100	0
14	$AgNO_3$	MeCN/H_2O	100	56[c]
15	$AgNO_3$	MeCN/H_2O	100	62[d]
16	$AgNO_3$	MeCN/H_2O	100	46[e]

[a]Reaction conditions: **1a** (0.4 mmol), **2a** (0.2 mmol), [Ag] (20 mol %), $K_2S_2O_8$ (1.5 equiv), and organic solvent/H_2O (2/1, 3.0 mL) at air atmosphere for 3 h. [b]Reported yields were based on **2a** and determined by ^1H NMR using CH_2Br_2 as an internal standard. [c]Under N_2 atmosphere. [d]Under O_2 atmosphere. [e]$K_2S_2O_8$ (3.0 equiv).

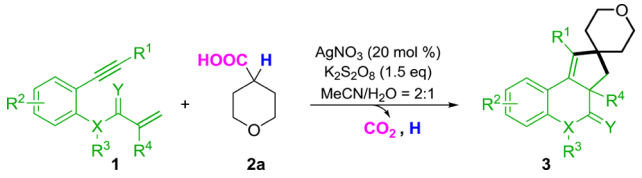
widespread screening of various parameters, the desired product **3aa**, formed by selective cycloalkylation of C(sp^3)-H bond of carboxylic acid after decarboxylation, was obtained in 65% yield with 1.5 equiv $K_2S_2O_8$ in mixed solvent (MeCN/H_2O = 2:1) at 100 °C for 3 h (entry 1). Encouraged by theses results, we further examined the effect of reaction temperature. The yield decreased to 46% when the temperature was increased to 120 °C (entry 2), and to 45% at a reaction temperature of 80 °C (entry 3). Notably, good yields were also achieved with other silver salts, for example, Ag_2CO_3, $AgBF_4$, AgOTf, and $AgSbF_6$ (entries 4−7), while without adding of catalyst or H_2O led to no detection of **3aa** (entries 8−9). Solvents that were miscible with H_2O turned to be more inferior than MeCN (entries 10−13). Besides, **3aa** was obtained in 56% yield under nitrogen and 62% under oxygen atmosphere (entries 14−15). Increasing of $K_2S_2O_8$ to 3.0 equiv led to decrease of the reaction efficiency (entry 16).

With the optimal reaction conditions in hand, a variety of templates, namely benzene-linked 1,7-enynes, were reacted with carboxylic acid **2a** to investigate the scope of this inert α-C(sp^3)-H bond cycloalkylation (Table 2). The electronic effect of the substituents on the aryl ring at alkyne moiety exerted observable effects on the efficiency of this transformation. For example, substrate **1b** with a Me group was transformed into **3ba** in good yield (entry 2), while strong electron-donating OMe group gave the desired **3ca** in only 32% yield (entry 3). Importantly, halogen functional groups, Cl and F, were well tolerated under the optimized reaction conditions (entries 4 and 5), thereby enabling subsequent functionalization at the halogenated positions. Aliphatic alkyne **1f**, even with a cyclopropyl group **1g**, were also applicable for this transformation, though giving the desired products **3fa** and **3ga** in only 44 and 26% yields, respectively, probably due to the poor ability to stabilize generated vinyl radical intermediates (entries 6 and 7). It is noteworthy that the complete desilylation was happening when trimethylsilyl alkyne **1h** was tested (entry 8). Screening revealed that the substituents, namely Me, Cl, F, and CF_3, on the aromatic ring of the aniline moiety were well-compatible (**3ia**−**la**), and have no obvious influence of this reaction (entries 9−12). Besides, the *N*-brosyl, mesyl, and sulfonyl substituted anilines also reacted smoothly to give the desired products **3ma**−**oa** (entries 13−15). It is worth noting that the cyclopenta[*c*]chromene skeleton **3pa**, cyclopenta[*c*]quinolin-4-one (**3qa**), and cyclopenta[*a*]naphthalene skelecton (**3ra**) were all constructed successfully in moderate yields (entries 16−18). Unfortunately, when aliphatic 1,7-enyne was applied, no desired cycloalkylation product was detected.

With enyne **1a** as the standard template, we next explored the scope of this inert C(sp^3)-H bond cycloalkylation and found it to be remarkably broad (Table 3). A range of secondary alkyl carboxylic acids were proven to be well-tolerated to react with **1a** under the standard reaction conditions. For example, carboxylic acids bearing small to large carbocycle **3ab**−**ae** (entries 1−4), bridged norbornene or adamantane skeleton **3af** and **3ag** (entries 5 and 6), and *O*-heterocycle **3ah**−**aj** (entries 7−9) all reacted efficiently to give the corresponding products in good yields. To our delight, various amino acids were also proven as viable partners involved in this transformation **3ak**−**am** (entries 10−12). Many of these structures would be either inconvenient or chemically intractable to access from the corresponding alkyl halides or aldehydes. The functional groups, such as Ts, F, CO_2Me, and CO etc., attached to the cyclohexane moiety, were well compatible under the optimal condition **3an**−**as** (entries 13−18). Besides, acyclic secondary alkyl acids were also transformed into the corresponding products **3at** and **3au** efficiently (entries 19 and 20). Primary alkyl carboxylic acids, and even acetic acid, representing one of the most inexpensive organic materials, could also be readily used (entries 21 and 22). Furthermore, the method could be used as a potential synthetic tool for the late stage modification of complex molecules. For example, naturally occurring oleic acid and man-made elaidic acid all reacted smoothly to give the corresponding products **4** and **4′** without olefin isomerization or oxidative degradation. Pharmaceutical, agrochemical, and steroid hormones, such as naproxen, 2,4-D, epiandrosterones, and cholesterol smoothly

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

Table 2. Cycloalkylations of 1,*n*-Enynes with Tetrahydro-2*H*-pyran-4-carboxylic Acids[a]



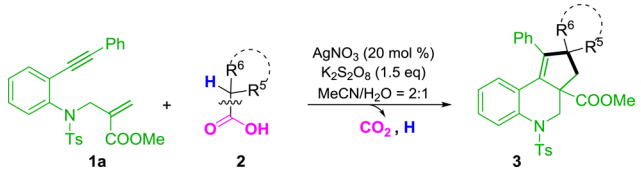
Entry	1	3	Yields (%)[b]
1	R^1 = Ph		**3aa**, 60
2	R^1 = 4-C_6H_4-Me,		**3ba**, 72
3	R^1 = 4-C_6H_4-OMe		**3ca**, 32
4	R^1 = 4-C_6H_4-Cl		**3da**, 60
5	R^1 = 4-C_6H_4-F		**3ea**, 55
6	R^1 = *n*-hex		**3fa**, 44
7	R^1 = ▷		**3ga**, 26
8	R^1 = TMS		**3ha**, 51[c]
9	R^2 = Me		**3ia**, 50
10	R^2 = Cl		**3ja**, 57
11	R^2 = F		**3ka**, 57
12	R^2 = CF_3		**3la**, 56
13	R^3 = Ms		**3ma**, 61
14	R^3 = Bs		**3na**, 60
15	R^3 = SO_2Ph		**3oa**, 56
16			**3pa**, 48
17			**3qa**, 60[d]
18			**3ra**, 46

[a]Reaction conditions: **1** (0.4 mmol), **2a** (0.2 mmol), $AgNO_3$ (20 mol %), $K_2S_2O_8$ (1.5 equiv), and MeCN/H_2O (2/1, 3.0 mL) at 100 °C at air atmosphere for 3 h. [b]Reported yields were isolated yields and based on **2a**. [c]A desilylation product **3ha** was obtained exclusively. [d]The rotational-isomeric ratio is 2:1.

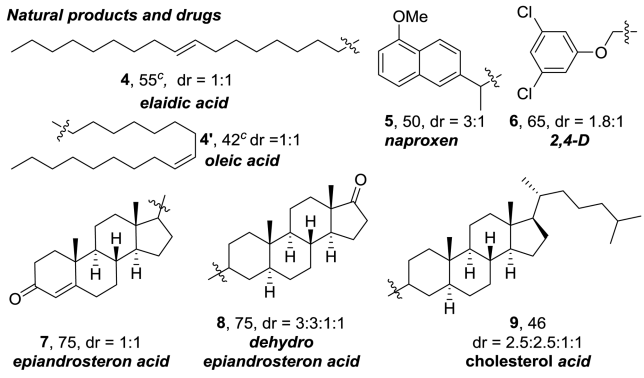
reacted with the standard template **1a** to afford good yields of the desired products **5**−**9**.

Preliminary synthetic transformation of **3aa** was studied (Scheme 2). For example, reduction with DIBAL-H afforded **10** in 97% yield under −78 °C. Deprotection of Ts group with magnesium chips in refluent methanol gave free aniline **11** in 82% yield. Alkali hydrolysis of the ester group, followed by azidation and subsequent Schmidt rearrangement, gave quaternary amine **12** in 96% yield. Besides, the *m*-CPBA mediated epoxidation delivered stereospecific fully substituted

Table 3. Cycloalkylations of Template 1a with Secondary and Primary Acids[a]



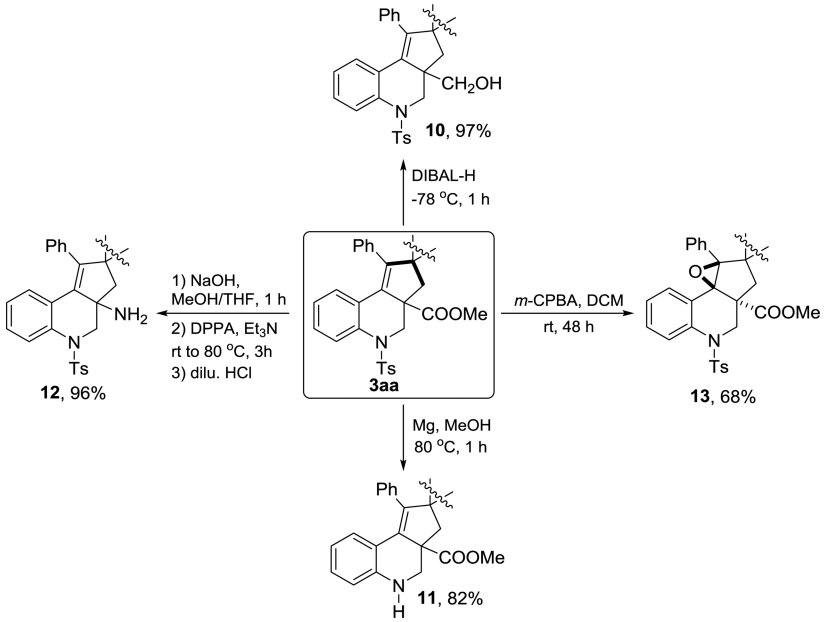
Entry	2	Yield of **3** (%)[b]	Entry	2	Yield of **3** (%)[b]
	R^5, R^6 =			R^5, R^6 =	
1		**3ab**, 67	12		**3am**, 61 dr = 1:1
2		**3ac**, 51	13		**3an**, 67
3		**3ad**, 62	14		**3ao**, 67
4		**3ae**, 72	15		**3ap**, 60
5		**3af**, 53 dr = 1.4:1	16		**3aq**, 53
6		**3ag**, 65	17		**3ar**, 65 dr = 1:1
7		**3ah**, 80 dr = 1.3:1	18		**3as**, 70 dr = 1:1
8		**3ai**, 67 dr = 2.6:1	19		**3at**, 60 dr = 1:1
9		**3aj**, 45 dr = 1.2:1	20		**3au**, 55
10		**3ak**, 50 dr = 1.8:1	21		**3av**, 47[c] dr = 1:1
11		**3al**, 60 dr = 1.6:1	22		**3aw**, 30[c]



[a]Reaction conditions: **1a** (0.4 mmol), **2** (0.2 mmol), $AgNO_3$ (20 mol %), $K_2S_2O_8$ (1.5 equiv), and MeCN/H_2O (2/1, 3.0 mL) at 100 °C at air atmosphere for 3 h. [b]Reported yields were isolated yields and based on **2**. [c]**6h**.

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

Scheme 2. Synthetic Transformation of 3aa



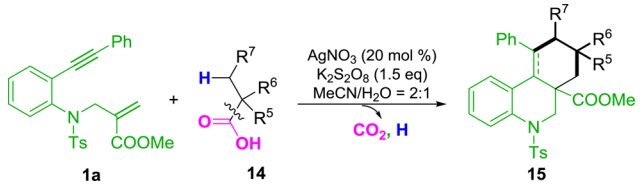
epoxide **13**. This structure was unambiguously confirmed by X-ray diffraction (see Figure S1 in Supporting Information).

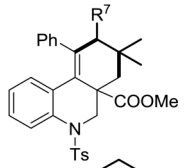
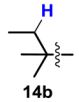
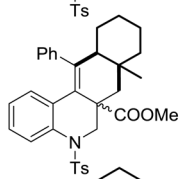
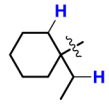
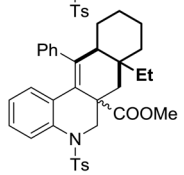
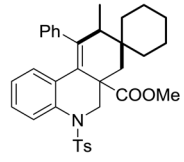
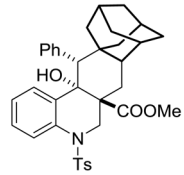
To our delight, the more inert β-C(sp^3)-H bond cycloalkylation took place when tertiary carboxylic acid reacted with the standard template under the aforementioned reaction conditions. For example, pivalic acid **14a**, which underwent decarboxylation/β-C(sp^3)-H cleavage to act as isobutene synthon, reacted with 1,7-enyne to afford **15aa** in 52% yield (Table 4, entry 1). When 2,2-dimethylbutanoic acid **14b** or 1-methylcyclohexane-1-carboxylic acid **14c** was applied, the hydrogen abstraction occurred exclusively on the methylene moiety to give **15ab** (entry 2) or tetracyclic hydrobenzophenanthridine **15ac** (entry 3) in a regiospecific manner. In contrast, **15ad** and **15ad′** were obtained in comparative yields when 1-ethylcyclohexane-1-carboxylic acid **14d** was examined (entry 4). These results indicated that the selectivity of this inert C(sp^3)-H bond alkylation probably depends on the stability of generated alkyl radical intermediate. Moreover, a twisted poly cyclized alcohol product **15ae** was selectively achieved when 1-adamantane carboxylic acid was applied (entry 5), probably due to the inherent torsional strain. This structure was unambiguously confirmed by X-ray diffraction (see Figure S2 in Supporting Information).

The enyne **16**, with a free hydroxyl group attached, was synthesized and applied to react with acetic acid d-4 under standard condition (Scheme 3). The poly-fused heterocyclic stereospecific product **17**, in which 100% D atom was captured, was obtained (eq 1). Changing the solvent to D_2O or CD_3CN led to no detection of D atom in **17′** (eqs 2 and 3). These results provided strong evidence that the intramolecular 1,5-H shift was involved in the transformation, which was eliminated in the final deprotonation step.[15,16] Besides, the reaction of **1a** with **2a** was completely suppressed when radical inhibitors, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or butylated hydroxytoluene (BHT), were added. The TEMPO-pyran adduct **18** was detected by HR-MS, which suggested that a radical pathway may be involved in this transformation (eq 4).

On the basis of the above results and previous reports,[13−15] a possible mechanism for this cycloalkylation of C(sp^3)-H bonds

Table 4. Cycloalkylations of Template 1a with Tertiary Acids[a]

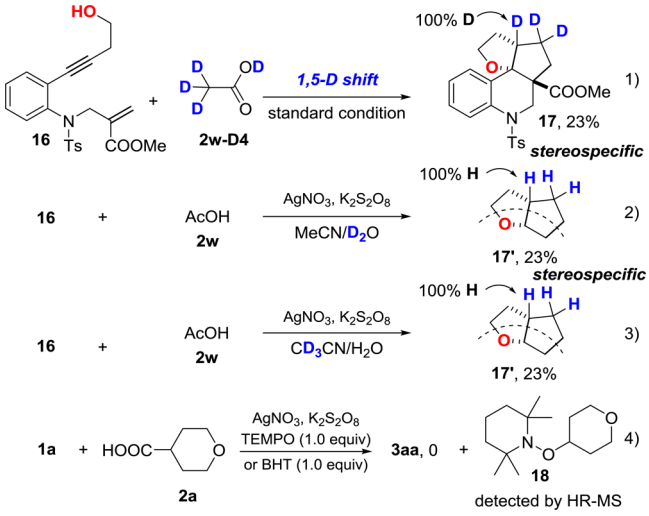


Entry	14	15	Yields (%)[b]
1	 14a		R^7 = H, **15aa**, 50
2	 14b		R^7 = Me, **15ab**, 55 dr = 1:1
3	 14c		**15ac**, 30, dr = 1:1
4	 14d	 **15ad**, 28, dr = 1:1 +  **15ad'**, 28, dr = 1:1	
5	 14e		**15ae**, 63, dr = 5.2:1

[a]Reaction conditions: **1a** (0.4 mmol), **14** (0.2 mmol), $AgNO_3$ (20 mol %), $K_2S_2O_8$ (1.5 equiv), and MeCN/H_2O (2/1, 3.0 mL) at 100 °C at air atmosphere for 3 h. [b]Reported yields were isolated yields and based on **14**.

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

Scheme 3. Deuterium-Labeled and Control Experiments



with neighboring carboxylic acid as a traceless activating group is depicted in Scheme 4. Initially, Ag^{I} was oxidized into Ag^{II} by $K_2S_2O_8$, then the aliphatic carboxylic acids underwent an SET process to generate the carbon radical **A** and release CO_2. Thereafter, radical tandem addition of **A** with enyne **1** gives the key vinyl radical intermediate **B**, which acts as an appropriate H-acceptor. In the case of primary and secondary alkyl carboxylic acids **2**, 1,5-H shift takes place exclusively to give intermediate **C**. The subsequent intramolecular radical cyclization and irreversible oxidation by silver catalyst gives a stable benzyl cation **F**. Finally, deprotonation of **F** delivers the five-membered product **3**. Alternatively, 1,6-H abstraction occurs when tertiary carboxylic acid **14** is used and the six-membered product **15** is generated accordingly.

CONCLUSION

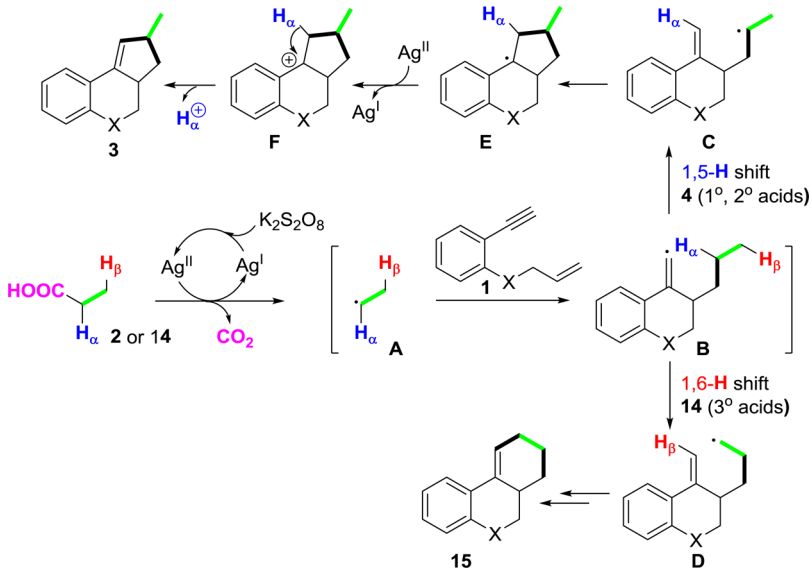
In summary, we have demonstrated a new strategy for decarboxylative functionalization of alkyl carboxylic acids with enynes, which enables regioselective cycloalkylation of its neighboring C(sp^3)-H bonds. The deuterium-labeled experiments provide strong evidence for the occurrence of intramolecular H shift in this transformation. The advantage of our protocol combines the traceless activating protocol and intramolecular H-transfer, thus allowing the subsequent cycloalkylation of its inert C(sp^3)-H bond after decarboxylation. Primary and secondary alkyl carboxylic acids undergo decarboxylation/α-C(sp^3)-H cleavage/cycloalkylation to give the five-membered cyclization products, while tertiary acids undergo decarboxylation/β-C(sp^3)-H cleavage/cycloalkylation to generate the six-membered cyclization products. The late stage functionalization of various natural products and drugs were also realized efficiently. Considering the abundance and feasibility of decarboxylation of aliphatic carboxylic acids, as well as efficiency of radical-initiated cyclization of enynes, the application of this protocol for inert alkyl C(sp^3)-H bond functionalization is envisioned.

EXPERIMENTAL SECTION

General Information. ^{1}H NMR spectra were recorded on 400 or 600 MHz spectrometer and the chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) for $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; q, quartet; m, multiplet. The coupling constants, J, are reported in Hertz (Hz). ^{13}C NMR spectra were obtained at 100 or 150 MHz and referenced to the internal solvent signals (central peak is 77.0 ppm in $CDCl_3$, 39.5 ppm in DMSO-d_6). $CDCl_3$ and DMSO-d_6 were used as the NMR solvents. Flash column chromatography was performed over silica gel 200−300. All reagents were weighed and handled in air at room temperature. All reagents were purchased from commercial source and used without further purification. The HRMS measurements were recorded on a FTMS analyzer using an ESI source in the positive mode.

General Procedure for Products 3 and 15. To a mixture of alkyl carboxylic acid **2** or **14** (0.2 mmol), enyne **1** (0.4 mmol), $AgNO_3$ (6.8 mg, 20 mol%), and $K_2S_2O_8$ (81.0 mg, 0.3 mmol), MeCN (2.0 mL) and H_2O (1.0 mL) were added under air at room temperature. The resulting mixture was stirred at 100 °C for 3 h. After the mixture was cooled to room temperature, EtOAc (10.0 mL) and H_2O (2.0 mL) were added sequentially. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to give the crude products. NMR yields were determined by ^{1}H NMR using dibromomethane as an internal standard. The residue was

Scheme 4. Proposed Mechanism



DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether) to give the pure product **3** or **15** in pale yellow oil.

*Methyl 1-Phenyl-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3aa**).* (64 mg, 60%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3); IR (neat): ν_{max} 2949, 2928, 2845, 1732, 1599, 1479, 1458, 1387, 1350, 1249, 1221, 1163, 1105, 1090, 1051, 917, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.2 Hz, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.39−7.33 (m, 3H), 7.28 (d, J = 8.2 Hz, 2H), 7.00−6.96 (m, 3H), 6.70 (dd, J = 7.8, 1.6 Hz, 1H), 6.62 (td, J = 7.6, 0.8 Hz, 1H), 5.08 (d, J = 12.0 Hz, 1H), 3.90 (dd, J = 11.6, 4.2 Hz, 1H), 3.78 (dd, J = 11.6, 3.8 Hz, 1H), 3.64 (s, 3H), 3.58 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (d, J = 12.0 Hz, 1H), 3.44 (td, J = 11.4, 1.8 Hz, 1H), 2.88 (d, J = 13.6 Hz, 1H), 2.41 (s, 3H), 1.97 (td, J = 13.0, 4.8 Hz, 1H), 1.83 (d, J = 13.6 Hz, 1H), 1.57 (td, J = 13.4, 4.8 Hz, 1H), 1.51 (dd, J = 13.4, 1.4 Hz, 1H), 1.03 (dd, J = 13.4, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 146.4, 143.8, 137.2, 136.0, 135.9, 130.7, 129.7, 129.1, 128.6, 127.8, 127.6, 127.5, 127.0, 123.5, 123.0, 120.2, 65.1, 64.3, 55.6, 55.4, 52.6, 50.0, 43.0, 36.9, 33.8, 21.5; HRMS (ESI) calcd for $C_{31}H_{31}NNaO_5S$ [M+Na^+], 552.1815; found: 552.1801.

*Methyl 1-(p-Tolyl)-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ba**).* (78 mg, 72%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2938, 2928, 2853, 1732, 1597, 1485, 1350, 1240, 1165, 1105, 1092, 1070, 1057, 1036, 959 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.48 (dd, J = 8.4, 0.8 Hz, 1H), 7.28 (d, J = 8.2 Hz, 2H), 7.15 (d, J = 7.8 Hz, 2H), 6.98 (td, J = 7.8, 1.6 Hz, 1H), 6.85 (d, J = 7.8 Hz, 2H), 6.76 (dd, J = 8.0, 1.6 Hz, 1H), 6.64 (td, J = 7.8, 1.0 Hz, 1H), 5.07 (d, J = 12.0 Hz, 1H), 3.89 (dd, J = 11.8, 4.0 Hz, 1H), 3.78 (dd, J = 11.6, 3.6 Hz, 1H), 3.63 (s, 3H), 3.57 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (td, J = 12.2, 1.8 Hz, 1H), 3.44 (d, J = 12.0 Hz, 1H), 2.87 (d, J = 13.6 Hz, 1H), 2.41 (s, 3H), 2.37 (s, 3H), 1.95 (td, J = 12.6, 4.0 Hz, 1H), 1.81 (d, J = 13.6 Hz, 1H), 1.58 (td, J = 13.2, 4.8 Hz, 1H), 1.48 (dd, J = 13.6, 1.8 Hz, 1H), 1.01 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 146.5, 143.8, 137.2, 137.1, 135.9, 132.8, 130.5, 129.7, 129.3, 128.9, 127.9, 127.6, 127.0, 123.7, 123.0, 120.2, 65.1, 64.3, 55.7, 55.4, 52.6, 49.9, 42.9, 36.9, 33.8, 21.5, 21.2; HRMS (ESI) calcd for $C_{32}H_{33}NNaO_5S$ [M+Na^+], 566.1972; found: 566.1964.

*Methyl 1-(4-Methoxyphenyl)-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ca**).* (36 mg, 32%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3); IR (neat): ν_{max} 2949, 2853, 1732, 1352, 1238, 1163, 1103, 1092, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.47 (dd, J = 8.4, 0.8 Hz, 1H), 7.28 (d, J = 8.2 Hz, 2H), 6.98 (td, J = 7.8, 1.6 Hz, 1H), 6.89 (s, 4H), 6.77 (dd, J = 8.0, 1.6 Hz, 1H), 6.65 (td, J = 7.8, 1.0 Hz, 1H), 5.06 (d, J = 12.0 Hz, 1H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.83 (s, 3H), 3.78 (dd, J = 11.6, 3.6 Hz, 1H), 3.63 (s, 3H), 3.57 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (td, J = 12.2, 1.8 Hz, 1H), 3.44 (d, J = 12.0 Hz, 1H), 2.86 (d, J = 13.6 Hz, 1H), 2.41 (s, 3H), 1.95 (td, J = 12.6, 4.0 Hz, 1H), 1.80 (d, J = 13.6 Hz, 1H), 1.59 (td, J = 13.2, 4.8 Hz, 1H), 1.48 (dd, J = 13.6, 1.8 Hz, 1H), 1.00 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 159.0, 146.2, 143.7, 137.2, 135.9, 130.7, 130.2, 129.7, 128.0, 127.9, 127.6, 127.0, 123.7, 123.0, 120.1, 114.1, 65.1, 64.3, 55.7, 55.3, 55.2, 52.6, 49.9, 42.9, 36.9, 33.8, 21.5; HRMS (ESI) calcd for $C_{32}H_{33}NNaO_6S$ [M+Na^+], 582.1921; found: 582.1913.

*Methyl 1-(4-Chlorophenyl)-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3da**).* (68 mg, 60%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2955, 2929, 2850, 1732, 1360, 1252, 1221, 1163, 1109, 1090 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.48 (dd, J = 8.4, 0.8 Hz, 1H), 7.33 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.01 (td, J = 7.8, 1.6 Hz, 1H), 6.92 (d, J = 8.2 Hz, 2H), 6.71−6.65 (m, 2H), 5.06 (d, J = 12.0 Hz, 1H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.79 (dd, J = 11.6, 3.6 Hz, 1H), 3.63 (s, 3H), 3.57 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (d, J = 12.0 Hz, 1H), 3.44 (td, J = 12.2, 1.8 Hz, 1H), 2.87 (d, J = 13.6 Hz, 1H), 2.42 (s, 3H), 1.91 (td, J = 12.6, 4.0 Hz, 1H), 1.83 (d, J = 13.6 Hz, 1H), 1.52 (td, J = 13.2, 4.8 Hz, 1H), 1.50 (dd, J = 13.6, 1.8 Hz, 1H), 1.01 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 144.9, 143.8, 137.1, 136.0, 134.5, 133.6, 131.5, 130.5, 129.7, 128.9, 127.9, 127.8, 127.0, 123.3, 123.1, 120.3, 65.1, 64.2, 55.6, 55.5, 52.6, 50.0, 43.0, 36.9, 33.9, 21.5; HRMS (ESI) calcd for $C_{31}H_{30}ClNNaO_5S$ [M+Na^+], 586.1425; found: 586.1416.

*Methyl 1-(4-Fluorophenyl)-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ea**).* (60 mg, 55%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2949, 2851, 1732, 1599, 1505, 1481, 1454, 1350, 1238, 1220, 1165, 1090, 1028, 1018 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.47 (dd, J = 8.4, 0.8 Hz, 1H), 7.28 (d, J = 8.2 Hz, 2H), 7.08−7.03 (m, 2H), 6.98 (td, J = 7.8, 1.6 Hz, 1H), 6.96−6.92 (m, 2H), 6.70−6.63 (m, 2H), 5.06 (d, J = 12.0 Hz, 1H), 3.91 (dd, J = 11.8, 4.0 Hz, 1H), 3.79 (dd, J = 11.6, 3.6 Hz, 1H), 3.63 (s, 3H), 3.57 (td, J = 12.2, 1.8 Hz, 1H), 3.46 (d, J = 12.0 Hz, 1H), 3.45 (td, J = 12.2, 1.8 Hz, 1H), 2.87 (d, J = 13.6 Hz, 1H), 2.41 (s, 3H), 1.92 (td, J = 12.6, 4.0 Hz, 1H), 1.84 (d, J = 13.6 Hz, 1H), 1.54 (td, J = 13.2, 4.8 Hz, 1H), 1.50 (dd, J = 13.6, 1.8 Hz, 1H), 1.02 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 162.3 (d, J_{C-F} = 245.4 Hz), 145.2, 143.8, 137.2, 136.0, 131.8, 131.4, 130.7 (d, J_{C-F} = 24.0 Hz), 129.7, 127.8 (d, J_{C-F} = 11.6 Hz), 127.0, 123.4, 123.0, 120.3, 115.7 (d, J_{C-F} = 21.2 Hz), 65.1, 64.2, 55.6, 55.4, 52.6, 49.9, 42.9, 36.9, 33.9, 21.5; HRMS (ESI) calcd for $C_{31}H_{30}FNNaO_5S$ [M+Na^+], 570.1721; found: 570.1711.

*Methyl 1-Hexyl-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta-[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3fa**).* (47 mg, 44%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.2); IR (neat): ν_{max} 3061, 3032, 2951, 2932, 2855, 1732, 1599, 1483, 1352, 1240, 1167, 1107, 1190, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.4, 1.0 Hz, 1H), 7.55 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 7.6, 1.6 Hz, 1H), 7.19 (d, J = 8.4 Hz, 2H), 7.15 (td, J = 7.8, 1.6 Hz, 1H), 7.06 (td, J = 7.6, 1.2 Hz, 1H), 4.73 (d, J = 12.0 Hz, 1H), 3.92−3.87 (m, 2H), 3.54−3.41 (m, 6H), 2.61 (d, J = 13.6 Hz, 1H), 2.36 (s, 3H), 2.25 (td, J = 12.6, 4.4 Hz, 1H), 2.03−1.80 (m, 3H), 1.69 (d, J = 13.6 Hz, 1H), 1.40−1.14 (m, 10H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 146.5, 143.5, 136.7, 135.9, 129.5, 128.9, 127.6, 127.0, 126.7, 126.3, 124.0, 122.0, 65.1, 64.5, 56.4, 52.4, 50.1, 43.2, 36.0, 34.9, 31.3, 30.0, 29.0, 26.0, 22.6, 21.4, 14.0; HRMS (ESI) calcd for $C_{31}H_{39}NNaO_5S$ [M+Na^+], 560.2441; found: 560.2431.

*Methyl 1-Cyclopropyl-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ga**).* (26 mg, 26%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3); IR (neat): ν_{max} 2951, 2851, 1734, 1354, 1240, 1220, 1169, 1107, 1092, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.2 Hz, 3H), 7.39 (d, J = 8.0 Hz, 1H), 7.11 (td, J = 7.8, 1.6 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.07 (td, J = 7.6, 1.0 Hz, 1H), 4.67 (d, J = 12.0 Hz, 1H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.78 (td, J = 12.4, 1.4 Hz, 1H), 3.53 (td, J = 12.6, 1.8 Hz, 1H), 3.43 (s, 3H), 3.39 (td, J = 12.4, 1.4 Hz, 1H), 3.28 (d, J = 12.0 Hz, 1H), 2.53 (d, J = 13.6 Hz, 1H), 2.37 (s, 3H), 2.27 (td, J = 12.6, 4.0 Hz, 1H), 1.96 (td, J = 12.6, 4.0 Hz, 1H), 1.64 (d, J = 13.6 Hz, 1H), 1.43 (td, J = 13.2, 4.8 Hz, 1H), 1.35−1.21 (m, 1H), 0.92 (dd, J = 13.6, 1.8 Hz, 1H), 0.78−0.71 (m, 1H), 0.61−0.54 (m, 1H), −0.11- −0.18 (m, 1H), −0.24- −0.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 144.8, 143.8, 136.0, 135.1, 129.6, 129.4, 129.3, 128.0, 127.0, 126.7, 123.8, 123.4, 65.0, 64.9, 57.5, 57.0, 52.3, 51.6, 43.3, 38.1, 34.9, 21.5, 9.9, 7.0, 5.2; HRMS (ESI) calcd for $C_{28}H_{31}NNaO_5S$ [M+Na^+], 516.1815; found: 516.1807.

*Methyl 5-Tosyl-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta[c]-quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ha**).* (46 mg, 51%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3); IR (neat): ν_{max} 2949, 2918, 2851, 1732, 1483, 1460, 1348, 1240, 1165, 1092, 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.60 (dd, J = 7.8, 1.6 Hz, 1H), 7.45 (dd, J = 8.4, 0.6 Hz, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.11 (td, J = 7.8, 1.6 Hz, 1H), 7.01 (td, J = 7.6, 1.0 Hz, 1H), 6.20 (s, 1H), 5.11 (d, J = 12.0 Hz, 1H), 3.84−3.78 (m, 1H), 3.76−3.72 (m, 1H), 3.70−3.61 (m, 2H), 3.66 (s, 3H), 3.21 (d, J = 12.0 Hz, 1H), 2.68 (d, J = 13.4 Hz, 1H), 2.40 (s, 3H), 1.75−1.66 (m, 2H), 1.67 (d, J = 13.4 Hz, 1H), 1.59−1.48 (m,

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 143.8, 137.9, 136.0, 135.4, 132.2, 129.8, 128.3, 126.8, 125.6, 123.3, 122.3, 119.5, 65.4, 65.0, 55.0, 54.7, 52.6, 46.0, 38.5, 36.4, 21.5; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_5S$ [M+Na$^+$], 476.1502; found: 476.1494.

*Methyl 8-Methyl-1-phenyl-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ia**).* (54 mg, 50%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2949, 2926, 1734, 1510, 1458, 1350, 1287, 1242, 1165, 1108, 1090, 1030 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 2H), 7.39−7.37 (m, 4H), 7.30 (d, J = 7.6 Hz, 2H), 7.00 (d, J = 5.8 Hz, 2H), 6.82 (d, J = 8.2 Hz, 1H), 6.48 (s, 1H), 5.07 (d, J = 12.0 Hz, 1H), 3.93 (dd, J = 11.8, 4.0 Hz, 1H), 3.81 (dd, J = 11.6, 3.6 Hz, 1H), 3.67 (s, 3H), 3.61 (td, J = 12.2, 1.8 Hz, 1H), 3.47 (d, J = 12.0 Hz, 1H), 3.45 (td, J = 12.2, 1.8 Hz, 1H), 2.91 (d, J = 13.6 Hz, 1H), 2.44 (s, 3H), 2.00 (td, J = 12.6, 4.0 Hz, 1H), 1.89 (s, 3H), 1.84 (d, J = 13.6 Hz, 1H), 1.63 (td, J = 13.2, 4.8 Hz, 1H), 1.53 (dd, J = 13.6, 1.8 Hz, 1H), 1.05 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.8, 146.3, 143.7, 137.3, 136.2, 133.5, 132.3, 130.9, 129.8, 129.2, 128.6, 128.5, 128.4, 127.5, 127.1, 123.4, 120.1, 65.2, 64.4, 55.7, 55.6, 52.7, 50.0, 43.1, 37.0, 33.9, 21.6, 20.5; HRMS (ESI) calcd for $C_{32}H_{33}NNaO_5S$ [M+Na$^+$], 566.1972; found: 566.1967.

*Methyl 8-Chloro-1-phenyl-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ja**).* (64 mg, 57%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3); IR (neat): ν_{max} 2955, 2928, 2851, 1734, 1350, 1240, 1221, 1165, 1107, 1090 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.43−7.36 (m, 4H), 7.30 (d, J = 8.2 Hz, 2H), 6.97−6.91 (m, 3H), 6.60 (d, J = 2.4 Hz, 1H), 5.07 (d, J = 12.0 Hz, 1H), 3.91 (dd, J = 11.8, 4.0 Hz, 1H), 3.78 (dd, J = 11.6, 3.6 Hz, 1H), 3.65 (s, 3H), 3.57 (td, J = 12.2, 1.8 Hz, 1H), 3.44 (td, J = 12.2, 1.8 Hz, 1H), 3.40 (d, J = 12.0 Hz, 1H), 2.89 (d, J = 13.6 Hz, 1H), 2.42 (s, 3H), 1.96 (td, J = 12.6, 4.0 Hz, 1H), 1.82 (d, J = 13.6 Hz, 1H), 1.60 (td, J = 13.2, 4.8 Hz, 1H), 1.47 (dd, J = 13.6, 1.8 Hz, 1H), 1.04 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 147.9, 144.1, 136.8, 135.2, 134.4, 129.8, 129.6, 128.8, 128.7, 128.4, 127.9, 127.5, 127.0, 124.9, 121.3, 65.1, 64.2, 55.5, 55.1, 52.7, 50.0, 42.9, 36.8, 33.6, 21.5; HRMS (ESI) calcd for $C_{31}H_{30}ClNNaO_5S$ [M+Na$^+$], 586.1425; found: 586.1417.

*Methyl 8-Fluoro-1-phenyl-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ka**).* (62 mg, 57%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.3); IR (neat): ν_{max} 2948, 2934, 2851, 1734, 1481, 1441, 1354, 1242, 1186, 1165, 1105, 1053 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.6 Hz, 2H), 7.47−7.43 (m, 1H), 7.38−7.34 (m, 3H), 7.29 (d, J = 7.6 Hz, 2H), 6.93−6.91 (m, 2H), 6.73−6.68 (m, 1H), 6.34 (dd, J = 10.0, 3.0 Hz, 1H), 5.00 (d, J = 12.0 Hz, 1H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.78 (dd, J = 11.6, 3.6 Hz, 1H), 3.64 (s, 3H), 3.57 (td, J = 12.2, 1.8 Hz, 1H), 3.44 (d, J = 12.0 Hz, 1H), 3.43 (td, J = 12.2, 1.8 Hz, 1H), 2.89 (d, J = 13.6 Hz, 1H), 2.42 (s, 3H), 1.98−1.90 (m, 1H), 1.83 (d, J = 13.6 Hz, 1H), 1.57 (td, J = 13.2, 4.8 Hz, 1H), 1.46 (dd, J = 13.6, 1.8 Hz, 1H), 1.02 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 158.3 (d, J_{C-F} = 241.4 Hz), 147.9, 143.9, 136.8, 135.2, 132.0, 130.0, 129.8, 128.8, 128.7, 127.9, 127.0, 125.8 (d, J_{C-F} = 8.2 Hz), 122.1 (d, J_{C-F} = 8.2 Hz), 114.6 (d, J_{C-F} = 22.8 Hz), 113.9 (d, J_{C-F} = 24.2 Hz), 65.1, 61.2, 55.6, 52.7, 50.1, 43.0, 36.8, 33.6, 21.5; HRMS (ESI) calcd for $C_{31}H_{30}FNNaO_5S$ [M+Na$^+$], 570.1721; found: 570.1715.

*Methyl 1-Phenyl-5-tosyl-8-(trifluoromethyl)-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3la**).* (67 mg, 56%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2951, 1732, 1618, 1597, 1487, 1439, 1387, 1338, 1240, 1165, 1123, 1088, 1053, 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.8 Hz, 1H), 7.43−7.36 (m, 3H), 7.32 (d, J = 8.4 Hz, 2H), 7.17 (dd, J = 7.8, 1.8 Hz, 1H), 7.05−7.02 (m, 2H), 6.94 (d, J = 1.6 Hz, 1H), 5.13 (d, J = 12.0 Hz, 1H), 3.92 (dd, J = 11.8, 4.0 Hz, 1H), 3.80 (dd, J = 11.6, 3.6 Hz, 1H), 3.67 (s, 3H), 3.60 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (td, J = 12.2, 1.8 Hz, 1H), 3.41 (d, J = 12.0 Hz, 1H), 2.91 (d, J = 13.6 Hz, 1H), 2.42 (s, 3H), 2.00 (td, J = 12.6, 4.0 Hz, 1H), 1.83 (d, J = 13.6 Hz, 1H), 1.66 (td, J = 13.2, 4.8 Hz, 1H), 1.50 (dd, J = 13.6, 1.8 Hz, 1H), 1.09 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 148.5, 144.3, 138.5, 137.1, 135.3, 129.9, 129.5, 128.9, 128.7, 128.0, 126.9, 125.0 (d, J_{C-F} = 3.6 Hz), 124.6 (q, J_{C-F} = 32.8 Hz), 124.1 (d, J_{C-F} = 3.0 Hz), 122.7, 122.2, 119.3, 65.1, 64.2, 55.3, 54.5, 52.7, 50.0, 42.7, 36.9, 33.5, 21.5; HRMS (ESI) calcd for $C_{32}H_{30}F_3NNaO_5S$ [M+Na$^+$], 620.1689; found: 620.1684.

*Methyl 5-(Methylsulfonyl)-1-phenyl-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3ma**).* (55 mg, 61%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2949, 2847, 1730, 1597, 1481, 1441, 1348, 1240, 1198, 1155, 1105, 1030, 957, 914 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, J = 7.8, 0.8 Hz, 1H), 7.44−7.35 (m, 3H), 7.14−7.08 (m, 3H), 6.80 (dd, J = 8.0, 1.6 Hz, 1H), 6.66 (td, J = 15.2, 1.0 Hz, 1H), 5.08 (d, J = 12.6 Hz, 1H), 3.92 (dd, J = 12.0, 4.6 Hz, 1H), 3.79 (dd, J = 11.6, 3.6 Hz, 1H), 3.67 (s, 3H), 3.58 (td, J = 12.2, 1.8 Hz, 1H), 3.44 (td, J = 12.2, 1.8 Hz, 1H), 3.34 (d, J = 12.6 Hz, 1H), 3.03 (s, 3H), 2.86 (d, J = 13.6 Hz, 1H), 1.99 (td, J = 12.6, 4.0 Hz, 1H), 1.77 (d, J = 13.6 Hz, 1H), 1.62 (td, J = 13.2, 4.8 Hz, 1H), 1.50 (dd, J = 13.6, 1.8 Hz, 1H), 1.11 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 147.0, 136.1, 135.7, 130.4, 129.0, 128.8, 128.5, 128.3, 127.6, 122.7, 122.2, 118.4, 65.1, 64.3, 54.4, 53.9, 52.5, 49.8, 42.4, 38.8, 37.1, 33.6; HRMS (ESI) calcd for $C_{25}H_{27}NNaO_5S$ [M+Na$^+$], 476.1502; found: 476.1495.

*Methyl 5-((4-Bromophenyl)sulfonyl)-1-phenyl-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3na**).* (71 mg, 60%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 3061, 3021, 2955, 2924, 2847, 1730, 1599, 1574, 1479, 1458, 1441, 1389, 1362, 1352, 1242, 1219, 1107, 1090, 1070, 1049, 1009 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67−7.62 (m, 4H), 7.45 (dd, J = 8.4, 0.6 Hz, 1H), 7.40−7.32 (m, 3H), 7.00 (dd, J = 7.8, 1.8 Hz, 1H), 6.96−6.92 (m, 2H), 6.72 (dd, J = 8.0, 1.6 Hz, 1H), 6.66 (td, J = 15.2, 1.0 Hz, 1H), 5.05 (d, J = 12.0 Hz, 1H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.79 (dd, J = 11.6, 3.6 Hz, 1H), 3.62 (s, 3H), 3.57 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (d, J = 12.0 Hz, 1H), 3.44 (td, J = 12.2, 1.8 Hz, 1H), 2.87 (d, J = 13.6 Hz, 1H), 1.96 (td, J = 12.6, 4.0 Hz, 1H), 1.84 (d, J = 13.6 Hz, 1H), 1.58 (td, J = 13.2, 4.8 Hz, 1H), 1.51 (dd, J = 13.6, 1.8 Hz, 1H), 1.03 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 146.8, 138.9, 135.7, 135.5, 132.4, 130.4, 129.0, 128.6, 128.5, 128.0, 127.8, 127.6, 124.0, 123.4, 120.3, 65.1, 64.3, 55.8, 55.5, 52.6, 50.1, 43.0, 36.9, 33.8; HRMS (ESI) calcd for $C_{30}H_{28}BrNNaO_5S$ [M+Na$^+$], 616.0764; found: 616.0756.

*Methyl 1-Phenyl-5-(phenylsulfonyl)-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta[c]quinoline-2,4′-pyran]-3a(3H)-carboxylate (**3oa**).* (58 mg, 56%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 3061, 3030, 2951, 2849, 1732, 1599, 1479, 1447, 1387, 1352, 1240, 1221, 1198, 1165, 1105, 1089, 1075, 1053, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.81 (m, 2H), 7.61−7.57 (m, 1H), 7.52−7.46 (m, 3H), 7.38−7.31 (m, 3H), 7.01−6.96 (m, 3H), 6.71 (dd, J = 8.0, 1.6 Hz, 1H), 6.63 (td, J = 15.2, 1.0 Hz, 1H), 5.09 (d, J = 12.0 Hz, 1H), 3.91 (dd, J = 11.8, 4.0 Hz, 1H), 3.78 (dd, J = 11.6, 3.6 Hz, 1H), 3.64 (s, 3H), 3.58 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (d, J = 12.0 Hz, 1H), 3.44 (td, J = 12.2, 1.8 Hz, 1H), 2.90 (d, J = 13.6 Hz, 1H), 1.96 (td, J = 12.6, 4.0 Hz, 1H), 1.83 (d, J = 13.6 Hz, 1H), 1.57 (td, J = 13.2, 4.8 Hz, 1H), 1.51 (dd, J = 13.6, 1.8 Hz, 1H), 1.03 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 146.6, 140.2, 136.0, 135.8, 132.9, 130.6, 129.2, 129.0, 128.6, 127.9, 127.7, 127.5, 126.9, 123.6, 123.1, 120.2, 65.1, 64.3, 55.7, 55.4, 52.6, 50.0, 42.9, 36.9, 33.8; HRMS (ESI) calcd for $C_{30}H_{29}NNaO_5S$ [M+Na$^+$], 538.1659; found: 538.1651.

*3a,5-Dimethyl-1-phenyl-2′,3,3a,3′,5′,6′-hexahydrospiro-[cyclopenta[c]quinoline-2,4′-pyran]-4(5H)-one (**3pa**).* (34 mg, 48%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.30 (m, 3H), 7.19−7.15 (m, 1H), 7.10−7.08 (m, 2H), 6.99 (d, J = 11.8 Hz, 1H), 6.74−6.69 (m, 2H), 3.95 (dd, J = 11.8, 4.0 Hz, 1H), 3.77 (dd, J = 11.6, 3.6 Hz, 1H), 3.69 (td, J = 12.2, 1.8 Hz, 1H), 3.56 (td, J = 12.2, 1.8 Hz, 1H), 3.41 (s, 3H), 2.58 (d, J = 13.8 Hz, 1H), 2.39 (d, J = 13.8 Hz, 1H), 2.12 (td, J = 12.6, 4.0 Hz, 1H), 1.61 (td, J = 13.2, 4.8 Hz, 1H), 1.51 (dd, J = 13.6, 1.8 Hz, 1H), 1.34 (s, 3H), 1.15 (dd, J = 13.6, 1.8 Hz, 1H);

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 146.7, 139.7, 135.9, 134.3, 129.5, 128.3, 128.2, 127.5, 127.3, 122.3, 121.4, 114.7, 65.1, 64.5, 52.0, 49.7, 43.3, 37.2, 36.0, 30.0, 27.5; HRMS (ESI) calcd for $C_{24}H_{25}NNaO_2$ [M+Na$^+$], 382.1778; found: 382.1782.

*Methyl 1-Phenyl-2′,3′,5′,6′-tetrahydro-3H-spiro[cyclopenta[c]-chromene-2,4′-pyran]-3a(4H)-carboxylate (**3qa**).* (45 mg, 60%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:2, R_f = 0.2); IR (neat): ν_{max} 2951, 2936, 2847, 1734, 1607, 1479, 1464, 1450, 1310, 1230, 1217, 1196, 1153, 1125, 1105, 1044, 1020 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.37 (m, 4H), 7.11−7.00 (m, 2H), 6.83−6.80 (m, 1H), 6.62−6.15 (m, 2H), 4.91 (d, J = 12.0 Hz, 0.7H), 4.79 (d, J = 12.0 Hz, 0.3H), 4.26 (d, J = 12.0 Hz, 0.3H), 3.92 (d, J = 12.0 Hz, 0.7H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.79 (dd, J = 11.6, 3.6 Hz, 1H), 3.72 (s, 0.9H), 3.68 (s, 2.1H), 3.58 (td, J = 12.2, 1.8 Hz, 0.7H), 3.50−3.35 (m, 1.3H), 2.77 (d, J = 13.6 Hz, 0.7H), 2.32 (d, J = 13.8 Hz, 0.3H), 2.00−1.92 (m, 0.7H), 1.81−1.61 (m, 2H), 1.59−1.58 (m, 0.2H), 1.53−1.49 (m, 0.7H), 1.46−1.38 (m, 0.7H), 1.16−1.11 (m, 0.7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 174.5, 156.0, 153.8, 145.2, 136.3, 132.3, 129.8, 129.5, 129.2, 128.8, 128.7, 128.6, 128.5, 127.5, 127.4, 127.2, 126.4, 120.9, 120.6, 119.4, 119.2, 116.8, 116.7, 79.1, 74.2, 70.1, 67.1, 65.2, 64.9, 64.3, 63.9, 54.3, 52.5, 52.4, 51.8, 49.7, 45.9, 41.3, 37.3, 34.8, 33.4, 32.3, 31.2; HRMS (ESI) calcd for $C_{24}H_{24}NaO_4$ [M+Na$^+$], 399.1567; found: 399.1560.

*Trimethyl 1-Phenyl-2′,3′,5′,6′-tetrahydrospiro[cyclopenta[a]-naphthalene-2,4′-pyran]-3a,5,5(3H,4H)-tricarboxylate (**3ra**).* (45 mg, 46%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2951, 2845, 1732, 1433, 1387, 1287, 1240, 1196, 1142, 1104, 1018 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.32 (m, 4H), 7.13−7.09 (m, 3H), 6.90 (td, J = 7.8, 1.0 Hz, 1H), 6.80 (td, J = 8.0, 1.0 Hz, 1H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.80−3.79 (m, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.58 (td, J = 11.6, 3.6 Hz, 1H), 3.50 (s, 3H), 3.47 (td, J = 12.2, 1.8 Hz, 1H), 3.31 (d, J = 14.0 Hz, 1H), 2.94 (d, J = 14.0 Hz, 1H), 2.84 (d, J = 14.0 Hz, 1H), 2.03 (td, J = 12.6, 4.0 Hz, 1H), 1.97 (d, J = 14.0 Hz, 1H), 1.59 (td, J = 13.2, 4.8 Hz, 1H), 1.46 (dd, J = 13.6, 1.8 Hz, 1H), 1.14 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 171.5, 171.1, 146.6, 136.5, 133.3, 132.6, 131.7, 129.4, 129.2, 128.5, 127.9, 127.4, 127.3, 127.0, 65.2, 64.4, 59.1, 53.8, 53.3, 53.0, 52.2, 50.0, 46.4, 41.6, 37.2, 33.8; HRMS (ESI) calcd for $C_{29}H_{30}NaO_7$ [M+Na$^+$], 513.1884; found: 513.1871.

*Methyl 1′-Phenyl-5′-tosyl-4′,5′-dihydrospiro[cyclobutane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ab**).* (67 mg, 67%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5); IR (neat): ν_{max} 2928, 1732, 1597, 1495, 1479, 1458, 1352, 1238, 1167, 1090, 1072, 1049 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.4 Hz, 1H), 7.41−7.35 (m, 3H), 7.25 (d, J = 8.2 Hz, 2H), 7.09−7.07 (m, 2H), 6.95 (td, J = 1.6 Hz, 1H), 6.77 (dd, J = 8.0, 1.4 Hz, 1H), 6.63−6.60 (m, 1H), 5.04 (J = 12.2 Hz, 1H), 3.63 (s, 3H), 3.45 (J = 12.2 Hz, 1H), 2.88 (J = 13.0 Hz, 1H), 2.38 (s, 3H), 2.35−2.30 (m, 1H), 2.05 (J = 13.0 Hz, 1H), 2.09−1.97 (m, 2H), 1.86−1.77 (m, 1H), 1.73−1.66 (m, 1H), 1.50−1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 145.7, 143.7, 137.4, 137.0, 136.0, 129.9, 129.7, 128.7, 127.5, 127.4, 127.3, 127.1, 123.9, 123.1, 120.4, 55.8, 54.6, 54.5, 52.5, 49.0, 33.0, 31.5, 21.5, 16.4; HRMS (ESI) calcd for $C_{30}H_{29}NNaO_4S$ [M+Na$^+$], 522.1710; found: 522.1715.

*Methyl-1′-Phenyl-5′-tosyl-4′,5′-dihydrospiro[cyclopentane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ac**).* (52 mg, 51%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.5); IR (neat): ν_{max} 2953, 2868, 1730, 1352, 1228, 1161, 1138, 1121, 1072, 989, 951, 864, 814, 754, 662, 575 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.4 Hz, 2H), 7.48 (dd, J = 8.4, 0.8 Hz, 1H), 7.35−7.30 (m, 3H), 7.27 (d, J = 8.2 Hz, 2H), 7.00−6.93 (m, 3H), 6.71 (dd, J = 8.0, 1.6 Hz, 1H), 6.62 (td, J = 7.6, 1.0 Hz, 1H), 5.03 (d, J = 12.0 Hz, 1H), 3.64 (s, 3H), 3.46 (d, J = 12.0 Hz, 1H), 2.54 (d, J = 13.2 Hz, 1H), 2.40 (s, 3H), 1.80 (d, J = 13.2 Hz, 1H), 1.70−1.40 (m, 7H), 1.26−1.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 146.0, 143.6, 137.3, 136.8, 135.7, 130.1, 129.6, 129.0, 128.4, 127.6, 127.3, 127.2, 127.0, 124.0, 123.0, 120.2, 59.1, 55.7, 55.3, 52.4, 48.2, 38.2, 36.4, 30.0, 25.8, 24.0, 23.9, 21.5; HRMS (ESI) calcd for $C_{31}H_{31}NNaO_4S$ [M+Na$^+$], 536.1866; found: 536.1875.

*Methyl-1′-Phenyl-5′-tosyl-4′,5′-dihydrospiro[cyclohexane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ad**).* (65 mg, 62%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.5); IR (neat): ν_{max} 2928, 2857, 1734, 1599, 1481, 1449, 1354, 1225, 1167, 1090, 1047, 916, 870, 814, 752, 704, 662, 575, 542 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 2H), 7.48 (dd, J = 8.4, 0.6 Hz, 1H), 7.35−7.31 (m, 3H), 7.27 (d, J = 8.4 Hz, 2H), 6.97−6.93 (m, 3H), 6.65 (dd, J = 8.0, 1.6 Hz, 1H), 6.59 (td, J = 7.6, 1.0 Hz, 1H), 5.05 (d, J = 12.0 Hz, 1H), 3.62 (s, 3H), 3.44 (d, J = 12.0 Hz, 1H), 2.72 (d, J = 13.6 Hz, 1H), 2.40 (s, 3H), 1.75 (d, J = 13.6 Hz, 1H), 1.68−1.59 (m, 3H), 1.58−1.51 (m, 2H), 1.33−1.24 (m, 2H), 1.19−1.18 (m, 2H), 0.97−0.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 146.0, 143.6, 137.3, 136.8, 135.7, 130.1, 129.6, 129.0, 128.4, 127.6, 127.3, 127.2, 127.0, 124.0, 123.0, 120.2, 59.1, 55.7, 55.3, 52.4, 48.2, 38.2, 36.4, 30.0, 25.8, 24.0, 23.9, 21.5; HRMS (ESI) calcd for $C_{32}H_{33}NNaO_4S$ [M+Na$^+$], 550.2023; found: 550.2032.

*Methyl 1′-Phenyl-5′-tosyl-4′,5′-dihydrospiro[cyclododecane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ae**).* (88 mg, 72%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.6); IR (neat): ν_{max} 3042, 2945, 2857, 1734, 1599, 1470, 1458, 1354, 1238, 1219, 1169, 1092, 1044, 1034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.6 Hz, 1H), 7.30−7.26 (m, 5H), 6.99−6.95 (m, 3H), 6.64−6.57 (m, 2H), 4.94 (d, J = 12.0 Hz, 1H), 3.62 (s, 3H), 3.48 (J = 12.0 Hz, 1H), 2.61 (J = 13.4 Hz, 1H), 2.40 (s, 3H), 1.90−1.83 (m, 1H), 1.66 (J = 13.4 Hz, 1H), 1.67−1.61 (m, 1H), 1.44−1.11 (m, 20 H), 0.98−0.87 (m, 1H), 0.58−0.55 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 148.6, 143.7, 138.0, 137.1, 136.0, 130.1, 129.7, 129.0, 128.4, 127.9, 127.3, 127.2, 127.1, 124.9, 123.2, 120.9, 55.9, 55.5, 54.9, 52.5, 46.3, 37.2, 33.8, 27.4, 27.3, 26.2, 23.4, 23.3, 23.2, 23.0, 21.6, 20.8, 19.9; HRMS (ESI) calcd for $C_{38}H_{45}NNaO_4S$ [M+Na$^+$], 634.2962; found: 634.2962.

*Methyl (1S,2R,4R)-1′-Phenyl-5′-tosyl-4′,5′-dihydrospiro[bicyclo-[2.2.1]heptane-2,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3af**).* (57 mg, 53%, dr = 1.4:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.6); IR (neat): ν_{max} 2949, 2930, 1734, 1356, 1169, 1090, 1053 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.72 (m, 1.5H), 7.65−7.57 (m, 2H), 7.45−7.35 (m, 3H), 7.18−6.92 (m, 4H), 6.75−6.45 (m, 2H), 6.04 (br, 0.5H), 5.05−4.84 (m, 1H), 3.70−3.58 (m, 3H), 3.54−3.40 (m, 1H), 2.75−2.46 (m, 1H), 2.40−2.28 (m, 3H), 2.07−1.89 (m, 3H), 1.72−1.08 (m, 6H), 0.93−0.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 174.5, 148.1, 146.8, 143.6, 138.4, 137.9, 137.3, 136.2, 136.0, 135.9, 130.8, 129.7, 129.6, 128.1, 127.2, 127.1, 127.0, 125.8, 123.6, 123.0, 121.9, 120.1, 57.1, 56.3, 56.2, 55.5, 54.9, 54.3, 52.5, 52.4, 48.0, 46.1, 45.7, 44.5, 43.2, 38.4, 37.9, 37.2, 37.0, 28.2, 26.6, 25.2, 21.5; HRMS (ESI) calcd for $C_{33}H_{33}NNaO_4S$ [M+Na$^+$], 562.2023; found: 562.2005.

*Methyl (1R,3S,5r,7r)-1′-Phenyl-5′-tosyl-4′,5′-dihydrospiro-[adamantane-2,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ag**).* (75 mg, 65%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.7); IR (neat): ν_{max} 2947, 2901, 2860, 1722, 1597, 1477, 1454, 1352, 1337, 1261, 1232, 1225, 1159, 1092, 1078, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 7.6 Hz, 1H), 7.40−7.37 (m, 2H), 7.29−7.26 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 6.94 (td, J = 7.8, 1.2 Hz, 1H), 6.72 (d, J = 1.2 Hz, 1H), 6.62−6.58 (m, 2H), 4.72 (d, J = 12.4 Hz, 1H), 3.65 (s, 3H), 3.53 (d, J = 12.4 Hz, 1H), 3.18 (d, J = 12.8 Hz, 1H), 2.41 (s, 3H), 2.37−2.33 (m, 1H), 2.24−2.20 (m, 1H), 2.02−1.98 (m, 2H), 1.83 (br, 1H), 1.78 (d, J = 12.8 Hz, 1H), 1.65−1.51 (m, 7H), 1.26−2.22 (m, 1H), 1.14−1.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 150.1, 143.6, 140.9, 137.8, 136.3, 132.9, 131.0, 129.7, 128.5, 127.7, 127.1, 126.9, 125.7, 123.3, 120.8, 57.3, 55.5, 55.0, 52.4, 47.8, 39.1, 37.6, 36.7, 36.4, 34.7, 33.5, 32.8, 27.1, 21.5; HRMS (ESI) calcd for $C_{36}H_{37}NNaO_4S$ [M+Na$^+$], 602.2336; found: 602.2322.

*Methyl 1′-Phenyl-5′-tosyl-4′,5′-dihydro-3H-spiro[benzo[b][1,4]-dioxine-2,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ah**).* (93 mg, 80%, dr = 1.3:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 2949, 2928, 1732, 1595, 1493, 1454, 1354, 1258, 1163, 1045, 916 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 12.2 Hz, 1.4H), 7.72 (d, J = 12.2 Hz, 0.6H), 7.63 (d, J = 7.6 Hz, 0.3H), 7.56 (dd, J = 8.4, 0.6 Hz,

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

0.7H), 7.35−7.27 (m, 5H), 7.20−7.15 (m, 2H), 7.13−7.04 (m, 1H), 6.98−6.66 (m, 6H), 5.15 (d, J = 12.0 Hz, 0.7H), 4.99 (d, J = 12.0 Hz, 0.3H), 4.30 (d, J = 11.0 Hz, 0.7H), 4.03 (d, J = 11.0 Hz, 0.3H), 4.02 (d, J = 11.0 Hz, 0.3H), 3.73 (d, J = 11.0 Hz, 0.7H), 3.72 (s, 2.1H), 3.59 (s, 0.9H), 3.58 (d, J = 12.0 Hz, 0.7H), 3.57 (d, J = 12.0 Hz, 0.3H), 2.97 (d, J = 14.2 Hz, 0.7H), 2.75 (d, J = 14.2 Hz, 0.3H), 2.43 (s, 2.1H), 2.40 (s, 0.9H), 2.16 (d, J = 14.2 Hz, 0.3H), 2.11 (d, J = 14.2, 1.5 Hz, 0.7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 173.0, 144.1, 144.0, 142.7, 142.6, 142.4, 138.0, 137.8, 136.9, 136.6, 136.5, 136.4, 135.3, 133.9, 133.6, 129.8, 129.7, 129.4, 129.1, 129.0, 128.7, 128.5, 128.4, 128.2, 128.0, 127.2, 127.0, 123.4, 123.1, 122.9, 121.9, 121.8, 121.7, 121.4, 121.1, 121.0, 119.9, 118.0, 117.5, 117.0, 116.9, 86.7, 86.4, 70.2, 68.3, 55.1, 54.9, 54.5, 54.3, 52.9, 52.6, 43.1, 42.8, 21.5; HRMS (ESI) calcd for $C_{34}H_{29}NNaO_6S$ [M+Na$^+$], 602.1608; found: 602.1599.

*Methyl 1-Phenyl-5-tosyl-4,4′,5,5′-tetrahydro-3′H-spiro-[cyclopenta[c]quinoline-2,2′-furan]-3a(3H)-carboxylate (**3ai**).* (69 mg, 67%, dr =2.6:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 3053, 2949, 2922, 2853, 1732, 1479, 1456, 1352, 1229, 1209, 1167, 1090, 1304 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.4 Hz, 1H), 7.28−7.25 (m, 5H), 7.07−7.03 (m, 3H), 6.81 (dd, J = 7.8, 1.4 Hz, 1H), 6.72 (td, J = 7.8, 0.8 Hz, 1H), 4.99 (d, J = 12.0 Hz, 1H), 3.83−3.78 (m, 2H), 3.58 (s, 3H), 3.47 (d, J = 12.0 Hz, 1H), 2.72 (d, J = 14.0 Hz, 1H), 2.39 (s, 3H), 1.96 (d, J = 14.0 Hz, 1H), 1.87−1.78 (m, 1H), 1.76−1.68 (m, 1H), 1.65−1.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 143.9, 140.2, 136.7, 136.2, 135.3, 134.0, 129.7, 128.9, 128.6, 128.3, 128.2, 127.5, 127.2, 123.9, 123.2, 120.8, 94.6, 68.1, 55.4, 54.8, 52.6, 48.0, 35.7, 26.6, 21.5; HRMS (ESI) calcd for $C_{30}H_{29}NNaO_5S$ [M+Na$^+$], 538.1659; found: 538.1644.

*Methyl 1-Phenyl-5-tosyl-4,4′,5,5′-tetrahydro-2′H-spiro-[cyclopenta[c]quinoline-2,3′-furan]-3a(3H)-carboxylate (**3aj**).* (46 mg, 45%, dr = 1.2:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3); IR (neat): ν_{max} 2951, 2928, 2866, 1732, 1599, 1481, 1458, 1352, 1244, 1161, 1092, 1076, 1047 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.69 (m, 2H), 7.51−7.47 (m, 1H), 7.38−7.34 (m, 3H), 7.29−7.27 (m, 2H), 7.05−6.97 (m, 3H), 6.76−6.72 (m, 1H), 6.67−6.21 (m, 1H), 5.08 (d, J = 12.2 Hz, 0.62H), 5.03 (d, J = 12.2 Hz, 0.38H), 3.88−3.76 (m, 3H), 3.66 (s, 3H), 3.59−3.55 (m, 0.62H), 3.52−3.48 (m, 1H), 3.40−3.38 (m, 0.38H), 2.78 (d, J = 13.4 Hz, 0.62H), 2.67 (d, J = 13.4 Hz, 0.38H), 2.41 (s, 3H), 2.26−2.19 (m, 0.38H), 2.03−1.87 (m, 2H), 1.60−1.54 (m, 0.62H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 174.2, 143.8, 142.0, 137.2, 136.0, 135.9, 135.7, 132.3, 132.1, 129.7, 128.9, 128.7, 128.0, 127.9, 127.8, 127.7, 127.6, 127.1, 127.0, 123.6, 123.2, 123.1, 123.0, 120.6, 120.1, 76.6, 75.9, 67.9, 67.7, 58.9, 58.6, 55.9, 55.6, 55.0, 52.6, 47.6, 47.2, 37.7, 37.4, 21.5; HRMS (ESI) calcd for $C_{30}H_{29}NNaO_5S$ [M+Na$^+$], 538.1659; found: 538.1654.

*1′-Benzyl 3a-Methyl 1-Phenyl-5-tosyl-4,5-dihydrospiro-[cyclopenta[c]quinoline-2,2′-pyrrolidine]-1′,3a(3H)-dicarboxylate (**3ak**).* (65 mg, 50%, dr = 1.8:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.4); IR (neat): ν_{max} 3059, 3032, 2951, 2924, 1734, 1695, 1599, 1481, 1456, 1404, 1352, 1217, 1188, 1169, 1093, 1059 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 1.36H), 7.64 (d, J = 8.4 Hz, 0.64H), 7.39−7.11 (m, 12H), 7.01−6.77 (m, 3H), 6.66−6.53 (m, 1H), 5.20 (d, J = 12.8 Hz, 0.64H), 5.12 (d, J = 12.0 Hz, 0.64H), 5.11 (d, J = 12.8 Hz, 0.36H), 5.04 (d, J = 12.0 Hz, 0.36H), 4.94 (d, J = 12.8 Hz, 0.64H), 4.81 (d, J = 12.0 Hz, 0.36H), 3.78 (d, J = 12.0 Hz, 0.64H), 3.70 (s, 2H), 3.68 (s, 1H), 3.62−3.50 (m, 1H), 3.00−2.89 (m, 1H), 2.88 (d, J = 12.8 Hz, 0.64H), 2.61 (d, J = 12.0 Hz, 0.36H), 2.54 (d, J = 12.8 Hz, 0.36H), 2.46−2.40 (m, 2H), 2.35 (s, 2H), 2.35−2.17 (m, 1H), 2.10−1.95 (m, 1H), 1.77−1.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 174.3, 154.2, 153.6, 143.6, 143.5, 141.8, 141.4, 138.3, 137.8, 137.1, 136.1, 135.5, 135.3, 131.4, 130.4, 129.7, 129.4, 129.1, 129.0, 128.4, 128.2, 128.1, 128.0, 127.6, 127.5, 127.4, 127.3, 126.9, 126.8, 122.5, 122.4, 122.3, 119.3, 119.2, 76.5, 75.9, 67.4, 65.9, 54.0, 53.8, 52.6, 52.5, 52.0, 48.5, 47.8, 44.4, 43.5, 38.5, 38.4, 23.1, 22.6, 21.5; HRMS (ESI) calcd for $C_{38}H_{36}N_2NaO_6S$ [M+Na$^+$], 671.2186; found: 671.2168.

*Methyl 5′-oxo-1-Phenyl-5-tosyl-4,5-dihydrospiro[cyclopenta[c]-quinoline-2,2′-pyrrolidine]-3a(3H)-carboxylate (**3al**).* (63 mg, 60%, dr = 1.6:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.2); IR (neat): ν_{max} 2951, 1732, 1694, 1682, 1447, 1237, 1207, 1184, 1161, 1098, 1026, 1013, 1003 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.70 (m, 2H), 7.50−7.47 (m, 0.7H), 7.39−7.26 (m, 5.5H), 7.17−6.89 (m, 3.5 H), 6.73−6.59 (m, 2.3H), 5.13−5.07 (m, 1H), 3.70−3.64 (m, 3H), 3.51−3.39 (m, 1H), 2.81−2.67 (m, 1H), 2.39 (s, 3H), 2.29−1.89 (m, 4.3H), 1.75−1.66 (m, 0.7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 176.7, 173.8, 173.7, 144.0, 143.9, 142.0, 140.8, 137.6, 136.9, 136.4, 134.7, 134.4, 133.2, 131.7, 129.9, 129.8, 129.1, 129.0, 128.9, 128.4, 128.3, 128.2, 127.6, 127.1, 126.8, 123.0, 122.9, 122.1, 121.6, 120.2, 119.8, 72.6, 54.4, 54.1, 54.0, 53.8, 53.1, 52.8, 49.2, 48.0, 32.4, 32.0, 30.4, 30.2, 21.5; HRMS (ESI) calcd for $C_{30}H_{28}N_2NaO_5S$ [M+Na$^+$], 551.1611; found: 551.1602.

*Methyl 2-Benzyl-2-(((benzyloxy)carbonyl)amino)-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**3am**).* (85 mg, 61%, dr = 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3); IR (neat): ν_{max} 2963, 2843, 1728, 1493, 1481, 1450, 1441, 1350, 1237, 1163, 1090 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 12.2 Hz, 2H), 7.43 (d, J = 7.6 Hz, 1H), 7.36−7.27 (m, 10H), 7.25−7.14 (m, 7H), 6.97 (t, J = 7.6 Hz, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.59 (t, J = 7.6 Hz, 1H), 5.12 (d, J = 12.0 Hz, 2H), 4.84 (s, 1H), 4.77 (d, J = 12.2 Hz, 1H), 3.84 (d, J = 12.2 Hz, 1H), 3.75 (s, 3H), 3.16 (d, J = 14.0 Hz, 1H), 3.03 (d, J = 14.0 Hz, 1H), 2.91 (d, J = 14.0 Hz, 1H), 2.63 (d, J = 14.0 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 154.5, 143.6, 141.8, 137.7, 136.5, 136.4, 135.7, 135.3, 132.6, 130.4, 129.8, 129.4, 128.9, 128.7, 128.5, 128.1, 128.0, 127.9, 127.8, 127.3, 127.0, 122.4, 122.3, 119.3, 69.5, 66.0, 53.8, 53.6, 52.6, 43.9, 38.7, 21.5; HRMS (ESI) calcd for $C_{42}H_{38}N_2NaO_6S$ [M+Na$^+$], 721.2343; found: 721.2348.

*Methyl 1-Phenyl-1′,5-ditosyl-4,5-dihydrospiro[cyclopenta[c]-quinoline-2,4′-piperidine]-3a(3H)-carboxylate (**3an**).* (91 mg, 67%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:3, R_f = 0.2); IR (neat): ν_{max} 2949, 2928, 2851, 1734, 1477, 1350, 1248, 1167, 1092 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.4 Hz, 1H), 7.35−7.32 (m, 3H), 7.32 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 6.70 (td, J = 7.8, 1.8 Hz, 1H), 6.92−6.89 (m, 2H), 6.66 (dd, J = 8.0, 1.6 Hz, 1H), 6.61 (td, J = 7.6, 0.8 Hz, 1H), 4.95 (d, J = 12.0 Hz, 1H), 3.76 (d, J = 11.8 Hz, 1H), 3.66 (d, J = 11.8 Hz, 1H), 3.58 (s, 3H), 3.36 (d, J = 12.0 Hz, 1H), 2.49 (d, J = 13.6 Hz, 1H), 2.45 (s, 3H), 2.40 (s, 3H), 2.35 (td, J = 12.0, 2.0 Hz, 1H), 2.23 (td, J = 12.0, 2.0 Hz, 1H), 1.94 (td, J = 12.8, 4.4 Hz, 1H), 1.64 (dd, J = 13.4, 2.0 Hz, 1H), 1.57−1.53 (m, 2H), 1.17 (dd, J = 13.4, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 145.7, 143.8, 143.6, 137.1, 135.8, 135.4, 132.8, 130.9, 129.7, 128.9, 128.7, 127.8, 127.7, 127.6, 127.5, 126.9, 123.4, 123.0, 120.2, 55.5, 55.3, 52.6, 49.8, 43.6, 42.8, 42.2, 35.8, 32.6, 21.5, 21.4; HRMS (ESI) calcd for $C_{38}H_{38}N_2NaO_6S_2$ [M+Na$^+$], 705.2063; found: 705.2061.

*Methyl-4,4-dimethyl-1″-phenyl-5′-tosyl-4′,5′-dihydrospiro-[cyclohexane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ao**).* (74 mg, 60%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.5); IR (neat): ν_{max} 2947, 2926, 2907, 2863, 1732, 1599, 1479, 1456, 1352, 1229, 1169, 1090, 917, 887, 864, 812, 754, 704, 662, 575 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 2H), 7.48 (dd, J = 8.4, 0.6 Hz, 1H), 7.35−7.30 (m, 3H), 7.26 (d, J = 8.4 Hz, 2H), 6.97−6.93 (m, 3H), 6.71 (dd, J = 8.0, 1.6 Hz, 1H), 6.62 (td, J = 7.6, 1.0 Hz, 1H), 5.03 (d, J = 12.0 Hz, 1H), 3.62 (s, 3H), 3.43 (d, J = 12.0 Hz, 1H), 2.72 (d, J = 13.6 Hz, 1H), 2.40 (s, 3H), 1.80−1.72 (m, 1H), 1.70 (d, J = 13.6 Hz, 1H), 1.48−1.44 (m, 1H), 1.38−1.20 (m, 5H), 0.98−0.96 (m, 1H), 0.88 (s, 3H), 0.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 148.0, 143.6, 137.2, 136.8, 135.8, 129.8, 129.7, 128.9, 128.4, 127.9, 127.3, 127.2, 127.0, 124.0, 122.9, 120.2, 55.9, 55.3, 52.4, 52.2, 43.2, 36.1, 35.2, 33.0, 32.9, 29.8, 29.1, 23.6, 21.5; HRMS (ESI) calcd for $C_{34}H_{37}NNaO_4S$ [M+Na$^+$], 578.2336; found: 578.2342.

*Methyl 4,4-Difluoro-1′-phenyl-5′-tosyl-4′,5′-dihydrospiro-[cyclohexane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3ap**).* (68 mg, 60%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5); IR (neat): ν_{max} 2965, 2841, 1730, 1494, 1453, 1442, 1352, 1238, 1165 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 12.2 Hz, 2H), 7.46 (d, J = 8.4 Hz, 1H), 7.36−7.33

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

(m, 3H), 7.29 (d, J = 12.2 Hz, 2H), 7.00−6.95 (m, 3H), 6.67 (dd, J = 7.8, 1.6 Hz, 1H), 6.62 (td, J = 7.6, 0.8 Hz, 1H), 5.05 (d, J = 12.2 Hz, 1H), 3.65 (s, 3H), 3.46 (d, J = 12.2 Hz, 1H), 2.79 (d, J = 13.4 Hz, 1H), 2.41 (s, 3H), 2.13−2.05 (m, 1H), 2.00−1.91 (m, 2H), 1.89−1.85 (m, 1H), 1.79−1.67 (m, 3H), 1.50−1.42 (m, 1H), 1.27−1.22 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 145.9, 143.8, 137.3, 135.9, 135.8, 130.8, 129.7, 128.8, 128.7, 127.9, 127.7, 127.6, 122.5 (m, J_{C-F} = 240.0 Hz), 126.9, 123.5, 123.0, 120.2, 55.5, 55.3, 52.6, 50.8, 42.3, 33.4 (d, J_{C-F} = 9.6 Hz), 31.2 (t, J_{C-F} = 24.0 Hz), 30.5 (t, J_{C-F} = 24.0 Hz), 30.1 (d, J_{C-F} = 9.6 Hz), 21.5; HRMS (ESI) calcd for $C_{32}H_{31}F_2NNaO_4S$ [M+Na$^+$], 586.1834; found: 586.1830.

*Methyl-4-oxo-1′-phenyl-5′-tosyl-4′,5′-dihydrospiro[cyclohexane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3aq**).* (63 mg, 53%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.4); IR (neat): ν_{max} 2951, 2932, 2864, 1730, 1718, 1458, 1352, 1227, 1161, 1090, 1074, 1051, 914, 870, 812, 663, 570, 540 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4 Hz, 2H), 7.46 (dd, J = 8.4, 0.6 Hz, 1H), 7.37−7.34 (m, 3H), 7.30 (d, J = 8.4 Hz, 2H), 7.02−6.97 (m, 3H), 6.70 (dd, J = 8.0, 1.6 Hz, 1H), 6.63 (td, J = 7.6, 1.0 Hz, 1H), 5.09 (d, J = 12.2 Hz, 1H), 3.67 (s, 3H), 3.52 (d, J = 12.2 Hz, 1H), 3.03 (d, J = 13.4 Hz, 1H), 2.59−2.50 (m, 1H), 2.42 (s, 3H), 2.42−2.36 (m, 2H), 2.27−2.24 (m, 1H), 2.05−2.01 (m, 2H), 1.97 (d, J = 13.4 Hz, 1H), 1.64−1.52 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.2, 174.4, 145.5, 143.8, 137.4, 136.0, 135.8, 130.9, 129.8, 128.8, 128.7, 127.9, 127.8, 127.7, 126.9, 123.4, 123.1, 120.2, 55.5, 52.7, 51.0, 42.6, 38.6, 37.9, 37.0, 33.6, 21.5; HRMS (ESI) calcd for $C_{32}H_{31}NNaO_5S$ [M+Na$^+$], 564.1815; found: 564.1800.

*Dimethyl 1′-Phenyl-5′-tosyl-4′,5′-dihydrospiro[cyclohexane-1,2′-cyclopenta[c]quinoline]-3a′,4(3′H)-dicarboxylate (**3ar**).* (76 mg, 65%, dr = 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.4); IR (neat): ν_{max} 2949, 2922, 2857, 1730, 1479, 1441, 1352, 1238, 1167, 1090, 1049 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.67 (m, 2H), 7.60−7.46 (m, 1H), 7.36−7.26 (m, 5H), 6.98−6.91 (m, 3H), 6.67−6.58 (m, 2H), 5.05 (d, J = 12.0 Hz, 0.5H), 5.03 (d, J = 12.0 Hz, 0.5H), 3.64 (s, 1.5H), 3.63 (s, 1.5H), 3.62 (s, 1.5H), 3.51 (s, 1.5H), 3.44 (d, J = 12.0 Hz, 0.5H), 3.43 (d, J = 12.0 Hz, 0.5H), 2.75 (d, J = 13.6 Hz, 0.5H), 2.73 (d, J = 13.6 Hz, 0.5H), 2.58 (br, 0.5H), 2.41 (s, 3H), 2.15−1.93 (m, 2H), 1.84−1.65 (m, 3.5H), 1.61−1.46 (m, 2H), 1.29−1.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 174.9, 174.8, 174.6, 147.6, 147.1, 143.7, 137.2, 137.1, 136.4, 136.3, 135.8, 130.3, 129.9, 129.7, 129.0, 128.8, 128.5, 128.3, 127.9, 127.8, 127.5, 127.4, 127.3, 127.0, 123.9, 123.6, 123.0, 122.9, 120.2, 120.1, 55.8, 55.6, 55.3, 52.5, 51.7, 51.5, 51.3, 43.2, 43.1, 42.0, 37.9, 36.1, 33.4, 32.7, 30.2, 25.8, 24.9, 24.0, 23.5, 21.5; HRMS (ESI) calcd for $C_{34}H_{35}NNaO_6S$ [M+Na$^+$], 608.2077; found: 608.2066.

*Methyl 4-Pentyl-1′-phenyl-5′-tosyl-4′,5′-dihydrospiro-[cyclohexane-1,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**3as**).* (84 mg, 70%, dr = 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.6); IR (neat): ν_{max} 3055, 3028, 2920, 2853, 1732, 1599, 1574, 1479, 1454, 1356, 1307, 1227, 1163, 1090, 1074, 1051, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.4 Hz, 1H), 7.35−7.30 (m, 3H), 7.28 (d, J = 8.2 Hz, 2H), 6.98−6.93 (m, 3H), 6.70 (dt, J = 7.8, 1.8 Hz, 1H), 6.60 (t, J = 7.4 Hz, 1H), 5.04 (d, J = 12.0 Hz, 0.5H), 5.03 (d, J = 12.0 Hz, 0.5H), 3.62 (s, 3H), 3.44 (d, J = 12.0 Hz, 1H), 2.76 (d, J = 13.6 Hz, 0.5H), 2.68 (d, J = 13.6 Hz, 0.5H), 2.40 (s, 3H), 1.76−1.50 (m, 6H), 1.40−1.05 (m, 12H), 0.85 (t, J = 7.2 Hz, 1.5H), 0.83 (t, J = 7.2 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 148.2, 148.0, 143.6, 137.2, 136.9, 136.7, 135.8, 129.7, 129.6, 129.1, 128.9, 128.4, 128.3, 127.9, 127.8, 127.3, 127.2, 127.0, 124.1, 122.9, 120.2, 55.9, 55.8, 55.4, 55.3, 52.4, 43.8, 43.4, 37.1, 37.0, 36.5, 33.9, 32.0, 31.8, 31.6, 31.5, 30.3, 30.0, 29.1, 28.8, 27.4, 26.8, 26.4, 26.0, 22.6, 22.5, 21.5, 14.0; HRMS (ESI) calcd for $C_{37}H_{43}NNaO_4S$ [M+Na$^+$], 620.2805; found: 620.2797.

*Methyl 2-(4-Isopropylbenzyl)-2-methyl-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**3at**).* (73 mg, 60%, dr = 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.5); IR (neat): ν_{max} 3053, 3007, 2959, 2926, 2870, 1734, 1599, 1479, 1458, 1242, 1163, 1092, 1074, 1049 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 12.2 Hz, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.40−7.35 (m, 3H), 7.29−7.26 (m, 2H), 7.14−6.96 (m, 7H), 6.77−6.70 (m, 1H), 6.65−6.61 (m, 1H), 5.07−5.01 (m, 1H), 3.73 (s, 2H), 3.58 (s, 1H), 3.52−3.40 (m, 1H), 2.90−2.75 (m, 3H), 2.40 (s, 3H), 2.43−2.36 (m, 1H), 1.26−1.23 (m, 8H), 0.84 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 148.1, 147.7, 146.8, 146.7, 143.8, 137.5, 137.3, 136.8, 136.7, 136.0, 135.5, 135.2, 130.7, 130.2, 129.8, 129.1, 129.0, 128.7, 128.0, 127.9, 127.6, 127.5, 127.1, 127.0, 126.1, 124.1, 123.7, 123.1, 123.0, 120.3, 120.0, 55.8, 55.4, 52.5, 52.4, 52.1, 46.4, 46.3, 43.7, 33.7, 25.9, 24.9, 24.1, 21.6; HRMS (ESI) calcd for $C_{38}H_{39}NNaO_4S$ [M+Na$^+$], 628.2492; found: 628.2491.

*Methyl-2,2-dimethyl-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**3au**).* (54 mg, 55%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.5); IR (neat): ν_{max} 2955, 2926, 1728, 1599, 1480, 1458, 1355, 1250, 1140, 1120, 1070 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.49 (d, J = 8.4 Hz, 1H), 7.35−7.30 (m, 3H), 7.27 (d, J = 8.2 Hz, 2H), 7.00−6.95 (m, 3H), 6.71 (dd, J = 7.8, 1.4 Hz, 1H), 6.62 (t, J = 7.6 Hz, 1H), 5.03 (d, J = 12.0 Hz, 1H), 3.64 (s, 3H), 3.45 (d, J = 12.0 Hz, 1H), 2.49 (d, J = 13.4 Hz, 1H), 2.40 (s, 3H), 1.88 (d, J = 13.4 Hz, 1H), 1.26 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 147.6, 143.7, 137.2, 136.7, 135.9, 129.7, 129.3, 128.7, 128.4, 127.7, 127.4, 127.2, 127.0, 124.0, 122.9, 120.2, 55.7, 55.4, 52.4, 49.0, 48.1, 28.6, 27.5, 21.5; HRMS (ESI) calcd for $C_{29}H_{29}NNaO_4S$ [M+Na$^+$], 510.1710; found: 510.1716.

*Methyl 2-Phenethyl-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**3av**).* (53 mg, 47%, dr = 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5); IR (neat): ν_{max} 2960, 2945, 2926, 1734, 1599, 1477, 1456, 1352, 1236, 1167, 1090, 1072, 1045 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.49 (m, 3H), 7.35−7.27 (m, 3H), 7.26−7.16 (m, 4H), 7.13−6.91 (m, 6H), 6.81−6.67 (m, 2H), 5.03 (d, J = 12.0 Hz, 0.3H), 4.85 (d, J = 12.0 Hz, 0.7H), 3.73−3.56 (m, 4H), 3.45 (d, J = 12.0 Hz, 1H), 2.85−2.70 (m, 1.4 H), 2.53−2.45 (m, 0.6H), 2.42−2.38 (m, 2.4H), 2.26 (s, 1.6H), 2.20−1.91 (m, 1H), 1.77−1.66 (m, 1.4H), 1.24−1.16 (m, 0.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 174.2, 143.8, 143.7, 142.8, 141.9, 141.8, 137.5, 137.2, 136.4, 136.2, 135.8, 135.7, 130.5, 130.3, 129.8, 129.6, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.6, 127.5, 127.2, 126.9, 125.9, 125.8, 124.0, 123.1, 123.0, 120.5, 58.4, 57.5, 55.9, 55.0, 52.6, 52.5, 50.5, 47.5, 40.7, 37.5, 35.5, 34.8, 34.3, 32.9, 21.5, 21.4; HRMS (ESI) calcd for $C_{35}H_{33}NNaO_4S$ [M+Na$^+$], 586.2023; found: 586.2019.

*Methyl 1-Phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]-quinoline-3a-carboxylate (**3aw**).* (27 mg, 30%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.4); IR (neat): ν_{max} 2955, 2872, 1734, 1594, 1480, 1462, 1368, 1240, 1172, 1072 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65−7.62 (m, 3H), 7.23−7.22 (m, 3H), 7.16−7.10 (m, 3H), 7.09−7.07 (m, 3H), 6.85−6.82 (m, 1H), 4.75 (d, J = 12.6 Hz, 1H), 3.75 (d, J = 12.6 Hz, 1H), 3.55 (s, 3H), 3.23−3.18 (m, 1H), 2.55−2.48 (m, 2H), 2.26 (s, 3H), 1.96−1.91 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.2, 143.6, 138.8, 136.7, 136.4, 130.1, 129.6, 128.2, 128.1, 127.6, 127.5, 127.2, 126.5, 124.1, 123.3, 60.7, 55.7, 52.3, 37.1, 34.4, 21.4; HRMS (ESI) calcd for $C_{27}H_{25}NNaO_4S$ [M+Na$^+$], 482.1397; found: 482.1399.

*Methyl (Z)-2-(Hexadec-7-en-1-yl)-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**4**).* (75 mg, 55%, dr = 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.8); IR (neat): ν_{max} 2924, 2853, 1732, 1599, 1352, 1167, 1090, 1072 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.4 Hz, 1H), 7.50 (dd, J = 8.4, 1.0 Hz, 1H), 7.40−7.22 (m, 10H), 7.09−7.05 (m, 3H), 7.01−6.98 (m, 2H), 6.92−6.90 (m, 2H), 6.79−6.66 (m, 3H), 5.38−5.29 (m, 4H), 5.00 (d, J = 12.0 Hz, 1H), 4.83 (d, J = 12.0 Hz, 1H), 3.68 (d, J = 12.2 Hz, 1H), 3.64 (s, 3H), 3.56 (s, 3H), 3.42 (d, J = 12.2 Hz, 1H), 3.38−3.30 (m, 1H), 2.77−2.68 (m, 2H), 2.43−2.33 (m, 1H), 2.39 (s, 3H), 2.35 (s, 3H), 2.17−2.11 (m, 1H), 2.02−1.95 (m, 8H), 1.57−1.52 (m, 2H), 1.40−1.14 (m, 47H), 0.90−0.85 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 174.3, 144.2, 143.7, 143.6, 137.8, 137.2, 136.7, 136.3, 136.1, 135.8, 130.2, 130.0, 129.7, 129.6, 128.5, 128.4, 128.3, 128.1, 127.9, 127.6, 127.5, 127.4, 127.3, 127.0, 125.8, 124.2, 123.9, 123.1, 122.7, 120.4, 58.2, 57.4, 55.9, 55.2, 52.5, 52.4,

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

51.0, 47.9, 41.0, 37.7, 33.6, 33.1, 31.9, 29.8, 29.7, 29.5, 29.3, 29.2, 28.1, 27.2, 27.1, 26.8, 22.7, 21.5, 14.1; HRMS (ESI) calcd for $C_{43}H_{55}NNaO_4S$ [M+Na$^+$], 704.3744; found: 704.3748.

*Methyl (E)-2-(Hexadec-7-en-1-yl)-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**4′**).* (57 mg, 42%, dr 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.8); IR (neat): ν_{max} 2951, 2926, 2851, 1732, 1479, 1352, 1238, 1161, 1090, 1072, 1049 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.4 Hz, 1H), 7.50 (dd, J = 8.4, 1.0 Hz, 1H), 7.35−7.25 (m, 10H), 7.09−7.05 (m, 3H), 7.01−6.97 (m, 2H), 6.92−6.90 (m, 2H), 6.79−6.75 (m, 2H), 6.67 (td, J = 7.6, 0.8 Hz, 1H), 5.38−5.35 (m, 4H), 5.00 (d, J = 12.0 Hz, 1H), 4.83 (d, J = 12.0 Hz, 1H), 3.68 (d, J = 12.2 Hz, 1H), 3.64 (s, 3H), 3.55 (s, 3H), 3.42 (d, J = 12.2 Hz, 1H), 3.38−3.30 (m, 1H), 2.77−2.67 (m, 2H), 2.39 (s, 3H), 2.37−2.33 (m, 1H), 2.35 (s, 3H), 2.17−2.11 (m, 1H), 1.61−0.86 (m, 57H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 174.3, 144.1, 143.6, 143.4, 137.8, 137.2, 136.7, 136.2, 136.1, 135.8, 130.4, 130.1, 129.9, 129.7, 129.6, 128.5, 128.4, 128.3, 128.0, 127.8, 127.5, 127.4, 127.3, 127.2, 127.0, 125.8, 124.1, 123.8, 123.0, 122.7, 120.4, 58.1, 57.3, 55.9, 55.1, 52.4, 50.9, 47.8, 40.9, 37.7, 33.5, 33.1, 32.6, 32.5, 31.8, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.0, 26.7, 22.6, 21.5, 14.1; HRMS (ESI) calcd for $C_{43}H_{55}NNaO_4S$ [M+Na$^+$], 704.3744; found: 704.3735.

*Methyl 2-(5-Methoxynaphthalen-2-yl)-2-methyl-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**5**).* (63 mg, 50%, dr =3:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.4); IR (neat): ν_{max} 2922, 1732, 1655, 1630, 1462, 1354, 1283, 1238, 1164, 1019 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 5.8 Hz, 1H), 7.60−7.56 (m, 2H), 7.49 (d, J = 1.4 Hz, 1H), 7.35 (d, J = 8.2 Hz, 2H), 7.15 (dd, J = 8.6, 1.8 Hz, 1H), 7.10−7.02 (m, 6H), 6.86−6.83 (m, 2H), 6.76 (dd, J = 8.0, 1.5 Hz, 1H), 6.67 (td, J = 7.6, 1.0 Hz, 1H), 5.16 (d, J = 12.0 Hz, 1H), 3.89 (s, 3H), 3.71 (s, 3H), 3.66 (d, J = 12.0 Hz, 1H), 2.72 (d, J = 14.2 Hz, 1H), 2.48 (d, J = 14.2 Hz, 1H), 2.44 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 157.5, 146.5, 143.8, 141.5, 136.9, 136.1, 136.0, 132.8, 131.3, 129.7, 129.4, 129.0, 128.3, 128.0, 127.8, 127.7, 127.2, 126.7, 126.5, 124.6, 123.8, 123.1, 120.5, 118.6, 105.4, 56.3, 55.9, 55.6, 55.2, 52.6, 51.4, 24.9, 21.6; HRMS (ESI) calcd for $C_{39}H_{35}NNaO_5S$ [M+Na$^+$], 652.2128; found: 652.2118.

*Methyl 2-(2,4-Dichlorophenoxy)-1-phenyl-5-tosyl-2,3,4,5-tetrahydro-3aH-cyclopenta[c]quinoline-3a-carboxylate (**6**).* (81 mg, 65%, dr = 1.8:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.6); IR (neat): ν_{max} 2951, 2922, 2851, 1736, 1477, 1352, 1285, 1242, 1167, 1090, 1059, 1034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 7.6 Hz, 1H), 7.67 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 2.8 Hz, 1H), 7.26−7.22 (m, 5H), 7.16 (td, J = 8.4, 1.4 Hz, 1H), 7.10 (dd, J = 8.8, 2.6 Hz, 1H), 7.00−6.97 (m, 3H), 6.81 (t, J = 7.4 Hz, 1H), 6.74 (d, J = 8.8 Hz, 1H), 5.78 (t, J = 6.3 Hz, 1H), 4.90 (d, J = 12.4 Hz, 1H), 3.84 (d, J = 12.4 Hz, 1H), 3.59 (s, 3H), 3.14 (dd, J = 13.8, 7.0 Hz, 1H), 2.32 (s, 3H), 2.09 (dd, J = 13.8, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 152.6, 144.0, 138.1, 136.6, 133.5, 130.1, 129.8, 129.0, 128.4, 128.2, 127.9, 127.5, 127.3, 127.2, 126.5, 124.8, 124.5, 124.0, 122.7, 116.5, 86.2, 57.5, 54.9, 52.8, 41.7, 21.5; HRMS (ESI) calcd for $C_{33}H_{27}Cl_2NNaO_5S$ [M+Na$^+$], 642.0879; found: 642.0871.

*Methyl (3a′R,8R,9S,10R,13S,14S)-10,13-Dimethyl-3-oxo-1′-phenyl-5′-tosyl-1,2,3,4′,5′,6,7,8,9,10,11,12,13,14,15,16-hexadecahydrospiro[cyclopenta[a]phenanthrene-17,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**7**).* (107 mg, 75%, dr = 1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3); IR (neat): ν_{max} 3053, 3028, 2949, 2868, 1732, 1672, 1614, 1599, 1477, 1456, 1435, 1354, 1267, 1232, 1169, 1092 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.58 (m, 2H), 7.57−7.49 (m, 1H), 7.40−7.38 (m, 0.5H), 7.34−7.25 (m, 5H), 7.11−6.96 (m, 2H), 6.79−6.77 (m, 0.5H), 6.66−6.58 (m, 1H), 6.39 (d, J = 7.8 Hz, 0.5H), 6.24 (dd, J = 7.8, 1.2 Hz, 0.5H), 5.64 (d, J = 15.4 Hz, 1H), 4.86 (d, J = 12.0 Hz, 0.5H), 4.78 (d, J = 12.0 Hz, 0.5H), 3.59 (s, 1.5H), 3.53 (s, 1.5H), 3.51 (d, J = 12.0 Hz, 0.5H), 3.39 (d, J = 12.0 Hz, 0.5H), 2.90 (d, J = 13.8 Hz, 0.5H), 2.52−2.20 (m, 8H), 2.13−1.52 (m, 9H), 1.39−1.21 (m, 3H), 1.13 (s, 1.5H), 1.11 (s, 1.5H), 1.13−1.08 (m, 1.5H), 0.86 (s, 1.5H), 0.76 (s, 1.5H), 0.67−0.60 (m, 0.5H), 0.49−0.36 (m, 1H), 0.22−0.16 (m, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 199.5, 174.7, 174.6, 171.2, 171.1, 146.0, 143.6, 143.5, 139.5, 139.1, 137.0, 136.2, 136.1, 136.0, 133.7, 132.1, 130.0, 129.7, 129.6, 128.2, 127.9, 127.7, 127.5, 127.4, 127.3, 127.2, 127.0, 125.8, 125.5, 123.8, 123.7, 123.5, 123.4, 122.2, 121.3, 66.5, 66.4, 56.4, 55.7, 55.5, 55.1, 53.6, 53.5, 52.4, 50.0, 49.5, 47.5, 47.2, 44.8, 42.8, 38.6, 38.5, 38.2, 36.8, 36.2, 36.1, 35.9, 35.8, 35.7, 34.0, 33.9, 32.7, 32.6, 32.0, 31.0, 26.9, 25.1, 24.5, 21.6, 20.8, 20.4, 17.5, 17.4, 17.3, 16.8; HRMS (ESI) calcd for $C_{45}H_{49}NNaO_5S$ [M+Na$^+$], 738.3224; found: 738.3205.

*Methyl (3a′R,5S,8R,9S,10S,13S,14S)-10,13-Dimethyl-17-oxo-1′-phenyl-5′-tosyl-1,2,4,4′,5,5′,6,7,8,9,10,11,12,13,14,15,16,17-octadecahydrospiro[cyclopenta[a]phenanthrene-3,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**8**).* (108 mg, 78%, dr =3:3:1:1). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.3); IR (neat): ν_{max} 3055, 3028, 2922, 2855, 1735, 1448, 1454, 1354, 1254, 1238, 1221, 1161, 1092, 1074, 1055 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.67 (m, 2H), 7.45−7.40 (m, 1H), 7.32−7.05 (m, 7H), 6.97−6.92 (m, 1H), 6.74−6.69 (m, 1H), 6.63−6.57 (m, 1H), 4.90 (d, J = 12.2 Hz, 0.5H), 4.88 (d, J = 12.2 Hz, 0.5H), 3.68 (s, 1.5H), 3.67 (s, 1.5H), 3.43 (d, J = 12.2 Hz, 0.5H), 3.41 (d, J = 12.2 Hz, 0.5H), 2.45−2.36 (m, 5H), 2.13−1.58 (m, 8H), 1.45−0.93 (m, 12H), 0.78 (s, 3H), 0.71 (s, 3H), 0.44−0.32 (m, 1H), 0.20−0.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 221.3, 174.9, 149.3, 149.2, 143.6, 143.5, 139.4, 139.2, 137.6, 137.5, 136.0, 130.2, 130.0, 128.8, 128.3, 127.8, 127.7, 127.4, 127.3, 127.2, 127.0, 126.9, 124.7, 124.5, 123.2, 123.1, 120.5, 120.3, 55.3, 55.0, 54.9, 54.4, 53.1, 52.5, 51.2, 51.1, 50.3, 50.2, 47.6, 41.4, 41.3, 41.1, 40.6, 35.7, 35.4, 35.0, 34.9, 34.3, 33.5, 31.4, 30.8, 30.6, 28.7, 28.2, 21.6, 21.5, 20.0, 19.9, 13.7, 11.4, 11.3; HRMS (ESI) calcd for $C_{45}H_{51}NNaO_5S$ [M+Na$^+$], 740.3380; found: 740.3367.

*Methyl (5S,8R,9S,10S,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-1′-phenyl-5′-tosyl-1,2,4,4′,5,5′,6,7,8,9,10,11,12,13,14,15,16,17-octadecahydrospiro-[cyclopenta[a]phenanthrene-3,2′-cyclopenta[c]quinoline]-3a′(3′H)-carboxylate (**9**).* (75g, 48%, dr =2.5:2.5:1:1). Isomer 1 (2.5:2.5): Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.55); IR (neat): ν_{max} 2932, 2886, 2855, 1734, 1599, 1477, 1458, 1356, 1228, 1167, 1090, 1072, 952, 870, 814, 756, 662, 573 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 8.4 Hz, 0.5H), 7.48 (d, J = 8.4 Hz, 0.5H), 7.33−7.29 (m, 3H), 7.26 (d, J = 8.4 Hz, 2H), 6.97−6.91 (m, 3H), 6.63 (td, J = 7.6, 1.6 Hz, 1H), 6.59 (td, J = 7.6, 1.6 Hz, 1H), 5.03 (d, J = 12.0 Hz, 0.5H), 5.01 (d, J = 12.0 Hz, 0.5H), 3.61 (s, 1.5H), 3.59 (s, 1.5H), 3.43 (d, J = 12.0 Hz, 1H), 2.75 (d, J = 13.6 Hz, 0.5H), 2.69 (d, J = 13.6 Hz, 0.5H), 2.40 (s, 3H), 1.97−1.93 (m, 1H), 1.81−1.74 (m, 2H), 1.63−1.45 (m, 6H), 1.34−0.98 (m, 20H), 0.91−0.86 (m, 4H), 0.87 (s, 3H), 0.85 (s, 3H), 0.74−0.64 (m, 2H), 0.62 (s, 3H), 0.51 (s, 1.5H), 0.49 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 147.8, 147.7, 143.6, 137.2, 137.0, 136.8, 136.6, 135.8, 129.9, 129.8, 129.7, 129.6, 129.0, 128.9, 128.4, 128.3, 127.9, 127.3, 127.2, 127.1, 127.0, 124.2, 124.0, 122.9, 122.8, 120.3, 120.1, 56.5, 56.2, 56.0, 55.9, 55.4, 55.3, 54.5, 54.4, 53.1, 53.0, 52.4, 44.8, 44.6, 43.2, 42.5, 42.2, 39.9, 39.5, 36.7, 36.1, 35.7, 35.6, 35.4, 35.3, 34.7, 32.5, 32.0, 29.6, 28.9, 28.7, 28.2, 27.9, 26.8, 24.1, 23.8, 22.8, 22.5, 21.5, 20.9, 18.6, 12.0, 11.4; HRMS (ESI) calcd for $C_{53}H_{69}NNaO_4S$ [M+Na$^+$], 838.4840; found: 838.4828.

Isomer 2 (1:1): Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5); IR (neat): ν_{max} 2930, 2866, 1734, 1597, 1448, 1356, 1240, 1161, 1121, 1092, 1070, 949, 864, 814, 750, 662, 571 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 8.4 Hz, 0.5H), 7.42 (d, J = 8.4 Hz, 0.5H), 7.32−7.26 (m, 5H), 7.05−6.91 (m, 3H), 6.72 (td, J = 7.6, 1.6 Hz, 0.5H), 6.70 (td, J = 7.6, 1.6 Hz, 0.5H), 6.63−6.57 (m, 1H), 4.89 (d, J = 12.0 Hz, 0.5H), 4.87 (d, J = 12.0 Hz, 0.5H), 3.66 (s, 1.5H), 3.65 (s, 1.5H), 3.42 (d, J = 12.2 Hz, 0.5H), 3.40 (d, J = 12.2 Hz, 0.5H), 2.42 (d, J = 12.2 Hz, 1H), 2.40 (s, 3H), 2.39 (d, J = 14.2 Hz, 0.5H), 2.08 (d, J = 14.2 Hz, 0.5H), 1.89−1.71 (m, 4H), 1.59−1.48 (m, 4H), 1.33−0.94 (m, 18H), 0.88−0.84 (m, 12H), 0.68 (s, 1.5H), 0.67 (s, 1.5H), 0.58 (s, 1.5H), 0.57 (s, 1.5H), 0.34−0.30 (m, 1H), 0.20−0.29 (m, 1H); ^{13}C

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

NMR (100 MHz, $CDCl_3$) δ 175.0, 149.6, 149.5, 143.6, 139.5, 139.4, 137.7, 137.6, 136.1, 130.1, 129.9, 129.8, 128.9, 128.3, 127.8, 127.4, 127.3, 127.2, 127.0, 125.0, 124.7, 123.2, 123.1, 120.7, 120.4, 56.4, 56.3, 56.2, 55.4, 55.1, 55.0, 54.4, 54.3, 53.3, 52.5, 50.5, 50.4, 42.5, 41.5, 41.4, 41.1, 40.8, 40.0, 39.6, 36.2, 35.7, 35.6, 35.4, 35.1, 34.8, 34.7, 34.4, 33.7, 32.1, 31.8, 29.1, 28.6, 28.2, 28.0, 24.1, 23.8, 22.9, 22.6, 21.6, 20.8, 20.7, 18.7, 12.1, 11.5, 11.4; HRMS (ESI) calcd for $C_{53}H_{69}NNaO_4S$ [M +Na^+], 838.4840; found: 838.4828.

*Methyl-8,8-dimethyl-10-phenyl-5-tosyl-5,7,8,9-tetrahydrophenanthridine-6a(6H)-carboxylate (**15aa**).* (50 mg, 50%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.5); IR (neat): ν_{max} 2951, 2870, 1736, 1597, 1479, 1458, 1356, 1242, 1169, 1072, 1047, 1036, 951, 920, 760, 720, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, J = 8.4, 0.8 Hz, 1H), 7.59 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 7.15−7.06 (m, 3H), 7.02−6.98 (m, 1H), 6.63 (td, J = 7.6, 1.1 Hz, 1H), 6.56−6.54 (m, 2H), 6.49 (dd, J = 7.8, 1.5 Hz, 1H), 4.56 (d, J = 11.6 Hz, 1H), 3.66 (d, J = 11.6 Hz, 1H), 3.40 (s, 3H), 2.48 (d, J = 17.2 Hz, 1H), 2.39 (s, 3H), 2.10 (dd, J = 14.0, 0.7 Hz, 1H), 2.00 (d, J = 17.2 Hz, 1H), 1.55 (d, J = 14.0 Hz, 1H), 1.04 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 143.8, 142.4, 135.6, 135.1, 135.0, 130.9, 130.3, 129.5, 128.6, 127.9, 127.5, 127.1, 126.8, 126.7, 123.5, 122.7, 55.7, 52.2, 49.5, 46.3, 44.0, 29.8, 29.7, 28.2, 21.5; HRMS (ESI) calcd for $C_{30}H_{31}NNaO_4S$ [M+Na^+], 524.1866; found: 524.1873.

*Methyl 8,8,9-Trimethyl-10-phenyl-5-tosyl-5,7,8,9-tetrahydrophenanthridine-6a(6H)-carboxylate (**15ab**).* (57 mg, 55%, dr = 1:1). Isomer 1: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.65); IR (neat): ν_{max} 3055, 3022, 2953, 2930, 2872, 1732, 1597, 1356, 1244, 1215, 1169, 1092, 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 7.15−7.05 (m, 3H), 6.97 (td, J = 7.8, 1.6 Hz, 1H), 6.59 (td, J = 7.6, 1.0 Hz, 1H), 6.53−6.29 (m, 3H), 4.68 (d, J = 11.2 Hz, 1H), 3.45 (d, J = 11.2 Hz, 1H), 3.39 (s, 3H), 2.41 (s, 3H), 2.25 (q, J = 6.8 Hz, 1H), 1.98 (dd, J = 14.6, 1.0 Hz, 1H), 1.73 (dd, J = 14.6 Hz, 1H), 1.13 (s, 3H), 0.97 (s, 3H), 0.66 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 144.0, 141.7, 140.9, 135.4, 134.9, 131.2, 130.6, 129.5, 129.3, 127.8, 127.6, 126.8, 126.6, 126.1, 123.5, 122.8, 58.6, 52.1, 48.5, 46.7, 40.6, 32.1, 28.5, 28.0, 21.6, 14.1; HRMS (ESI) calcd for $C_{31}H_{33}NNaO_4S$ [M+Na^+], 538.2023; found: 538.2016.

Isomer 2: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.6); IR (neat): ν_{max} 3055, 3030, 2972, 2953, 2922, 1734, 1356, 1240, 1229, 1169, 1090, 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.23 (d, J = 8.2 Hz, 2H), 7.13−7.09 (m, 1H), 7.05−7.00 (m, 3H), 6.65 (td, J = 7.8, 1.6 Hz, 1H), 6.55 (td, J = 7.6, 1.0 Hz, 1H), 6.54−6.50 (m, 1H), 4.50 (d, J = 11.2 Hz, 1H), 3.82 (d, J = 11.2 Hz, 1H), 3.39 (s, 3H), 2.40 (s, 3H), 2.10 (d, J = 14.6 Hz, 1H), 1.95 (q, J = 6.8 Hz, 1H), 1.57 (s, 3H), 1.48 (dd, J = 14.6, 1.0 Hz, 1H), 1.35 (d, J = 6.8 Hz, 3H), 0.96 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 143.8, 143.0, 141.2, 135.6, 135.0, 131.1, 131.0, 129.5, 128.5, 127.8, 127.5, 127.4, 126.6, 126.3, 123.9, 123.6, 52.9, 52.4, 49.9, 46.9, 38.6, 33.1, 29.1, 28.3, 21.6, 16.6; HRMS (ESI) calcd for $C_{31}H_{33}NNaO_4S$ [M+Na^+], 538.2023; found: 538.2016.

*Methyl (6a,7a,11a)-7a-Methyl-12-phenyl-5-tosyl-5,7,7a,8,9,10,11,11a-octahydrobenzo[j]phenanthridine-6a(6H)-carboxylate (**15ac**).* (32 mg, 30%, dr = 1:1). Isomer 1: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.55); IR (neat): ν_{max} 2928, 2862, 1736, 1454, 1356, 1240, 1169, 1088, 1037, 918, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, J = 8.4, 0.6 Hz, 1H), 7.58 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 7.15−7.05 (m, 3H), 6.98−6.94 (m, 1H), 6.63 (td, J = 7.6, 1.1 Hz, 1H), 6.39 (dd, J = 7.8, 1.5 Hz, 1H), 6.38 (br, 2H), 4.74 (d, J = 11.4 Hz, 1H), 3.50 (d, J = 11.4 Hz, 1H), 3.38 (s, 3H), 2.40 (s, 3H), 2.11 (d, J = 14.6 Hz, 1H), 2.10−2.06 (m, 1H), 1.75 (dd, J = 14.6, 1.0 Hz, 1H), 1.65−1.50 (m, 3H), 1.44−1.27 (m, 3H), 1.12 (s, 3H), 1.07−0.97 (m, 1H), 0.88−0.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 143.9, 141.4, 139.9, 135.3, 134.8, 131.1, 130.5, 129.5, 129.2, 127.7, 127.5, 126.8, 126.5, 126.0, 123.3, 122.6, 58.9, 52.0, 49.8, 48.2, 39.9, 37.6, 32.0, 28.7, 27.7, 26.1, 21.6, 21.5; HRMS (ESI) calcd for $C_{33}H_{35}NNaO_4S$ [M +Na^+], 564.2179; found: 564.2172.

Isomer 2: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.5); IR (neat): ν_{max} 2930, 2882, 1734, 1479, 1456, 1358, 1221, 1169, 1074, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 8.4, 0.8 Hz, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 7.13−7.09 (m, 1H), 7.05−7.00 (m, 3H), 6.64 (td, J = 7.6, 1.1 Hz, 1H), 6.54 (dd, J = 7.8, 1.5 Hz, 1H), 7.52−7.49 (m, 2H), 4.51 (d, J = 11.8 Hz, 1H), 3.89 (d, J = 11.8 Hz, 1H), 3.41 (s, 3H), 2.48 (d, J = 14.6 Hz, 1H), 2.40 (s, 3H), 2.21−2.17 (m, 1H), 1.83−1.79 (m, 2H), 1.73−1.66 (m, 1H), 1.62−1.48 (m, 3H), 1.26−1.22 (m, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 143.8, 143.3, 140.0, 135.5, 135.0, 131.2, 130.9, 129.5, 128.3, 127.8, 127.5, 127.4, 126.6, 126.5, 123.9, 123.7, 53.1, 52.4, 50.5, 49.7, 39.9, 35.1, 32.6, 30.1, 29.8, 26.9, 26.2, 21.6, 21.3; HRMS (ESI) calcd for $C_{33}H_{35}NNaO_4S$ [M +Na^+], 564.2179; found: 564.2172.

*Methyl-7a-ethyl-12-phenyl-5-tosyl-5,7,7a,8,9,10,11,11a-octahydrobenzo[j]phenanthridine-6a(6H)-carboxylate (**15ad**) Methyl-9′-methyl-10′-phenyl-5′-tosyl-5′,9′-dihydro-6′H-spiro-[cyclohexane-1,8′-phenanthridine]-6a′(7′H)-carboxylate (**15ad**).* (62 mg, dr = 1:1). Isomer 1: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.55); IR (neat): ν_{max} 2930, 2855, 1738, 1730, 1360, 1242, 1207, 1669, 1090, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76−7.74 (m, 1H), 7.58−7.55 (m, 2H), 7.26−7.24 (m, 2H), 7.15−7.05 (m, 3H), 6.98−6.95 (m, 1H), 6.61−6.57 (m, 1H), 6.50−6.28 (m, 3H), 4.78−4.71 (m, 1H), 3.50−3.40 (m, 1H), 3.88 (s, 3H), 2.40 (s, 3H), 2.46−2.19 (m, 1H), 2.10−1.64 (m, 4H), 1.56−0.80 (m, 8H), 0.71 (t, J = 7.4 Hz, 1.5H), 0.64 (d, J = 7.0 Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 174.2, 143.9, 141.8, 141.5, 140.6, 139.9, 135.3, 135.2, 134.8, 131.1, 131.0, 130.5, 129.5, 127.8, 127.7, 127.6, 126.8, 126.6, 126.1, 126.0, 123.4, 122.7, 59.1, 59.0, 52.1, 50.0, 48.0, 47.9, 36.4, 35.3, 34.7, 34.5, 34.4, 33.2, 32.3, 27.7, 26.2, 26.1, 21.8, 21.7, 21.6, 12.8, 7.1; HRMS (ESI) calcd for $C_{34}H_{37}NNaO_4S$ [M+Na^+], 578.2336; found:578.2319.

Isomer 2: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:7, R_f = 0.50); IR (neat): ν_{max} 2926, 2852, 1734, 1479, 1449, 1356, 1229, 1169, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86−7.83 (m, 1H), 7.52−7.50 (m, 2H), 7.26−7.22 (m, 2H), 7.13−7.09 (m, 1H), 7.06−7.00 (m, 3H), 6.68−6.62 (m, 1H), 6.59−6.47 (m, 3H), 4.52 (d, J = 11.8 Hz, 1H), 3.75−3.71 (m, 1H), 3.41 (s, 3H), 2.41 (s, 3H), 2.33−2.16 (m, 2H), 1.92−1.65 (m, 3H), 1.50−0.84 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 174.6, 143.8, 143.3, 140.9, 139.9, 135.5, 134.8, 131.2, 131.1, 130.9, 129.4, 128.2, 127.8, 127.5, 127.4, 127.3, 126.5, 123.9, 123.8, 53.0, 52.4, 50.3, 49.5, 36.5, 35.9, 35.5, 35.3, 35.0, 32.6, 30.8, 29.9, 26.1, 21.6, 21.2, 21.1, 15.3, 7.2; HRMS (ESI) calcd for $C_{34}H_{37}NNaO_4S$ [M+Na^+], 578.2336; found: 578.2319.

*Methyl (7aS,8R,10R,12S,13aR)-14a-Hydroxy-14-phenyl-5-tosyl-5,6,7,7a,8,9,10,11,12,13,14,14a-dodecahydro-6aH-8,12:10,13a-dimethanocycloocta[j]phenanthridine-6a-carboxylate (**15ae**).* (75 mg, 63%, dr =5.2:1). Major isomer: Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:5, R_f = 0.6); IR (neat): ν_{max} 3061, 3024, 2907, 2849, 1732, 1485, 1450, 1352, 1246, 1169, 1092, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 8.4, 1.0 Hz, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.50−7.43 (m, 3H), 7.35−7.31 (m, 1H), 7.27−7.22 (m, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.08 (dd, J = 7.8, 1.4 Hz, 1H), 6.74 (dd, J = 7.8, 1.4 Hz, 1H), 4.18 (d, J = 11.4 Hz, 1H), 3.88 (d, J = 11.8 Hz, 1H), 3.85 (d, J = 11.8 Hz, 1H), 3.51 (s, 3H), 2.40 (s, 3H), 2.10−2.07 (m, 1H), 1.95−1.83 (m, 4H), 1.73−1.65 (m, 2H), 1.61−1.53 (m, 4H), 1.47−1.40 (m, 2H), 1.27−1.23 (m, 1H), 1.10−1.07 (m, 1H), 0.92 (s, 1H), 0.87 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 143.8, 143.6, 135.1, 135.0, 134.9, 132.6, 129.5, 129.0, 128.1, 127.9, 127.6, 127.5, 127.1, 126.3, 123.3, 123.1, 72.6, 52.5, 51.8, 51.6, 49.1, 47.1, 46.3, 44.3, 39.1, 37.3, 35.6, 33.0, 28.6, 28.2, 28.0, 21.5; HRMS (ESI) calcd for $C_{36}H_{39}NNaO_5S$ [M+Na^+], 620.2441; found: 620.2429.

*Synthesis of Product **10**.* To a stirred solution of **3aa** (106 mg, 0.2 mmol) in THF (3.0 mL) under nitrogen at −78 °C, DIBAl-H (1.0 M in hexane, 0.6 mL, 0.6 mmol) was added dropwise and the mixture was stirred at −78 °C for 1 h. The resulting mixture was quenched by water and extracted with EtOAc three times. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

chromatography on silica gel (ethyl acetate/petroleum ether = 1:1, R_f = 0.2) to give the desired product **10** (97 mg, 97%). IR (neat): ν_{max} 3053, 2934, 2853, 1597, 1477, 1387, 1349, 1163, 1105, 1092, 1049, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2H), 7.40−7.32 (m, 6H), 7.01−6.97 (m, 3H), 6.65−6.58 (m, 2H), 4.73 (d, J = 12.0 Hz, 1H), 3.90 (td, J = 11.8, 4.0 Hz, 2H), 3.78 (dd, J = 11.8, 4.0 Hz, 1H), 3.70 (t, J = 11.8 Hz, 1H), 3.49 (td, J = 12.2, 1.8 Hz, 1H), 3.45 (td, J = 12.2, 1.8 Hz, 1H), 3.26 (d, J = 12.4 Hz, 1H), 2.80 (t, J = 8.8 Hz, 1H), 2.79 (d, J = 12.4 Hz, 1H), 2.45 (s, 3H), 2.00 (td, J = 12.6, 4.0 Hz, 1H), 1.64−1.56 (m, 2H), 1.47 (d, J = 13.6 Hz, 1H), 1.02 (d, J = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 144.0, 137.8, 136.7, 135.7, 132.0, 130.0, 129.1, 128.7, 128.1, 127.4, 127.3, 126.5, 123.0, 122.9, 120.3, 65.2, 64.8, 64.2, 53.8, 49.7, 39.5, 38.0, 35.5, 21.5; HRMS (ESI) calcd for $C_{30}H_{31}NNaO_4S$ [M+Na$^+$], 524.1866; found: 524.1859.

*Synthesis of Product **11**.* To a stirred solution of **3aa** (106 mg, 0.2 mmol) in MeOH (3.0 mL) under nitrogen at room temperature, magnesium chips (24 mg, 1.0 mmol) were added and the mixture was refluxed at 80 °C for 1 h. The resulting mixture was quenched by diluted. HCl and extracted with EtOAc three times. The combined organic phase was washed with brine, saturated $NaCO_3$, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether = 1:2, R_f = 0.2) to give the desired product **11**. (61 mg, 82%). IR (neat): ν_{max} 3431, 3080, 3020, 2951, 2922, 2849, 1719, 1487, 1389, 1350, 1314, 1240, 1217, 1145, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43−7.10 (m, 5H), 6.76 (td, J = 7.6, 1.4 Hz, 1H), 6.46 (dd, J = 8.0, 0.6 Hz, 1H), 6.35 (dd, J = 8.0, 1.2 Hz, 1H), 6.11 (d, J = 3.8 Hz, 1H), 6.07 (td, J = 7.6, 1.0 Hz, 1H), 3.83 (dd, J = 11.4, 4.2 Hz, 1H), 3.74 (dd, J = 11.8, 4.0 Hz, 1H), 3.62 (td, J = 11.6, 3.6 Hz, 1H), 3.55 (s, 3H), 3.43 (td, J = 12.2, 1.8 Hz, 1H), 3.30 (td, J = 12.2, 1.8 Hz, 1H), 3.09 (d, J = 12.0 Hz, 1H), 2.61 (d, J = 11.4 Hz, 1H), 1.76 (d, J = 11.4 Hz, 1H), 1.72 (td, J = 13.2, 4.8 Hz, 1H), 1.34 (d, J = 12.6 Hz, 1H), 1.30 (td, J = 13.2, 4.8 Hz, 1H), 1.12 (d, J = 12.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 171.5, 171.1, 146.6, 136.5, 133.3, 132.6, 131.7, 129.4, 129.2, 128.5, 127.9, 127.4, 127.3, 127.0, 65.2, 64.4, 59.1, 53.8, 53.3, 53.0, 52.2, 50.0, 46.4, 41.6, 37.2, 33.8; HRMS (ESI) calcd for $C_{24}H_{26}NO_3$ [M+H$^+$], 376.1907; found: 376.1920.

*Synthesis of Product **12**.* To a stirred solution of **3aa** (106 mg, 0.2 mmol) in mixed solvent (MeOH/THF/H_2O = 2.5 mL/2.5 mL/1.0 mL) at room temperature, NaOH (40 mg, 1.0 mmol) was added. The mixture was heated to reflux for 5 h. Then cooled to room temperature, 2 M HCl was added to adjust the pH value to 2. Then the resulting mixture was extracted with EtOAc three times, the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo to give the pure acid in quantitative yield.

1-Phenyl-5-tosyl-2′,3′,4,5,5′,6′-hexahydrospiro[cyclopenta[c]-quinoline-2,4′-pyran]-3a(3H)-carboxylic Acid. (103 mg, 100%). IR (neat): ν_{max} 3053, 2934, 2853, 1597, 1477, 1387, 1349, 1163, 1105, 1092, 1049, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.4 Hz, 1H), 7.36−7.32 (m, 3H), 7.25 (d, J = 8.2 Hz, 2H), 6.99 (td, J = 7.8, 1.6 Hz, 1H), 6.98−6.93 (m, 2H), 6.68 (dd, J = 7.8, 1.4 Hz, 1H), 6.62 (t, J = 7.4 Hz, 1H), 5.06 (d, J = 12.0 Hz, 1H), 3.88 (dd, J = 11.8, 4.0 Hz, 1H), 3.79 (dd, J = 11.6, 3.6 Hz, 1H), 3.56 (td, J = 12.2, 1.8 Hz, 1H), 3.46 (d, J = 12.0 Hz, 1H), 3.44 (td, J = 12.2, 1.8 Hz, 1H), 2.89 (d, J = 13.6 Hz, 1H), 2.42 (s, 3H), 1.94 (td, J = 12.6, 4.0 Hz, 1H), 1.84 (d, J = 13.6 Hz, 1H), 1.60 (dd, J = 13.6, 1.8 Hz, 1H), 1.57 (td, J = 13.2, 4.8 Hz, 1H), 1.02 (dd, J = 13.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4, 146.7, 143.9, 136.8, 135.9, 135.8, 130.2, 129.7, 129.1, 128.6, 127.9, 127.8, 127.5, 127.1, 123.5, 123.1, 120.3, 65.2, 64.2, 55.5, 55.3, 50.1, 43.0, 36.9, 33.7, 21.5; HRMS (ESI) calcd for $C_{30}H_{29}NNaO_5S$ [M+Na$^+$], 538.1659; found: 538.1654.

Then to the stirred solution of acid (0.2 mmol) and Et_3N (0.6 mmol) in THF (3.0 mL) at room temperature, $(PhO)_2PON_3$ (83 mg, 0.3 mmol) was added dropwise. The resulting mixture was stirred for 3 h at room temperature. Then 2 M HCl (2.0 mL) was added and the resulting mixture was heated to reflux for 2 h. After the solution was cooled to room temperature, the mixture was treated with saturated K_2CO_3 solution and extracted with EtOAc three times. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered through a pad of silica gel using EtOAc as eluent. The solvent was evaporated in vacuo and the residue was purified by flash column chromatography on silica gel (dichloromethane/methanol = 20:1, R_f = 0.6) to give the desired amine **12**. (93 mg, 96%). IR (neat): ν_{max} 2947, 2928, 2851, 1597, 1477, 1458, 1385, 1348, 1163, 1105, 1092 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.4 Hz, 1H), 7.40−7.34 (m, 3H), 7.29 (d, J = 8.2 Hz, 2H), 7.03−6.97 (m, 3H), 6.68 (dd, J = 7.8, 1.0 Hz, 1H), 6.62 (t, J = 7.2 Hz, 1H), 4.66 (d, J = 12.2 Hz, 1H), 3.90 (dd, J = 11.8, 4.0 Hz, 1H), 3.79 (dd, J = 11.8, 4.0 Hz, 1H), 3.66 (t, J = 11.8 Hz, 1H), 3.47 (td, J = 12.2, 1.8 Hz, 1H), 3.44 (d, J = 12.2 Hz, 1H), 2.44 (d, J = 13.6 Hz, 1H), 2.41 (s, 3H), 2.06 (td, J = 12.6, 4.6 Hz, 1H), 1.87 (d, J = 13.6 Hz, 1H), 1.74 (d, J = 13.6 Hz, 1H), 1.65 (br, 2H), 1.57 (td, J = 12.6, 4.6 Hz, 1H), 1.02 (d, J = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 143.8, 137.5, 136.4, 135.5, 134.9, 129.8, 128.9, 128.7, 128.6, 127.7, 127.4, 126.9, 123.0, 122.0, 120.0, 65.2, 64.5, 59.1, 58.7, 49.3, 46.0, 36.8, 35.7, 21.5; HRMS (ESI) calcd for $C_{29}H_{30}N_2NaO_3S$ [M+Na$^+$], 509.1869; found: 509.1863.

*Synthesis of Product **13**.* To a stirred solution of **3aa** (106 mg, 0.2 mmol) in dichloromethane (5.0 mL) at room temperature, *m*-CPBA (87 mg, 0.5 mmol) was added and the mixture was stirred at room temperature for 48 h. The mixture was treated with saturated $NaHCO_3$ solution and extracted with EtOAc three times. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether = 1:5, R_f = 0.3)) to give the desired epoxide **13** (74 mg, 68%). IR (neat): ν_{max} 2951, 2851, 1734, 1605, 1493, 1454, 1352, 1242, 1163, 1089, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.2 Hz, 2H), 7.54 (d, J = 8.4 Hz, 1H), 7.50−7.41 (m, 5H), 7.28−7.25 (m, 2H), 7.02 (td, J = 7.8, 1.6 Hz, 1H), 6.61 (td, J = 7.8, 0.6 Hz, 1H), 6.29 (dd, J = 7.8, 1.4 Hz, 1H), 5.13 (d, J = 12.0 Hz, 1H), 3.85 (dd, J = 11.8, 4.0 Hz, 1H), 3.78 (dd, J = 11.6, 3.6 Hz, 1H), 3.71 (s, 3H), 3.66 (d, J = 12.0 Hz, 1H), 3.47 (td, J = 12.2, 1.8 Hz, 1H), 3.39 (td, J = 12.2, 1.8 Hz, 1H), 2.45 (d, J = 13.6 Hz, 1H), 2.39 (s, 3H), 1.71 (td, J = 12.6, 4.0 Hz, 1H), 1.64 (td, J = 13.6, 4.6 Hz, 1H), 1.55 (dd, J = 13.6, 1.8 Hz, 1H), 1.50−4.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 144.0, 138.5, 136.8, 132.2, 129.9, 129.8, 128.7, 128.6, 128.5, 128.4, 127.4, 127.1, 126.9, 122.8, 122.4, 119.0, 79.5, 68.4, 64.8, 63.9, 52.5, 51.6, 50.9, 45.8, 36.5, 32.3, 31.3, 21.5; HRMS (ESI) calcd for $C_{31}H_{31}NNaO_6S$ [M+Na$^+$], 568.1764; found: 568.1758.

Deuterium-Labled Experiment. To a mixture of d_4-acetic acid (0.2 mmol), enyne **16** (0.4 mmol), $AgNO_3$ (6.8 mg, 20 mol%), and $K_2S_2O_8$ (81.0 mg, 0.3 mmol), MeCN (2.0 mL) and H_2O (1.0 mL) were added under air at room temperature. The resulting mixture was stirred at 100 °C for 6 h. After the mixture was cooled to room temperature, EtOAc (10.0 mL) and H_2O (2.0 mL) were added sequentially. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to give the crude products. The residue was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether) to give the pure product **17′**. **17** was obtained with the similar procedure unless D_2O or CD_3CN was used.

*Methyl 7-Tosyl-3,3a,4,5,6,7-hexahydrofuro[2′,3′:2,3]cyclopenta-[1,2-c]quinoline-5a(2H)-carboxylate (**17′**).* (20 mg, 23%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:10, R_f = 0.3); IR (neat): ν_{max} 3063, 3028, 2951, 2872, 1732, 1485, 1454, 1350, 1325, 1227, 1165, 1045, 1024 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 1H), 7.49 (d, J = 8.2 Hz, 2H), 7.21−7.17 (m, 1H), 7.13 (d, J = 8.2 Hz, 2H), 7.02−6.97 (m, 2H), 4.53 (d, J = 10.6 Hz, 1H), 3.80 (d, J = 10.6 Hz, 1H), 3.47−3.40 (m, 1H), 3.37 (s, 3H), 3.38−3.33 (m, 1H), 3.26 (td, J = 8.6, 3.8 Hz, 1H), 2.33 (s, 3H), 2.41−2.23 (m, 2H), 1.91−1.80 (m, 3H), 1.51−1.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 143.0, 135.9, 135.2, 130.7, 128.8, 128.3, 127.6, 123.8, 123.6, 123.3, 90.4, 66.2, 59.5, 51.8, 50.6, 41.6 (t, J_{C-D} = 21.2 Hz), 35.0, 32.5, 32.1−31.7 (m), 21.4; HRMS (ESI) calcd for $C_{23}H_{22}D_3NNaO_5S$ [M+Na$^+$], 453.1534; found: 453.1524.

*Methyl 7-Tosyl-3,3a,4,5,6,7-hexahydrofuro[2′,3′:2,3]cyclopenta-[1,2-c]quinoline-5a(2H)-carboxylate-3a,4,4-d3 (**17**).* (20 mg, 23%). Isolated by flash column chromatography (ethyl acetate/petroleum ether = 1:10, R_f = 0.3); IR (neat): ν_{max} 3067, 3036, 2951, 2872, 1732, 1483, 1456, 1348, 1232, 1165, 1090, 1041, 1030 cm^{-1}; ^1H NMR (400

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702

MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 1H), 7.49 (d, J = 8.2 Hz, 2H), 7.21−7.17 (m, 1H), 7.13 (d, J = 8.2 Hz, 2H), 7.02−6.97 (m, 2H), 4.53 (d, J = 10.6 Hz, 1H), 3.80 (d, J = 10.6 Hz, 1H), 3.47−3.40 (m, 1H), 3.37 (s, 3H), 3.26 (td, J = 8.6, 3.8 Hz, 1H), 2.33 (s, 3H), 2.30−2.23 (m, 1H), 1.89−1.80 (m, 3H);); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 143.0, 135.9, 135.2, 130.7, 128.8, 128.3, 127.6, 123.8, 123.6, 123.3, 90.4, 66.2, 59.5, 51.8, 50.6, 42.1, 35.0, 32.7, 32.5, 21.4; HRMS (ESI) calcd for $C_{23}H_{25}NNaO_5S$ [M+Na$^+$], 450.1346; found: 450.1332.

Radical Trapping Experiment. To a mixture of tetrahydro-2*H*-pyran-4-carboxylic acid **2a** (0.2 mmol), enyne **1a** (0.4 mmol) $AgNO_3$ (6.8 mg, 20 mol%), $K_2S_2O_8$ (81.0 mg, 0.3 mmol), TEMPO (0.2 mmol) or BHT (0.2 mol), MeCN (2.0 mL) and H_2O (1.0 mL) were added under air at room temperature. The resulting mixture was stirred at 100 °C for 3 h. After the mixture was cooled to room temperature, EtOAc (10.0 mL) and H_2O (2.0 mL) were added sequentially. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to give the crude products. ^{1}H NMR did not dectect the formation of **3aa**. HR-MS detected the formation of TEMPO-pyran adduct **18**. HRMS (ESI) calcd for $C_{14}H_{28}NO_2$ [M+H$^+$], 242.2115; found: 242.2113.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b03091.

X-ray crystallographic data of compound **13** (CIF)
X-ray crystallographic data of compound **15ae** (CIF)
Copies of ^{1}H and ^{13}C NMR spectra of all new compounds and (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*zhipingli@ruc.edu.cn

ORCID

Leiyang Lv: 0000-0002-2850-8952
Zhiping Li: 0000-0001-7987-279X

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the National Science Foundation of China (21672259) and the Fundamental Research Funds for the Central Universities, the Research Funds of Renmin University of China (10XNL017).

■ REFERENCES

(1) Qin, T.; Cornella, J.; Li, C.; Malins, L. R.; Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. *Science* **2016**, *352*, 801−805.

(2) For selected examples, see: (a) Liu, C.; Wang, X.; Li, Z.; Cui, L.; Li, C. *J. Am. Chem. Soc.* **2015**, *137*, 9820−9823. (b) Wang, Z.; Zhu, L.; Yin, F.; Su, Z.; Li, Z.; Li, C. *J. Am. Chem. Soc.* **2012**, *134*, 4258−4263. (c) Bi, H.-P.; Zhao, L.; Liang, Y.-M.; Li, C.-J. *Angew. Chem., Int. Ed.* **2009**, *48*, 792−795.

(3) For selected reviews, see: (a) Xuan, J.; Zhang, Z.-G.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2015**, *54*, 15632−15641. (b) Dzik, W. I.; Lange, P. P.; Goossen, L. J. *Chem. Sci.* **2012**, *3*, 2671−2678. (c) Rodriguez, N.; Goossen, L. J. *Chem. Soc. Rev.* **2011**, *40*, 5030−5048.

(4) For selected recent reviews, see: (a) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369−375. (b) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960−9009. (c) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890−931.

(5) For selected recent reviews, see: (a) Hartwig, J. F. *J. Am. Chem. Soc.* **2016**, *138*, 2−24. (b) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem., Int. Ed.* **2014**, *53*, 74−100. (c) White, M. C. *Science* **2012**, *335*, 807−809.

(6) For photochemically induced functionalization of inert C(sp^3)-H bonds, see: (a) Yoshioka, S.; Nagatomo, M.; Inoue, M. *Org. Lett.* **2015**, *17*, 90−93. (b) Amaoka, Y.; Nagatomo, M.; Watanabe, M.; Tao, K.; Kamijo, S.; Inoue, M. *Chem. Sci.* **2014**, *5*, 4339−4345.

(7) For selected recent reviews, see; (a) Xie, J.; Pan, C.; Abdukader, A.; Zhu, C. *Chem. Soc. Rev.* **2014**, *43*, 5245−5256. (b) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788−802. (c) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147−1169.

(8) For selected examples, see: (a) Zhang, F.-L.; Hong, K.; Li, T.-J.; Park, H.; Yu, J.-Q. *Science* **2016**, *351*, 252−256. (b) Bedford, R. B.; Coles, S. J.; Hursthouse, M. B.; Limmert, M. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 112−114. (c) Jun, C.-H.; Lee, H.; Hong, J.-B. *J. Org. Chem.* **1997**, *62*, 1200−1201.

(9) For selected recent reviews, see: (a) Zhang, F.; Spring, D. R. *Chem. Soc. Rev.* **2014**, *43*, 6906−6919. (b) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236−10254. (c) Rousseau, G.; Breit, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2450−2494.

(10) For selected reviews, see: (a) Wang, L.; Xiao, J. *Top. Curr. Chem. (Z)* **2016**, *374*, 17. (b) Haibach, M. C.; Seidel, D. *Angew. Chem., Int. Ed.* **2014**, *53*, 5010−5036. (c) Peng, B.; Maulide, N. *Chem. - Eur. J.* **2013**, *19*, 13274−13287.

(11) For alkyl carboxylic acid as a traceless activating group for C(sp^3)-H functionalization, see: (a) Johnston, C. P.; Smith, R. T.; Allmendinger, S.; MacMillan, D. W. C. *Nature* **2016**, *536*, 322−325. (b) Zuo, Z.; Cong, H.; Li, W.; Choi, J.; Fu, G. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2016**, *138*, 1832−1835. (c) Nawrat, C. C.; Jamison, C. R.; Slutskyy, Y.; MacMillan, D. W. C.; Overman, L. E. *J. Am. Chem. Soc.* **2015**, *137*, 11270−11273.

(12) For aromatic carboxylic acid as a traceless directing group for C(sp^2)-H functionalization, see: (a) Zhang, Y.; Zhao, H.; Zhang, M.; Su, W. *Angew. Chem., Int. Ed.* **2015**, *54*, 3817−3821. (b) Luo, J.-F.; Preciado, S.; Larrosa, I. *J. Am. Chem. Soc.* **2014**, *136*, 4109−4112. (c) Cornella, J.; Righi, M.; Larrosa, I. *Angew. Chem., Int. Ed.* **2011**, *50*, 9429−9432.

(13) For seminal two examples on the radical cyclization of 1,n-enynes, see: (a) Qiu, J.-K.; Jiang, B.; Zhu, Y.-L.; Hao, W.-J.; Wang, D.-C.; Sun, J.; Wei, P.; Tu, S.-J.; Li, G. *J. Am. Chem. Soc.* **2015**, *137*, 8928−8931. (b) Hu, M.; Fan, J.-H.; Liu, Y.; Ouyang, X.-H.; Song, R.-J.; Li, J.-H. *Angew. Chem., Int. Ed.* **2015**, *54*, 9577−9580.

(14) For recent reviews on radical chemistry, see: (a) Studer, A.; Curran, D. P. *Nat. Chem.* **2014**, *6*, 765−773. (b) Studer, A.; Curran, D. P. *Angew. Chem., Int. Ed.* **2016**, *55*, 58−102. (c) Yan, M.; Lo, J. C.; Edwards, J. T.; Baran, P. S. *J. Am. Chem. Soc.* **2016**, *138*, 12692−12714.

(15) For recent examples on 1,5-H transfer, see: (a) Wang, L.; Xiao, J. *Org. Chem. Front.* **2016**, *3*, 635−638. (b) Mori, K.; Kurihara, K.; Yabe, S.; Yamanaka, M.; Akiyama, T. *J. Am. Chem. Soc.* **2014**, *136*, 3744−3747. (c) Zhang, C.; De, C. K.; Mal, R.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 416−417.

(16) For another evidence for the occurrence of 1,5-H shift, see: Hu, M.; Zou, H.-X.; Song, R.-J.; Xiang, J.-N.; Li, J.-H. *Org. Lett.* **2016**, *18*, 6460−6463.

DOI: 10.1021/acs.joc.6b03091
J. Org. Chem. 2017, 82, 2689−2702