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Iodocyclization of Ethoxyethyl Ethers to Ynamides: An Immediate Construction to Benzo[*b*]furans

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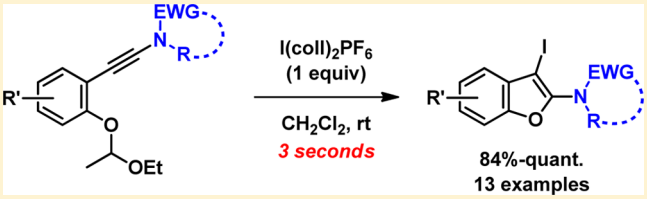
Supporting Information

ABSTRACT: The iodocyclization of ethoxyethyl ethers to ynamides was completed within three seconds. The corresponding benzo[*b*]furans were obtained in high yields (84%–quant.) under mild conditions.

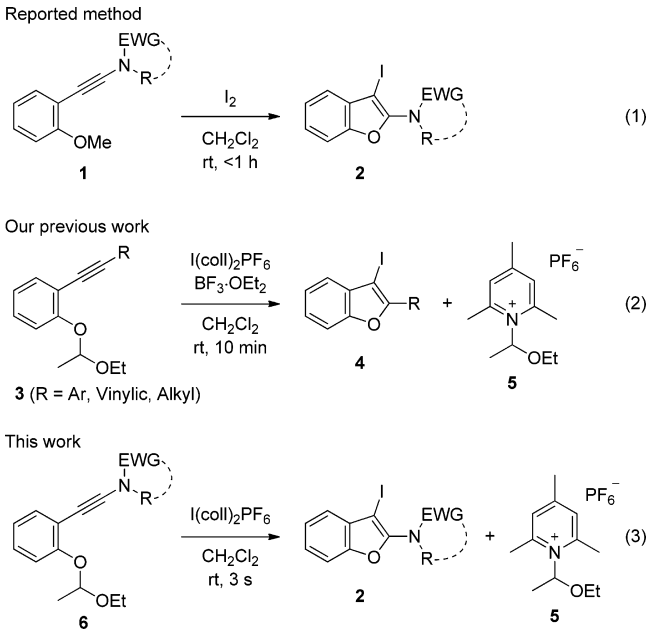


Iodocyclization, an electrophilic cyclization by iodonium ion, is one of the most powerful methodologies for the creation of not only ring structures but also further functionalizable iodo components.[1,2] In general, the ease of iodocyclization for alkyne-containing substrates depends on the substituent effect of alkynes: conjugated sp^2 carbon, sulfur, and selenium-substituted alkynes are good substrates for the iodocyclization because the formed iodonium intermediates are stabilized by the resonance and/or inductive effects.[3] Thus, nitrogen-substituted alkynes would also be desirable substrates for iodocyclization.

Ynamides, amide-substituted alkynes, have been established by Hsung as the ultimate synthetic units because of their electron-rich and relatively stable nature.[4] Although there have been several reports on the electrophilic cyclization of ynamides,[5] their electrophiles have been limited to Brønsted acids,[6] transition metals,[7] and carbocations.[8] Very recently, iodine-mediated electrophilic cyclization of *o*-anisole-substituted ynamides **1** for the synthesis of 2-amidobenzo[*b*]furans **2** was accomplished by Cao et al. (Scheme 1, eq 1).[9] The iodocyclization of ynamides by their methods afforded benzo[*b*]furans **2** in moderate to high yields, and one of the reactions was finished less than 1 h, albeit each reaction time was not reported. We thought this type of the iodocyclization would be accelerated if the leaving group on phenolic oxygen and the iodonium reagent were appropriately chosen.

We have already achieved the versatile synthesis of benzo[*b*]furans **4** by iodocyclization of the corresponding ethoxyethyl ether-substituted alkynes **3** (Scheme 1, eq 2).[10,11] The ethoxyethyl ether serves not only as the protecting group and the directing group for the preparation of the precursors but also as a good leaving group for the cyclization step. In addition, the formed byproducts based on the *N*,*O*-acetal salt **5** can be easily removed by extraction and column chromatography. Thus, we applied our methodology to the ynamides **6** and found that the iodocyclization was finished within only 3 s under milder conditions than those previously reported (Scheme 1, eq 3). To the best of our knowledge, this reaction

Scheme 1. Benzo[*b*]furan Synthesis by Iodocyclization



time is the shortest among the reported iodocyclization. In this paper, we present a remarkable reaction of ynamides having ethoxyethyl ether mediated by bis(2,4,6-collidine)iodonium hexafluorophosphate [$I(coll)_2PF_6$] as the iodonium reagent.[2q,12]

Initially, ynamide **6a** was used as a precursor for the examination of iodocyclization (Table 1). In previous work, the iodocyclization of alkyne **3a** was performed in 2 equiv of $I(coll)_2PF_6$ and the same molar amount of $BF_3{\cdot}OEt_2$ as an activator (entry 1), and the conditions without $BF_3{\cdot}OEt_2$ required 24 h for almost complete consumption of **3a** (entry

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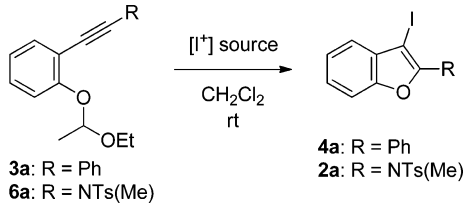
Table 1. Comparison of Reactivity with Alkyne 3a and Ynamide 6a[a]



3a: R = Ph
6a: R = NTs(Me)

4a: R = Ph
2a: R = NTs(Me)

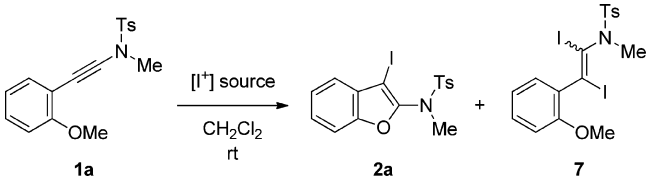
entry	substrate	[I+] source (equiv)	time	product (% yield)[b]
1[c]	**3a**	I(coll)$_2$PF$_6$ (2)	10 min	**4a** (quant.)
2	**3a**	I(coll)$_2$PF$_6$ (2)	24 h	**4a** (92%)
3	**6a**	I(coll)$_2$PF$_6$ (1)	20 min	**2a** (91%)
4	**6a**	I(coll)$_2$PF$_6$ (1)	1 min	**2a** (86%)
5	**6a**	I(coll)$_2$PF$_6$ (1)	10 s	**2a** (95%)
6	**6a**	**I(coll)$_2$PF$_6$ (1)**	**3 s**	**2a (98%)**
7	**6a**	I_2 (1)	10 s	**2a** (43%)
8	**6a**	NIS (1)	5 s	**2a** (81%)

[a]All reactions were carried out in CH_2Cl_2 (0.1 M). [b]Isolated yields. [c]2 equiv of BF_3·OEt_2 were added.

2).[10] On the other hand, iodocyclization of ynamide **6a** was accomplished with only 1 equiv of I(coll)$_2$PF$_6$ (entry 3). Surprisingly, this reaction was very rapid: when reaction time was shortened gradually from 20 min to 10 s, starting material **6a** was completely consumed and benzo[*b*]furan **2a** was obtained in high yields for each case (entries 3−5). Finally we found that this reaction time could be shortened to only 3 s to afford **2a** in 98% yield (entry 6). At this time, I(coll)$_2$PF$_6$ quickly dissolved in CH_2Cl_2. In contrast with the reported method by Cao,[9] **6a** was treated with iodine for 10 s to obtain **2a** in 43% yield, and the partially insoluble iodine was observed before the reaction mixture was quenched (entry 7). *N*-Iodosuccinimide (NIS) was also applicable for this rapid reaction to yield **2a** in 81%, but the starting material **6a** was recovered in 19% (entry 8). Therefore, I(coll)$_2$PF$_6$ was the most suitable iodinating reagent for the rapid synthesis of iodobenzo[*b*]furan **2** using ethoxyethyl ether-tethered ynamide **6**.[13,14]

Next, we examined the iodocyclization of methyl ether **1a** to compare with ethoxyethyl ether **6a** (Table 2). By a previously reported method,[9] **1a** was completely consumed for 30 min and benzo[*b*]furan **2a** was obtained in 68% yield along with diiodinated enamide **7** in 25% yield (entry 1). The use of 1

Table 2. Reactivity of Ynamide 1a



1a **2a** **7**

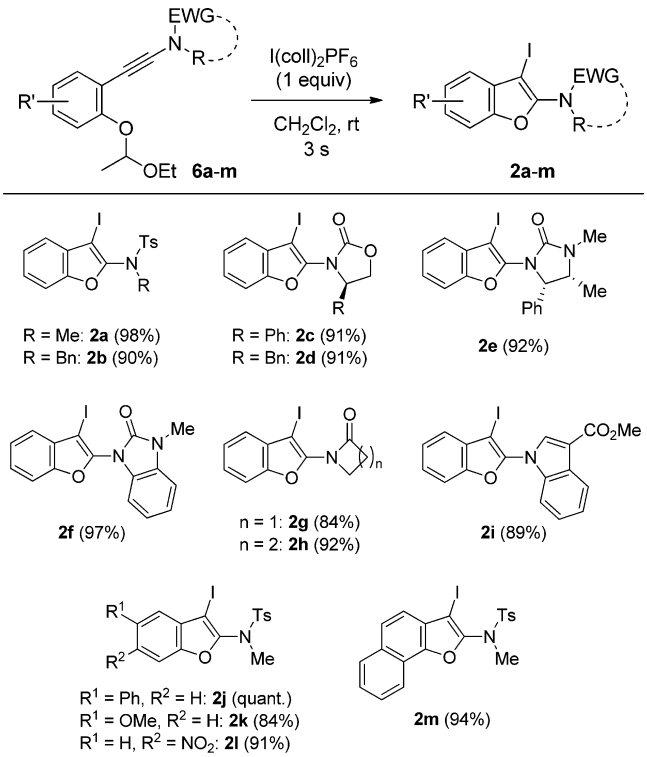
entry	[I+] source (equiv)	time	product (% yield)[a]
1[b]	I_2 (1.5)	30 min	**2a** (68%), 7 (25%)[d]
2[c]	I_2 (1)	10 s	**2a** (7%), 7 (40%),[d] **1a** (49%)
3[c]	NIS (1)	3 s	**2a** (9%), **1a** (74%)
4[c]	I(coll)$_2$PF$_6$ (1)	3 s	**2a** (60%)

[a]Isolated yields. [b]Reaction was carried out in CH_2Cl_2 (0.125 M). [c]Reactions were carried out in CH_2Cl_2 (0.1 M). [d]Ratio of stereoisomers of 7 is 2:1 in each case.

equiv of iodine and a short reaction time resulted in a poor yield of **2a** and the recovery of **1a** (entry 2). These results indicated that the use of iodine caused the production of undesirable side-product **7** and the reaction time of **1a** was longer than that of **6a** (Table 1, entry 7). NIS was also adopted for the iodocyclization of **1a**; however, the yield of **2a** was low when the reaction was quenched 3 s later (entry 3). On the other hand, the use of I(coll)$_2$PF$_6$ as the iodinating reagent resulted in the complete consumption of **1a** within 3 s affording **2a** in moderate yield (entry 4). Therefore, the choices of the ether unit and the iodinating reagent were important for the effective iodocyclization of the ynamide. Although the substrate having no protected phenolic hydroxyl group would be an alternative precursor for this reaction, we could not prepare such a compound due to its instability.

Having defined the optimized conditions and substrate system for the iodocyclization (Table 1, entry 6), we next examined the scope and limitations of the benzo[*b*]furan substrates (Table 3). Toward the substrate scope, all ynamides

Table 3. Iodocyclization of Ynamides 6a−m[a]



[a]All reactions were carried out in CH_2Cl_2 (0.1 M). Isolated yields are listed.

6a−m were prepared by the oxidative coupling with corresponding terminal alkynes and amides according to Stahl's procedure.[15] Notably, the ethoxyethyl ether has important roles as the protecting group and the directing group for the preparation of precursors. For example, α-lithiation and subsequent iodination of 1-(1-ethoxyethyl)naphthalene, Sonogashira coupling with ethynyltrimethylsilane, deprotection of silyl group,[10] and the oxidative coupling of corresponding terminal alkyne with *N*-methyl-*p*-tosylamide provided ynamide **6m**. As the amide part, sulfonamide **6a−b**, oxazolidinone **6c−d**, imidazolidinone **6e−f**, and lactam **6g−h** were applicable for this reaction. In addition, **6i**, a substituted indole having an electron-withdrawing group at the 3-position, also worked

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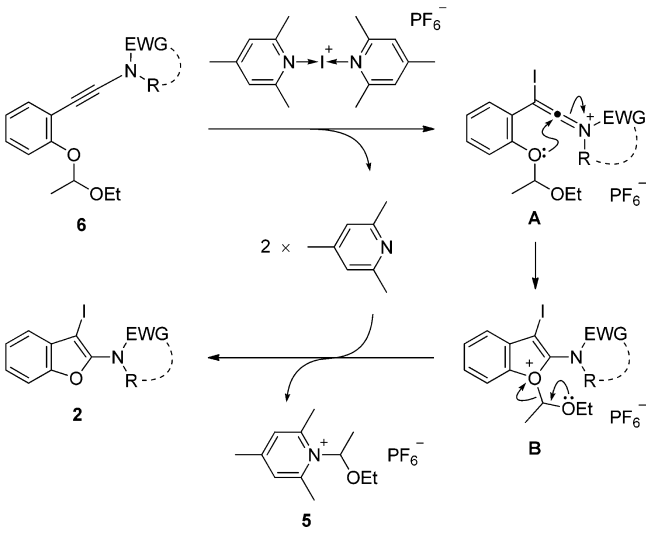
well to afford benzo[*b*]furan-indole biaryl system **2i** in 89% yield. The reactions were not affected by the presence of phenyl (**6j**), methoxy (**6k**), and nitro (**6l**) substituents. A bicyclic system such as naphthalene derivative **6m** gave the corresponding naphtho[1,2-*b*]furan **2m** in 94% yield. This reaction could be applied to gram scale synthesis and 1.18 g of **2c** was prepared at once in 85% yield within 3 s, albeit this reaction was not performed in a microflow reaction system. It is noteworthy that the efficient construction of benzo[*b*]furan was accomplished within 3 s to afford **2a**−**m** in high yields in all cases.

On the basis of the outcomes of these reactions, we have proposed a plausible mechanism for the iodocyclization as illustrated in Scheme 2. An electrophilic addition of ynamide **6**

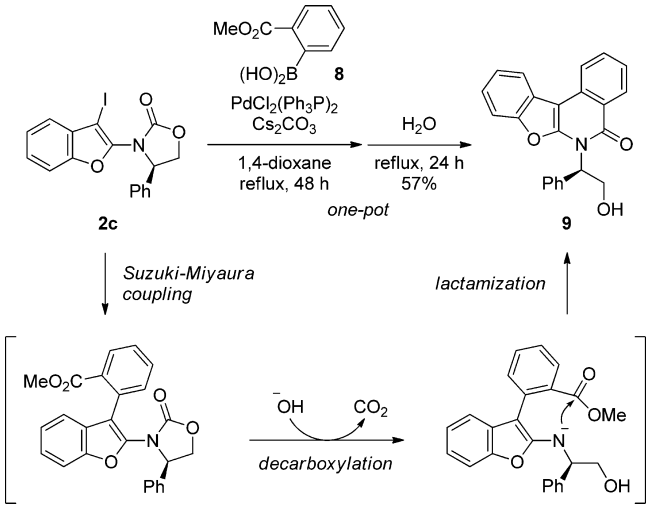
Scheme 2. Plausible Reaction Mechanism



with the iodinating reagent, $I(coll)_2PF_6$, forms keteniminium ion **A** and 2,4,6-collidine. The nucleophilic addition of the oxygen of the ethoxyethyl ether **A** gives intermediate **B**, which undergoes the loss of the ethoxyethyl group by the trap of 2,4,6-collidine to afford benzo[*b*]furan **2** and collidinium salt **5**.[10,16] We consider that all steps, the formation of **A**, cyclization, and the elimination of the ethoxyethyl group, are very rapid so that this reaction finished within 3 s. In contrast, the iodocyclization of alkyne **3** with $I(coll)_2PF_6$ was slow (Table 1, entry 2) because the formation of the iodonium ion might be the rate-determining step due to its thermodynamic instability. In addition, the ethoxyethyl group is a better leaving group than methyl ether **1** so that the transformation from **B** to benzo[*b*]furan **2** proceeds effectively by being trapped by 2,4,6-collidine. Moreover, our method produced 1 equiv of collidinium salt **5** and same molar amount of 2,4,6-collidine, which were easily removable by column chromatography on silica gel. Thus, the reaction could proceed under mild conditions, and our synthetic protocol was handy to user.

The 3-iodobenzofurans can be further functionalized by palladium-catalyzed coupling reactions at the C−I bond. Cao et al. reported the Suzuki-Miyaura coupling, the Sonogashira coupling, and Heck reaction of **2**.[9] To discover the new transformation, we developed a novel one-pot, tandem reaction of the Suzuki-Miyaura coupling/decarboxylation/lactamization of **2c** and arylboronic acid **8** to afford tetracyclic isoquinolinone **9** in 57% yield (Scheme 3).

Scheme 3. Transformation of 2c to 9



In summary, we have developed the most rapid construction of benzo[*b*]furans by iodocyclization of ethoxyethyl ethers to ynamides. Our protocol was user-friendly and the benzo[*b*]-furans were obtained in high yields under mild conditions. In addition, we found a new tandem reaction of the Suzuki-Miyaura coupling/decarboxylation/lactamization leading to a polycyclic isoquinolinone structure.

EXPERIMENTAL SECTION

General Information. IR spectra were measured using $CHCl_3$. Chemical shifts (δ) are reported in ppm relative to tetramethylsilane as internal reference ($CDCl_3$: δ = 0 ppm for ^1H) and residual solvent signal ($CDCl_3$: δ = 77.0 ppm for ^{13}C; DMSO-d_6: δ = 39.5 ppm for ^{13}C). *J*-values are given in Hz. MS was performed on an Exactive Orbitrap mass spectrometer.

***N*-((2-Methoxyphenyl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (1a).** According to the literature,[17] to a mixture of *N*-methyl-*p*-toluenesulfonamide (643 mg, 3.47 mmol), K_2CO_3 (959 mg, 6.94 mmol), $CuSO_4{\cdot}5H_2O$ (86.6 mg, 0.347 mmol), and 1,10-phenanthroline (125 mg, 0.694 mmol) in a reaction vial was added a solution of 1-(bromoethynyl)-2-methoxybenzene (805 mg, 3.81 mmol) in toluene (3.81 mL). The reaction mixture was filled with argon and heated at 70 °C for 24 h. The reaction mixture was cooled to room temperature and diluted with EtOAc and filtered through Celite, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with hexane/EtOAc = 4:1 to yield **1a** (817 mg, 75%): Colorless solid; IR ν_{max}: 3013, 2241, 1598, 1367, 1249, 1168 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.32 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.28−7.22 (m, 1H), 6.88 (td, *J* = 7.5, 1.2 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H) 3.87 (s, 3H), 3.16 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 144.6, 133.3, 133.2, 129.7, 129.2, 128.0, 120.4, 111.9, 110.6, 87.6, 65.3, 55.7, 39.4, 21.6; HR-ESIMS calcd for $C_{17}H_{18}NO_3S$ $[M + H]^+$ 316.1002. Found 316.1005.

General Procedure for the Preparation of Ynamides 6a-m (GP-1). According to the literature,[15] in a 1 L three-neck round-bottom flask equipped with a stir-bar, $CuCl_2$ (0.2 equiv), amide **B** (4−5 equiv) and Na_2CO_3 (2.0 equiv) were combined. The reaction flask was purged with oxygen gas. A solution of pyridine (2 equiv) in 0.1 M dry toluene was added to the reaction flask via a syringe. A balloon filled with oxygen gas was connected to the reaction flask via a needle. The flask was placed in an oil-bath and heated to 70 °C. A solution of terminal alkyne **A** (1 equiv) in 0.1 M dry toluene was added to the flask over 4 h by using a syringe pump. After the addition of **1** in toluene solution, the reaction mixture was allowed to stir at 70 °C for another 4 h, and then cooled to room temperature. After the crude

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mixture was concentrated in vacuo, the reaction mixture was purified by flash chromatography on silica gel to yield the ynamide **6**.

***N*-((2-(1-Ethoxyethoxy)phenyl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (6a).** According to **GP-1**, **6a** (780 mg, 79%) was obtained from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (502 mg, 2.64 mmol). Eluent: hexane/EtOAc = 7:1. Yellow oil; IR ν_{max}: 3034, 2241, 1599, 1368, 1169 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 8.7 Hz, 2H), 7.33 (dd, J = 7.5, 1.8 Hz, 1H), 7.24−7.19 (m, 1H), 7.01 (dd, J = 8.1, 1.5 Hz, 1H), 6.94 (dt, J = 7.5, 1.2 Hz, 1H), 5.42 (q, J = 5.4 Hz, 1H), 3.89−3.79 (m, 1H), 3.60−3.50 (m, 1H), 3.15 (s, 3H), 2.45 (s, 3H), 1.52 (d, J = 5.4 Hz, 3H) 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 144.6, 133.3, 132.9, 129.7, 128.9, 127.9, 121.8, 117.0, 114.2, 100.7, 87.5, 65.5, 61.7, 39.3, 21.6, 20.4, 15.1; HR-ESIMS calcd for $C_{20}H_{24}NO_4S$ $[M + H]^+$ 374.1421. Found 374.1423.

***N*-Benzyl-*N*-((2-(1-ethoxyethoxy)phenyl)ethynyl)-4-methylbenzenesulfonamide (6b).** According to **GP-1**, **6b** (221 mg, 33%) was obtained from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (285 mg, 1.50 mmol). Eluent: hexane/EtOAc = 5:1. Yellow oil; IR ν_{max}: 3034, 2238, 1598, 1366, 1170 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, J = 8.7 Hz, 2H), 7.38−7.34 (m, 2H), 7.31−7.26 (m, 5H), 7.20−7.14 (m, 2H), 6.98 (d, J = 8.1 Hz, 1H), 6.88 (t, J = 8.7 Hz, 1H), 5.35 (q, J = 5.4 Hz, 1H), 4.62 (d, J = 14.1 Hz, 1H), 4.55 (d, J = 14.1 Hz, 1H), 3.80−3.70 (m, 1H), 3.52−3.42 (m, 1H), 2.41 (s, 3H), 1.42 (d, J = 5.1 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.9, 144.4, 134.8, 134.5, 132.7, 129.6, 128.74, 128.70, 128.4, 128.1, 127.7, 121.6, 116.7, 114.2, 100.2, 86.2, 67.7, 61.5, 55.7, 21.5, 20.2, 15.1; HR-ESIMS calcd for $C_{26}H_{28}NO_4S$ $[M + H]^+$ 450.1734. Found 450.1735.

(4*R*)-3-((2-(1-Ethoxyethoxy)phenyl)ethynyl)-4-phenyloxazolidin-2-one (6c). According to **GP-1**, **6c** (1.55 g, 49%) was obtained as 1:1 diastereomer mixture from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (1.71 g, 8.98 mmol). Eluent: hexane/EtOAc = 2:1. Yellow oil; $[\alpha]_D^{22}$ −169 (c 1.02, $CHCl_3$); IR ν_{max}: 3013, 2257, 1776, 1597 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47−7.44 (m, 2H), 7.42−7.39 (m, 3H), 7.26 (d, J = 8.0 Hz, 1H), 7.19−7.15 (m, 1H), 6.99 (dd, J = 3.0, 1.0 Hz, 0.5H), 6.97 (dd, J = 2.5, 1.0 Hz, 0.5H), 6.90−6.86 (m, 1H), 5.28−5.25 (m, 1H), 5.16 (t, J = 6.5 Hz, 0.5H), 5.14 (t, J = 6.5 Hz, 0.5H), 4.78 (t, J = 9.0 Hz, 1H), 4.31−4.26 (m, 1H), 3.73−3.61 (m, 1H), 3.43−3.39 (m, 1H), 1.32 (d, J = 5.0 Hz, 1.5H), 1.31 (d, J = 5.0 Hz, 1.5H), 1.15 (t, J = 7.0 Hz, 1.5H), 1.12 (t, J = 7.0 Hz, 1.5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 157.0, 155.50, 155.49, 136.3, 136.2, 133.3, 133.2, 129.37, 129.35, 129.27, 129.26, 129.25, 129.20, 126.85, 126.78, 121.8, 117.45, 117.44, 113.84, 113.81, 100.4, 100.2, 81.5, 70.76, 70.72, 69.3, 69.2, 62.18, 62.16, 61.3, 61.0, 20.0, 19.9, 15.13, 15.11; HR-ESIMS calcd for $C_{21}H_{21}NNaO_4$ $[M + Na]^+$ 374.1363. Found 374.1357.

(4*R*)-4-Benzyl-3-((2-(1-ethoxyethoxy)phenyl)ethynyl)oxazolidin-2-one (6d). According to **GP-1**, **6d** (384 mg, 70%) was obtained as 1:1 diastereomer mixture from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (285 mg, 1.50 mmol). Eluent: hexane/EtOAc = 3:2. Yellow oil; $[\alpha]_D^{23}$ −77.5 (c 1.12, $CHCl_3$); IR ν_{max}: 3025, 2258, 1772, 1598 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (td, J = 7.5, 1.5 Hz, 1H), 7.37−7.34 (m, 2H), 7.31−7.24 (m, 4H), 7.07 (d, J = 7.5 Hz, 1H), 6.97 (dt, J = 7.5, 1.5 Hz, 1H), 5.47 (t, J = 5.5 Hz, 0.5H), 5.46 (t, J = 5.5 Hz, 0.5H), 4.40−4.33 (m, 2H), 4.20−4.15 (m, 1H), 3.86−3.78 (m, 1H), 3.61−3.53 (m, 1H), 3.32 (td, J = 14.0, 3.5 Hz, 1H), 3.10−3.05 (m, 1H), 1.54 (d, J = 5.5 Hz, 1.5H), 1.53 (d, J = 5.5 Hz, 1.5H), 1.19 (t, J = 7.0 Hz, 1.5H), 1.16 (t, J = 7.0 Hz, 1.5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 157.4, 155.3, 134.17, 134.16, 133.2, 133.1, 129.49, 129.47, 129.42, 129.39, 129.0, 127.5, 121.73, 121.71, 116.56, 116.50, 113.57, 113.55, 100.5, 100.4, 81.52, 81.49, 70.03, 70.00, 67.3, 67.2, 61.52, 61.47, 58.6, 58.5, 37.6, 37.5, 20.4, 15.2, 15.1; HR-ESIMS calcd for $C_{22}H_{23}NNaO_4$ $[M + Na]^+$ 388.1525. Found 388.1511.

(4*S*,5*R*)-1-((2-(1-Ethoxyethoxy)phenyl)ethynyl)-1,5-dimethyl-4-phenyl-imidazolidin-2-one (6e). According to **GP-1**, **6e** (56.4 mg, 13%) was obtained as 1:1 diastereomer mixture from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (218 mg, 1.15 mmol). Eluent: hexane/EtOAc = 1:1. Yellow oil; $[\alpha]_D^{21}$ +167 (c 0.792, $CHCl_3$); IR ν_{max}: 3018, 2246, 1720, 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.37 (m, 2H), 7.35−7.32 (m, 1H), 7.29−7.26 (m, 3H), 7.13−7.09 (m, 1H), 6.96 (dd, J = 8.5, 1.0 Hz, 0.5H), 6.95 (dd, J = 8.5, 1.0 Hz, 0.5H), 6.87 (td, J = 7.5, 1.5 Hz, 0.5H), 6.86 (td, J = 7.5, 1.5 Hz, 0.5H), 5.26−5.20 (m, 1H), 5.06 (d, J = 6.0 Hz, 0.5H), 5.04 (d, J = 6.0 Hz, 0.5H), 3.97−3.92 (m, 1H), 3.68−3.57 (m, 1H), 3.47−3.34 (m, 1H), 2.86 (s, 3H), 1.27 (d, J = 5.0 Hz, 1.5H), 1.24 (d, J = 5.0 Hz, 1.5H), 1.12 (t, J = 7.0 Hz, 1.5H), 1.09 (t, J = 7.0 Hz, 1.5H), 0.79 (d, J = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.62, 157.61, 156.7, 156.5, 134.8, 133.1, 132.9, 128.5, 128.42, 128.40, 128.3, 128.2, 127.71, 127.70, 122.0, 121.8, 118.4, 117.9, 115.5, 115.4, 100.6, 100.1, 85.1, 67.94, 67.88, 64.1, 61.3, 61.0, 55.7, 28.9, 20.04, 20.00, 15.15, 15.12, 14.8; HR-ESIMS calcd for $C_{23}H_{27}N_2O_3$ $[M + H]^+$ 379.2016. Found 379.2016.

1-((2-(1-Ethoxyethoxy)phenyl)ethynyl)-3-methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (6f). According to **GP-1**, **6f** (206 mg, 42%) was obtained from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (278 mg, 1.46 mmol). Eluent: hexane/EtOAc = 3:1. Yellow oil; IR ν_{max}: 3012, 2259, 1732, 1621 cm^{-1}; ^1H NMR (300 MHz, $CHCl_3$) δ 7.54 (dd, J = 7.5, 1.2 Hz, 1H), 7.38−7.35 (m, 1H), 7.31−7.25 (m, 1H), 7.23−7.14 (m, 2H), 7.09 (d, J = 7.8 Hz, 1H), 7.02−6.97 (m, 1H), 5.52 (q, J = 5.4 Hz, 1H), 3.92−3.82 (m, 1H), 3.67−3.55 (m, 1H), 3.44 (s, 3H), 1.59 (d, J = 5.4 Hz, 3H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4, 152.9, 133.0, 129.7, 129.4, 128.3, 123.4, 122.1, 121.7, 116.7, 113.5, 109.9, 107.8, 100.5, 79.1, 71.9, 61.5, 27.5, 20.4, 15.1; HR-ESIMS calcd for $C_{20}H_{20}N_2NaO_3$ $[M + Na]^+$ 359.1366. Found 359.1359.

1-((2-(1-Ethoxyethoxy)phenyl)ethynyl)azetidin-2-one (6g). According to **GP-1**, **6g** (514 mg, 87%) was obtained from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (432 mg, 2.27 mmol). Eluent: hexane/EtOAc = 5:1. Yellow oil; IR ν_{max}: 3012, 2243, 1770, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, J = 7.5, 1.8 Hz, 1H), 7.25−7.21 (m, 1H), 7.05 (dd, J = 8.4, 1.2 Hz, 1H), 6.96 (dd, J = 7.5, 0.9 Hz, 1H), 5.41 (q, J = 5.1 Hz, 1H), 3.91−3.80 (m, 1H), 3.72 (t, J = 4.8 Hz, 2H), 3.64−3.54 (m, 1H), 3.10 (t, J = 4.8 Hz, 2H), 1.54 (d, J = 5.1 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 157.3, 133.4, 129.4, 122.0, 117.5, 113.8, 101.0, 82.2, 66.3, 61.7, 43.1, 37.9, 20.4, 15.2; HR-ESIMS calcd for $C_{15}H_{17}NNaO_3$ $[M + Na]^+$ 282.1101. Found 282.1099.

1-((2-(1-Ethoxyethoxy)phenyl)ethynyl)pyrrolidin-2-one (6h). Modifying to **GP-1** (Cs_2CO_3 was used as a base instead of Na_2CO_3 and pyridine; DMSO was used as solvent instead of toluene), **6h** (218 mg, 33%) was obtained from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (460 mg, 2.42 mmol), pyrrolidin-2-one (1.03 g, 12.1 mmol), $CuCl_2$ (650 mg, 4.83 mmol), and Cs_2CO_3 (1.57 g, 4.83 mmol). Eluent: hexane/EtOAc = 3:1 to 1:1. Yellow oil; IR ν_{max}: 3012, 2250, 1714, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 7.5 Hz, 1H), 7.28−7.20 (m, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 5.43 (q, J = 5.1 Hz, 1H), 3.90−3.78 (m, 1H), 3.79 (t, J = 7.2 Hz, 2H), 3.64−3.54 (m, 1H), 2.48 (t, J = 7.8 Hz, 2H), 2.22−2.12 (m, 2H), 1.55 (d, J = 5.1 Hz, 3H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 157.1, 133.2, 129.0, 121.9, 117.5, 114.3, 100.9, 84.0, 68.9, 61.6, 50.0, 29.6, 20.3, 18.7, 15.1; HR-ESIMS calcd for $C_{16}H_{19}NNaO_3$ $[M + Na]^+$ 296.1257. Found 296.1252.

Methyl 1-((2-(1-ethoxyethoxy)phenyl)ethynyl)-1*H*-indole-3-carboxylate (6i). According to **GP-1**, **6i** (470 mg, 86%) was obtained from 1-(1-ethoxyethoxy)-2-ethynylbenzene[10] (285 mg, 1.50 mmol). Eluent: hexane/EtOAc = 7:1. Red oil; IR ν_{max}: 3012, 2258, 1708, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.20−8.17 (m, 1H), 7.98 (s, 1H), 7.76−7.73 (m, 1H), 7.51 (dd, J = 7.8, 1.8 Hz, 1H), 7.44−7.28 (m, 3H), 7.12 (d, J = 8.4 Hz, 1H), 7.02 (dt, J = 7.8, 0.9 Hz, 1H), 5.52 (q, J = 5.4 Hz, 1H), 3.94 (s, 3H), 3.92−3.82 (m, 1H), 3.66−3.56 (m, 1H), 1.60 (d, J = 5.4 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 157.4, 138.5, 134.5, 132.8, 129.7, 125.3, 124.4, 123.6, 121.8, 121.7, 116.3, 112.8, 111.6, 110.8, 100.3, 82.7, 68.8, 61.4, 51.3, 20.3, 15.1; HR-ESIMS calcd for $C_{22}H_{21}NNaO_4$ $[M + Na]^+$ 386.1363. Found 386.1368.

***N*-((4-(1-Ethoxyethoxy)-[1,1′-biphenyl]-3-yl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (6j).** According to **GP-1**, **6j** (418 mg, 58%) was obtained from 4-(1-ethoxyethoxy)-3-ethynyl-1,1′-biphenyl[10] (428 mg, 1.61 mmol). Eluent: hexane/EtOAc = 5:1. Yellow oil; IR

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ν_{max}: 3011, 2239, 1599, 1368, 1168 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.94−7.89 (m, 2H), 7.56−7.51 (m, 3H), 7.45−7.29 (m, 6H), 7.09 (d, J = 8.4 Hz, 1H), 5.46 (q, J = 5.4 Hz, 1H), 3.92−3.82 (m, 1H), 3.63−3.53 (m, 1H), 3.17 (s, 3H), 2.45 (s, 3H), 1.55 (d, J = 5.4 Hz, 3H), 1.21 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 144.7, 139.9, 134.9, 133.4, 131.4, 129.8, 128.7, 127.9, 127.5, 127.1, 126.7, 117.2, 114.6, 100.7, 87.6, 65.6, 61.7, 39.3, 21.6, 20.4, 15.2; HR-ESIMS calcd for $C_{26}H_{28}NO_4S$ $[M + H]^+$ 450.1734. Found 450.1732.

***N*-((2-(1-Ethoxyethoxy)-5-methoxyphenyl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (6k).** According to **GP-1**, **6k** (426 mg, 64%) was obtained from 1-(1-ethoxyethoxy)-2-ethynyl-4-methoxybenzene (364 mg, 1.65 mmol). Eluent: hexane/EtOAc = 5:1. Yellow oil; IR ν_{max}: 2962, 2156, 1603, 1384, 1175 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 6.96 (d, J = 9.0 Hz, 1H), 6.85 (d, J = 3.3 Hz, 1H), 6.77 (dd, J = 9.0, 3.3 Hz, 1H), 5.29 (q, J = 5.4 Hz, 1H), 3.88−3.78 (m, 1H), 3.76 (s, 3H), 3.60−3.50 (m, 1H), 3.15 (s, 3H), 2.45 (s, 3H), 1.46 (d, J = 5.4 Hz, 3H), 1.18 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 151.0, 144.7, 133.2, 129.7, 127.8, 119.7, 117.0, 115.5, 115.0, 101.6, 87.4, 65.6, 61.9, 55.6, 39.3, 21.6, 20.4, 15.1; HR-ESIMS calcd for $C_{21}H_{25}NNaO_5S$ $[M + Na]^+$ 426.1346. Found 426.1345.

***N*-((2-(1-Ethoxyethoxy)-4-nitrophenyl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (6l).** According to **GP-1**, **6l** (542 mg, 41%) was obtained from 2-(1-ethoxyethoxy)-1-ethynyl-4-nitrobenzene (743 mg, 3.16 mmol). Eluent: hexane/EtOAc = 4:1. Yellow oil; IR ν_{max}: 3030, 2232, 1598, 1520, 1373, 1342, 1170 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.92−7.89 (m, 3H), 7.84−7.80 (m, 1H), 7.41−7.37 (m, 3H), 5.54 (q, J = 5.1 Hz, 1H), 3.90−3.80 (m, 1H), 3.65−3.55 (m, 1H), 3.20 (s, 3H), 2.46 (s, 3H), 1.60 (d, J = 5.1 Hz, 3H), 1.22 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.5, 146.9, 145.1, 133.2, 131.6, 129.9, 127.8, 121.5, 116.7, 110.8, 100.7, 93.0, 65.7, 61.7, 39.2, 21.7, 20.0, 15.1; HR-ESIMS calcd for $C_{20}H_{22}N_2NaO_6S$ $[M + Na]^+$ 441.1091. Found 441.1092.

***N*-((1-(1-Ethoxyethoxy)naphthalen-2-yl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (6m).** According to **GP-1**, **6m** (387 mg, 59%) was obtained from 1-(1-ethoxyethoxy)-2-ethynylnaphthalene[10] (374 mg, 1.56 mmol). Eluent: hexane/EtOAc = 5:1. Yellow oil; IR ν_{max}: 3010, 2236, 1598, 1369, 1169 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.36−8.32 (m, 1H), 7.88−7.86 (m, 2H), 7.77−7.74 (m, 1H), 7.51−7.47 (m, 3H), 7.39−7.34 (m, 3H), 5.78 (q, J = 5.1 Hz, 1H), 3.52−3.36 (m, 2H), 3.20 (s, 3H), 2.45 (s, 3H), 1.55 (d, J = 5.1 Hz, 3H), 1.00 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 144.9, 134.2, 133.3, 129.9, 129.7, 129.0, 128.0, 127.8, 127.4, 127.0, 126.2, 123.3, 110.3, 104.4, 88.2, 66.6, 64.9, 39.3, 21.7, 21.6, 15.3; HR-ESIMS calcd for $C_{24}H_{26}NO_4S$ $[M + H]^+$ 424.1577. Found 424.1579.

General Procedure for the Iodocyclization of Ynamides 6 (Table 1, entry 6 and Table 3, GP-2). Three seconds was precisely counted by stopwatch just after $I(coll)_2PF_6$ (1 equiv) was added in one portion to a stirred solution of **6a** (1 equiv) in CH_2Cl_2 (0.1 M) at 23 °C, and the reaction mixture was immediately quenched with a saturated aqueous solution of $Na_2S_2O_3$/$NaHCO_3$ (1:1) and was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by flash column chromatography on silica gel to give **2**.

***N*-(3-Iodobenzofuran-2-yl)-*N*,4-dimethylbenzenesulfonamide (2a).** According to **GP-2**, **2a** (90.6 mg, 98%) was obtained from **6a** (80.7 mg, 0.216 mmol). Eluent: hexane/EtOAc = 5:1. Colorless amorphous solid; IR ν_{max}: 3032, 1602, 1362, 1172, 1068 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 2H), 7.39−7.28 (m, 6H), 3.22 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 149.6, 144.4, 134.7, 130.4, 129.8, 128.2, 126.4, 123.7, 122.0, 111.4, 64.7, 37.3, 21.7; HR-ESIMS calcd for $C_{16}H_{15}INO_3S$ $[M + H]^+$ 427.9812. Found 427.9803.

***N*-Benzyl-*N*-(3-iodobenzofuran-2-yl)-4-methylbenzenesulfonamide (2b).** According to **GP-2**, **2b** (89.6 mg, 90%) was obtained from **6b** (88.4 mg, 0.197 mmol). Eluent: hexane/EtOAc = 6:1. Colorless amorphous solid; IR ν_{max}: 3020, 1600, 1362, 1168, 1092 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.28−7.19 (m, 7H), 4.72 (s, 2H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.3, 147.8, 144.4, 135.7, 134.2, 130.4, 129.8, 128.9, 128.4, 128.2, 128.1, 126.3, 123.5, 122.0, 111.3, 67.5, 53.9, 21.7; HR-ESIMS calcd for $C_{22}H_{19}INO_3S$ $[M + H]^+$ 504.0125. Found 504.0126.

***(R)*-3-(3-Iodobenzofuran-2-yl)-4-phenyloxazolidin-2-one (2c).** According to **GP-2**, **2c** (53.3 mg, 91%) was obtained from **6c** (50.5 mg, 0.144 mmol). Eluent: hexane/EtOAc = 3:1. Colorless amorphous solid; $[\alpha]_D^{24}$ −177 (c 0.874, $CHCl_3$); IR ν_{max}: 3028, 1775, 1613, 1082 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47−7.43 (m, 2H), 7.39−7.28 (m, 5H), 7.27−7.21 (m, 2H), 5.56 (t, J = 8.4 Hz, 1H), 4.89 (t, J = 8.4 Hz, 1H), 4.39 (t, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 152.0, 145.7, 136.1, 130.3, 129.4, 129.1, 127.2, 125.9, 123.6, 121.4, 111.3, 70.9, 62.4, 61.3; HR-ESIMS calcd for $C_{17}H_{13}INO_3$ $[M + H]^+$ 405.9935. Found 405.9934.

***(R)*-4-Benzyl-3-(3-iodobenzofuran-2-yl)oxazolidin-2-one (2d).** According to **GP-2**, **2d** (94.2 mg, 91%) was obtained from **6d** (90.1 mg, 0.247 mmol). Eluent: hexane/EtOAc = 2:1. Colorless amorphous solid; $[\alpha]_D^{23}$ −29.2 (c 0.806, $CHCl_3$); IR ν_{max}: 3030, 1774, 1613, 1094 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.39 (m, 3H), 7.36−7.29 (m, 1H), 7.25−7.12 (m, 5H), 4.76−4.66 (m, 1H), 4.49 (t, J = 8.4 Hz, 1H), 4.28 (dd, J = 8.4, 6.6 Hz, 1H), 3.09 (dd, J = 13.5, 4.8 Hz, 1H), 2.91 (dd, J = 13.5, 9.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 152.2, 145.6, 134.6, 130.4, 128.9, 128.8, 127.2, 126.2, 123.8, 121.6, 111.5, 68.1, 63.2, 58.4, 39.3; HR-ESIMS calcd for $C_{18}H_{15}INO_3$ $[M + H]^+$ 420.0091. Found 420.0090.

***(4S,5R)*-1-(3-Iodobenzofuran-2-yl)-3,4-dimethyl-5-phenylimidazolidin-2-one (2e).** According to **GP-2**, **2e** (50.7 mg, 92%) was obtained from **6e** (48.3 mg, 0.128 mmol). Eluent: hexane/EtOAc = 7:3. Colorless oil; $[\alpha]_D^{21}$ +132 (c 0.658, $CHCl_3$); IR ν_{max}: 3026, 1720, 1612, 1078 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37−7.35 (m, 2H), 7.31−7.28 (m, 3H), 7.26−7.20 (m, 4H), 5.53 (d, J = 9.0 Hz, 1H), 4.07−4.01 (m, 1H), 2.92 (s, 3H), 0.86 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.8, 151.8, 148.4, 135.2, 130.9, 128.41, 128.39, 127.9, 125.1, 123.2, 121.0, 111.1, 62.7, 60.6, 56.0, 28.9, 14.7; HR-ESIMS calcd for $C_{19}H_{18}IN_2O_2$ $[M + H]^+$ 433.0407. Found 433.0404.

1-(3-Iodobenzofuran-2-yl)-3-methyl-1*H*-benzo[*d*]imidazol-2(3*H*)-one (2f). According to **GP-2**, **2f** (88.5 mg, 97%) was obtained from **6f** (78.5 mg, 0.234 mmol). Eluent: hexane/EtOAc = 2:1. Colorless amorphous solid; IR ν_{max}: 3023, 1728, 1612, 1088 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.47 (m, 2H), 7.47−7.34 (m, 2H), 7.21 (d, J = 7.8 Hz, 1H), 7.09 (d, J = 7.8 Hz, 2H), 6.97−6.94 (m, 1H), 3.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 152.1, 144.2, 130.6, 130.3, 128.2, 126.4, 123.9, 123.1, 122.0, 121.8, 111.7, 109.7, 108.1, 63.5, 27.5; HR-ESIMS calcd for $C_{16}H_{12}IN_2O_2$ $[M + H]^+$ 390.9938. Found 390.9934.

1-(3-Iodobenzofuran-2-yl)azetidin-2-one (2g). According to **GP-2**, **2g** (67.4 mg, 84%) was obtained from **6g** (66.0 mg, 0.255 mmol). Eluent: hexane/EtOAc = 2:1. Colorless amorphous solid; IR ν_{max}: 3027, 1769, 1606, 1099 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.41 (m, 1H), 7.40−7.26 (m, 3H), 4.00 (t, J = 4.8 Hz, 2H), 3.26 (t, J = 4.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 151.1, 146.5, 130.5, 125.1, 123.9, 120.8, 111.1, 49.5, 41.2, 38.2; HR-ESIMS calcd for $C_{11}H_9INO_2$ $[M + H]^+$ 313.9672. Found 313.9671.

1-(3-Iodobenzofuran-2-yl)pyrrolidin-2-one (2h). According to **GP-2**, **2h** (74.9 mg, 92%) was obtained from **6h** (87.2 mg, 0.260 mmol). Eluent: hexane/EtOAc = 1:1. Colorless amorphous solid; IR ν_{max}: 3011, 1720, 1608, 1103 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.35 (m, 2H), 7.31 (dd, J = 7.8, 1.8 Hz, 2H), 3.90 (t, J = 7.2 Hz, 2H), 2.60 (t, J = 8.1 Hz, 2H), 2.32−2.22 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 151.8, 148.0, 130.6, 125.6, 123.5, 121.2, 111.2, 59.6, 48.7, 30.8, 19.1; HR-ESIMS calcd for $C_{12}H_{11}INO_2$ $[M + H]^+$ 327.9829. Found 327.9828.

Methyl 1-(3-iodobenzofuran-2-yl)-1*H*-indole-3-carboxylate (2i). According to **GP-2**, **2i** (74.6 mg, 89%) was obtained from **6i** (72.8 mg, 0.200 mmol). Eluent: hexane/EtOAc = 5:1. Colorless amorphous solid; IR ν_{max}: 3017, 1710, 1614, 1061 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.29−8.25 (m, 1H), 8.18 (s, 1H), 7.54−7.49 (m, 3H), 7.44 (dd, J = 7.2, 1.8 Hz, 2H), 7.39−7.35 (m, 2H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 152.0, 147.1, 136.8, 133.7, 130.6,

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126.4, 126.3, 124.34, 124.30, 123.4. 122.0, 121.9, 112.2, 111.5, 111.4, 57.8, 51.4; HR-ESIMS calcd for $C_{18}H_{13}INO_3$ $[M + H]^+$ 417.9935. Found 417.9931.

***N*-(3-Iodo-5-phenylbenzofuran-2-yl)-*N*,4-dimethylbenzenesulfonamide (2j).** According to **GP-2**, **2j** (95.2 mg, quant.) was obtained from **6j** (81.2 mg, 0.181 mmol). Eluent: hexane/EtOAc = 5:1. Colorless amorphous solid; IR ν_{max}: 3033, 1602, 1362, 1171, 1068 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.1 Hz, 2H), 7.63−7.56 (m, 4H), 7.45 (t, J = 7.8 Hz, 2H), 7.41−7.33 (m, 4H), 3.23 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 150.1, 144.4, 140.9, 137.5, 134.7, 130.8, 129.8, 128.8, 128.2, 127.4, 127.2, 126.0, 120.4, 111.7, 64.9, 37.3, 21.6; HR-ESIMS calcd for $C_{22}H_{19}INO_3S$ $[M + H]^+$ 504.0125. Found 504.0124.

***N*-(3-Iodo-5-methoxybenzofuran-2-yl)-*N*,4-dimethylbenzenesulfonamide (2k).** According to **GP-2**, **2k** (74.9 mg, 84%) was obtained from **6k** (79.1 mg, 0.196 mmol). Eluent: hexane/EtOAc = 5:1. Colorless amorphous solid; IR ν_{max}: 3030, 1600, 1361, 1168, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 9.0 Hz, 1H), 6.96 (dd, J = 9.0, 2.7 Hz, 1H), 6.82 (d, J = 2.7 Hz, 1H), 3.87 (s, 3H), 3.21 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 150.0, 146.9, 144.4, 134.7, 130.9, 129.7, 128.2, 115.6, 112.2, 103.8, 64.7, 55.9, 37.3, 21.6; HR-ESIMS calcd for $C_{17}H_{17}INO_4S$ $[M + H]^+$ 457.9916. Found 457.9917.

***N*-(3-Iodo-6-nitrobenzofuran-2-yl)-*N*,4-dimethylbenzenesulfonamide (2l).** According to **GP-2**, **2l** (78.1 mg, 91%) was obtained from **6l** (76.1 mg, 0.182 mmol). Eluent: hexane/EtOAc = 3:1. Colorless amorphous solid; IR ν_{max}: 2927, 1599, 1526, 1363, 1347, 1172, 1090 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 1.8 Hz, 1H), 8.24 (dd, J = 8.4, 1.8 Hz, 1H) 7.76 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.4 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 3.25 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 150.6, 146.3, 145.0, 136.3, 134.2, 130.0, 128.1, 122.3, 119.2, 107.8, 64.2, 37.2, 21.7; HR-ESIMS calcd for $C_{16}H_{13}IN_2NaO_5S$ $[M + Na]^+$ 494.9482. Found 494.9485.

***N*-(3-Iodonaphtho[1,2-*b*]furan-2-yl)-*N*,4-dimethylbenzenesulfonamide (2m).** According to **GP-2**, **2m** (88.3 mg, 94%) was obtained from **6m** (83.6 mg, 0.197 mmol). Eluent: hexane/EtOAc = 5:1. Colorless amorphous solid; IR ν_{max}: 2927, 1600, 1361, 1171, 1068 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (td, J = 8.1, 0.6 Hz, 1H), 7.92 (d, J = 7.5 Hz, 1H), 7.83−7.79 (m, 2H), 7.72 (d, J = 8.7 Hz, 1H), 7.61−7.49 (m, 2H), 7.43 (d, J = 8.7 Hz, 1H), 7.36 (dd, J = 8.7, 0.6 Hz, 2H), 3.29 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 148.0, 144.4, 134.8, 132.3, 129.7, 128.6, 128.3, 126.8, 126.1, 126.0, 124.3, 120.7, 119.8, 119.6, 65.8, 37.7, 21.7; HR-ESIMS calcd for $C_{20}H_{16}INNaO_3S$ $[M + Na]^+$ 499.9788. Found 499.9791.

***N*-(1,2-Diiodo-2-(2-methoxyphenyl)vinyl)-*N*,4-dimethylbenzenesulfonamide (7) (Table 2, entry 1).** According to the literature,[9] to a solution of **1a** (52.3 mg, 0.166 mmol) in dry CH_2Cl_2 (1.33 mL) was added I_2 (61.1 mg, 0.249 mmol) at rt and the reaction mixture was stirred for 30 min. The reaction mixture was quenched with a saturated aqueous solution of $Na_2S_2O_3$/$NaHCO_3$ (1:1), and was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by flash column chromatography on silica gel eluting with hexane/EtOAc = 6:1 to give **2a** (48.4 mg, 68%) and **7** (23.6 mg, 25%) as the mixture of 2:1 stereoisomer. Colorless solid; IR ν_{max}: 2929, 1597, 1361, 1167, 1046 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 4/3H), 7.87 (d, J = 8.0 Hz, 2/3H), 7.36−7.31 (m, 3H), 7.21 (dd, J = 7.5, 1.5 Hz, 2/3H), 7.06 (dd, J = 7.5, 1.5 Hz, 1/3H), 7.00 (t, J = 7.5 Hz, 2/3H), 6.96 (t, J = 7.5 Hz, 1/3H), 6.91 (d, J = 8.0 Hz, 1/3H), 6.87 (d, J = 8.0 Hz, 2/3H), 3.96 (s, 1H), 3.85 (s, 2H), 2.82 (s, 1H), 2.79 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 154.9, 144.6, 144.5, 134.1, 133.9, 133.5, 133.1, 130.6, 130.1, 129.4, 129.3, 129.2, 120.8, 120.6, 112.1, 111.6, 100.9, 99.9, 99.8, 98.8, 56.1, 55.7, 37.8, 37.2, 21.7; HR-ESIMS calcd for $C_{17}H_{18}I_2NO_3S$ $[M + H]^+$ 569.9091. Found 569.9095.

***(R)*-6-(2-Hydroxy-1-phenylethyl)benzofuro[2,3-*c*]isoquinolin-5(6*H*)-one (9).** A solution of **2c** (81.0 mg, 0.200 mmol), **8** (108 mg, 0.600 mmol), $PdCl_2(PPh_3)_2$ (14.0 mg, 0.0200 mmol) and Cs_2CO_3 (195 mg, 0.600 mmol) in dry 1,4-dioxane (1.2 mL) was heated under reflux for 48 h. After checking the consumption of **2c** using TLC, water (0.20 mL) was added and the mixture was heated under reflux for 24 h. Then, the mixture was diluted with water, and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by flash column chromatography on silica gel eluting with hexane/EtOAc = 3:1 to 2:1 to give **9** (40.3 mg, 57%). Colorless crystals; mp 167−168 °C; $[\alpha]_D^{24}$ −6.6 (c 0.501, $CHCl_3$); IR ν_{max}: 3421, 3013, 1652, 1620, 1587 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 8.39 (d, J = 7.8 Hz, 1H), 8.34 (dd, J = 7.8, 3.3 Hz, 1H), 8.24 (dd, J = 7.8, 3.6 Hz, 1H), 7.91 (t, J = 7.8 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H), 7.50−7.41 (m, 3H), 7.39−7.25 (m, 4H), 6.48 (br s, 1H), 5.30 (t, J = 5.7 Hz, 1H), 4.69 (ddd, J = 11.4, 9.9, 5.7 Hz, 1H), 4.45 (dt, J = 11.4, 5.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.1, 151.2, 151.1, 137.1, 133.7, 132.1, 129.1, 128.5, 127.6, 127.2, 125.4, 124.5, 124.0, 123.4, 122.7, 122.5, 119.7, 111.4, 94.5, 60.2, 59.2; HR-ESIMS calcd for $C_{23}H_{18}NO_3$ $[M + H]^+$ 356.1281. Found 356.1281.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H and ^{13}C NMR spectra of **1a**, **6a-m**, **2a-m**, **7**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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