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Cyclization and *N*-Iodosuccinimide-Induced Electrophilic Iodocyclization of 3-Aza-1,5-enynes To Synthesize 1,2-Dihydropyridines and 3-Iodo-1,2-dihydropyridines

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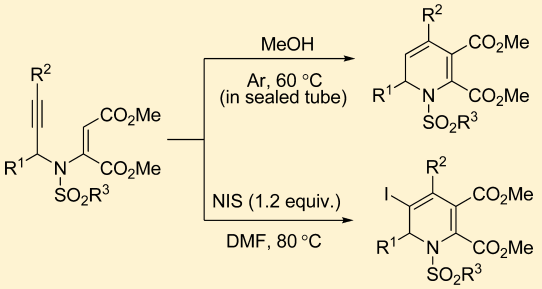
Supporting Information

ABSTRACT: Metal-free cyclization and *N*-iodosuccinimide-induced electrophilic iodocyclization of readily available 3-aza-1,5-enynes have been developed. The reactions selectively give 1,2-dihydropyridines and 3-iodo-1,2-dihydropyridines involving an aza-Claisen rearrangement and a 6π-electrocyclization step. Furthermore, the reaction could be carried out in 10 g scale for the synthesis of 1,2-dihydropyridines.



INTRODUCTION

Dihydropyridines (DHPs)[1] are an important class of heterocyclic compounds that have found widespread applications in therapeutically active compounds[2] and have been recognized as versatile synthetic intermediates for a broad variety of nitrogen-containing heterocycles such as piperidines[3] and pyridines.[4] Moreover, iodinated dihydropyridines are useful building blocks for allowing further structural elaboration via cross-coupling reactions.[5] Historically, 1,4-dihydropyridines (1,4-DHPs) have been extensively studied, whereas 1,2-dihydropyridines (1,2-DHPs) have received limited attention. Although 1,2-dihydropyridines are accessible via several routes,[1,6] the most popular approaches to 1,2-dihydropyridine synthesis is nucleophilic addition of a variety of nucleophiles to *N*-acyl, *N*-alkyl, or *N*-heteroatom pyridinium salts, and these processes usually require harsh reaction conditions and often yield regioisomeric products. The development of alternative methods for the synthesis of 1,2-dihydropyridines and iodo-1,2-dihydropyridines from readily available starting materials under mild conditions continues to be of intense interest.

3-Aza-1,5-enyne substrate is a versatile framework for the synthesis of a broad variety of heterocyclic compounds.[7] Cacchi and co-workers reported that *N*-propargylic β-enaminones could be selectively transformed into pyrroles or pyridines via 5-*exo*-*dig* or 6-*endo*-*dig* cyclization (Scheme 1, eq 1, left).[7a] Recently, the electrophilic cyclizations of *N*-propargylic β-enaminones with molecular iodine leading to iodo-substituted pyridines were studied by the Zora research group (Scheme 1, eq 1, right),[7b] and the resulting iodo-substituted pyridines were successfully elaborated to more complex molecules via palladium-catalyzed reactions.[7c] Saito and co-workers described that the similar structure, *N*-tosyl, *N*-propargylic β-enaminones, underwent Au(I)-catalyzed amino-Claisen rearrangement and heterocyclization to yield pyrroles (Scheme 1, eq 2).[7d] 1,2-Dihydropyridines (three examples) were also obtained as a dominant product or accompanied with pyrroles by changing the reaction conditions or the structure of starting materials.[7d] Recently, in a short communication, we reported that 3-aza-1,5-enyne **1** was selectvely trasformed into two kinds of functionalized pyrroles via regioselective sulfonyl group migration under thermal or base conditions (Scheme 1, eq 3, left).[7e] As a continuation of this work, we found that 1,2-dihydropyridines **2** and 3-iodo-1,2-dihydropyridines **3** were selectively synthesized by changing the reaction conditions via cyclization or *N*-iodosuccinimide (NIS)-induced electrophilic iodocyclization[8] of 3-aza-1,5-enynes **1** (Scheme 1, eq 3, right). Herein, we report the detailed results for selective synthesis of 1,2-dihydropyridines and 3-iodo-1,2-dihydropyridines via cyclization or NIS-induced electrophilic iodocyclization of 3-aza-1,5-enynes.

RESULTS AND DISCUSSION

Synthesis of 1,2-Dihydropyridines. In the course of our continuing investigation on the transformation of aza-enyne **1** to *N*-heterocycles, we found that treatment of the model substrate **1a** (R^1 = R^2 = Ph, R^3 = *p*-tolyl) in methanol at 60 °C for 48 h, a different type of heterocycle, 1,2-dihydropyridine **2a**, was obtained in 95% yield (Table 1, entry 1). The structure of **2a** was unambiguously confirmed by X-ray crystallography (see Supporting Information).

We directly explored the scope and generality of this reaction, and the results are given in Table 1. Aryl R^1 groups bearing different substituents, including electron-neutral groups (entry 1), electron-donating groups (entries 2−4), electron-withdrawing groups (entry 5), and halogen groups (entries 6−

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Scheme 1. Synthetic Variability of 3-Aza-1,5-enynes

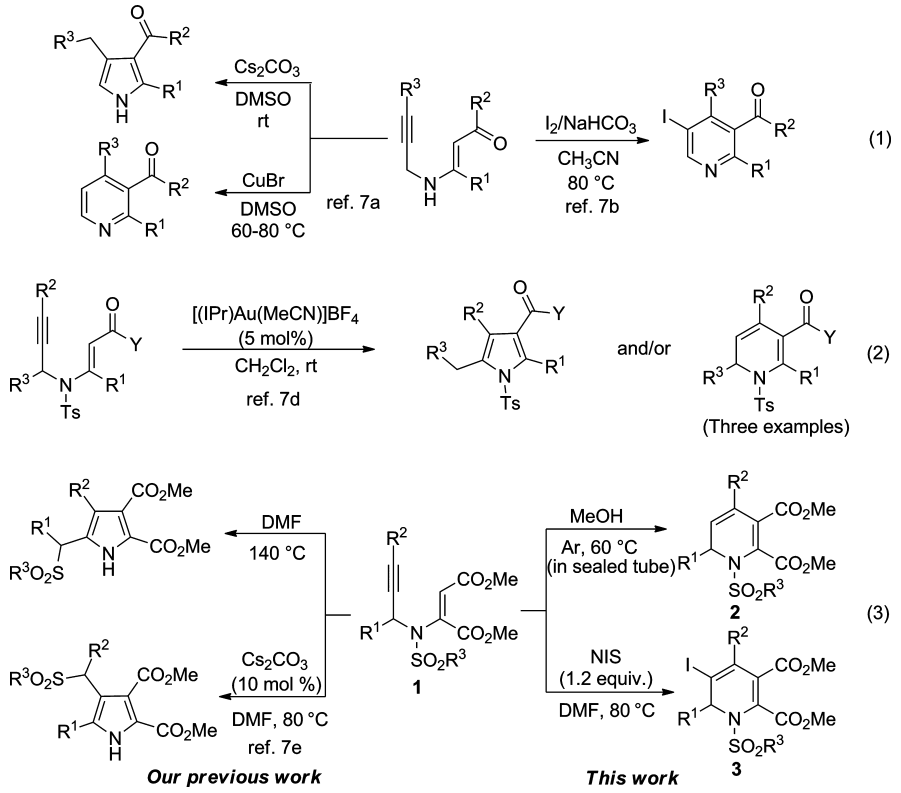
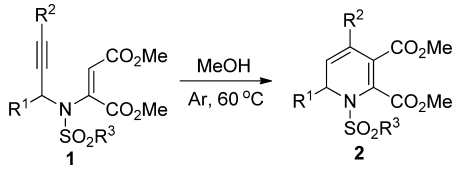


Table 1. Scope of the Synthesis of 1,2-Dihydropyridines[a]



entry	1	R^1	R^2	R^3	yield (%)
1	**1a**	Ph	Ph	4-MeC_6H_4	95 (**2a**)
2	**1b**	2-MeC_6H_4	Ph	4-MeC_6H_4	91 (**2b**)
3	**1c**	3-MeC_6H_4	Ph	4-MeC_6H_4	92 (**2c**)
4	**1d**	4-MeC_6H_4	Ph	4-MeC_6H_4	78 (**2d**)
5	**1e**	2-$CF_3C_6H_4$	Ph	4-MeC_6H_4	81 (**2e**)
6	**1f**	4-FC_6H_4	Ph	4-MeC_6H_4	88 (**2f**)
7	**1g**	2-ClC_6H_4	Ph	4-MeC_6H_4	87 (**2g**)
8	**1h**	2-BrC_6H_4	Ph	4-MeC_6H_4	86 (**2h**)
9	**1i**	1-naphthyl	Ph	4-MeC_6H_4	72 (**2i**)
10[b]	**1j**	^{i}Pr	Ph	4-MeC_6H_4	97 (**2j**)
11[c]	**1k**	^{c}Pr	Ph	4-MeC_6H_4	69 (**2k**)
12	**1l**	Ph	3-MeC_6H_4	4-MeC_6H_4	95 (**2l**)
13	**1m**	Ph	4-MeC_6H_4	4-MeC_6H_4	93 (**2m**)
14	**1n**	Ph	4-FC_6H_4	4-MeC_6H_4	95 (**2n**)
15	**1o**	Ph	4-ClC_6H_4	4-MeC_6H_4	97 (**2o**)
16	**1p**	Ph	^{n}Pr	4-MeC_6H_4	96 (**2p**)
17	**1q**	Ph	^{n}Bu	4-MeC_6H_4	97 (**2q**)
18	**1r**	Ph	Ph	Ph	92 (**2r**)
19	**1s**	Ph	Ph	2-ClC_6H_4	95 (**2s**)

[a]Reaction conditions: in sealed tube, 0.2 mmol of **1** in 2.0 mL of methanol was heated at 60 °C under an argon atmosphere until the consumption of the starting material unless otherwise noted. [b]At 140 °C. [c]At 100 °C.

8), were well-tolerated, and the desired products were isolated with moderate to high yields (78−95%). A fused ring was also suitable for this process, although a relatively lower yield was obtained (72%, entry 9). Alkyl R^1 substituents were also tolerated (entries 10 and 11) but only at elevated temperature (140 and 100 °C). Both aryl- and alkyl-substituted alkyne (R^2) units in the substrate were well-tolerated (entries 12−17). It is worthwhile to note that alkyl-substituted alknyl substrates also reacted in high yield (entries 16 and 17). The electronic properties of the sulfonyl group (R^3) had a relatively small impact on the yield (entries 1, 18, and 19).

Deuterium-labeling experiments were performed to explore the reaction mechanism. Substrate deuterated at the C4 position (**1a-D**) was subjected to the standard reaction conditions (Scheme 2a), where no deuterium scrambling was detected based on ^{1}H NMR spectroscopy, indicating that C−H cleavage is not involved at this position. When substrate **1a** was allowed to react in deuterium/methanol, 95% of the D atom was incorporated in the olefinic position of product **2a-D′** (Scheme 2b). A control experiment was also performed. 1,2-DHP **2a** was heated in deuterium/methanol, and no deuterated product was detected (Scheme 2c). This result ruled out a postreaction H/D exchange.

A plausible reaction mechanism is depicted in Scheme 3. Aza-Claisen rearrangement[7d,e] of **1** leads to **A**. Enamine **B** is the equilibrium form of imine **A** via 1,3-H-shift. H-shift (H^b) of **A** results in azatriene **C**. Subsequent 6π-electrocyclization[6d−f] of **C** generates 1,2- dihydropyridine **2**. The H atom (N−C−H, H^a) of the reactant connects to the same carbon atom in product **2**. This goes well with the deuterium-labeling experiment (Scheme 2a). The olefinic H atom (H^b) of **1** appears in the olefinic position of product **2**. When the reaction was performed in CD_3OD, H/D exchange takes place between

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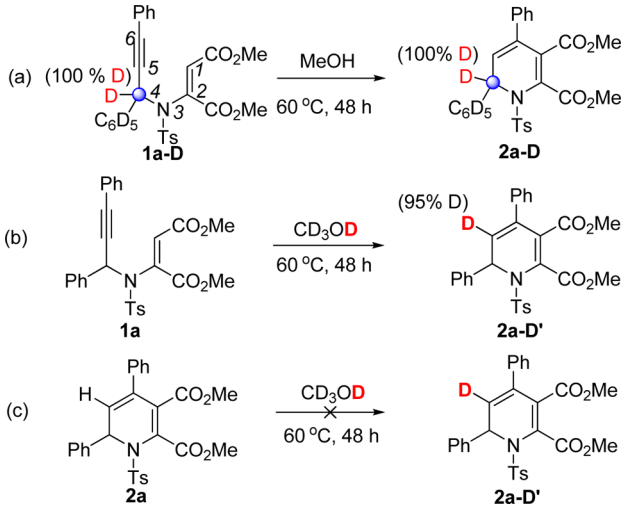
Scheme 2. Mechanistic Studies



intermediate **B** (H^b) and CD_3OD, thus the D atom appears in the olefinic position of the product **2**. This illustrates the D-incorporated experiment (Scheme 2b).

This reaction could also be carried out *under air atmosphere* and in 10 g scale (Scheme 4). The product **2a** was obtained in 96% yield after simple precipitation and recrystallization. Reactant **1a** was readily prepared from commercially available starting materials.[7e,9] This method provided a highly efficient, operationally convenient approach to access polysubstituted 1,2-dihydropyridines.

Synthesis of 3-Iodo-1,2-dihydropyridines. After successful transformation of aza-enyne **1** to 1,2-dihydropyridines, we attempted to synthesize 3-iodo-1,2-dihydropyridines through a simple NIS-induced electrophilic cyclization. When model substrate **1a** (R^1 = R^2 = Ph, R^3 = *p*-tolyl) was treated with NIS (1.2 equiv) in THF at 80 °C under argon atmosphere, to our delight, the desired product **3a** was obtained in 66% yield (Table 2, entry 1). The structure of **3a** was also unambiguously confirmed by X-ray crystallography (see Supporting Information). The solvent effect was then investigated. The use of 1,2-dichloroethane or 1,4-dioxane as solvent did not greatly improve the product yield (Table 2, entries 2 and 3). Gratifyingly, the yield was improved to 87% when the reaction was performed in acetonitrile (Table 2, entry 4). Fortunately, **3a** was obtained in 93% yield when using DMF as solvent. Therefore, we performed the reaction in DMF at 80 °C under argon atmosphere.

Scheme 4. Synthesis of 1,2-DHP in 10 Gram Scale via Simple Operation

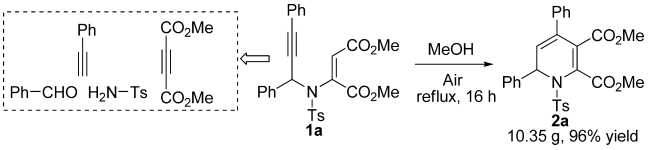
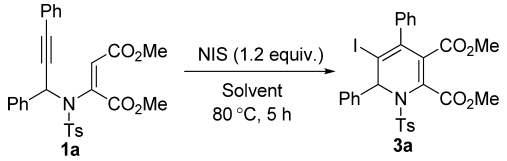


Table 2. Solvent Screening for 3-Iodo-1,2-dihydropyridines[a]



entry	solvent	yield (%)
1	THF	66
2	1,2-dichloroethane	64
3	1,4-dioxane	70
4	CH_3CN	87
5	DMF	93

[a]Reaction conditions: **1** (0.2 mmol), NIS (0.24 mmol) in 1 mL of solvent was heated at 80 °C under an argon atmosphere for 5 h.

Following the optimization of the reaction conditions, we explored the reaction scope, and the results are given in Table 3. Aryl R^1 and R^2 groups bearing different substituents were well-tolerated, and the desired products were isolated with moderate to high yields. A fused ring was also suitable for this process (entry 9). When R^1 was changed to an isopropyl or cyclopropyl group, the products were very complicated and the desired compounds were not obtained. Alkyl-substituted alkyne (R^2) units in the substrate were also tolerated (entries 16 and 17), but the yields were very low. The electronic properties of the sulfonyl group (R^3) had a relatively small impact on the yields (entries 1, 18, and 19).

A plausible reaction mechanism is depicted in Scheme 5. An initial attack of iodonium ion to the alkyne moiety leads to cation **D** and succinimide anion. Subsequent cyclization of cation **D** generates cation **E**. The succinimide anion traps a proton of **E** to furnish 3-iodo-1,2-dihydropyridine product **3** and succinimide.

Scheme 3. Proposed Mechanism

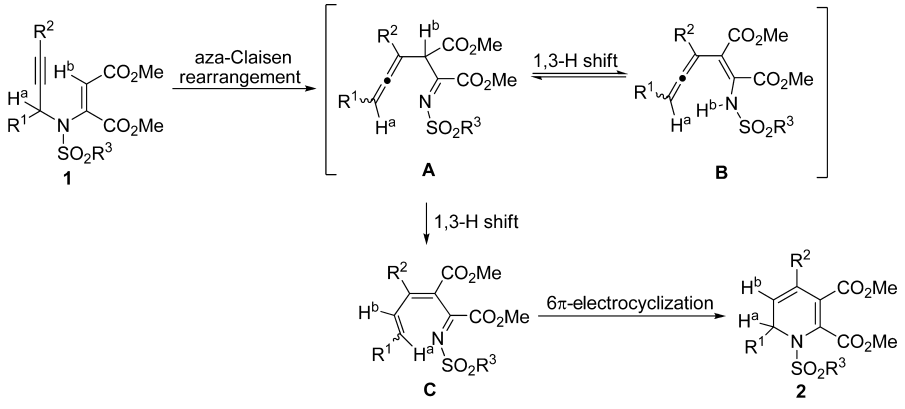


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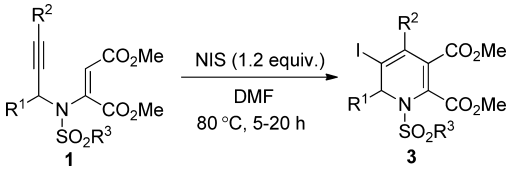
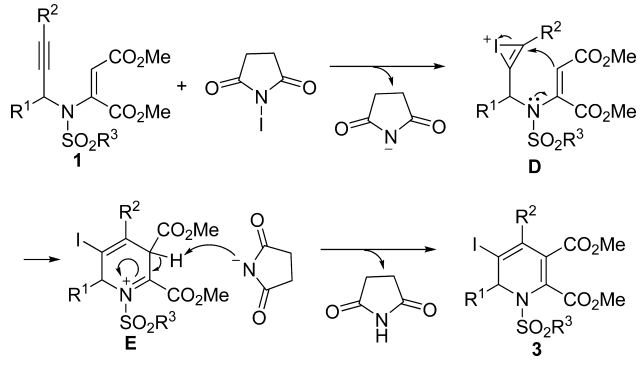
Table 3. Scope of Synthesis of 3-Iodo-1,2-dihydropyridines[a]



entry	1	R^1	R^2	R^3	yield (%)
1	**1a**	Ph	Ph	4-MeC_6H_4	93 (**3a**)
2	**1b**	2-MeC_6H_4	Ph	4-MeC_6H_4	89 (**3b**)
3	**1c**	3-MeC_6H_4	Ph	4-MeC_6H_4	88 (**3c**)
4	**1d**	4-MeC_6H_4	Ph	4-MeC_6H_4	71 (**3d**)
5[b]	**1e**	2-$CF_3C_6H_4$	Ph	4-MeC_6H_4	69 (**3e**)
6	**1f**	4-FC_6H_4	Ph	4-MeC_6H_4	92 (**3f**)
7[b]	**1g**	2-ClC_6H_4	Ph	4-MeC_6H_4	85 (**3g**)
8[b]	**1h**	2-BrC_6H_4	Ph	4-MeC_6H_4	80 (**3h**)
9	**1i**	1-naphthyl	Ph	4-MeC_6H_4	63 (**3i**)
10[c]	**1j**	^{i}Pr	Ph	4-MeC_6H_4	*d*
11[c]	**1k**	^{c}Pr	Ph	4-MeC_6H_4	*d*
12	**1l**	Ph	3-MeC_6H_4	4-MeC_6H_4	89 (**3l**)
13	**1m**	Ph	4-MeC_6H_4	4-MeC_6H_4	83 (**3m**)
14	**1n**	Ph	4-FC_6H_4	4-MeC_6H_4	80 (**3n**)
15	**1o**	Ph	4-ClC_6H_4	4-MeC_6H_4	93 (**3o**)
16[b]	**1p**	Ph	^{n}Pr	4-MeC_6H_4	23 (**3p**)
17[b]	**1q**	Ph	^{n}Bu	4-MeC_6H_4	33 (**3q**)
18	**1r**	Ph	Ph	Ph	90 (**3r**)
19	**1s**	Ph	Ph	2-ClC_6H_4	91 (**3s**)

[a]Reaction conditions: **1** (0.2 mmol), NIS (0.24 mmol) in DMF (1 mL) was heated at 80 °C under an argon atmosphere for 5 h unless otherwise noted. [b]For 10 h. [c]At 140 °C, 20 h. [d]The products were very complicated, and the desired compounds were not obtained.

Scheme 5. Proposed Mechanism of NIS-Induced Cyclization of 3-Aza-1,5-enynes

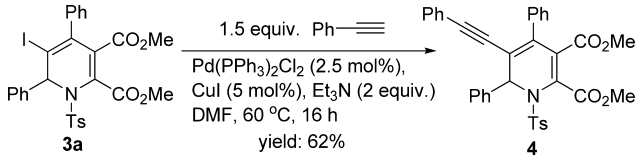


The presence of iodine at the product allows further structural elaboration for increasing molecular complexity via palladium-catalyzed reactions. For example, when compound **3a** was exposed to Sonogashira coupling conditions[10] with phenylacetylene, the corresponding coupling product **4** was obtained in 62% yield (Scheme 6).

CONCLUSIONS

In summary, we have developed highly efficient cyclization and iodocyclization of 3-aza-1,5-enynes for the synthesis of 1,2-dihydropyridines and 3-iodo-1,2-dihydropyridines. The metal-free approach to 1,2-dihydropyridines involves an aza-Claisen rearrangement and a 6π-electrocyclization step. This reaction can be carried out under air atmosphere in 10 g scale via simple operation. 3-Iodo-1,2-dihydropyridines are obtained via NIS-induced electrophilic iodocyclization of 3-aza-1,5-enyne, which makes it possible to allow further structural derivatization using palladium-catalyzed cross-coupling reactions. Studies to explore more versatile reactions of the aza-enyne building block by changing the substituent patterns or altering reaction conditions are currently in process.

Scheme 6. Further Structural Elaboration of the Iodide Product



EXPERIMENTAL SECTION

General. All reactions were carried out under an atmosphere of argon using standard Schlenk techniques unless otherwise noted. Column chromatography was carried out on silica gel (300−400 mesh) using a forced flow of eluent at 0.3−0.5 bar pressure. For TLC, silica gel GF254 was used and visualized by fluorescence quenching under UV light. Solvents were dried according to the standard procedure and were distilled prior to use. Starting materials **1** were prepared according to literature procedures.[7e,9]

^{1}H NMR, ^{13}C NMR, ^{19}F NMR spectra were recorded with 400 or 500 MHz spectrometers. The ^{1}H NMR spectra of **1**, **2**, **3p**−**3q**, and **4** were recorded at room temperature. The ^{1}H NMR spectra of **3a**−**3i**, **3l**−**3o**, and **3r**−**3s** were recorded in $(CD_3)_2SO$ at 60 °C. The chemical shifts for ^{1}H NMR were recorded in parts per million downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard (7.26 ppm for $CDCl_3$, 2.05 ppm for CD_3COCD_3, or 2.50 ppm for $(CD_3)_2SO$). The chemical shifts for ^{13}C NMR were recorded in parts per million downfield using the central peak of $CDCl_3$ (77.16 ppm) or CD_3COCD_3 (29.84 ppm) as the internal standard. Coupling constants (*J*) are reported in hertz and refer to apparent peak multiplications. The abbreviations s, d, t, q, and m stand for singlet, doublet, triplet, quartet, and multiplet in that order. All ^{13}C NMR spectra were proton decoupled.

General Procedure To Prepare the Starting Materials 3-Aza-1,5-enynes 1. The 3-aza-1,5-enynes were prepared following the procedure described in the literature:[7e,9] the corresponding propargyl amines and dimethyl acetylenedicarboxylate (1.2 equiv) were placed in a dried flask under argon atmosphere, and CH_2Cl_2 was added until the dissolution of the solid. Subsequently, 10−20 mol % of Cs_2CO_3 was added. The resulting mixture was stirred at 0 °C or room temperature until the consumption of propargyl amines was detected by TLC. The solvent was evaporated, and the crude product was directly purified by silica gel flash column chromatography (eluent: 10:1 petroleum ether/ethyl acetate) to give the desired complex **1**.

*Dimethyl 2-(N-(1,3-Diphenylprop-2-ynyl)-4-methylphenylsulfonamido)maleate (**1a**) (ref 7e):* white solid; 31% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.40−7.27 (m, 8H), 7.16 (dd, *J* = 8.1, 1.4 Hz, 2H), 6.54 (s, 1H), 6.10 (s, 1H), 3.76 (s, 3H), 3.60 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 164.2, 144.9, 139.7, 135.3, 133.9, 131.7, 129.8, 129.1, 128.8, 128.7, 128.5, 128.4, 128.0, 121.7, 117.4, 89.7, 82.8, 55.0, 53.0, 52.0, 21.7.

*Dimethyl 2-(N-(1,3-Diphenylprop-2-ynyl)-4-methylphenylsulfonamido)-maleate-d_6 (**1a-D**):* white solid; 59% yield; mp 100−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.30 (m, 5H), 7.15 (m, 2H), 6.10 (s, 1H), 3.76 (s, 3H), 3.59 (s, 3H), 2.31 (s, 3H); HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{19}D_6NO_6NaS$ $[M + Na]^+$ 532.1677, found 532.1671.

*Dimethyl 2-(4-Methyl-N-(3-phenyl-1-o-tolylprop-2-ynyl)phenylsulfonamido)maleate (**1b**):* white solid; 66% yield; mp 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J*

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= 7.7 Hz, 1H), 7.28 (m, 7H), 7.13 (m, 3H), 6.65 (s, 1H), 6.38 (s, 1H), 3.66 (s, 3H), 3.61 (s, 3H), 2.63 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.9, 144.6, 138.6, 137.7, 135.1, 131.6, 131.4, 131.2, 130.3, 129.6, 129.4, 129.0, 128.7, 128.4, 125.6, 124.1, 121.8, 89.4, 84.2, 53.9, 52.7, 52.3, 21.6, 19.5; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{27}NO_6NaS$ $[M + Na]^+$ 540.1457, found 540.1448.

*Dimethyl 2-(4-Methyl-N-(3-phenyl-1-m-tolylprop-2-ynyl)phenylsulfonamido)maleate (**1c**) (ref 7e):* white solid; 25% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 7.5 Hz, 2H), 7.32 (m, 2H), 7.29 (m, 2H), 7.24 (m, 2H), 7.15 (m, 2H), 7.11 (d, J = 7.8 Hz, 1H), 6.50 (s, 1H), 6.10 (s, 1H), 3.77 (s, 3H), 3.60 (s, 3H), 2.35 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.2, 144.9, 139.7, 138.4, 135.3, 133.7, 131.7, 129.8, 129.5, 129.4, 129.0, 128.6, 128.5, 128.4, 125.0, 121.8, 117.1, 89.5, 82.9, 54.9, 53.0, 52.0, 21.6, 21.5.

*Dimethyl 2-(4-Methyl-N-(3-phenyl-1-p-tolylprop-2-ynyl)phenylsulfonamido)maleate (**1d**) (ref 7e):* white solid; 51% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.31 (m, 5H), 7.15 (m, 4H), 6.50 (s, 1H), 6.10 (s, 1H), 3.77 (s, 3H), 3.61 (s, 3H), 2.34 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.3, 144.8, 139.8, 138.6, 135.3, 131.7, 130.8, 129.8, 129.4, 129.0, 128.5, 128.4, 127.9, 121.8, 117.1, 89.5, 83.0, 54.8, 53.0, 52.1, 21.7, 21.3.

*Dimethyl 2-(4-Methyl-N-(3-phenyl-1-(2-(trifluoromethyl)phenyl)-prop-2-ynyl)phenylsulfonamido)maleate (**1e**) (ref 7e):* white solid; 53% yield; mp 89−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (m, 3H), 7.72 (d, J = 7.7 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.32 (m, 3H), 7.22 (m, 4H), 6.89 (s, 1H), 6.52 (s, 1H), 3.74 (s, 3H), 3.39 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.4, 144.5, 135.5, 135.2, 133.2, 132.2, 131.8, 131.6, 131.4, 129.4, 129.3, 129.19, 128.90 (q, J = 31.0 Hz), 128.89, 128.4, 126.7 (q, J = 5.6 Hz), 124.0 (q, J = 274.4 Hz), 121.5, 89.4, 84.3, 52.5, 52.4, 52.0 (q, J = 2.5 Hz), 21.6.

*Dimethyl 2-(N-(1-(4-Fluorophenyl)-3-phenylprop-2-ynyl)-4-methylphenylsulfonamido)maleate (**1f**) (ref 7e):* white solid; 40% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 2H), 7.63 (m, 2H), 7.32 (m, 5H), 7.15 (d, J = 7.4 Hz, 2H), 7.06 (t, J = 8.2 Hz, 2H), 6.50 (s, 1H), 6.12 (s, 1H), 3.77 (s, 3H), 3.63 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.2, 162.9 (d, J = 244.7 Hz), 145.0, 139.5, 135.2, 131.7, 130.0, 129.9, 129.8, 129.2, 128.5, 128.4, 121.5, 118.1, 115.7 (d, J = 21.9 Hz), 89.8, 82.7, 54.4, 53.1, 52.2, 21.7.

*Dimethyl 2-(N-(1-(2-Chlorophenyl)-3-phenylprop-2-ynyl)-4-methylphenylsulfonamido)maleate (**1g**) (ref 7e):* white solid; 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.3 Hz, 2H), 7.66 (dd, J = 7.5, 1.6 Hz, 1H), 7.41 (dd, J = 7.8, 1.2 Hz, 1H), 7.27 (m, 9H), 6.81 (s, 1H), 6.44 (s, 1H), 3.69 (s, 3H), 3.53 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.7, 144.4, 137.3, 135.5, 135.2, 131.9, 131.69, 131.67, 130.6, 130.2, 129.4, 129.2, 128.8, 128.5, 126.7, 126.5, 121.7, 89.3, 83.8, 53.5, 52.6, 52.4, 21.7.

*Dimethyl 2-(N-(1-(2-Bromophenyl)-3-phenylprop-2-ynyl)-4-methylphenylsulfonamido)maleate (**1h**) (ref 7e):* white solid; 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.3 Hz, 2H), 7.67 (dd, J = 7.7, 1.6 Hz, 1H), 7.60 (dd, J = 7.9, 1.2 Hz, 1H), 7.31 (m, 4H), 7.20 (m, 5H), 6.77 (s, 1H), 6.45 (s, 1H), 3.69 (s, 3H), 3.53 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.6, 144.4, 137.2, 135.3, 133.6, 133.3, 132.3, 131.7, 130.8, 129.4, 129.2, 128.8, 128.5, 127.1, 126.9, 125.4, 121.7, 89.4, 83.9, 55.8, 52.5, 52.4, 21.7.

*Dimethyl 2-(4-Methyl-N-(1-(naphthalen-1-yl)-3-phenylprop-2-ynyl)phenylsulfonamido)maleate (**1i**) (ref 7e):* white solid; 38% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 8.6 Hz, 1H), 7.91 (d, J = 8.2 Hz, 2H), 7.84 (t, J = 8.5 Hz, 3H), 7.68 (t, J = 7.7 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.7 Hz, 1H), 7.32 (m, 3H), 7.23 (m, 3H), 7.17 (m, 2H), 6.42 (s, 1H), 3.64 (s, 3H), 3.12 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.5, 144.5, 137.0, 135.3, 133.9, 131.6, 131.4, 130.5, 129.5, 129.2, 129.0, 128.9, 128.8, 128.6, 128.4, 127.1, 126.9, 126.2, 124.7, 124.2, 121.9, 89.6, 84.2, 53.6, 52.3, 52.1, 21.6.

*Dimethyl 2-(4-Methyl-N-(4-methyl-1-phenylpent-1-yn-3-yl)-phenylsulfonamido)maleate (**1j**):* white solid; 52% yield; mp 85−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.3 Hz, 2H), 7.35−7.18 (m, 5H), 7.03 (dd, J = 8.1, 1.4 Hz, 2H), 6.49 (s, 1H), 4.70 (d, J = 10.4 Hz, 1H), 3.83 (s, 3H), 3.73 (s, 3H), 2.30 (s, 3H), 2.27−2.18 (m, 1H), 1.14 (d, J = 0.6 Hz, 3H), 1.13 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 164.6, 144.7, 141.4, 135.2, 131.5, 129.6, 128.7, 128.5, 128.3, 122.0, 117.1, 87.6, 84.8, 58.5, 53.1, 52.2, 30.5, 21.6, 20.4, 19.5; HRMS (Q-TOF, m/z) calcd for $C_{25}H_{27}NO_6NaS$ $[M + Na]^+$ 492.1457, found 492.1453.

*Dimethyl 2-(N-(1-Cyclopropyl-3-phenylprop-2-ynyl)-4-methylphenylsulfonamido)maleate (**1k**):* white solid; 45% yield; mp 79−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.7 Hz, 2H), 7.25 (m, 5H), 7.08 (d, J = 6.3 Hz, 2H), 6.46 (s, 1H), 4.77 (d, J = 6.6 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 2.33 (s, 3H), 1.40 (d, J = 3.5 Hz, 1H), 0.74−0.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 164.5, 144.4, 139.5, 135.5, 131.6, 129.6, 128.8, 128.4, 128.3, 122.5, 121.8, 86.7, 83.7, 56.3, 53.0, 52.3, 21.6, 14.2, 5.3, 3.6; HRMS (Q-TOF, m/z) calcd for $C_{25}H_{25}NO_6NaS$ $[M + Na]^+$ 490.1300, found 490.1314.

*Dimethyl 2-(4-Methyl-N-(1-phenyl-3-m-tolylprop-2-ynyl)phenylsulfonamido)maleate (**1l**):* white solid; 53% yield; mp 102−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.31 (m, 3H), 7.21−7.13 (m, 2H), 6.97 (d, J = 9.4 Hz, 2H), 6.54 (s, 1H), 6.11 (s, 1H), 3.76 (s, 3H), 3.60 (s, 3H), 2.33 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.2, 144.8, 139.7, 138.1, 135.3, 134.0, 132.2, 129.9, 129.8, 128.8, 128.7, 128.6, 128.5, 128.3, 128.0, 121.5, 117.4, 89.9, 82.4, 55.0, 53.0, 52.0, 21.7, 21.3; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{27}NO_6NaS$ $[M + Na]^+$ 540.1457, found 540.1439.

*Dimethyl 2-(4-Methyl-N-(1-phenyl-3-p-tolylprop-2-ynyl)phenylsulfonamido)maleate (**1m**) (ref 7e):* white solid; 29% yield; mp 107−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 7.8 Hz, 2H), 7.37 (t, J = 7.3 Hz, 2H), 7.32 (d, J = 7.1 Hz, 1H), 7.28 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 6.53 (s, 1H), 6.10 (s, 1H), 3.76 (s, 3H), 3.60 (s, 3H), 2.36 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.2, 144.8, 139.7, 139.3, 135.3, 134.0, 131.6, 129.8, 129.1, 128.7, 128.6, 128.5, 128.0, 118.7, 117.4, 89.9, 82.1, 55.0, 53.0, 52.1, 21.7, 21.6.

*Dimethyl 2-(N-(3-(4-Fluorophenyl)-1-phenylprop-2-ynyl)-4-methylphenylsulfonamido)maleate (**1n**):* white solid; 18% yield; mp 104−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.8 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H), 7.38 (t, J = 7.4 Hz, 2H), 7.33 (d, J = 7.1 Hz, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.16 (m, 2H), 6.99 (t, J = 8.3 Hz, 2H), 6.52 (s, 1H), 6.08 (s, 1H), 3.75 (s, 3H), 3.61 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 164.2, 162.9 (d, J = 245.5 Hz), 144.8, 139.6, 135.4, 133.8, 133.7, 133.6, 129.8, 128.8, 128.7, 128.6, 127.9, 117.6, 115.8 (d, J = 22.1 Hz), 88.6, 82.7, 54.9, 53.0, 52.1, 21.7.

*Dimethyl 2-(N-(3-(4-Chlorophenyl)-1-phenylprop-2-ynyl)-4-methylphenylsulfonamido)maleate (**1o**):* white solid; 31% yield; mp 85−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 7.4 Hz, 2H), 7.37 (t, J = 7.2 Hz, 2H), 7.34−7.24 (m, 5H), 7.09 (d, J = 7.6 Hz, 2H), 6.52 (s, 1H), 6.06 (s, 1H), 3.74 (s, 3H), 3.60 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 164.1, 144.9, 139.6, 135.4, 135.2, 133.7, 132.9, 129.8, 128.9, 128.8, 128.7, 128.6, 127.9, 120.2, 117.7, 88.5, 84.0, 54.9, 53.0, 52.1, 21.7; HRMS (Q-TOF, m/z) calcd for $C_{28}H_{24}NO_6NaSCl$ $[M + Na]^+$ 560.0911, found 560.0923.

*Dimethyl 2-(4-Methyl-N-(1-phenylhex-2-ynyl)phenylsulfonamido)maleate (**1p**):* white solid; 63% yield; mp 86−87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 2H), 7.56 (d, J = 6.8 Hz, 2H), 7.38−7.24 (m, 5H), 6.30 (s, 1H), 6.04 (s, 1H), 3.76 (s, 3H), 3.59 (s, 3H), 2.45 (s, 3H), 2.00 (s, 2H), 1.44−1.29 (m, 2H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 164.2, 144.6, 139.8, 135.5, 134.4, 129.1, 128.54, 128.49, 127.9, 116.5, 90.6, 74.1, 54.8, 52.9, 51.9, 21.7, 20.7, 13.6; inverse gated decoupling ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0 (1C), 164.2 (1C), 144.6 (1C), 139.8 (1C), 135.5 (1C), 134.4 (1C), 129.6 (2C), 128.54 (2C), **128.49 (3C)**, 127.9 (2C), 116.4 (1C), 90.6 (1C), 74.0 (1C), 54.8 (1C), 52.9 (1C), 51.9 (1C), **21.72 (2C)**, 20.7 (1C), 13.6 (1C); *Note: as shown in inverse gated decoupling ^{13}C NMR (integrate carbon singles), two sp^2 carbon peaks overlap at δ 128.49 ppm; two sp^3 carbon peaks overlap at δ*

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21.72 ppm. HRMS (Q-TOF, *m*/*z*) calcd for $C_{25}H_{27}NO_6NaS$ $[M + Na]^+$ 492.1457, found 492.1450.

*Dimethyl 2-(4-Methyl-N-(1-phenylhept-2-ynyl)phenylsulfonamido)maleate (**1q**) (ref 7e):* white solid; 63% yield; mp 97−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 8.3 Hz, 4H), 7.28 (m, 1H), 6.30 (s, 1H), 6.04 (s, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 2.45 (s, 3H), 2.03 (m, 2H), 1.28 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.2, 144.6, 139.9, 135.5, 134.4, 129.6, 128.6, 128.5, 127.9, 116.3, 90.8, 73.9, 54.8, 53.0, 52.0, 30.3, 22.1, 21.8, 18.4, 13.6.

*Dimethyl 2-(N-(1,3-Diphenylprop-2-ynyl)phenylsulfonamido)maleate (**1r**):* white solid; 35% yield; mp 105−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.2 Hz, 2H), 7.64 (d, *J* = 6.8 Hz, 2H), 7.54 (m, 3H), 7.34 (m, 6H), 7.18 (d, *J* = 6.6 Hz, 2H), 6.57 (s, 1H), 6.13 (s, 1H), 3.73 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.1, 139.2, 138.3, 133.9, 133.7, 131.7, 129.1, 128.8, 128.7, 128.4, 128.3, 128.0, 121.5, 118.6, 89.7, 82.7, 55.1, 53.0, 52.1; HRMS (Q-TOF, *m*/*z*) calcd for $C_{27}H_{23}NO_6NaS$ $[M + Na]^+$ 512.1144, found 512.1148.

*Dimethyl 2-(2-Chloro-N-(1,3-diphenylprop-2-ynyl)phenylsulfonamido)maleate (**1s**):* white solid; 41% yield; mp 116−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 6.1 Hz, 2H), 7.38 (m, 11H), 6.53 (s, 1H), 6.26 (s, 1H), 3.62 (6H, two CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.7, 138.2, 136.6, 134.6, 134.2, 133.8, 132.7, 132.2, 131.8, 129.2, 129.0, 128.7, 128.5, 128.4, 127.2, 124.3, 121.8, 89.2, 83.0, 55.6, 52.8, 52.2; HRMS (Q-TOF, *m*/*z*) calcd for $C_{27}H_{22}NO_6NaSCl$ $[M + Na]^+$ 546.0754, found 546.0747.

General Procedure A for the Synthesis of 1,2-Dihydropyridine 2. In a glass pressure tube (15 mL) equipped with a magnetic stir bar, starting material **1** (0.2 mmol) and methanol (2 mL) were added. The pressure tube was closed with a Teflon cap, and the resulting mixture was stirred at 60 °C under argon protection until the consumption of the starting material monitored by HPLC. After cooling to room temperature, the solvent was removed under vacuum. The residue was directly purified by flash chromatography (eluent: 10:1 petroleum ether/ethyl acetate) to give the desired 1,2-dihydropyridine **2**.

*Dimethyl 4,6-Diphenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2a**):* following general procedure A, 60 °C, 48 h; white solid; 95.3 mg; 95% yield; mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 7.4 Hz, 2H), 7.34 (m, 5H), 7.24 (m, 3H), 6.80 (d, *J* = 7.1 Hz, 2H), 5.86 (d, *J* = 6.2 Hz, 1H), 5.67 (d, *J* = 6.2 Hz, 1H), 3.80 (s, 3H), 3.49 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 164.3, 144.8, 137.0, 136.6, 135.8, 135.1, 130.9, 129.9, 128.8, 128.6, 128.2, 128.1, 128.0, 127.9, 127.8, 127.2, 127.1, 56.6, 53.1, 52.5, 21.7; HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{25}NO_6NaS$ $[M + Na]^+$ 526.1300, found 526.1308.

*Dimethyl 4,6-Diphenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate-d_6 (**2a-D**):* following general procedure A, 60 °C, 48 h; white solid; mp 133−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.27−7.19 (m, 3H), 6.88−6.73 (m, 2H), 5.67 (s, 1H), 3.81 (s, 3H), 3.50 (s, 3H), 2.43 (s, 3H); HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{19}D_6NO_6NaS$ $[M + Na]^+$ 532.1677, found 532.1686.

*Dimethyl 4,6-Diphenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate-d_1 (**2a-D′**) (partly deuterated product):* Following general procedure A, **1a** (0.1 mmol, 50.4 mg) in CD_3OD (1 mL) was heated at 60 °C under argon protection for 48 h. After cooling to room temperature, the solvent was removed under vacuum. The residue was directly purified by flash chromatography (eluent: 10:1 petroleum ether/ethyl acetate) to give the desired **2a-D′**: white solid, mp 130−131 °C; mp 137−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 7.3 Hz, 2H), 7.35 (m, 5H), 7.27−7.19 (m, 3H), 6.83−6.76 (m, 2H), 5.85 (s, **0.95H**), 5.67 (d, *J* = 6.3 Hz, **0.05H**), 3.81 (s, 3H), 3.50 (s, 3H), 2.42 (s, 3H); HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{24}DNO_6NaS$ $[M + Na]^+$ 527.1363, found 527.1351.

*Dimethyl 4-Phenyl-6-o-tolyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2b**):* following general procedure A, 60 °C, 72 h; white solid; 93.9 mg; 91% yield; mp 146−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.22 (m, 9H), 6.73 (d, *J* = 7.3 Hz, 2H), 6.10 (d, *J* = 6.0 Hz, 1H), 5.61 (d, *J* = 6.0 Hz, 1H), 3.76 (s, 3H), 3.53 (s, 3H), 2.67 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.4, 144.7, 137.0, 136.3, 135.1, 135.0, 133.6, 132.8, 131.5, 129.7, 128.8, 128.2, 128.1, 127.8, 127.7, 127.6, 126.3, 54.8, 53.0, 52.5, 21.6, 20.1; HRMS (Q-TOF, *m*/*z*) calcd for $C_{29}H_{27}NO_6NaS$ $[M + Na]^+$ 540.1457, found 540.1451.

*Dimethyl 4-Phenyl-6-m-tolyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2c**):* following general procedure A, 60 °C, 48 h; white solid; 95.0 mg; 92% yield; mp 136−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.29−7.18 (m, 6H), 7.13 (s, 1H), 6.79 (d, *J* = 7.6 Hz, 2H), 5.82 (d, *J* = 6.2 Hz, 1H), 5.66 (d, *J* = 6.2 Hz, 1H), 3.81 (s, 3H), 3.50 (s, 3H), 2.42 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 164.4, 144.7, 138.4, 136.9, 136.7, 135.8, 134.9, 130.9, 129.9, 129.5, 129.4, 128.6, 128.1, 128.0, 127.9, 127.9, 127.8, 127.3, 124.1, 56.6, 53.1, 52.4, 21.7, 21.6; HRMS (Q-TOF, *m*/*z*) calcd for $C_{29}H_{27}NO_6NaS$ $[M + Na]^+$ 540.1457, found 540.1458.

*Dimethyl 4-Phenyl-6-p-tolyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2d**):* following general procedure A, 60 °C, 72 h; white solid; 80.8 mg; 78% yield; mp 169−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.32 (m, 4H), 7.22 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.80 (dd, *J* = 7.9, 1.4 Hz, 2H), 5.82 (d, *J* = 6.2 Hz, 1H), 5.65 (d, *J* = 6.2 Hz, 1H), 3.79 (s, 3H), 3.49 (s, 3H), 2.42 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.4, 144.7, 138.4, 136.7, 135.9, 134.9, 133.9, 130.9, 129.9, 129.5, 128.1, 127.9, 127.7, 127.3, 127.2, 56.5, 53.1, 52.4, 21.7, 21.3; HRMS (Q-TOF, *m*/*z*) calcd for $C_{29}H_{27}NO_6NaS$ $[M + Na]^+$ 540.1457, found 540.1454.

*Dimethyl 4-Phenyl-1-tosyl-6-(2-(trifluoromethyl)phenyl)-1,6-dihydropyridine-2,3-dicarboxylate (**2e**):* following general procedure A, 60 °C, 48 h; white solid; 92.2 mg; 81% yield; mp 154−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.42 (dd, *J* = 17.1, 9.4 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.23−7.15 (m, 3H), 6.79 (d, *J* = 6.9 Hz, 2H), 6.22 (d, *J* = 6.3 Hz, 1H), 5.61 (d, *J* = 6.3 Hz, 1H), 3.93 (s, 3H), 3.54 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.6, 145.1, 138.1, 136.6, 135.0, 133.5, 132.7, 130.0, 129.9, 128.5, 128.4, 128.1, 128.0, 127.9, 127.1, 127.0, 126.3 (q, *J* = 5.9 Hz), 125.8, 125.2, 54.7, 53.3, 52.5, 21.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ −58.64; HRMS (Q-TOF, *m*/*z*) calcd for $C_{29}H_{24}NO_6F_3NaS$ $[M + Na]^+$ 594.1174, found 594.1168.

*Dimethyl 6-(4-Fluorophenyl)-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2f**):* following general procedure A, 60 °C, 48 h; white solid; 91.9 mg; 88% yield; mp 163−164 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.44 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.24 (m, 3H), 7.05 (m, 2H), 6.80 (m, 2H), 5.82 (d, *J* = 6.2 Hz, 1H), 5.64 (d, *J* = 6.2 Hz, 1H), 3.81 (s, 3H), 3.50 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 164.2, 163.0 (d, *J* = 247.3 Hz), 144.9, 136.5, 135.9, 135.4, 132.8, 130.7, 130.0, 129.1, 129.0, 128.3, 128.1, 128.0, 127.8, 126.6, 115.8 (d, *J* = 21.6 Hz), 55.9, 53.1, 52.5, 21.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ −114.4; HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{24}NO_6FNaS$ $[M + Na]^+$ 544.1206, found 544.1210.

*Dimethyl 6-(2-Chlorophenyl)-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2g**):* following general procedure A, 60 °C, 48 h; white solid; 93.6 mg; 87% yield; mp 138−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.0 Hz, 2H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 1H), 7.25 (m, 7H), 6.77 (d, *J* = 7.0 Hz, 2H), 6.23 (d, *J* = 6.1 Hz, 1H), 5.84 (d, *J* = 6.3 Hz, 1H), 3.93 (s, 3H), 3.52 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 164.6, 144.9, 136.7, 136.3, 135.7, 135.4, 135.2, 133.5, 130.7, 130.0, 129.9, 129.5, 128.16, 128.12, 128.09, 128.0, 127.9, 127.8, 125.9, 55.3, 53.3, 52.41, 21.7; HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{24}NO_6NaSCl$ $[M + Na]^+$ 560.0911, found 560.0905.

*Dimethyl 6-(2-Bromophenyl)-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2h**):* following general procedure A, 60 °C, 48 h; white solid; 100.3 mg; 86% yield; mp 137−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.31 (m, 3H), 7.23−7.11 (m, 4H), 6.78 (d, *J* = 6.6 Hz, 2H), 6.21 (d, *J* = 6.4 Hz, 1H), 5.87 (d, *J* = 6.4 Hz, 1H), 3.93 (s, 3H), 3.52 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 165.6, 164.6, 144.9, 138.2, 136.7, 135.2, 133.1, 129.8, 129.7, 129.6, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 125.9, 120.3, 57.3, 53.3, 52.4, 21.7; HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{24}NO_6NaSBr$ [M + Na]$^+$ 604.0405, found 604.0408.

*Dimethyl 6-(Naphthalen-1-yl)-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2i**):* following general procedure A, 60 °C, 66 h; white solid; 80.1 mg; 72% yield; mp 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.3 Hz, 1H), 7.86 (m, 4H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.54 (m, 2H), 7.42 (m, 1H), 7.31 (d, *J* = 7.3 Hz, 2H), 7.22 (m, 3H), 6.75 (d, *J* = 8.1 Hz, 3H), 5.72 (d, *J* = 4.6 Hz, 1H), 3.68 (s, 3H), 3.54 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 164.5, 148.6, 146.1, 144.8, 136.4, 135.2, 135.1, 134.4, 130.9, 130.7, 129.8, 129.7, 129.0, 128.3, 128.2, 128.1, 128.0, 127.9, 127.1, 126.2, 126.0, 125.5, 123.7, 54.4, 53.0, 52.5, 21.7; HRMS (Q-TOF, *m*/*z*) calcd for $C_{32}H_{27}NO_6NaS$ [M + Na]$^+$ 576.1457, found 576.1465.

*Dimethyl 6-Isopropyl-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2j**):* following general procedure A, 140 °C, 96 h; white solid; 90.8 mg; 97% yield; mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.23−7.13 (m, 3H), 6.67 (d, *J* = 7.7 Hz, 2H), 5.44 (d, *J* = 6.0 Hz, 1H), 4.23 (dd, *J* = 8.9, 6.0 Hz, 1H), 3.90 (s, 3H), 3.53 (s, 3H), 2.40 (s, 3H), 1.95−1.80 (m, 1H), 1.11 (d, *J* = 6.6 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 164.7, 144.5, 136.8, 136.0, 133.7, 131.1, 129.7, 128.8, 128.1, 128.0, 127.9, 127.8, 127.6, 60.6, 53.1, 52.4, 31.8, 21.6, 18.6, 18.3; HRMS (Q-TOF, *m*/*z*) calcd for $C_{25}H_{27}NO_6NaS$ [M + Na]$^+$ 492.1457, found 492.1460.

*Dimethyl 6-Cyclopropyl-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2k**):* following general procedure A, 100 °C, 48 h; white solid; 64.6 mg; 69% yield; mp 137−138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76−7.67 (m, 2H), 7.28 (m, 2H), 7.24−7.16 (m, 3H), 6.82−6.63 (m, 2H), 5.41 (d, *J* = 6.0 Hz, 1H), 4.08 (dd, *J* = 8.1, 6.0 Hz, 1H), 3.90 (s, 3H), 3.53 (s, 3H), 2.40 (s, 3H), 1.11 (m, 1H), 0.64−0.52 (m, 2H), 0.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 164.7, 144.5, 136.8, 136.1, 134.1, 130.4, 129.8, 128.4, 128.1, 128.0, 127.8, 127.7, 127.2, 58.9, 53.1, 52.4, 21.7, 14.0, 2.8, 2.4; HRMS (Q-TOF, *m*/*z*) calcd for $C_{25}H_{25}NO_6NaS$ [M + Na]$^+$ 490.1300, found 490.1296.

*Dimethyl 6-Phenyl-4-m-tolyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2l**):* following general procedure A, 60 °C, 66 h; white solid; 98.4 mg; 95% yield; mp 158−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.47 (d, *J* = 7.3 Hz, 2H), 7.41−7.29 (m, 5H), 7.15−7.04 (m, 2H), 6.72−6.48 (m, 2H), 5.85 (d, *J* = 6.1 Hz, 1H), 5.66 (d, *J* = 6.2 Hz, 1H), 3.80 (s, 3H), 3.51 (s, 3H), 2.43 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.4, 144.6, 137.5, 137.1, 136.6, 135.9, 135.2, 131.2, 129.9, 128.9, 128.8, 128.6, 127.8, 127.2, 126.9, 125.2, 56.6, 53.1, 52.4, 21.7, 21.5; HRMS (Q-TOF, *m*/*z*) calcd for $C_{29}H_{27}NO_6NaS$ [M + Na]$^+$ 540.1457, found 540.1448.

*Dimethyl 6-Phenyl-4-p-tolyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2m**):* following general procedure A, 60 °C, 48 h; white solid; 96.4 mg; 93% yield; mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 2H), 7.46 (d, *J* = 7.1 Hz, 2H), 7.34 (m, 5H), 7.02 (d, *J* = 7.3 Hz, 2H), 6.69 (d, *J* = 7.3 Hz, 2H), 5.84 (d, *J* = 5.8 Hz, 1H), 5.64 (d, *J* = 6.1 Hz, 1H), 3.79 (s, 3H), 3.51 (s, 3H), 2.42 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.4, 144.7, 138.0, 137.2, 136.0, 135.9, 135.0, 133.7, 131.2, 129.9, 128.8, 128.6, 128.5, 128.1, 127.8, 127.2, 126.8, 56.6, 53.0, 52.4, 21.7, 21.3; HRMS (Q-TOF, *m*/*z*) calcd for $C_{29}H_{27}NO_6NaS$ [M + Na]$^+$ 540.1457, found 540.1450.

*Dimethyl 4-(4-Fluorophenyl)-6-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2n**):* following general procedure A, 60 °C, 48 h; white solid; 99.1 mg; 95% yield; mp 135−136 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.45 (m, 2H), 7.35 (m, 5H), 6.91 (m, 2H), 6.80 (m, 2H), 5.86 (d, *J* = 6.3 Hz, 1H), 5.67 (d, *J* = 6.3 Hz, 1H), 3.81 (s, 3H), 3.51 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 164.3, 162.7 (d, *J* = 247.8 Hz), 144.8, 137.0, 135.9, 134.2, 132.6, 130.4, 130.1 (d, *J* = 8.2 Hz), 129.9, 128.9, 128.7, 128.6, 127.8, 127.2, 127.1, 114.9 (d, *J* = 21.6 Hz), 56.6, 53.1, 52.5, 21.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ −114.6; HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{24}NO_6FNaS$ [M + Na]$^+$ 544.1206, found 544.1213.

*Dimethyl 4-(4-Chlorophenyl)-6-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2o**):* following general procedure A, 60 °C, 48 h; white solid; 104.7 mg; 97% yield; mp 165−166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83−7.76 (m, 2H), 7.44 (dd, *J* = 5.1, 3.8 Hz, 2H), 7.39−7.29 (m, 5H), 7.23−7.18 (m, 2H), 6.80−6.71 (m, 2H), 5.87 (d, *J* = 6.3 Hz, 1H), 5.67 (d, *J* = 6.3 Hz, 1H), 3.81 (s, 3H), 3.52 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 164.2, 144.8, 136.9, 135.9, 135.1, 134.3, 134.1, 129.9, 129.8, 129.6, 128.9, 128.8, 128.7, 128.1, 127.8, 127.3, 127.1, 56.6, 53.2, 52.6, 21.7; HRMS (Q-TOF, *m*/*z*) calcd for $C_{28}H_{24}NO_6NaSCl$ [M + Na]$^+$ 560.0911, found 560.0904.

*Dimethyl 6-Phenyl-4-propyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2p**):* following general procedure A, 60 °C, 96 h; white solid; 90.2 mg; 96% yield; mp 101−102 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74−7.70 (m, 2H), 7.38−7.34 (m, 2H), 7.29 (m, 5H), 5.64 (d, *J* = 6.3 Hz, 1H), 5.47 (dt, *J* = 6.3, 1.3 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 2.40 (s, 3H), 1.95−1.89 (m, 2H), 1.23−1.13 (m, 1H), 1.04−0.97 (m, 1H), 0.73 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 164.6, 144.6, 137.6, 135.9, 132.8, 131.0, 129.7, 128.6, 128.3, 128.2, 127.6, 127.0, 123.5, 56.3, 53.0, 52.6, 33.6, 22.0, 21.6, 13.8; HRMS (Q-TOF, *m*/*z*) calcd for $C_{25}H_{27}NO_6NaS$ [M + Na]$^+$ 492.1457, found 492.1442.

*Dimethyl 4-Butyl-6-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**2q**):* following general procedure A, 60 °C, 66 h; colorless oil; 93.9 mg; 97% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 7.3 Hz, 2H), 7.28 (m, 5H), 5.65 (d, *J* = 6.2 Hz, 1H), 5.47 (d, *J* = 6.3 Hz, 1H), 3.77 (s, 3H), 3.70 (s, 3H), 2.40 (s, 3H), 1.93 (t, *J* = 7.1 Hz, 2H), 1.13 (m, 3H), 0.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 164.5, 144.5, 137.6, 135.9, 133.0, 131.1, 129.7, 128.5, 128.3, 128.2, 127.6, 127.0, 123.4, 56.2, 52.9, 52.6, 31.4, 31.2, 22.4, 21.6, 14.0; HRMS (Q-TOF, *m*/*z*) calcd for $C_{26}H_{29}NO_6NaS$ [M + Na]$^+$ 506.1613, found 506.1610.

*Dimethyl 4,6-Diphenyl-1-(phenylsulfonyl)-1,6-dihydropyridine-2,3-dicarboxylate (**2r**):* following general procedure A, 60 °C, 96 h; white solid; 90.2 mg; 92% yield; mp 121−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (m, 2H), 7.63 (m, 1H), 7.54 (m, 2H), 7.47 (m, 2H), 7.36 (m, 3H), 7.23 (m, 3H), 6.82 (m, 2H), 5.86 (d, *J* = 6.3 Hz, 1H), 5.69 (d, *J* = 6.3 Hz, 1H), 3.81 (s, 3H), 3.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 164.3, 139.0, 137.0, 136.6, 135.3, 133.7, 130.9, 129.4, 128.9, 128.7, 128.2, 128.1, 128.0, 127.7, 127.2, 127.0, 125.6, 56.7, 53.1, 52.5; HRMS (Q-TOF, *m*/*z*) calcd for $C_{27}H_{23}NO_6NaS$ [M + Na]$^+$ 512.1144, found 512.1143.

*Dimethyl 1-(2-Chlorophenylsulfonyl)-4,6-diphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**2s**):* following general procedure A, 60 °C, 66 h; white solid; 99.9 mg; 95% yield; mp 131−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.7 Hz, 1H), 7.57−7.48 (m, 4H), 7.46−7.33 (m, 4H), 7.29−7.22 (m, 3H), 6.95 (d, *J* = 6.5 Hz, 2H), 5.98 (d, *J* = 6.2 Hz, 1H), 5.93 (d, *J* = 6.3 Hz, 1H), 3.78 (s, 3H), 3.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.9, 136.9, 136.8, 136.6, 135.8, 134.6, 132.8, 132.6, 132.3, 130.6, 128.8, 128.7, 128.3, 128.2, 128.1, 128.0, 127.2, 127.1, 127.0, 56.5, 53.1, 52.4; HRMS (Q-TOF, *m*/*z*) calcd for $C_{27}H_{22}NO_6NaSCl$ [M + Na]$^+$ 546.0754, found 546.0758.

Procedure for the Syntheses 1,2-DHP 2a in 10 Gram Scale. In a Schlenk tube (500 mL) equipped with a condenser and a magnetic stir bar, starting material **1a** (10.78 g, 0.0214 mol) and methanol (215 mL) were added. The resulting mixture was stirred *under air atmosphere* in reflux condition for 16 h. After cooling to room temperature, the resulting mixture was kept undisturbed for 3 h and 8.83 g product **2a** precipitated from the solution. After removal of the residual solvent, the solid was washed with the solution of ethyl acetate/petroleum ether = 10:1 (50 mL) to give the second batch of product (1.52 g). Yield 10.35 g, 96% yield.

General Procedure for the Syntheses of 3-Iodo-1,2-dihydropyridines 3. In a glass pressure tube (10 mL) equipped with a magnetic stir bar, starting material **1** (0.2 mmol), NIS (0.24 mmol, 54.0 mg), and DMF (1 mL) were added. The resulting mixture was stirred at 80 °C under argon protection until the consumption of the starting material monitored by HPLC. After cooling to room temperature, the solvent was removed under vacuum. The residue

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was directly purified by flash chromatography (eluent: 20:1 petroleum ether/ethyl acetate) to give the desired 3-iodo-1,2-dihydropyridine **3**.

*Dimethyl 5-Iodo-4,6-diphenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3a**):* white solid; 117.0 mg; 93% yield; mp 110−111 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.84−7.77 (m, 2H), 7.56 (d, J = 7.9 Hz, 2H), 7.47−7.40 (m, 5H), 7.34−7.28 (m, 3H), 6.59 (s, 2H), 5.97 (s, 1H), 3.64 (s, 3H), 3.30 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 164.1, 145.1, 140.2, 138.9, 135.4, 134.1, 130.4, 130.2, 129.2, 129.0, 128.6, 128.5, 128.2, 128.0, 127.9, 126.6, 99.6, 67.3, 53.1, 52.5, 21.8; HRMS (Q-TOF, m/z) calcd for $C_{28}H_{24}NO_6NaSI$ [M + Na]$^+$ 652.0267, found 652.0264.

*Dimethyl 5-Iodo-4-phenyl-6-(o-tolyl)-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3b**):* white solid; 114.9 mg; 89% yield; mp 142−143 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.79 (d, J = 8.3 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 7.37−7.29 (m, 5H), 7.24 (m, 2H), 6.48 (s, 2H), 6.23 (s, 1H), 3.63 (s, 3H), 3.35 (s, 3H), 2.65 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 164.3, 145.0, 140.0, 138.8, 138.4, 134.6, 132.7, 131.8, 130.5, 130.0, 129.4, 128.6, 128.5, 128.3, 128.1, 127.4, 126.5, 125.8, 102.7, 65.3, 53.0, 52.5, 21.8, 20.2; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{26}NO_6NaSI$ [M + Na]$^+$ 666.0423, found 666.0431.

*Dimethyl 5-Iodo-4-phenyl-6-(m-tolyl)-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3c**):* white solid; 113.5 mg; 88% yield; mp 169−170 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.86−7.78 (m, 2H), 7.58 (d, J = 7.9 Hz, 2H), 7.38−7.30 (m, 4H), 7.28−7.19 (m, 3H), 6.60 (s, 2H), 5.93 (s, 1H), 3.66 (s, 3H), 3.32 (s, 3H), 2.52 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 164.2, 145.0, 140.0, 138.9, 138.7, 135.3, 133.9, 130.5, 130.2, 130.0, 128.9, 128.8, 128.6, 128.5, 128.2, 127.9, 126.5, 124.7, 99.8, 67.3, 53.1, 52.5, 21.8, 21.7; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{26}NO_6NaSI$ [M + Na]$^+$ 666.0423, found 666.0406.

*Dimethyl 5-Iodo-4-phenyl-6-(p-tolyl)-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3d**):* white solid; 91.5 mg; 71% yield; mp 183−184 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.84−7.77 (m, 2H), 7.62−7.54 (m, 2H), 7.33 (m, 5H), 7.26 (d, J = 8.0 Hz, 2H), 6.59 (s, 2H), 5.93 (s, 1H), 3.66 (s, 3H), 3.32 (s, 3H), 2.51 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.2, 145.0, 140.0, 139.1, 138.9, 135.3, 130.8, 130.5, 130.2, 129.8, 128.6, 128.5, 128.2, 128.1, 127.8, 126.4, 100.0, 67.1, 53.1, 52.5, 21.8, 21.4; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{26}NO_6NaSI$ [M + Na]$^+$ 666.0423, found 666.0413.

*Dimethyl 5-Iodo-4-phenyl-1-tosyl-6-(2-(trifluoromethyl)phenyl)-1,6-dihydropyridine-2,3-dicarboxylate (**3e**):* white solid; 96.0 mg; 69% yield; mp 136−137 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.92 (d, J = 7.8 Hz, 1H), 7.81−7.67 (m, 4H), 7.56 (m, 3H), 7.38−7.25 (m, 3H), 6.54 (s, 1H), 6.45 (s, 2H), 3.62 (s, 3H), 3.38 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 164.3, 145.1, 140.2, 138.2, 134.4, 132.9, 132.8, 131.6, 129.9, 129.8, 129.5, 129.4 (d, J = 30.7 Hz), 128.7, 128.6, 128.5, 128.2, 127.5 (q, J = 6.0 Hz), 126.1, 123.9 (d, J = 274.8 Hz), 103.0, 63.2, 53.1, 52.6, 21.8; ^{19}F NMR (471 MHz, $CDCl_3$) δ −58.08; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{23}NO_6F_3NaSI$ [M + Na]$^+$ 720.0141, found 720.0123.

*Dimethyl 6-(4-Fluorophenyl)-5-iodo-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3f**):* white solid; 118.8 mg; 92% yield; mp 173−174 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.86−7.78 (m, 2H), 7.58 (dd, J = 8.5, 0.5 Hz, 2H), 7.51−7.45 (m, 2H), 7.36−7.26 (m, 5H), 6.60 (s, 2H), 5.98 (s, 1H), 3.66 (s, 3H), 3.32 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 164.0, 163.2 (d, J = 248.2 Hz), 145.2, 140.3, 138.7, 135.2, 130.3, 130.2, 129.8, 129.7, 128.7, 128.4, 128.3, 127.8, 126.5, 116.1 (d, J = 21.8 Hz), 99.1, 66.7, 53.2, 52.5, 21.8; ^{19}F NMR (471 MHz, $CDCl_3$) δ −113.47; HRMS (Q-TOF, m/z) calcd for $C_{28}H_{23}NO_6FNaSI$ [M + Na]$^+$ 670.0173, found 670.0190.

*Dimethyl 6-(2-Chlorophenyl)-5-iodo-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3g**):* white solid; 113.2 mg; 85% yield; mp 143−144 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.83−7.76 (m, 2H), 7.66−7.53 (m, 3H), 7.49 (td, J = 7.6, 1.8 Hz, 1H), 7.43 (td, J = 7.6, 1.4 Hz, 1H), 7.37 (dd, J = 7.8, 1.7 Hz, 1H), 7.35−7.28 (m, 3H), 6.53 (s, 3H), 3.65 (s, 3H), 3.37 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.2, 145.0, 139.8, 138.3, 134.7, 134.7, 131.8, 131.4, 130.9, 130.8, 130.0, 128.9, 128.7, 128.5, 128.3, 128.2, 127.7, 126.3, 101.8, 64.5, 53.1, 52.6, 21.8.; HRMS (Q-TOF, m/z) calcd for $C_{28}H_{23}NO_6NaSCII$ [M + Na]$^+$ 685.9877, found 685.9880.

*Dimethyl 6-(2-Bromophenyl)-5-iodo-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3h**):* white solid; 113.0 mg; 80% yield; mp 149−150 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.79 (dd, J = 10.9, 8.2 Hz, 3H), 7.58 (d, J = 8.1 Hz, 2H), 7.47 (dd, J = 11.0, 4.0 Hz, 1H), 7.39 (dd, J = 10.9, 4.5 Hz, 2H), 7.36−7.26 (m, 3H), 6.53 (d, J = 1.5 Hz, 3H), 3.66 (s, 3H), 3.38 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.2, 145.0, 139.3, 138.2, 134.6, 134.2, 133.4, 131.8, 131.1, 130.0, 128.9, 128.7, 128.5, 128.3, 128.2, 126.2, 124.6, 102.6, 66.5, 53.1, 52.6, 21.8; HRMS (Q-TOF, m/z) calcd for $C_{28}H_{23}NO_6NaSBrI$ [M + Na]$^+$ 729.9372, found 729.9376.

*Dimethyl 5-Iodo-6-(naphthalen-1-yl)-4-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3i**):* white solid; 85.3 mg; 63% yield; mp 210−211 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 8.80 (d, J = 8.5 Hz, 1H), 8.12−7.99 (m, 2H), 7.88 (d, J = 8.3 Hz, 2H), 7.75 (ddd, J = 8.4, 6.8, 1.3 Hz, 1H), 7.67−7.63 (m, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.59−7.53 (m, 1H), 7.48−7.44 (m, 1H), 7.41−7.26 (m, 3H), 6.86 (s, 1H), 6.54 (s, 2H), 3.50 (s, 3H), 3.37 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 164.2, 145.1, 140.7, 138.4, 134.6, 134.6, 133.0, 132.0, 130.6, 130.1, 128.9, 128.7, 128.6, 128.5, 128.2, 127.3, 127.1, 126.3, 126.2, 125.7, 125.2, 124.1, 102.2, 64.8, 52.9, 52.6, 21.8; HRMS (Q-TOF, m/z) calcd for $C_{32}H_{26}NO_6NaSI$ [M + Na]$^+$ 702.0423, found 702.0397.

*Dimethyl 5-Iodo-6-phenyl-4-m-tolyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3l**):* white solid; 114.4 mg; 89% yield; mp 153−154 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.89−7.78 (m, 2H), 7.59 (d, J = 8.0 Hz, 2H), 7.51−7.40 (m, 5H), 7.21 (t, J = 7.6 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 6.43 (s, 1H), 6.35 (s, 1H), 5.98 (s, 1H), 3.65 (s, 3H), 3.33 (s, 3H), 2.52 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.1, 144.9, 140.2, 138.6, 135.3, 134.0, 130.6, 130.2, 129.3, 129.1, 129.0, 128.8, 127.9, 127.8, 127.2, 126.3, 125.4, 110.1, 99.4, 67.2, 53.1, 52.5, 31.7, 22.8, 21.8, 21.5, 14.2; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{26}NO_6NaSI$ [M + Na]$^+$ 666.0423, found 666.0416.

*Dimethyl 5-Iodo-6-phenyl-4-(p-tolyl)-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3m**):* white solid; 107.4 mg; 83% yield; mp 191−192 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.81 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 7.50−7.39 (m, 5H), 7.13 (d, J = 7.9 Hz, 2H), 6.48 (s, 2H), 5.96 (s, 1H), 3.65 (s, 3H), 3.34 (s, 3H), 2.51 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.1, 145.0, 140.1, 138.4, 135.7, 135.2, 134.0, 130.7, 130.1, 129.1, 129.0, 128.9, 128.3, 127.9, 127.8, 126.3, 99.8, 67.2, 53.1, 52.5, 21.8, 21.5; HRMS (Q-TOF, m/z) calcd for $C_{29}H_{26}NO_6NaSI$ [M + Na]$^+$ 666.0423, found 666.0422.

*Dimethyl 4-(4-Fluorophenyl)-5-iodo-6-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3n**):* white solid; 103.9 mg; 80% yield; mp 183−184 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.82 (d, J = 8.3 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 7.50−7.39 (m, 5H), 7.21−7.11 (m, 2H), 6.65 (s, 2H), 5.99 (s, 1H), 3.66 (s, 3H), 3.36 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.525, 164.0, 162.7 (d, J = 248.8 Hz), 145.1, 139.3, 135.3, 134.7, 133.9, 130.5 (d, J = 8.2 Hz, 1H), 130.1, 130.0, 129.2, 129.0, 127.9, 127.8, 127.0, 115.4 (d, J = 21.4 Hz), 100.1, 67.3, 53.2, 52.6, 21.8; ^{19}F NMR (471 MHz, $CDCl_3$) δ −113.33; HRMS (Q-TOF, m/z) calcd for $C_{28}H_{23}NO_6FNaSI$ [M + Na]$^+$ 670.0173, found 670.0190.

*Dimethyl 4-(4-Chlorophenyl)-5-iodo-6-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3o**):* white solid; 123.0 mg; 93% yield; mp 157−158 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.89−7.74 (m, 2H), 7.58 (d, J = 7.9 Hz, 2H), 7.50−7.42 (m, 5H), 7.41 (dd, J = 7.3, 1.4 Hz, 2H), 6.63 (s, 2H), 5.99 (s, 1H), 3.67 (s, 3H), 3.37 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 164.1, 145.1, 139.2, 137.2, 135.2, 134.7, 133.9, 130.2, 130.1, 129.7, 129.3, 129.1, 128.6, 128.5, 127.9, 127.8, 99.8, 67.3, 53.2, 52.7, 21.8; HRMS (Q-TOF, m/z) calcd for $C_{28}H_{23}NO_6NaSClI$ [M + Na]$^+$ 685.9877, found 685.9885.

*Dimethyl 5-Iodo-6-phenyl-4-propyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3p**):* white solid; 27.6 mg; 23% yield; mp 158−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.46−7.29 (m, 7H), 5.89 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.44 (s,

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3H), 2.32−2.19 (m, 1H), 1.99−1.88 (m, 1H), 1.20−1.03 (m, 1H), 0.83 (t, J = 7.1 Hz, 3H), 0.78−0.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 164.0, 144.6, 137.3, 134.8, 133.9, 130.4, 129.7, 129.2, 128.7, 128.5, 127.6, 127.2, 96.5, 66.9, 52.8, 52.6, 37.9, 21.4, 14.0; HRMS (Q-TOF, m/z) calcd for $C_{25}H_{26}NO_6NaSI$ $[M + Na]^+$ 618.0423, found 618.0422.

*Dimethyl 4-Butyl-5-iodo-6-phenyl-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**3q**):* white solid; 40.0 mg; 33% yield; mp 149−150 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78−7.72 (m, 2H), 7.41−7.37 (m, 2H), 7.35 (m, 5H), 5.89 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.43 (s, 3H), 2.26 (td, J = 12.5, 4.9 Hz, 1H), 2.02−1.91 (m, 1H), 1.28−1.19 (m, 2H), 1.08 (tdd, J = 8.2, 5.8, 3.3 Hz, 1H), 0.87 (t, J = 7.3 Hz, 3H), 0.66−0.55 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 164.3, 144.8, 137.7, 135.3, 134.3, 130.1, 129.5, 129.0, 128.8, 128.1, 127.9, 127.6, 96.6, 67.2, 53.1, 52.9, 36.2, 30.3, 22.9, 21.8, 14.0; HRMS (Q-TOF, m/z) calcd for $C_{26}H_{28}NO_6NaSI$ $[M + Na]^+$ 632.0580, found 632.0583.

*Dimethyl 5-Iodo-4,6-diphenyl-1-(phenylsulfonyl)-1,6-dihydropyridine-2,3-dicarboxylate (**3r**):* white solid; 113.3 mg; 90% yield; mp 162−163 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 7.96 (dt, J = 8.5, 1.6 Hz, 2H), 7.93−7.88 (m, 1H), 7.82−7.76 (m, 2H), 7.50−7.42 (m, 5H), 7.36−7.30 (m, 3H), 6.64 (s, 2H), 5.99 (s, 1H), 3.66 (s, 3H), 3.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 164.0, 140.3, 138.7, 138.4, 134.0, 133.9, 130.4, 129.6, 129.2, 129.0, 128.6, 128.5, 128.2, 127.9, 127.7, 126.4, 99.4, 67.2, 53.1, 52.5; HRMS (Q-TOF, m/z) calcd for $C_{27}H_{22}NO_6NaSI$ $[M + Na]^+$ 638.0110, found 638.0098.

*Dimethyl 1-((2-Chlorophenyl)sulfonyl)-5-iodo-4,6-diphenyl-1,6-dihydropyridine-2,3-dicarboxylate (**3s**):* white solid; 117.7 mg; 91% yield; mp 129−130 °C; ^{1}H NMR (500 MHz, DMSO, 60 °C) δ 8.21 (dd, J = 8.0, 1.5 Hz, 1H), 7.88 (dd, J = 8.0, 1.2 Hz, 1H), 7.82 (td, J = 7.7, 1.6 Hz, 1H), 7.67 (ddd, J = 8.0, 7.5, 1.3 Hz, 1H), 7.56−7.52 (m, 2H), 7.50−7.44 (m, 3H), 7.42−7.34 (m, 3H), 6.89 (d, J = 6.7 Hz, 2H), 5.91 (s, 1H), 3.64 (s, 3H), 3.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 163.5, 141.0, 139.0, 137.7, 134.8, 134.0, 133.1, 132.8, 132.7, 129.3, 129.2, 129.0, 128.7, 128.6, 128.4, 127.9, 127.4, 127.2, 98.5, 66.9, 53.1, 52.4; HRMS (Q-TOF, m/z) calcd for $C_{27}H_{21}NO_6NaSClI$ $[M + Na]^+$ 671.9721, found 671.9703.

Procedure for the Synthesis of Sonogashira Product 4. *Dimethyl 4,6-Diphenyl-5-(phenylethynyl)-1-tosyl-1,6-dihydropyridine-2,3-dicarboxylate (**4**).* To a solution of **3a** (125.9 mg, 0.2 mmol) in anhydrous DMF (1 mL) were added $PdCl_2(PPh_3)_2$ (3.5 mg, 2.5 mol %), CuI (1.9 mg, 5 mol %), and Et_3N (40.5 mg, 2.0 equiv). The reaction mixture was stirred for 5 min under argon protection at room temperature. Phenylacetylene (30.6 mg, 0.3 mmol) was then added. The resulting solution was stirred at 60 °C for 16 h. After cooling to room temperature, the solvent was removed under vacuum. The residue was directly purified by flash chromatography (eluent: 20:1 petroleum ether/ethyl acetate) to give the desired product **4**: yellow solid; 74.6 mg; 62% yield; mp 150−151 °C; ^{1}H NMR (400 MHz, acetone) δ 7.90 (d, J = 7.9 Hz, 2H), 7.66 (d, J = 7.5 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 7.44 (t, J = 7.3 Hz, 2H), 7.41−7.28 (m, 7H), 7.16 (d, J = 7.2 Hz, 2H), 6.87 (s, 2H), 6.00 (s, 1H), 3.77 (s, 3H), 3.42 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, acetone) δ165.4, 164.4, 146.2, 138.7, 137.3, 136.4, 136.0, 132.4, 132.3, 130.9, 130.2, 129.7, 129.6, 129.5, 129.4, 129.0, 128.5, 128.4, 127.9, 127.7, 123.0, 120.4, 100.0, 88.7, 60.6, 53.2, 52.6, 21.5; HRMS (Q-TOF, m/z) calcd for $C_{36}H_{29}NO_6NaS$ $[M + Na]^+$ 626.1613, found 626.1614.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C, and ^{19}F NMR spectra, HRMS spectra, and crystallographic information files (CIF) for compounds **2a** and **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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