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One-Pot Synthesis of Substituted Benzo[*b*]furans and Indoles from Dichlorophenols/Dichloroanilines Using a Palladium–Dihydroxyterphenylphosphine Catalyst

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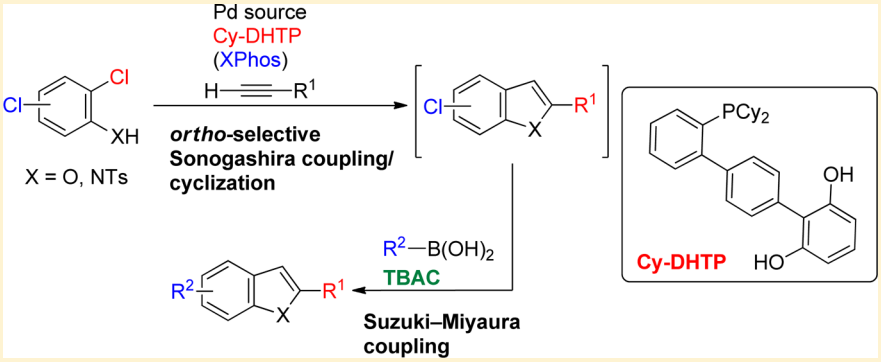
Supporting Information



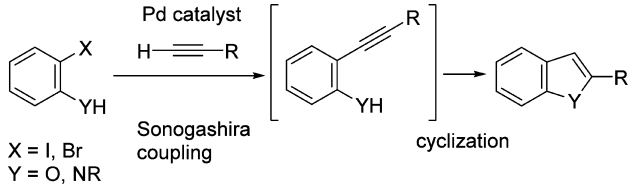
ABSTRACT: Disubstituted benzo[*b*]furans were synthesized by *ortho*-selective Sonogashira coupling of dichlorophenols and terminal alkynes, followed by cyclization and Suzuki–Miyaura coupling in one pot, using a palladium–dihydroxyterphenylphosphine (Cy-DHTP) catalyst. The use of substoichiometric amounts of tetrabutylammonium chloride was effective in accelerating the Suzuki–Miyaura coupling. This protocol was also successfully applied to the one-pot synthesis of disubstituted indoles from dichloroaniline derivatives.

INTRODUCTION

Benzo-fused five-membered heterocyclic compounds have attracted considerable interest from synthetic organic chemists due to their importance as frameworks in natural products and pharmaceuticals.[1−6] Benzo[*b*]furan is one such framework, with various synthetic methods being developed over the years to obtain the desired derivatives.[7−9] Furthermore, considerable effort has been devoted to the synthesis of indoles,[7,9−13] including palladium-catalyzed cross-coupling.[14−16] Among these methods, the Sonogashira coupling of 2-halophenols or 2-haloanilines with terminal alkynes, followed by cyclization, has been used to construct 2-substituted benzo[*b*]furans[17−27] and indoles[17−19,22,24,27−33] (Scheme 1). However, in general, iodo- or bromo-substituted substrates were employed, with only a few examples using the less reactive 2-chlorophenols[34−36] or 2-chloroanilines[37] being reported. As these chloro compounds are generally cheaper and more readily available, the development of efficient synthetic methods toward benzo[*b*]furans and indoles from chloro-substituted substrates is highly desirable.

We previously reported the syntheses of benzo[*b*]furans from 2-chlorophenols using a catalyst derived from palladium and terphenylphosphine ligands bearing hydroxy groups (Figure 1a).[38,39] This catalyst remarkably accelerates oxidative addition of the C–Cl bond *ortho* to the substrate hydroxy

Scheme 1. Synthesis of 2-Substituted Benzo[*b*]furans/Indoles by Sonogashira Coupling and Subsequent Cyclization



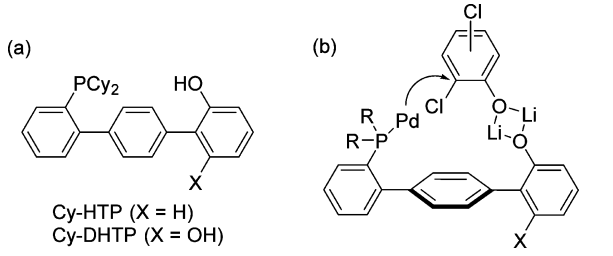


Figure 1. (a) Hydroxyterphenylphosphines and (b) assumed heteroaggregates.

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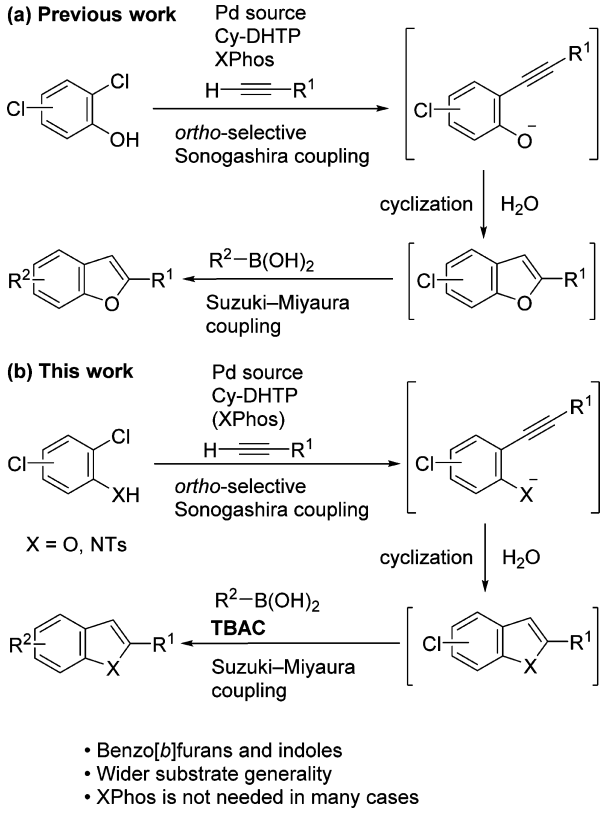
J. Org. Chem. 2016, 81, 5450–5463

group, allowing the Sonogashira coupling of 2-chlorophenols with terminal alkynes to take place. This catalyst also enables the *ortho*-selective Sonogashira coupling of dichlorophenols, and so chlorobenzo[*b*]furan was easily obtained from dichlorophenols by employing this catalyst. We assume that the origin of this rate acceleration and *ortho*-selectivity is based on heteroaggregate formation between lithium phenoxides of both the ligand and the substrate (Figure 1b). In our previous studies, we found that dihydroxyterphenylphosphine (Cy-DHTP)[40−42] bearing two hydroxy groups is more effective in the Sonogashira coupling than hydroxyterphenylphosphine (Cy-HTP),[43−47] which bears a single hydroxy group.

The Pd−Cy-DHTP system was further applied to the sequential one-pot synthesis of disubstituted benzo[*b*]furans by conducting Suzuki−Miyaura coupling reactions[48] with boronic acids following chlorobenzo[*b*]furan formation (Scheme 2a).[39]

Scheme 2. One-Pot Synthesis of Disubstituted Benzo[*b*]furans/Indoles from Dichlorophenols/Dichloroanilines Using a Pd−Cy-DHTP Catalyst

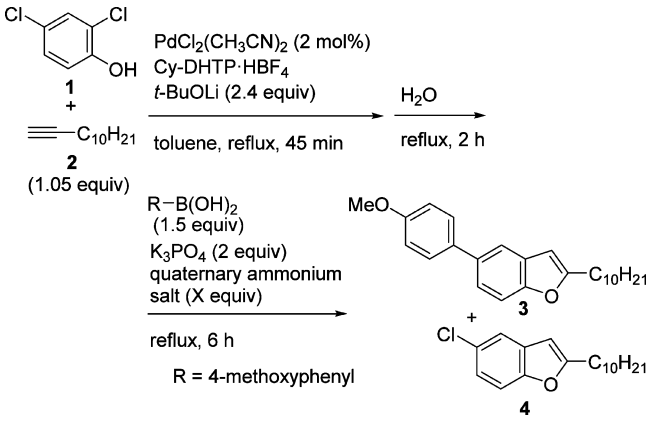


However, the use of XPhos (2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl)[49] in addition to Cy-DHTP was necessary to obtain the Suzuki−Miyaura coupling products in good yield. In addition, substrate scope was limited as a number of boronic acids afforded the desired products only in very low yield, even in the presence of XPhos. These drawbacks prompted us to investigate a more efficient catalytic system for the synthesis of a wide range of disubstituted benzo[*b*]furans. In addition, we envisaged that this one-pot procedure would also be applicable to the preparation of disubstituted indoles from dichloroaniline derivatives. Here, we report the effects of tetrabutylammonium chloride (TBAC) addition on the Suzuki−Miyaura coupling reaction to improve the one-pot sequential synthesis of disubstituted benzo[*b*]furans from dichlorophenols (Scheme 2b). Application of this protocol to the sequential one-pot synthesis of disubstituted indoles from *N*-tosyl-dichloroanilines is also presented in detail.[50]

RESULTS AND DISCUSSION

Effect of Quaternary Ammonium Salts in the One-Pot Synthesis of Disubstituted Benzo[*b*]furans from Dichlorophenols. The previously reported one-pot synthesis (see Scheme 2a)[39] of disubstituted benzo[*b*]furans via a Suzuki−Miyaura coupling following chlorobenzo[*b*]furan formation[51,52] required two ligands, namely, Cy-DHTP and XPhos. To carry out the one-pot synthesis using a Pd−Cy-DHTP catalyst in the absence of XPhos, we investigated the effect of various quaternary ammonium salts in the Suzuki−Miyaura coupling (Table 1), as it is well-known that quaternary ammonium salts

Table 1. Optimization of Reaction Conditions for the Synthesis of 2,5-Disubstituted Benzo[*b*]furan 3 from 2,4-Dichlorophenol



entry	quaternary ammonium salt (equiv)	yield (%)[a] 3	4
1	none	31	41
2	TBAC (2)	71	<12
3	TBAB (2)	68	<6
4[b]	TBAOH (2)	47	<17
5	Me_4NBr (2)	27	<26
6	TBAC (1)	65	<15
7	TBAC (0.5)	78	trace

[a]Isolated yield. [b]Without K_3PO_4.

enhance Suzuki−Miyaura coupling.[53−55] The synthesis of 2-decyl-5-(4-methoxyphenyl)benzo[*b*]furan (**3**) was selected as our model reaction, which employed the HBF_4 salt of Cy-DHTP (Cy-DHTP·HBF_4).[56] Thus, for the initial Sonogashira coupling step between 2,4-dichlorophenol (**1**) and 1-dodecyne (**2**) and for the following cyclization, the previously reported reaction conditions for benzo[*b*]furan synthesis were applied.[39] Following chlorobenzo[*b*]furan formation, the Suzuki−Miyaura coupling was performed with the addition of 4-methoxyphenylboronic acid, K_3PO_4 as base, and a quaternary ammonium salt. Without the addition of a quaternary ammonium salt, the Suzuki−Miyaura coupling did not reach completion and a significant amount of chlorobenzo[*b*]furan **4** was recovered (entry 1). However, the reaction proceeded smoothly in the presence of 2 equiv of tetrabutylammonium chloride (TBAC), and the desired **3** was obtained in good yield (71%, entry 2). Changing the counterion of TBA from chloride to either

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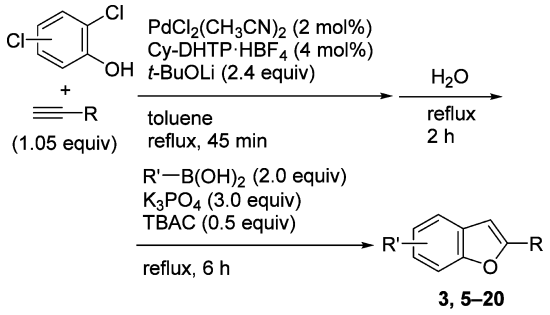
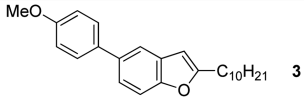
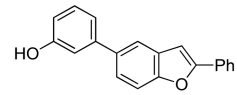
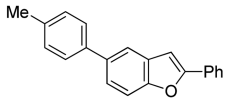
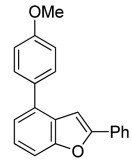
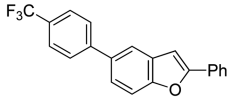
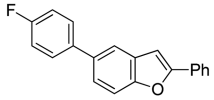
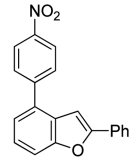
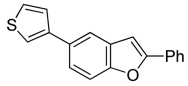
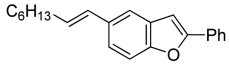
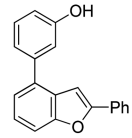
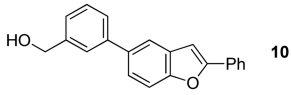
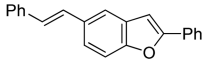
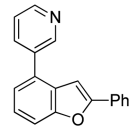
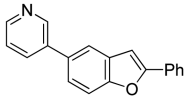
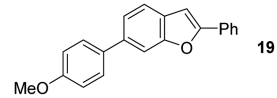
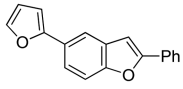
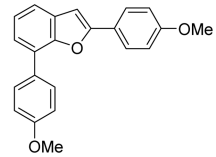
Table 2. One-Pot Benzo[*b*]furan Synthesis from Dichlorophenols, Alkynes, and Boronic Acids



entry	product	yield (%)[a]	entry	product	yield (%)[a]
1	 3	78	11	 14	22 (31)[f]
2	 5	82 (89)[b]	12	 15	85 (83)[g]
3[c]	 6	74			
4[d]	 7	81	13	 16	76
5	 8	73			
6	 9	53	14[f]	 17	71
7[c]	 10	72			
8[e]	 11	<23	15	 18	87
9[e]	 12	37	16[c]	 19	32
10[e]	 13	42	17[c]	 20	32

[a]Isolated yield. [b]Pd 1 mol %. [c]Suzuki–Miyaura coupling 8 h. [d]Suzuki–Miyaura coupling 10 h. [e]Suzuki–Miyaura coupling 20 h. [f]TBAOH (2 equiv) instead of TBAC and K_3PO_4. [g]2 mmol scale.

bromide (TBAB) or hydroxide (TBAOH) resulted in lower yield (68%, entry 3, and 47%, entry 4). The use of tetramethylammonium bromide was ineffective (27%, entry 5). TBAC was, therefore, selected as the optimal salt for the reaction, with 0.5 equiv being found to afford the highest yield of product (entries 6 and 7), with the desired product being obtained in good yield (78%) in the absence of XPhos as a second ligand. We, therefore, assumed that the TBA salt works as a phase transfer catalyst, transporting boronic acid from the aqueous phase to the organic phase, thus accelerating the Suzuki–Miyaura coupling step.

Substrate Scope of the One-Pot Syntheses of Disubstituted Benzo[*b*]furans from Dichlorophenols. With the optimized conditions in hand, substrate generality

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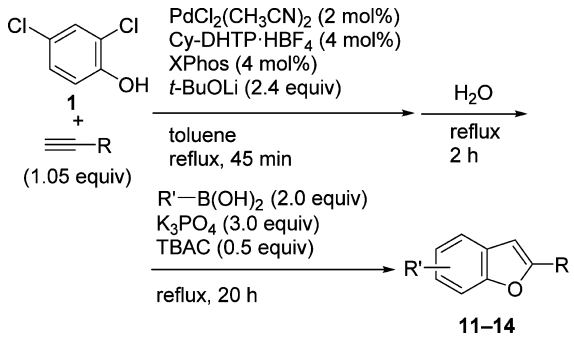
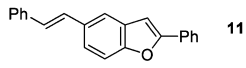
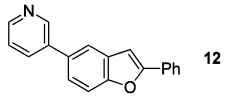
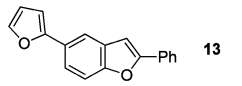
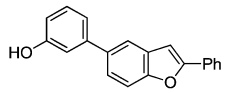
was examined for the syntheses of disubstituted benzo[*b*]furans (Table 2). Initially, 2,5-disubstituted benzo[*b*]furans were prepared using 2,4-dichlorophenol (**1**), terminal alkynes, and a range of boronic acids. Boronic acids bearing either electron-donating (entries 1 and 2) or electron-withdrawing groups (entries 3 and 4) reacted smoothly with 5-chlorobenzo[*b*]furan under the optimized conditions, and the corresponding disubstituted benzo[*b*]furans **3** and **5**–**7** were obtained in high yields (74–82%). For the synthesis of benzo[*b*]furan **5**, reduction of the catalyst loading to 1 mol % gave an improved yield (89%, entry 2). 3-Thienyl (entry 5) and alkenyl (entry 6) groups were also successfully introduced to give compounds **8** and **9**, respectively. Furthermore, 3-(hydroxymethyl)phenylboronic acid reacted smoothly to give the desired product **10** in good yield (72%, entry 7). However, the Suzuki–Miyaura coupling did not proceed efficiently under the optimized conditions when *trans*-2-phenylvinylboronic acid was employed (<23% **11**, entry 8). In addition, the use of 3-pyridylboronic acid and 2-furylboronic acid resulted in moderate yields (37% **12**, entry 9, and 42% **13**, entry 10). The introduction of a 3-hydroxyphenyl group was also not successful, although a slightly higher yield of **14** was obtained using TBAOH (31%) rather than TBAC and K_3PO_4 (22%, entry 11).

The optimized reaction conditions were also applicable to the synthesis of 2,4-disubstituted benzo[*b*]furans from 2,3-dichlorophenol. A 4-methoxyphenyl group was successfully introduced at the 4-position of the benzo[*b*]furan, giving the desired product **15** in high yields (83–85%, entry 12, Table 2). Surprisingly, 4-nitrophenylboronic acid, which gave a poor result in the synthesis of 2,5-disubstituted benzo[*b*]furans (data not shown), reacted smoothly with 4-chlorobenzo[*b*]furan to afford the desired 2,4-disubstituted product **16** in moderate yield (76%, entry 13). Furthermore, the reactions with 3-hydroxyphenyl and 3-pyridyl groups were also successful, giving the desired products **17** and **18** in good yields (71%, entry 14, and 87%, entry 15). We, therefore, assumed that these intermediates, i.e., the 4-chlorobenzo[*b*]furans, were more reactive than the 5-chlorobenzo[*b*]furans. The reactions of 2,5- and 2,6-dichlorophenols also gave the desired products, albeit in lower yields (entries 16 and 17).

As shown above, the Suzuki–Miyaura coupling of 5-chlorobenzo[*b*]furans with a number of different boronic acids afforded the desired products in low yields (<50%, entries 8–11, Table 2). To accelerate the reaction with these boronic acids, we revisited the effect of XPhos as a second ligand in the Suzuki–Miyaura coupling (Table 3). Among the conditions tested, use of XPhos and Cy-DHTP as ligands and the addition of 0.5 equiv of TBAC gave optimal results, with a significant improvement in yields of the desired 2,5-disubstituted benzo[*b*]furans being observed. In the case of *trans*-2-phenylvinylboronic acid, the corresponding benzo[*b*]furan **11** was obtained in good yield (68%, entry 1). Although the reason is unclear, the procedure in which XPhos was added together with the boronic acid, TBAC, and K_3PO_4 in the Suzuki–Miyaura coupling step resulted in lower yield (36%, entry 1). The 3-pyridyl and 2-furyl groups were also successfully introduced with the addition of XPhos (84%, entry 2, and 64%, entry 3). Coupling with 3-hydroxyphenylboronic acid resulted in a moderate yield only (57%, entry 4). In this case, the use of TBAOH rather than TBAC gave a higher yield (71%, entry 4). However, in the absence of TBAC and TBAOH, the Suzuki–Miyaura coupling reaction did not take place, and chlorobenzo[*b*]furan was recovered (entry 5). This result indicates that both XPhos and a TBA salt are required to obtain the products in good yields.

Table 3. One-Pot Benzo[*b*]furan Synthesis Using XPhos as a Secondary Ligand



entry	product	yield (%)[a]
1	 **11**	68 (36)[b]
2	 **12**	84
3	 **13**	64
4[c]	 **14**	57[d] (71)[e]
5[c]		0[f]

[a]Isolated yield. [b]Sonogashira coupling was conducted without XPhos, which was added together with TBAC and K_3PO_4 in the Suzuki–Miyaura coupling step. [c]Suzuki–Miyaura coupling 6 h. [d]TBAC (2 equiv). [e]TBAOH (2 equiv) instead of TBAC and K_3PO_4. [f]In the absence of TBAC.

Optimization of the Synthesis of Monosubstituted Indoles from Monochloroaniline Derivatives. We then turned our attention to the synthesis of indoles, which are also important targets in synthetic organic chemistry. We expected that the reaction conditions for the synthesis of benzo[*b*]furan using the Pd–Cy-DHTP catalyst could also be applied for the one-pot synthesis of disubstituted indoles from dichloroanilines and terminal alkynes. To confirm this hypothesis, we first investigated the synthesis of monosubstituted indoles from monochloroanilines. The Sonogashira coupling of 2-chloroanilines **21a–g** with ethynylbenzene (**22**) and subsequent cyclization were tested using the Pd–Cy-DHTP catalyst (Table 4). Fortunately, with only a slight modification of the reaction conditions optimized for the benzo[*b*]furan synthesis, the Pd–Cy-DHTP system was applicable to the synthesis of *N*-tosylindole from *N*-tosyl-2-chloroaniline (**21a**) and alkyne **22** (Table 4, entry 1).[S7] In this case, the catalyst allowed the Sonogashira coupling to take place at the less reactive and sterically hindered 2-chloro group. Following the Sonogashira coupling, the addition of water was necessary to cyclize the alkynylaniline to afford the desired 2-substituted indole **23a**

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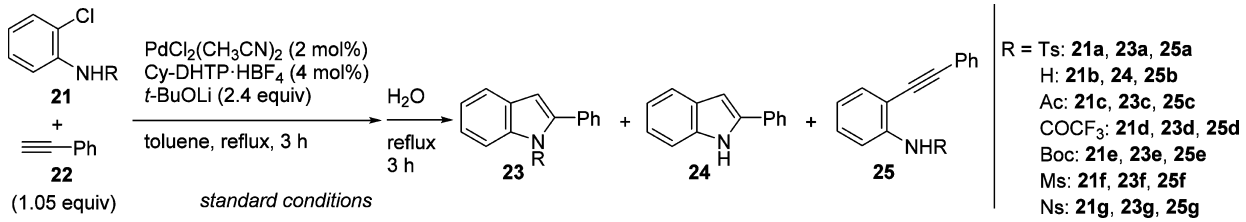
Table 4. Optimization of Reaction Conditions for Indole Synthesis from 2-Chloroaniline Derivatives



		yield (%)[a]		
entry	variation from the standard conditions	23	24	25
1	none	68	nd[b]	nd[b]
2	*t*-BuOLi (3.6 equiv), without H_2O addition, 19 h	trace	nd[b]	38
3	MeOH instead of H_2O	25	nd[b]	trace
4	LiOH instead of *t*-BuOLi	trace	nd[b]	nd[b]
5	Li_3PO_4 instead of *t*-BuOLi	trace	nd[b]	nd[b]
6	*t*-BuOK instead of *t*-BuOLi	nd[b]	nd[b]	nd[b]
7	K_2CO_3 instead of *t*-BuOLi	nd[b]	nd[b]	nd[b]
8	K_3PO_4 instead of *t*-BuOLi	nd[b]	nd[b]	nd[b]
9	DMF instead of toluene	nd[b]	nd[b]	nd[b]
10	Cy-HTP·HBF_4 instead of Cy-DHTP·HBF_4	11	nd[b]	nd[b]
11	**21b** instead of **21a**		nd[b]	nd[b]
12	**21c** instead of **21a**	nd[b]	12	23
13	**21c** instead of **21a**, without H_2O addition, 6 h	nd[b]	nd[b]	65
14	**21d** instead of **21a**	nd[b]	nd[b]	23[c]
15	**21e** instead of **21a**	nd[b]	nd[b]	nd[b]
16	**21f** instead of **21a**	trace	nd[b]	nd[b]
17	**21g** instead of **21a**	nd[b]	nd[b]	nd[b]

[a]Isolated yield. [b]Not detected. [c]**25b** was obtained instead of **25d**.

(entry 1 vs entry 2), as in the benzo[*b*]furan synthesis. Methanol was not suitable as cosolvent for this reaction (entry 3). Furthermore, the use of *t*-BuOLi as a base was key in promoting the Sonogashira coupling, with other lithium salts (entries 4 and 5) and potassium salts (entries 6–8) failing to yield the desired product. When DMF was used as a solvent instead of toluene, the reaction did not proceed at all (entry 9). Monohydroxylated terphenylphosphine Cy-HTP (Figure 1a) was also ineffective (entry 10). We then screened several *N*-protecting groups. In the case of 2-chloroaniline (**21b**), neither the desired indole **24** nor the alkynylaniline **25b** was obtained (entry 11). *N*-Acetylated **21c** afforded the deacylated indole **24** along with the Sonogashira coupling product **25c** (entry 12). In the absence of water following the Sonogashira coupling of **21c** and **22**, **25c** was obtained in moderate yield (65%, entry 13), suggesting that the cyclization of **25c** was problematic under these conditions. Finally, 2-chloroanilines bearing other protecting groups, such as trifluoroacetyl, *t*-butyloxycarbonyl (Boc), mesyl, and 2-nitrobenzenesulfonyl (Ns), failed to yield the desired products **25d–g** (entries 14–17).

Substrate Scope for Indole Synthesis from 2-Chloroaniline Derivatives. The optimized reaction conditions were then applied to the syntheses of a range of 2-substituted indoles from 2-chloroaniline derivatives (Table 5). Initially, various *N*-tosyl-2-chloroanilines **26–34** were prepared from their corresponding 2-chloroanilines and tosyl chloride. Reaction of **21a** with 1-dodecyne (**2**) afforded 2-decyl-substituted indole **35** in high yield (82%, entry 1), while the 4-methyl-substituted substrate gave the corresponding 5-methylindoles **36–39** in moderate to good yields (60–72%, entries 2–5). Both aliphatic (entries 2 and 3) and aromatic (entries 4 and 5) alkynes reacted smoothly. Furthermore, the electron-withdrawing fluoro group was successfully introduced using the 4-fluoro-substituted substrate **27** to give the desired products **40** and **41** (entries 6 and 7). Trifluoromethyl-substituted indole **42** was also obtained by this method (entry 8). In addition, the 5-methoxy-substituted substrate afforded 6-methoxyindoles **43** and **44** (entries 9 and 10), while the reaction of tosylated 3-amino-2-chloropyridine and **2** proceeded efficiently and gave the corresponding pyrrolo[3,2-*b*]pyridine **45** (entry 11). Similarly, pyrrolo[2,3-*b*]pyridine **46** was obtained from tosylated 2-amino-3-chloropyridine in moderate yield (64%, entry 12). The high *ortho*-selectivity in this Sonogashira coupling reaction also enabled the preparation of various 2-substituted chloroindoles **47–52** from the dichloroaniline derivatives (entries 13–18), with the second Sonogashira coupling being almost completely suppressed even in the presence of an excess amount of alkyne. These results indicate the effectiveness of the Pd–Cy-DHTP system for the *ortho*-selective cross-coupling.

One-Pot Synthesis of Disubstituted Indoles from Dichloroaniline Derivatives. We then conducted the one-pot synthesis of disubstituted indoles through a Sonogashira coupling/cyclization/Suzuki–Miyaura coupling sequence using the Pd–Cy-DHTP system (Table 6). 2,4-Disubstituted indoles were selected as synthetic targets due to the synthetic difficulty of functionalizing at the 4-position using conventional methods.[58−67] As a result, various 2,4-disubstituted indoles were successfully synthesized (**53–68**) from *N*-tosyl-2,3-dichloroaniline (**32**) using the Pd–Cy-DHTP catalyst (entries 1–16). In these reactions, the addition of a substoichiometric amount of TBAC was also found to be effective in promoting the Suzuki–Miyaura coupling of 4-chloroindoles and boronic acids. Phenylboronic acids bearing not only electron-donating

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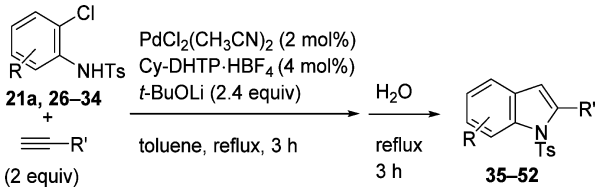
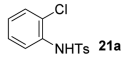
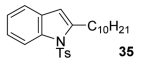
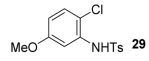
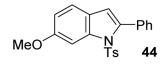
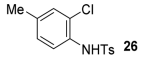
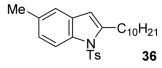
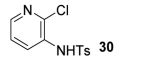
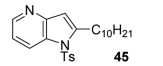
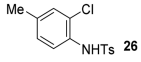
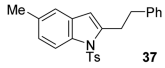
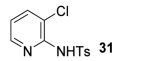
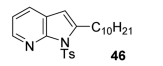
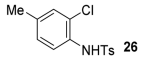
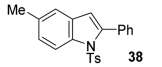
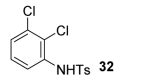
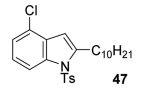
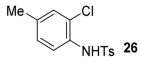
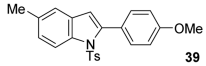
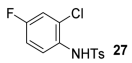
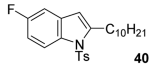
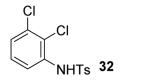
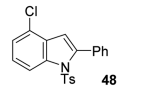
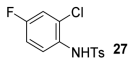
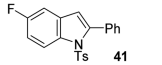
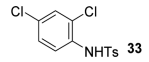
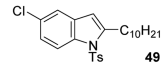
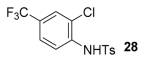
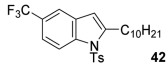
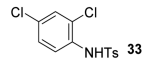
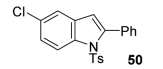
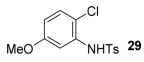
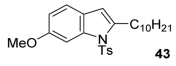
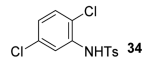
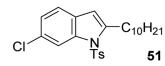
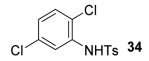
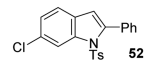
J. Org. Chem. 2016, 81, 5450–5463

Table 5. Indole Synthesis from 2-Chloroaniline Derivatives



entry	*N*-tosylaniline	product	yield (%)[a]	entry	*N*-tosylaniline	product	yield (%)[a]
1			82	10[c]			75
2[b]			72	11			67
3[c]			64	12			64
4			60	13			83
5			64				
6[c]			66	14			88
7[c]			73	15			83
8			70	16[d]			67
9[c]			47	17			37
				18			57

[a]Isolated yield. [b]Sonogashira coupling 5 h. [c]Sonogashira coupling 6 h. [d]Alkyne 1.05 equiv, mesitylene instead of toluene, 140 °C, 2 h; H_2O, reflux, 1.5 h.

but also electron-withdrawing groups afforded the desired products (entries 1−4, 6−13, and 16). Furthermore, 3-thienyl (entries 5 and 14) and alkenyl groups (entry 15) were also successfully introduced. This method was applicable to the synthesis of various disubstituted indoles bearing substituents at different positions; namely, 2,5-disubstituted indoles **69**−**71** (entries 17−19) and 2,6-disubstituted indoles **72**−**74** (entries 20−22), which were obtained in moderate yields (36−63%).

Mechanistic Study Using ESI-TOF-MS. We previously conducted electrospray ionization time-of flight mass spectrometry (ESI-TOF-MS) on the mixture of Cy-DHTP and 2-chlorophenol in the presence of *t*-BuOLi, allowing the observation of complex formation between the lithium phenoxides of Cy-DHTP and 2-chlorophenol.[39] The obtained results support our hypothesis regarding the formation of a heteroaggregate between the Pd−Cy-DHTP catalyst and 2-chlorophenols, which leads to acceleration of the Sonogashira coupling reaction at the *ortho*-position. We then turned our attention to the reaction mechanism in the preparation of indoles from *N*-tosyl-chloroanilines. On the basis of the above-mentioned results and previous examples of single-crystal X-ray structure determination for lithium salts of sulfonamides shown to form dimers via N−Li−O linkages,[68,69] Pd−Cy-DHTP was expected to form heteroaggregates, such as structures **A** and **B**, with *N*-tosyl-2-chloroanilines in the presence of *t*-BuOLi (Scheme 3). We performed ESI-TOF-MS on the mixture of Cy-DHTP and **21a** with *t*-BuOLi. Under an argon atmosphere, **21a**, Cy-DHTP (40 mol %), and *t*-BuOLi (1.4 equiv) were dissolved in toluene and stirred for 30 min at room temperature. An aliquot was then taken, diluted with acetonitrile, and analyzed by ESI-TOF-MS in the negative ion mode.

As a result, a signal corresponding to the 1:1 complex between the Cy-DHTP monophenoxide and the lithium salt of **21a** was observed at m/z 744 in the negative ion mode (Figure 2a). The observed isotopic distribution of the signal is consistent with the theoretical isotopic pattern of the complex (Figure 2b,c). We assume the structure of the complex as shown in Figure 3. Signals corresponding to the 1:2 and 1:3 complexes between the Cy-DHTP phenoxide and the lithium

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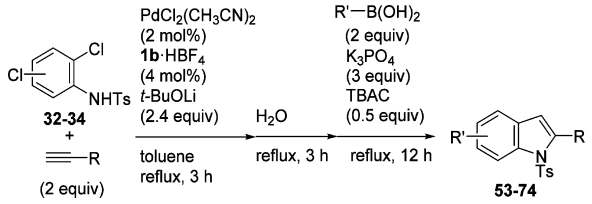
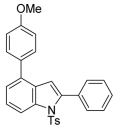
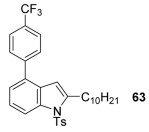
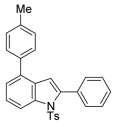
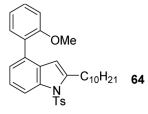
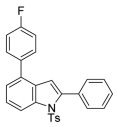
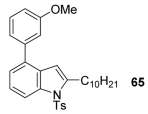
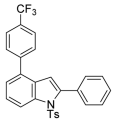
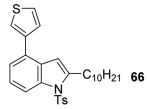
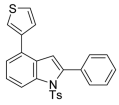
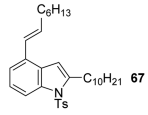
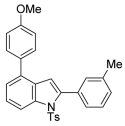
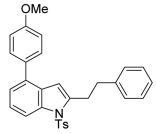
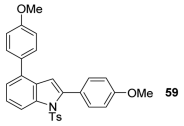
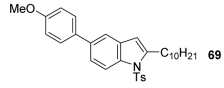
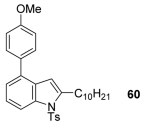
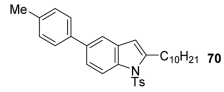
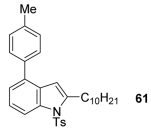
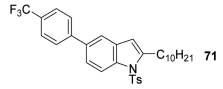
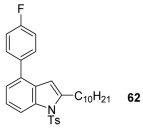
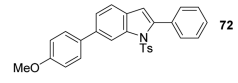
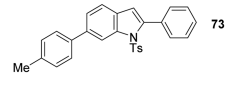
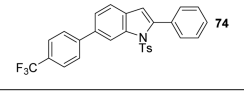
Table 6. One-Pot Indole Synthesis from Dichloroaniline Derivatives



entry	product	yield (%)[a]	entry	product	yield (%)[a]
1	 **53**	69	11[c]	 **63**	72
2	 **54**	38	12[c]	 **64**	58
3	 **55**	28	13[c]	 **65**	58
4	 **56**	42	14[c]	 **66**	64
5[b]	 **57**	31	15[c]	 **67**	36
6	 **58**	47	16	 **68**	56
7	 **59**	49	17	 **69**	62
8[c]	 **60**	87 (73)[d]	18	 **70**	54
9[c]	 **61**	55	19	 **71**	63
10[c]	 **62**	48	20	 **72**	44
			21[e]	 **73**	53
			22	 **74**	36

[a]Isolated yield. [b]Boronic acid (3 equiv), K_3PO_4 (4.5 equiv), Suzuki–Miyaura coupling 20 h. [c]Alkyne 1.05 equiv. [d]2 mmol scale. [e]Suzuki–Miyaura coupling 20 h.

salt of **21a** were observed at *m/z* 1031 and *m/z* 1320, respectively (Figure S2). In addition, signals corresponding to the aggregates of the lithium salt of **21a** were also observed at *m/z* 856 (trimer), 1143 (tetramer), and 1430 (pentamer)

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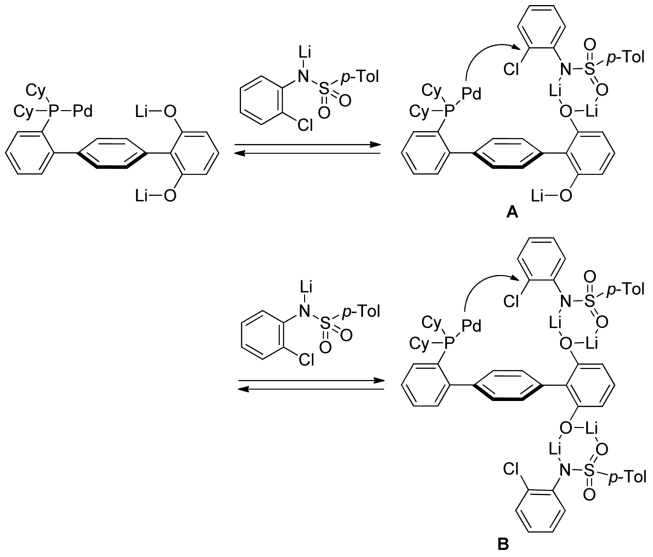
J. Org. Chem. 2016, 81, 5450–5463

Scheme 3. Formation of the Proposed Intermediate between Lithium Salts of Pd−Cy-DHTP and 21a.



(Figure S3). These results indicate that Cy-DHTP has the ability to form complexes with *N*-tosyl-2-chloroanilines in the presence of *t*-BuOLi, and is consistent with our hypothesis regarding heteroaggregate formation, as shown in Scheme 3.

CONCLUSION

A one-pot synthesis for the preparation of disubstituted benzo[*b*]furans from dichlorophenols, terminal alkynes, and boronic acids was established using an *ortho*-selective Sonogashira coupling, followed by cyclization and Suzuki−Miyaura coupling. TBAC was found to play an important role in improving the Suzuki−Miyaura coupling step. Furthermore, the novel protocol was also successfully applied in the one-pot synthesis of disubstituted indoles from *N*-tosyldichloroanilines. Mechanistic studies using ESI-TOF-MS suggested complex formation between the lithium salts of Cy-DHTP and the *N*-tosyldichloroanilines, which is similar to the mechanism

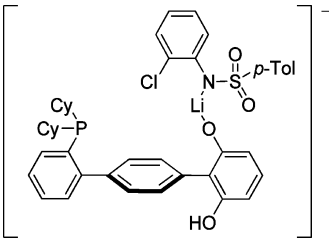


Figure 3. Assumed structure of the complex observed at *m*/*z* 744 in ESI-TOF-MS, as shown in Figure 2.

determined for 2-chlorophenols. These synthetic methods are expected to be useful in the preparation of benzo[*b*]furan and indole derivatives bearing a range of substituent patterns.

EXPERIMENTAL SECTION

All reactions were performed under an argon atmosphere. For ^{1}H NMR spectroscopic analysis, tetramethylsilane (TMS) (δ = 0) in $CDCl_3$ served as an internal standard. For ^{13}C NMR spectroscopic analysis, $CDCl_3$ (δ = 77.0) served as an internal standard. For ^{19}F NMR spectroscopic analysis, $CFCl_3$ (δ = 0) served as an external standard. For IR spectroscopic analysis, ZnSe was used as an ATR crystal. DART-TOF mass spectrometric analyses were conducted using glass rods, which were dipped in the sample solution (dissolved in dichloromethane or methanol) and placed in the open gap between the DART source and the orifice of the API interface. Melting points were uncorrected. All reagents were purchased from commercial suppliers and used without further purification. Anhydrous solvents were also purchased from commercial suppliers. Cy-DHTP·HBF_4,[42] *N*-(2-chlorophenyl)-4-methylbenzenesulfonamide (**21a**),[70,71] *N*-(2-chlorophenyl)acetamide (**21c**),[72,73] *N*-(2-chlorophenyl)-2,2,2-trifluoroacetamide (**21d**),[74,75] *N*-(2-chlorophenyl)methanesulfonamide (**21e**),[76,77] *N*-(2-chlorophenyl)-2-nitrobenzenesulfonamide (**21f**),[78,79] *tert*-butyl (2-chlorophenyl)carbamate (**21g**),[80,81] *N*-(2,3-dichlorophenyl)-4-methylbenzenesulfonamide (**32**),[50,82] *N*-(2,4-dichlorophenyl)-4-methylbenzenesulfonamide (**33**),[50,83] and *N*-(2,5-dichlorophenyl)-4-methylbenzenesulfonamide (**34**)[50] were prepared according to reported procedures.

Typical Experimental Procedure for the Synthesis of Disubstituted Benzo[*b*]furans (Method A, Table 1, Entry 7). *2-Decyl-5-(4-methoxyphenyl)benzo[b]furan* (*3*).[39] Toluene (1.0 mL) was added to $PdCl_2(CH_3CN)_2$ (2.6 mg, 0.01 mmol), Cy-DHTP·HBF_4

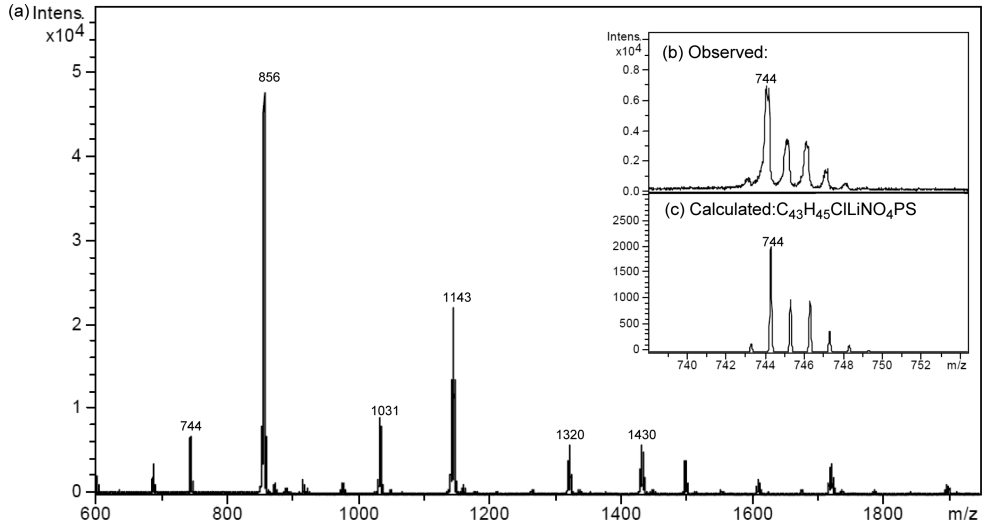


Figure 2. Complex formation between **21a** and Cy-DHTP (0.4 equiv) in the presence of *t*-BuOLi (1.4 equiv) as observed by ESI-TOF-MS in the negative ion mode. (a) ESI-TOF mass spectrum obtained following stirring for 30 min. Detailed view of (b) the observed isotopic distribution compared to (c) the theoretical isotopic pattern of the complex shown in Figure 3.

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J. Org. Chem. 2016, 81, 5450−5463

(10.6 mg, 0.02 mmol), *t*-BuOLi (144 mg, 1.20 mmol), and **1** (82.0 mg, 0.50 mmol) in a two-neck flask under argon. The reaction mixture was stirred at rt for 15 min, after which time **2** (112 μL, 0.53 mmol) was added. The reaction mixture was then stirred at reflux for 45 min. After cooling to rt, degassed water (1 mL) was added, and the reaction mixture stirred at reflux for 2 h. After cooling to rt, 4-methoxyphenylboronic acid (114 mg, 0.75 mmol), K_3PO_4 (213 mg, 1.0 mmol), and tetrabutylammonium chloride (71.7 mg. 0.26 mmol) were added, and the reaction mixture stirred at reflux for 6 h. The resulting suspension was quenched with 1 M aq. HCl (6 mL) at rt and extracted using ethyl acetate (2 × 20 mL). The combined organic layers were then dried over anhydrous Na_2SO_4 and concentrated *in vacuo*, and the resulting residue was purified by preparative TLC (PTLC) (SiO_2, hexanes/dichloromethane = 4/1) to give **3** (142 mg, 78%) as a white solid.

*5-Chloro-2-decylbenzo[b]furan (**4**, Table 1, Entry 1).*[39] A pale-yellow solid (60 mg, 41%).

*5-(4-Methylphenyl)-2-phenylbenzo[b]furan (**5**).*[39] Prepared from **1**, **22**, and 4-methylphenylboronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexanes/dichloromethane = 6/1) afforded **5** as colorless needles (116 mg, 82%).

*2-Phenyl-5-(4-trifluoromethylphenyl)benzo[b]furan (**6**).*[39] Prepared from **1**, **22**, and 4-trifluoromethylphenylboronic acid following the typical procedure (Method A). Purification by PTLC (SiO_2, hexanes/dichloromethane = 6/1) afforded **6** as a pale yellow solid (126 mg, 74%).

*5-(4-Fluorophenyl)-2-phenylbenzo[b]furan (**7**).*[39] Prepared from **1**, **22**, and 4-fluorophenylboronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexanes/dichloromethane = 10/1) afforded **7** as yellow plates (117 mg, 81%).

*2-Phenyl-5-(thiophene-3-yl)benzo[b]furan (**8**).*[39] Prepared from **1**, **22**, and 3-thiopheneboronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexanes/dichloromethane = 10/1) afforded **8** as colorless cubes (101 mg, 73%).

*(E)-5-(Octo-1-en-1-yl)-2-phenylbenzo[b]furan (**9**).*[39] Prepared from **1**, **22**, and *trans*-1-octen-1-ylboronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexanes/dichloromethane = 20/1) afforded **9** as a white solid (81 mg, 53%).

*(3-(2-Phenylbenzo[b]furan-5-yl)phenyl)methanol (**10**).* Prepared from **1**, **22**, and (3-(hydroxymethyl)phenyl)boronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexane/EtOAc = 2/1) afforded **10** (113 mg, 72%) as a yellow solid. Mp. 134.5−136.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (2H, dd, *J* = 7.2, 1.6 Hz), 7.72 (1H, d, *J* = 1.5 Hz), 7.59 (1H, s), 7.54−7.52 (2H, m), 7.47 (1H, dd, *J* = 8.5, 1.7 Hz), 7.45−7.39 (3H, m), 7.32 (2H, dd, *J* = 16.8, 7.6 Hz), 6.99 (1H, s), 4.72 (2H, s), 2.08 (1H, s). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 156.6, 154.5, 141.9, 141.3, 136.3, 130.3, 129.7, 128.9, 128.8, 128.6, 126.6, 126.0, 125.4, 124.9, 123.9, 119.3, 111.2, 101.4, 65.3. IR (ATR) cm^{-1}: 3447, 3422, 1464, 1441, 1269, 1177, 1152, 1126, 1072, 1038, 1023. HRMS (DART-TOF) *m*/*z*: calcd for $C_{21}H_{17}O_2$ ([M + H]$^+$), 301.1229; found, 301.1221.

Typical Experimental Procedure for the Synthesis of Disubstituted Benzo[*b*]furans (Method B, Table 3, Entry 1). *(E)-2-Phenyl-5-styrylbenzo[b]furan (**11**).* Toluene (1.0 mL) was added to $PdCl_2(CH_3CN)_2$ (2.6 mg, 0.01 mmol), Cy-DHTP·HBF$_4$ (10.6 mg, 0.02 mmol), XPhos (9.5 mg, 0.02 mmol), *t*-BuOLi (144 mg, 1.20 mmol), and **1** (81.6 mg, 0.50 mmol) in a two-neck flask under argon. The reaction mixture was stirred at rt for 15 min, after which time **22** (58 μL, 0.53 mmol) was added. The reaction mixture was then stirred at reflux for 45 min. After cooling to rt, degassed water (1 mL) was added, and the reaction mixture stirred at reflux for 2 h. After cooling to rt, *trans*-2-phenylvinylboronic acid (149 mg, 1.01 mmol), K_3PO_4 (318 mg, 1.5 mmol), and tetrabutylammonium chloride (70.7 mg, 0.25 mmol) were added, and the reaction mixture stirred at reflux for 20 h. The resulting suspension was quenched with 1 M aq. HCl (6 mL) at rt and extracted using ethyl acetate (2 × 20 mL). The combined organic layers were then dried over anhydrous Na_2SO_4 and concentrated *in vacuo*, and the resulting residue was purified by preparative TLC (PTLC) (SiO_2, hexanes/dichloromethane = 4/1) to give **11** (101 mg, 68%) as a white solid. Mp. 211.4−211.9 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (2H, d, *J* = 7.4 Hz), 7.70 (1H, s), 7.53 (2H, t, *J* = 7.4 Hz), 7.49 (2H, t, *J* = 1.7 Hz), 7.45 (2H, t, *J* = 7.7 Hz), 7.38−7.35 (3H, m), 7.26 (1H, t, *J* = 7.5 Hz), 7.21 (1H, d, *J* = 16.0 Hz), 7.10 (1H, d, *J* = 16.4 Hz), 7.02 (1H, s). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 154.7, 137.6, 132.7, 130.3, 129.7, 129.0, 128.8, 128.7, 127.8, 127.4, 126.4, 124.9, 123.1, 118.8, 111.3, 101.3, 99.9 (one carbon signal is overlapped). IR (ATR) cm^{-1}: 1489, 1466, 1449, 1271, 1254, 1119, 1072, 1038, 1018. HRMS (DART-TOF) *m*/*z*: calcd for $C_{22}H_{17}O$ ([M + H]$^+$), 297.1274; found, 297.1294.

*2-Phenyl-5-(pyridine-3-yl)benzo[b]furan (**12**, Table 3, Entry 2).* Prepared from **1**, **22**, and 3-pyridineboronic acid following the typical procedure (Method B). Purification by column chromatography (SiO_2, hexane/dichloromethane = 1/5) afforded **12** (114 mg, 84%) as a yellow solid. Mp. 159.7−160.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (1H, d, *J* = 2.0 Hz), 8.59 (1H, dd, *J* = 4.9, 1.5 Hz), 7.91 (3H, dt, *J* = 10.4, 3.0 Hz), 7.77 (1H, d, *J* = 2.0 Hz), 7.62 (1H, d, *J* = 8.3 Hz), 7.50−7.45 (3H, m), 7.40−7.36 (2H, m), 7.08 (1H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.0, 154.9, 148.5, 148.1, 137.1, 134.5, 133.1, 130.2, 130.0, 128.8, 125.0, 123.7, 123.5, 119.5, 111.6, 101.3 (one carbon signal is overlapped). IR (ATR) cm^{-1}: 3028, 1566, 1491, 1445, 1406, 1267, 1246, 1155, 1123, 1105. HRMS (DART-TOF) *m*/*z*: calcd for $C_{19}H_{14}NO$ ([M + H]$^+$), 272.1075; found, 272.1065.

*5-(Furan-2-yl)-2-phenylbenzo[b]furan (**13**, Table 3, Entry 3).* Prepared from **1**, **22**, and 2-furylboronic acid following the typical procedure (Method B). Purification by column chromatography (SiO_2, hexane/dichloromethane = 5/1) afforded **13** (84 mg, 64%) as an orange solid. Mp. 134 °C (decomposed). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (3H, d, *J* = 9.3 Hz), 7.58 (1H, dd, *J* = 8.8, 1.5 Hz), 7.43 (4H, m), 7.32 (1H, t, *J* = 7.3 Hz), 6.95 (1H, s), 6.59 (1H, d, *J* = 3.4 Hz), 6.45 (1H, dd, *J* = 2.0, 0.8 Hz). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 156.7, 154.41, 154.36, 141.7, 130.3, 129.6, 128.8, 128.6, 126.4, 124.9, 120.9, 116.1, 111.6, 111.3, 104.1, 101.4. IR (ATR) cm^{-1}: 3109, 3057, 1489, 1458, 1445, 1431, 1269, 1240, 1213, 1163, 1038, 1011. HRMS (DART-TOF) *m*/*z*: calcd for $C_{18}H_{13}O_2$ ([M + H]$^+$), 261.0916; found, 261.0915.

*5-(3-Hydroxyphenyl)-2-phenylbenzo[b]furan (**14**, Table 3, Entry 4).* Prepared from **1**, **22**, and 3-hydroxyphenylboronic acid following the typical procedure (Method B), except for the use of TBAOH (2 equiv) instead of TBAC and K_3PO_4. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 1/4) afforded **14** (102 mg, 71%) as yellow plates. Mp. 171.8−172.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (2H, dd, *J* = 3.6, 1.6 Hz), 7.75 (1H, d, *J* = 2.0 Hz), 7.56 (1H, d, *J* = 8.3 Hz), 7.50−7.45 (3H, m), 7.39−7.34 (1H, m), 7.31 (1H, d, *J* = 7.8 Hz), 7.21 (1H, d, *J* = 7.8 Hz), 7.10 (1H, t, *J* = 2.2 Hz), 7.06 (1H, s), 6.82 (1H, ddd, *J* = 8.2, 2.8, 1.0 Hz), 4.80 (1H, s). ^{13}C{^{1}H} NMR (100 MHz, acetone-d_6): δ 158.6, 157.2, 155.3, 143.7, 137.4, 131.1, 130.68, 130.66, 129.7, 129.5, 125.6, 124.7, 120.1, 119.3, 114.8, 111.9, 102.6. IR (ATR) cm^{-1}: 3503, 3402, 1607, 1576, 1443, 1294, 1254, 1192, 1148, 1038, 1018. HRMS (DART-TOF) *m*/*z*: calcd for $C_{20}H_{15}O_2$ ([M + H]$^+$), 287.1072; found, 287.1080.

*4-(4-Methoxylphenyl)-2-phenylbenzo[b]furan (**15**).*[39] Prepared from 2,3-dichlorophenol, **22**, and 4-methoxyphenylphenylboronic acid following the typical procedure (Method A). Purification by PTLC (SiO_2, hexane/ethyl acetate = 10/1) afforded **15** as a yellow oil (127 mg, 85%).

*4-(4-Nitrophenyl)-2-phenylbenzo[b]furan (**16**).* Prepared from 2,3-dichlorophenol, **22**, and 4-nitrophenylboronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexane/dichloromethane = 2/1) afforded **16** (121 mg, 76%) as yellow needles. Mp. 177.7−180.9 °C. ^{1}H NMR ($CDCl_3$): δ 8.35 (2H, d, *J* = 8.8 Hz), 7.87 (2H, dd, *J* = 8.7, 1.6 Hz), 7.79 (2H, dd, *J* = 6.8, 2.0 Hz), 7.58 (1H, d, *J* = 8.3 Hz), 7.45 (2H, dt, *J* = 7.6, 2.0 Hz), 7.35 (3H, m), 7.13 (1H, d, *J* = 0.8 Hz). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 157.2, 155.2, 147.0, 146.7, 132.3, 129.9, 129.04, 129.01, 128.9, 127.6, 126.0, 124.6, 124.1, 122.9, 111.6, 100.0. IR (ATR) cm^{-1}: 3082, 3032, 2924, 1591, 1508, 1474, 1398, 1341, 1258, 1163, 1109, 1024. HRMS (DART-TOF) *m*/*z*: calcd for $C_{20}H_{14}NO_3$ ([M + H]$^+$), 316.0974; found, 316.0973.

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J. Org. Chem. 2016, 81, 5450−5463

*4-(3-Hydroxyphenyl)-2-phenylbenzo[b]furan (**17**).* Prepared from 2,3-dichlorophenol, **22**, and 3-hydroxyphenylboronic acid following the typical procedure (Method A), except for the use of TBAOH (2 equiv) instead of TBAC and K_3PO_4. Purification by column chromatography (SiO_2, hexane/dichloromethane = 1/3) afforded **17** (102 mg, 71%) as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (2H, dd, J = 6.8, 0.8 Hz), 7.47 (1H, d, J = 7.9 Hz), 7.39 (2H, t, J = 7.7 Hz), 7.35−7.27 (3H, m), 7.24 (1H, dd, J = 7.4, 1.1 Hz), 7.20 (1H, dd, J = 8.5, 1.0 Hz), 7.16 (1H, s), 7.11 (1H, t, J = 2.0 Hz), 6.86 (1H, dd, J = 7.9, 1.7 Hz), 5.38 (1H, s). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 156.2, 155.7, 155.1, 141.8, 134.4, 130.3, 130.0, 128.7, 128.6, 127.5, 124.9, 124.4, 122.4, 121.1, 115.3, 114.3, 110.3, 100.8. IR (ATR) cm^{-1}: 3319, 3057, 1578, 1447, 1414, 1306, 1252, 1207, 1186, 1155, 1042, 1022. HRMS (DART-TOF) m/z: calcd for $C_{20}H_{15}O_2$ ([M + H]$^+$), 287.1067; found, 287.1085.

*2-Phenyl-4-(pyridine-3-yl)benzo[b]furan (**18**).* Prepared from 2,3-dichlorophenol, **22**, and 3-pyridineboronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexane/EtOAc = 1/1) afforded **18** (118 mg, 87%) as a brown solid. Mp. 159.7−160.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.92 (1H, d, J = 1.5 Hz), 8.62 (1H, dd, J = 4.9, 1.5 Hz), 7.91−7.89 (1H, m), 7.83 (2H, dd, J = 8.4, 1.2 Hz), 7.51 (1H, d, J = 8.3 Hz), 7.45−7.40 (3H, m), 7.35−7.30 (2H, m), 7.26 (1H, dd, J = 7.2, 0.8 Hz), 7.14 (1H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.8, 155.2, 149.3, 148.4, 135.7, 135.5, 121.1, 130.0, 128.78, 128.77, 127.7, 124.9, 124.6, 123.6, 122.7, 110.9, 100.0. IR (ATR) cm^{-1}: 3028, 1585, 1489, 1466, 1431, 1402, 1265, 1165, 1038, 1020. HRMS (DART-TOF) m/z: calcd for $C_{19}H_{14}NO$ ([M + H]$^+$), 272.1075; found, 272.1076.

*6-(4-Methoxyphenyl)-2-phenylbenzo[b]furan (**19**).*[39] Prepared from 2,5-dichlorophenol, **22**, and 4-methoxyphenylboronic acid following the typical procedure (Method A). Purification by column chromatography (SiO_2, hexanes/dichloromethane = 10/1) and preparative TLC (hexanes/dichloromethane = 4/1) afforded **19** as a white solid (48 mg, 32%).

*2-(4-Methoxyphenyl)-7-(4-methoxyphenyl)benzo[b]furan (**20**).*[39] Prepared from 2,6-dichlorophenol, 4-ethynylanisole, and 4-methoxyphenylboronic acid following the typical procedure (Method A). Purification by preparative TLC (hexanes/dichloromethane = 5/2) and preparative HPLC afforded **20** as a colorless oil (53 mg, 32%).

Typical Experimental Procedure for the Syntheses of 2-Substituted Indoles (Table 4, entry 1). *2-Phenyl-1-tosyl-1H-indole (**23a**).*[84] Toluene (2 mL) was added to $PdCl_2(CH_3CN)_2$ (2.6 mg, 0.01 mmol), Cy-DHTP·HBF_4 (10.9 mg, 0.02 mmol), *t*-BuOLi (96 mg, 1.2 mmol), and **21a** (140 mg, 0.50 mmol) in a two-neck flask under argon. The reaction mixture was stirred at rt for 40 min, and then **22** (112 μL, 1.0 mmol) was added, and the resulting mixture stirred at reflux for 3 h. Water (2 mL) was then added, and the reaction mixture was stirred at reflux for 3 h. The resulting suspension was quenched with saturated aq. NH_4Cl (5 mL) at rt and extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated, and the resulting residue was purified by preparative TLC (SiO_2, hexanes/dichloromethane = 1/1) to give **23a** (118 mg, 68%) as a pale yellow solid.

*2-Phenyl-1H-indole (**24**, Table 4, Entry 12).*[85] A white solid (12 mg, 12%).

*4-Methyl-N-(2-(phenylethynyl)phenyl)benzenesulfonamide (**25a**, Table 4, Entry 2).*[86] A pale yellow solid (67 mg, 38%).

*2-(Phenylethynyl)aniline (**25b**, Table 4, Entry 14).*[87] A pale orange solid (22 mg, 23%).

*N-(2-(Phenylethynyl)phenyl)acetamide (**25c**, Table 4, Entry 12).*[88,89] A pale yellow solid (36 mg, 23%).

Typical Experimental Procedure for the Syntheses of *N*-Tosylchloroanilines. *N-(2-Chloro-4-methylphenyl)-4-methylbenzenesulfonamide (**26**).* *p*-Toluenesulfonyl chloride (4.56 g, 24 mmol) was added in small portions to a mixture of 2-chloro-4-methylaniline (20 mmol) and pyridine (10 mL, 120 mmol) dissolved in dichloromethane (66 mL). The reaction mixture was then stirred at rt for 3.5 h, after which time 1 M aq. HCl (50 mL) was added and the organic phase was washed with 1 M aq. HCl (3 × 50 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuo to give a residue, which was recrystallized from ethanol to give **26** (5.46 g, 92%) as colorless needles. Mp. 104.8−105.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (2H, d, J = 8.0 Hz), 7.54 (1H, d, J = 8.0 Hz), 7.21 (2H, d, J = 8.4 Hz), 7.02−7.05 (2H, m), 6.83 (1H, brs), 2.38 (3H, s), 2.26 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.0, 136.3, 135.9, 130.7, 129.63, 129.59, 128.6, 127.3, 125.3, 122.9, 21.6, 20.6. IR (ATR) cm^{-1}: 3258, 1495, 1414, 1385, 1310, 1234, 1167, 1094, 1053, 916. HRMS (ESI-TOF) m/z: calcd for $C_{14}H_{13}ClNO_2S$ ([M-H]$^-$), 294.0361; found, 294.0369.

*N-(2-Chloro-4-fluorophenyl)-4-methylbenzenesulfonamide (**27**).* Prepared from 2-chloro-4-fluoroaniline following the typical procedure. Recrystallization from ethanol afforded **27** (5.70 g, 95%) as colorless needles. Mp. 115.1−115.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (1H, dd, J = 6.4, 7.6 Hz), 7.61 (2H, d, J = 6.8 Hz), 7.23 (2H, d, J = 7.2 Hz), 7.01−6.95 (2H, m), 6.81, (1H, s) 2.39, (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.9 (d, J = 247.8 Hz), 144.3, 135.7, 129.8 (d, J = 3.3 Hz), 129.7, 127.2, 126.9 (d, J = 10.7 Hz), 125.0 (d, J = 9.1 Hz), 116.8 (d, J = 25.6 Hz), 115.2 (d, J = 21.4 Hz), 21.6; ^{19}F NMR (471 MHz, $CDCl_3$): δ −114.1 (m). IR (ATR) cm^{-1}: 3250, 1597, 1489, 1425, 1381, 1339, 1258, 1165, 1092, 1043. HRMS (DART-TOF) m/z: calcd for $C_{13}H_{12}ClFNO_2S$ ([M + H]$^+$), 300.0256; found, 300.0262.

*N-(2-Chloro-4-(trifluoromethyl)phenyl)-4-methylbenzenesulfonamide (**28**).*[90] Prepared from 2-chloro-4-trifluoromethylaniline (10 mmol) following the typical procedure. Recrystallization from dichloromethane/hexanes afforded **28** (1.72 g, 49%) as colorless cubes. Mp. 98.3−99.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76−7.70 (3H, m), 7.54 (1H, d, J = 2.0 Hz), 7.46 (1H, dd, J = 8.8, 1.6 Hz), 7.28−7.26 (3H, m), 2.40 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.9, 136.9, 135.7, 127.3, 127.3 (q, J = 33.1 Hz), 126.8 (q, J = 4.0 Hz), 125.1 (q, J = 4.0 Hz), 124.0, 123.1 (q, J = 271.1 Hz), 120.4, 21.5. ^{19}F NMR (471 MHz, $CDCl_3$): δ −62.4 (s). IR (ATR) cm^{-1}: 3273, 1612, 1508, 1429, 1395, 1323, 1165, 1115, 1082, 905. HRMS (DART-TOF) m/z: calcd for $C_{14}H_{12}NO_2ClF_3S$ ([M + H]$^+$), 350.0224; found, 350.0229.

*N-(2-Chloro-5-methoxyphenyl)-4-methylbenzenesulfonamide (**29**).* Prepared from 2-chloro-5-methoxyaniline following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **29** (5.45 g, 87%) as colorless needles. Mp. 90.7−91.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (2H, d, J = 8.4 Hz), 7.24−7.22 (3H, m), 7.12 (1H, d, J = 8.4 Hz), 6.96 (1H, brs), 6.57 (1H, dd, J = 3.2, 9.2 Hz), 3.78 (3H, s), 2.38 (3H, s). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.0, 144.3, 135.8, 134.1, 129.7, 129.6, 127.3, 116.0, 111.9, 107.2, 55.6, 21.6. IR (ATR) cm^{-1}: 3252, 1595, 1580, 1489, 1395, 1337, 1298, 1263, 1240, 1200, 1163. HRMS (DART-TOF) m/z: calcd for $C_{14}H_{15}ClNO_3S$ ([M + H]$^+$), 312.0456; found, 312.0467.

*N-(2-Chloropyridin-3-yl)-4-methylbenzenesulfonamide (**30**).*[91] Prepared from 3-amino-2-chloropyridine (10 mmol) following the typical procedure. Recrystallization from ethanol afforded **30** (2.29 g, 81%) as colorless cubes. Mp. 111.5−112.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (1H, dd, J = 4.6, 1.7 Hz), 8.00 (1H, dd, J = 8.0, 1.7 Hz), 7.67 (2H, d, J = 8.3 Hz), 7.28−7.21 (3H, m) 7.15 (1H, s), 2.39 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.2, 144.7, 142.2, 135.5, 130.9, 129.92, 129.89, 127.1, 123.3, 21.5. IR (ATR) cm^{-1}: 3138, 3069, 1599, 1568, 1439, 1329, 1163, 1092, 1076, 894. HRMS (DART-TOF) m/z: calcd for $C_{12}H_{12}N_2O_2ClS$ ([M + H]$^+$), 283.0303; found, 283.0314.

*N-(3-Chloropyridin-2-yl)-4-methylbenzenesulfonamide (**31**).* Prepared from 2-amino-3-chloropyridine (7.8 mmol) following the typical procedure. Recrystallization from dichloromethane/hexanes afforded **31** (0.60 g, 27%) as colorless needles. Mp. 128.1−128.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (1H, s), 8.05 (2H, d, J = 7.3 Hz), 7.78 (1H, s), 7.57 (1H, d, J = 7.3 Hz), 7.29 (2H, d, J = 7.8 Hz), 6.87 (1H, s), 2.40 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 147.2, 146.1, 144.2, 137.4, 136.6, 129.2, 128.5, 119.1, 117.2, 21.5. IR (ATR) cm^{-1}: 3252, 1580, 1443, 1385, 1339, 1159, 1088, 1040, 920. HRMS (DART-TOF) m/z: calcd for $C_{12}H_{12}N_2O_2ClS$ ([M + H]$^+$), 283.0303; found, 283.0308.

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*2-Decyl-1-tosyl-1H-indole (**35**).* Prepared from **21a** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/chloroform = 2/1) afforded **35** (169 mg, 82%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (1H, d, J = 8.4 Hz), 7.60 (2H, d, J = 8.4 Hz), 7.39 (1H, d, J = 8.0 Hz), 7.25−7.13 (4H, m), 6.36 (1H, s), 2.97 (2H, t, J = 7.9 Hz), 2.29 (3H, s), 1.76−1.69 (2H, m), 1.42−1.27 (14H, m), 0.88 (3H, t, J = 6.8 Hz). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 144.5, 142.6, 137.2, 136.3, 129.8, 129.7, 126.2, 123.7, 123.4, 120.0, 114.8, 108.6, 31.9, 29.59, 29.57, 29.44, 29.36, 29.3, 29.0, 28.8, 22.7, 21.5, 14.1. IR(ATR) cm^{-1}: 2922, 2853, 1597, 1566, 1495, 1450, 1368, 1306, 1217, 1173, 1144. HRMS (DART-TOF) m/z: calcd for $C_{25}H_{34}NO_2S$([M + H]$^+$), 412.2310; found, 412.2328.

*2-Decyl-5-methyl-1-tosyl-1H-indole (**36**).* Prepared from **26** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 2/1) afforded **36** (153 mg, 72%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (1H, d, J = 8.0 Hz), 7.60 (2H, d, J = 8.0 Hz), 7.17 (1H, s), 7.15 (2H, d, J = 8.0 Hz), 7.06 (1H, d, J = 8.8 Hz), 6.29 (1H, s), 2.95 (2H, t, J = 7.6 Hz), 2.38 (3H, s), 2.30 (3H, s), 1.74−1.68 (2H, m), 1.39−1.27 (14H, m), 0.88 (3H, t, J = 6.8 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.4, 142.6, 136.3, 135.5, 132.9, 130.1, 129.7, 126.2, 125.0, 120.0, 114.5, 108.5, 31.9, 29.60, 29.56, 29.43, 29.36, 29.3, 29.0, 28.9, 22.7, 21.5, 21.1, 14.1. IR (ATR) cm^{-1}: 2922, 2853, 1466, 1368, 1219, 1153, 1134, 1090, 1047, 804. HRMS (DART-TOF) m/z: calcd for $C_{26}H_{36}NO_2S$ ([M + H]$^+$), 426.2461; found, 426.2460.

*5-Methyl-2-(2-phenylethyl)-1-tosyl-1H-indole (**37**).* Prepared from **26** and 4-phenyl-1-butyne following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 1/1) afforded **37** (124 mg, 64%) as a pale brown solid. Mp. 90.5−91.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (1H, d, J = 8.8 Hz), 7.60 (2H, d, J = 8.4 Hz), 7.31−7.07 (9H, m), 6.30 (1H, s), 3.27 (2H, t, J = 8.0 Hz), 3.06 (2H, t, J = 7.8 Hz), 2.38 (3H, s), 2.30 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.5, 141.4, 141.2, 136.1, 135.5, 133.1, 130.0, 129.7, 128.5, 128.4, 126.2, 126.1, 125.3, 120.1, 114.6, 109.3, 35.6, 31.1, 21.5, 21.2. IR (ATR) cm^{-1}: 1597, 1452, 1364, 1213, 1150, 1090, 1040, 885, 808, 752. HRMS (DART-TOF) m/z: calcd for $C_{24}H_{24}NO_2S$ ([M + H]$^+$), 390.1522; found, 390.1515.

*5-Methyl-2-phenyl-1-tosyl-1H-indole (**38**).*[28] Prepared from **26** and **22** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 2/1) afforded **38** (109 mg, 60%) as a dark purple solid. Mp. 105.0−107.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (1H, d, J = 8.8 Hz), 7.51−7.48 (2H, m), 7.44−7.38 (3H, m), 7.26−7.14 (4H, m), 7.02 (2H, d, J = 8.0 Hz), 6.46 (1H, s), 2.40 (3H, s), 2.26 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.4, 142.2, 136.5, 134.6, 133.9, 132.5, 130.8, 130.2, 129.1, 128.5, 127.4, 126.8, 126.1, 120.6, 116.3, 113.5, 21.5, 21.2. IR (ATR) cm^{-1}: 1462, 1371, 1171, 1140, 1092, 1047, 1026, 984, 804, 760. HRMS (DART-TOF) m/z: calcd for $C_{22}H_{20}NO_2S$ ([M + H]$^+$), 362.1209; found, 362.1200.

*2-(4-Methoxyphenyl)-5-methyl-1-tosyl-1H-indole (**39**).*[28] Prepared from **26** and 4-ethynylanisole following the typical procedure. Purification by PTLC (SiO_2, hexanes/chloroform = 1/1) afforded **39** (125 mg, 64%) as an orange solid. Mp. 136.3−137.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (1H, d, J = 8.8 Hz), 7.42 (2H, d, J = 8.8 Hz), 7.26 (2H, d, J = 8.4 Hz), 7.19 (1H, s), 7.15 (1H, d, J = 8.8 Hz), 7.03 (2H, d, J = 8.4 Hz), 6.95 (2H, d, J = 8.8 Hz), 6.40 (1H, s), 3.87 (3H, s), 2.40 (3H, s), 2.27 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.0, 144.3, 142.1, 136.4, 134.7, 133.9, 131.6, 130.9, 129.1, 126.8, 125.9, 124.8, 120.4, 116.4, 112.9, 112.8, 55.3, 21.5, 21.2. IR (ATR) cm^{-1}: 1612, 1503, 1458, 1358, 1287, 1246, 1169, 1092, 1018, 841. HRMS (DART-TOF) m/z: calcd for $C_{23}H_{22}NO_3S$ ([M + H]$^+$), 392.1315; found, 392.1302.

*2-Decyl-5-fluoro-1-tosyl-1H-indole (**40**).* Prepared from **27** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 1/1) afforded **40** (142 mg, 66%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (1H, dd, J = 4.4, 8.8 Hz), 7.59 (2H, d, J = 8.4 Hz), 7.19 (2H, d, J = 8.0 Hz), 7.05 (1H, dd, J = 2.4, 8.4 Hz), 6.96 (1H, td, J = 9.0, 2.9 Hz), 6.33 (1H, s), 2.96 (2H, t, J = 7.6 Hz), 2.32 (3H, s), 1.76−1.68 (2H, m), 1.40−1.27 (14H, m), 0.88 (3H, t, J = 6.8 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.8 (d, J 38= 240.0 Hz), 144.8, 144.5, 136.1, 133.5, 131.0 (d, J = 10.0 Hz), 129.9, 126.3, 115.9 (d, J = 9.0 Hz), 111.4 (d, J = 24.1 Hz), 108.5 (d, J = 4.0 Hz), 105.6 (d, J = 24.1 Hz), 31.8, 29.6, 29.5, 29.4, 29.34, 29.25, 29.0, 28.7, 22.6, 21.4, 14.0. ^{19}F NMR (471 MHz, $CDCl_3$): δ −119.9 (m). IR (ATR) cm^{-1}: 2922, 2853, 1597, 1466, 1369, 1155, 1090, 1051, 856, 810. HRMS (DART-TOF) m/z: calcd for $C_{25}H_{33}FNO_2S$ ([M + H]$^+$), 430.2211; found, 430.2195.

*5-Fluoro-2-phenyl-1-tosyl-1H-indole (**41**).*[92,93] Prepared from **27** and **22** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 1/1) afforded **41** (134 mg, 73%) as a pale orange solid. Mp. 108.8−110.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (1H, dd, J = 4.4, 9.6 Hz), 7.50−7.39 (5H, m), 7.24 (2H, d, J = 8.8 Hz), 7.07 (4H, dd, J = 8.4, 16.8 Hz), 6.49 (1H, s), 2.28 (3H, s). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 160.3 (d, J = 242.0 Hz), 144.8, 144.0, 134.6, 134.4, 132.1, 131.7 (d, J = 10.0 Hz), 130.3, 129.3, 129.0, 127.6, 126.8, 117.9 (d, J = 9.0 Hz), 113.3 (d, J = 4.0 Hz), 112.6 (d, J = 25.1 Hz), 106.3 (d, J = 24.1 Hz), 21.4. ^{19}F NMR (471 MHz, $CDCl_3$): δ −118.5 (m). IR (ATR) cm^{-1}: 1597, 1458, 1377, 1173, 1130, 1090, 1055, 1026, 988, 957. HRMS (DART-TOF) m/z: calcd for $C_{21}H_{17}FNO_2S$ ([M + H]$^+$), 366.0959; found, 366.0957.

*2-Decyl-5-trifluoromethyl-1-tosyl-1H-indole (**42**).* Prepared from **28** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 2/1) afforded **42** (167 mg, 70%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 8.0 Hz), 1.20−1.46 (14H, m), 1.74 (2H, quin, J = 7.4 Hz), 2.33 (3H, s) 2.99 (2H, t, J = 7.6 Hz), 6.44 (1H, s) 7.20 (2H, d, J = 8.3 Hz), 7.49 (1H, d, J = 8.8 Hz), 7.63 (2H, d, J = 8.0 Hz), 7.69 (1H, s), 8.27 (1H, d, J = 8.78 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.1, 144.5, 138.7, 136.0, 129.9, 129.5, 126.3, 125.7, (q, J = 32.1 Hz), 124.6 (q, J = 270.8 Hz), 120.4 (q, J = 3.3 Hz), 117.4 (q, J = 4.0 Hz), 114.9, 108.1, 31.9, 29.6, 29.5, 29.4, 29.3, 28.9, 28.7, 22.6, 21.5, 14.1. ^{19}F NMR (471 Hz, $CDCl_3$): δ −61.1 (s). IR (ATR) cm^{-1}: 2922, 2853, 1589, 1460, 1364, 1163, 1138, 1092, 1057, 883. HRMS (DART-TOF) m/z: calcd for $C_{26}H_{33}NO_2F_3S$ ([M + H]$^+$), 480.2179; found, 480.2170.

*2-Decyl-6-methoxy-1-tosyl-1H-indole (**43**).* Prepared from **29** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 2/1) afforded **43** (103 mg, 47%) as a pale yellow solid. Mp. 78.6−79.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (1H, d, J = 2.4 Hz), 7.61 (2H, d, J = 8.0 Hz), 7.27 (1H, d, J = 8.4 Hz), 7.19 (2H, d, J = 8.8 Hz), 6.84 (1H, dd, J = 1.6, 8.0 Hz), 6.29 (1H, s), 3.86 (3H, s), 2.91 (2H, t, J = 7.6 Hz), 2.32 (3H, s), 1.71−1.66 (2H, m), 1.38−1.26 (14H, m), 0.87 (3H, t, J = 6.6 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.3, 144.5, 141.3, 138.2, 136.3, 129.7, 126.2, 123.6, 120.3, 112.3, 108.3, 99.7, 55.8, 31.9, 29.60, 29.57, 29.4, 29.35, 29.32, 29.0, 28.9, 22.7, 21.5, 14.1; IR (ATR) cm^{-1}: 2924, 2853, 1595, 1489, 1468, 1431, 1358, 1163, 1134, 1090. HRMS (DART-TOF) m/z: calcd for $C_{26}H_{36}NO_3S$ ([M + H]$^+$), 442.2410; found, 442.2419.

*6-Methoxy-2-phenyl-1-tosyl-1H-indole (**44**).* Prepared from **29** and **22** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 2/1) afforded **44** (141 mg, 75%) as a pale orange solid. Mp. 132.9−133.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (1H, s), 7.49−7.45 (2H, m), 7.41−7.38 (3H, m), 7.29 (1H, s), 7.25 (2H, d, J = 7.6 Hz), 7.03 (2H, d, J = 8.8 Hz), 6.89 (1H, dd, J = 2.0, 8.4 Hz), 6.44 (1H, s), 3.91 (3H, s), 2.26 (3H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.9, 144.5, 140.9, 139.4, 134.5, 132.6, 130.1, 129.1, 128.3, 127.4, 126.7, 124.3, 121.0, 113.5, 113.3, 101.1, 55.8, 21.4. IR (ATR) cm^{-1}: 1611, 1489, 1364, 1265, 1163, 1111, 1092, 1051, 1028, 993. HRMS (DART-TOF) m/z: calcd for $C_{22}H_{20}NO_3S$ ([M + H]$^+$), 378.1158; found, 378.1152.

*2-Decyl-1-tosyl-1H-pyrrolo[3,2-b]pyridine (**45**).* Prepared from **30** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/EtOAc = 2/1) afforded **45** (139 mg, 67%) as a pale yellow solid. Mp. 62.1−63.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (1H, d, J = 4.8 Hz), 8.42 (1H, d, J = 7.6 Hz), 7.61 (2H, d, J = 8.4 Hz), 7.20 (2H, d, J = 8.4 Hz), 7.16 (1H, dd, J = 8.4, 4.8 Hz), 6.59 (1H, s), 3.00 (2H, t, J = 7.6 Hz), 2.33 (3H, s), 1.75 (2H, quin, J = 7.2 Hz), 1.45−1.17 (14H, m), 0.88 (3H, t, J = 7.6 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.0, 146.4, 145.9, 145.1, 135.8, 130.6, 129.9, 126.2, 121.7, 118.2, 109.4, 31.8, 29.5, 29.4, 29.3, 29.2, 28.7, 28.5, 22.5, 21.4, 14.0. IR (ATR) cm^{-1}: 3075, 2918, 2851, 1582, 1468, 1410, 1366, 1175, 1146,

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J. Org. Chem. 2016, 81, 5450−5463

1090, 1045, 1034. HRMS (DART-TOF) m/z: calcd for $C_{24}H_{33}N_2O_2S$ ($[M + H]^+$), 413.2257; found, 413.2262.

*2-Decyl-1-tosyl-1H-pyrrolo[2,3-b]pyridine (**46**).* Prepared from **31** and **22** following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 1/4) afforded **46** (132 mg, 64%) as a pale yellow solid. Mp. 84.1−85.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (1H, dd, J = 1.0, 4.9 Hz), 8.00 (2H, d, J = 8.3 Hz), 7.67 (1H, dd, J = 1.0, 7.8 Hz), 7.22 (2H, d, J = 8.3 Hz), 7.09 (1H, dd, J = 4.9, 7.8 Hz), 6.30 (1H, s), 3.12 (2H, t, J = 7.6 Hz), 2.33 (s, 3 H), 1.79 (quin, J = 7.6 Hz, 2H), 1.50−1.20 (14H, m), 0.88 (3H, t, J = 8.0 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.2, 144.6, 143.5, 143.4, 136.5, 129.4, 127.7, 127.6, 121.8, 118.8, 104.5, 31.8, 29.53, 29.51, 29.40, 29.36, 29.33, 29.25, 28.7, 22.6, 21.5, 14.0. IR (ATR) cm^{-1}: 2922, 2851, 1597, 1560, 1468, 1398, 1369, 1258, 1192, 1175, 1090, 1036. HRMS (DART-TOF) m/z: calcd for $C_{24}H_{33}N_2O_2S$ ($[M + H]^+$), 413.2257; found, 413.2243.

*4-Chloro-2-decyl-1-tosyl-1H-indole (**47**).*[50] Prepared from **32** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 3/1) afforded **47** as a pale yellow oil (186 mg, 83%).

*4-Chloro-2-phenyl-1-tosyl-1H-indole (**48**).*[50] Prepared from **32** and **22** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 3/1) afforded **48** as a pale yellow solid (169 mg, 88%).

*5-Chloro-2-decyl-1-tosyl-1H-indole (**49**).*[50] Prepared from **33** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 3/1) afforded **49** as a pale yellow oil (186 mg, 83%).

*5-Chloro-2-phenyl-1-tosyl-1H-indole (**50**).*[93,94] Prepared from **33** and **22** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 3/1) afforded **50** as a pale yellow solid (127 mg, 67%).

*6-Chloro-2-decyl-1-tosyl-1H-indole (**51**).*[50] Prepared from **34** and **2** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 3/1) afforded **51** as a pale yellow solid (83 mg, 37%).

*6-Chloro-2-phenyl-1-tosyl-1H-indole (**52**).*[95] Prepared from **34** and **22** following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 3/1) afforded **52** as a pale yellow solid (109 mg, 57%).

Typical Experimental Procedure for the Synthesis of Disubstituted Indoles (Table 6, Entry 1). *4-(4-Methoxyphenyl)-2-phenyl-1-tosyl-1H-indole (**53**).*[50] Toluene (2 mL) was added to $PdCl_2(CH_3CN)_2$ (2.6 mg, 0.01 mmol), Cy-DHTP·HBF_4 (10.6 mg, 0.02 mmol), *t*-BuOLi (144 mg, 1.20 mmol), and **32** (158.1 mg, 0.50 mmol) in a two-neck flask under argon. The reaction mixture was stirred at rt for 40 min, **22** (110 μL, 1.0 mmol) was added, and the resulting mixture was stirred at reflux for 3 h. After cooling to rt, degassed water (2 mL) was added, and the reaction mixture was stirred at reflux for 3 h. After cooling to rt, 4-methoxyphenylboronic acid (152 mg, 1.0 mmol), K_3PO_4 (318 mg, 1.5 mmol), and tetrabutylammonium chloride (69 mg, 0.25 mmol) were added, and the reaction mixture was stirred at reflux for 12 h. The resulting suspension was then quenched with 1 M aq. HCl (6 mL) at rt and filtered through a pad of Celite, which was subsequently washed with ethyl acetate (50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated, and the residue was purified by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) to give **53** (157 mg, 69%) as a pale yellow solid.

*4-(4-Methylphenyl)-2-phenyl-1-tosyl-1H-indole (**54**).*[50] Prepared from **32**, **22**, and 4-methylphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **54** as a pale yellow solid (68 mg, 38%).

*4-(4-Fluorophenyl)-2-phenyl-1-tosyl-1H-indole (**55**).*[50] Prepared from **32**, **22**, and 4-fluorophenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **55** as a pale yellow solid (62 mg, 28%).

*2-Phenyl-4-(4-trifluoromethylphenyl)-1-tosyl-1H-indole (**56**).*[50] Prepared from **32**, **22**, and 4-trifluoromethylphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **56** as a pale yellow solid (103 mg, 42%).

*2-Phenyl-4-(3-thienyl)-1-tosyl-1H-indole (**57**).*[50] Prepared from **32**, **22**, and 3-thienylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **57** as a pale yellow solid (67 mg, 31%).

*4-(4-Methoxyphenyl)-2-(3-methylphenyl)-1-tosyl-1H-indole (**58**).*[50] Prepared from **32**, 1-ethynyl-3-methylbenzene, and 4-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **58** as a pale yellow solid (109 mg, 47%).

*2,4-Di-(4-methoxyphenyl)-1-tosyl-1H-indole (**59**).*[50] Prepared from **32**, 4-ethynylanisole, and 4-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **59** as a pale brown solid (118 mg, 49%).

*2-Decyl-4-(4-methoxyphenyl)-1-tosyl-1H-indole (**60**).*[50] Prepared from **32**, **2**, and 4-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **60** as a yellow oil (226 mg, 87%).

*2-Decyl-4-(4-methylphenyl)-1-tosyl-1H-indole (**61**).*[50] Prepared from **32**, **2**, and 4-methylphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **61** as a yellow oil (138 mg, 55%).

*2-Decyl-4-(4-fluorophenyl)-1-tosyl-1H-indole (**62**).*[50] Prepared from **32**, **2**, and 4-fluorophenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **62** as a yellow oil (122 mg, 48%).

*2-Decyl-4-(4-trifluoromethylphenyl)-1-tosyl-1H-indole (**63**).*[50] Prepared from **32**, **2**, and 4-trifluoromethylphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **63** as a yellow oil (201 mg, 72%).

*2-Decyl-4-(2-methoxyphenyl)-1-tosyl-1H-indole (**64**).*[50] Prepared from **32**, **2**, and 2-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **64** as a pale yellow oil (150 mg, 58%).

*2-Decyl-4-(3-methoxyphenyl)-1-tosyl-1H-indole (**65**).*[50] Prepared from **32**, **2**, and 3-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **65** as a pale yellow oil (150 mg, 58%).

*2-Decyl-4-(3-thienyl)-1-tosyl-1H-indole (**66**).*[50] Prepared from **32**, **2**, and 3-thienylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **66** as a yellow oil (158 mg, 64%).

*2-Decyl 4-(1-trans-1-Octen-1-yl)-1-tosyl-1H-indole (**67**).*[50] Prepared from **32**, **2**, and 1-*trans*-1-octen-1-ylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **67** as a pale yellow oil (93 mg, 36%).

*4-(4-Methoxyphenyl)-2-phenethyl-1-tosyl-1H-indole (**68**).*[50] Prepared from **32**, 4-phenyl-1-butyne, and 4-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **68** as a yellow solid (135 mg, 56%).

*2-Decyl-5-(4-methoxyphenyl)-1-tosyl-1H-indole (**69**).* Prepared from **33**, **2**, and 4-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **69** (161 mg, 62%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (1H, d, J = 8.8 Hz), 7.64 (2H, d, J = 8.4 Hz), 7.57−7.47 (m, 3 H), 7.44 (1H, dd, J = 2.0, 8.8 Hz), 7.18 (2H, d, J = 8.3 Hz), 6.96 (2H, d, J = 9.2 Hz), 6.40 (s, 1 H), 3.83 (3H, s), 2.97 (2H, t, J = 8.0 Hz), 2.32 (s, 3 H), 1.74 (2H, quin, J = 7.6 Hz), 1.45−1.15 (14 H, m), 0.88 (3H, t, J = 7.6 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.9, 144.6, 143.1, 136.4, 136.3, 133.9, 130.4,

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129.8, 128.2, 126.3, 122.9, 117.9, 115.0, 114.2, 108.7, 55.3, 31.9, 29.60, 29.57, 29.44, 29.36, 29.31, 29.0, 28.9, 22.7, 21.5, 14.1 (one carbon signal is overlapped). IR (ATR) cm^{-1}: 2920, 2851, 1597, 1464, 1445, 1369, 1227, 1165, 1148, 1090, 1038, 812. HRMS (DART-TOF) *m/z*: calcd for $C_{32}H_{40}NO_3S$ ($[M + H]^+$), 518.2723; found, 518.2720.

*2-Decyl-5-(4-methylphenyl)-1-tosyl-1H-indole (**70**).* Prepared from **33**, **2**, and 4-methylphenylboronic acid following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 1/1) afforded **70** (137 mg, 54%) as a pale yellow solid. Mp. 85.3−85.7 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.20 (1H, d, J = 8.8 Hz), 7.63 (2H, d, J = 8.3 Hz), 7.56 (1H, s), 7.51−7.42 (3H, m), 7.21 (2H, d, J = 8.3 Hz), 7.13 (2H, d, J = 8.3 Hz), 6.38 (1H, s), 2.97 (2H, t, J = 7.6 Hz), 2.36 (3H, s), 2.27 (3H, s), 1.73 (2H, quin, J = 7.4 Hz), 1.47−1.10 (14H, m), 0.88 (3H, t, J = 6.8 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 144.5, 143.1, 138.4, 136.7, 136.5, 136.4, 136.3, 130.3, 129.7, 129.4, 127.0, 126.2, 123.0, 118.1, 114.9, 108.7, 31.9, 29.58, 29.56, 29.4, 29.34, 29.30, 29.0, 28.8, 22.6, 21.4, 21.0, 14.1. IR (ATR) cm^{-1}: 2930, 2855, 1614, 1464, 1325, 1273, 1192, 1161, 1109, 1090. HRMS (DART-TOF) *m/z*: calcd for $C_{32}H_{40}NO_2S$ ($[M + H]^+$), 502.2774; found, 502.2756.

*2-Decyl-5-(4-trifluoromethylphenyl)-1-tosyl-1H-indole (**71**).* Prepared from **33**, **2**, and 4-trifluoromethylphenylboronic acid following the typical procedure. Purification by PTLC (SiO_2, hexanes/dichloromethane = 1/1) afforded **71** (174 mg, 63%) as a pale yellow solid. Mp. 103.4−104.3 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.26 (1H, d, J = 8.8 Hz), 7.72−7.62 (6H, m), 7.60 (1H, d, J = 1.5 Hz), 7.46 (1H, dd, J = 2.0, 8.8 Hz), 7.16 (2H, d, J = 7.8 Hz), 6.42 (1H, s), 2.99 (2H, t, J = 7.6 Hz), 2.30 (3H, s), 1.74 (2H, quin, J = 7.6 Hz), 1.49−1.10 (14H, m), 0.88 (3H, t, J = 8.0 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 144.9, 144.8, 143.7, 137.1, 136.3, 135.2, 130.5, 129.9, 129.0 (q, J = 32.0 Hz), 127.5, 126.3, 125.7 (q, J = 3.0 Hz), 124.4 (q, J = 271.0 Hz), 123.1, 118.7, 115.2, 108.6, 31.8, 29.54, 29.51, 29.4, 29.30, 29.26, 28.9, 28.7, 22.6, 21.4, 13.4. ^{19}F NMR (471 MHz, $CDCl_3$): δ −62.2 (s). IR (ATR) cm^{-1}: 2922, 2853, 1589, 1460, 1364, 1234, 1192, 1161, 1140, 1092, 1057, 802. HRMS (DART-TOF) *m/z*: calcd for $C_{32}H_{37}NO_2F_3S$ ($[M + H]^+$), 556.2492; found, 556.2488.

*6-(4-Methoxyphenyl)-2-phenyl-1-tosyl-1H-indole (**72**).* Prepared from **34**, **22**, and 4-methoxyphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **72** (110 mg, 44%) as a pale yellow solid. Mp. 160.0−161.1 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (1H, s), 7.70−7.59 (2H, m), 7.55−7.48 (2H, m), 7.48−7.45 (2H, m), 7.45−7.40 (3H, m), 7.29 (2H, d, J = 8.8 Hz), 7.03 (4H, d, J = 8.3 Hz), 6.54 (1H, s), 3.88 (3H, s), 2.27 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.2, 144.5, 142.4, 139.1, 137.8, 134.7, 134.0, 132.5, 130.3, 129.3, 129.2, 128.6, 128.4, 127.5, 126.8, 123.5, 120.7, 114.6, 114.3, 113.5, 55.4, 21.5. IR (ATR) cm^{-1}: 2934, 2839, 1605, 1522, 1477, 1366, 1273, 1159, 1049, 1018, 827. HRMS (DART-TOF) *m/z*: calcd for $C_{28}H_{24}NO_3S$ ($[M + H]^+$), 454.1471; found, 454.1492.

*6-(4-Methylphenyl)-2-phenyl-1-tosyl-1H-indole (**73**).* Prepared from **34**, **22**, and 4-methylphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) and PTLC (SiO_2, hexanes/dichloromethane = 1/1) afforded **73** (116 mg, 53%) as a white solid. Mp. 161.7−163.3 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.56 (1H, s), 7.60 (2H, td, J = 8.2, 1.8 Hz), 7.55−7.47 (3H, m), 7.44−7.40 (4H, m), 7.29 (4H, dd, J = 8.3, 2.0 Hz), 7.01 (2H, d, J = 8.8 Hz), 6.53 (1H, s), 2.41 (3H, s), 2.25 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 144.5, 142.5, 139.0, 138.5, 138.1, 137.0, 134.7, 132.4, 130.2, 129.5, 129.2, 128.6, 127.5, 127.2, 126.8, 123.7, 120.7, 114.9, 113.4, 21.4, 21.1. IR (ATR) cm^{-1}: 3026, 2924, 1597, 1472, 1362, 1161, 1092, 1047, 991, 808. HRMS (DART-TOF) *m/z*: calcd for $C_{28}H_{24}NO_2S$ ($[M + H]^+$), 438.1522; found, 438.1544.

*2-Phenyl-6-(4-trifluoromethylphenyl)-1-tosyl-1H-indole (**74**).* Prepared from **34**, **22**, and 4-trifluoromethylphenylboronic acid following the typical procedure. Purification by column chromatography (SiO_2, hexanes/dichloromethane = 2/1) afforded **74** (88 mg, 36%) as a white solid. Mp. 194.7−195.3 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (1H, s), 7.82−7.75 (2H, m), 7.72 (2H, d, J = 6.8 Hz), 7.54−7.46 (4H, m), 7.45−7.36 (3H, m), 7.27 (2H, dd, J = 2.0, 8.8 Hz), 7.03 (2H, d, J = 6.8 Hz), 6.55 (1H, d, J = 2.0 Hz), 2.26 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 144.9, 144.7, 143.2, 138.9, 136.4, 134.7, 132.1, 130.4, 130.3, 129.3, 129.2 (q, J = 32.2 Hz), 128.8, 127.6, 127.5, 126.8, 125.7 (q, J = 3.3 Hz), 124.3 (q, J = 269.2 Hz), 123.7, 121.1, 115.3, 113.1, 21.4. ^{19}F NMR (471 MHz, $CDCl_3$): δ −62.2 (s). IR (ATR) cm^{-1}: 3015, 2924, 1614, 1373, 1319, 1190, 1163, 1107, 1067, 1053. HRMS (DART-TOF) *m/z*: calcd for $C_{28}H_{21}NO_2F_3S$ ($[M + H]^+$), 492.1240; found, 492.1224.

Detection of Heteroaggregate Formation of Lithium Salts of Cy-DHTP and 21a by ESI-TOF-MS. **21a** (0.03 mmol, 8.5 mg), Cy-DHTP (5.5 mg, 40 mol %), and *t*-BuOLi (3.4 mg, 1.4 equiv) were dissolved in toluene (1 mL), and the resulting solution was stirred at rt for 30 min. Following stirring, an aliquot (10 μL) was taken, diluted using acetonitrile (1 mL), and filtered, and the resulting solution was subjected to ESI-TOF-MS.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00824.

Additional ESI mass spectra and ^1H and ^{13}C spectra (PDF)

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Notes

The authors declare no competing financial interest.

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