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Synthesis of 3- and 6-Sulfonylindoles from *ortho*-Alkynyl-*N*-sulfonylanilines by the Use of Lewis Acidic Transition-Metal Catalysts

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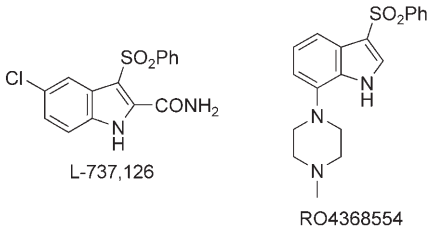
Dedicated to Professor Teruaki Mukaiyama on the occasion of his 80th birthday

Abstract: Gold-catalyzed reactions of *ortho*-alkynyl-*N*-sulfonylanilines produced the corresponding 3-sulfonylindoles in good to high yields. For example, the reaction of *N*-mesyl-*N*-methyl-2-(1-pentynyl)aniline, *N*-mesyl-*N*-methyl-2-(phenylethynyl)-aniline, and 2-ethynyl-*N*-mesyl-*N*-methylaniline in the presence of 10 mol% of $AuBr_3$ in toluene at 80°C gave 3-mesyl-1-methyl-2-propylindole, 3-mesyl-1-methyl-2-phenylindole, and 3-mesyl-1-methylindole in 95, 92, and 71% yield, respectively. Furthermore, we found that the reactions of 2-alkynyl-6-methoxy-*N*-sulfonyl-anilines in the presence of indium catalyst ($InBr_3$) afforded the corresponding 6-sulfonylindoles as the major product in good yields. For example, the reaction of 6-methoxy-*N*-methyl-2-(1-pentynyl)-*N*-tosylaniline in the presence of 5 mol% of $InBr_3$ in toluene at 80°C gave an 87:13 mixture of 7-methoxy-1-methyl-2-propyl-6-tosylindole and 7-methoxy-1-methyl-2-propyl-3-tosylindole in 95% yield. Most probably, the gold-catalyzed reactions of *ortho*-alkynyl-*N*-sulfonylanilines proceed through a [1,3] sulfonyl migration, whereas the indium-catalyzed cyclizations of 2-alkynyl-6-methoxy-*N*-sulfonylanilines, which produce 6-sulfonylindoles, proceed by an unprecedented [1,7] sulfonyl migration.

Keywords: addition reactions · gold · indium · indoles · sulfonyl migration

Introduction

3-Sulfonylindoles are found in a wide variety of biologically active compounds. For example, it has been shown that indolyl aryl sulfones (IASs) such as L-737,126 potentially inhibit the growth of wild-type and drug-resistant HIV-1.[1] Moreover, it has been reported that the 3-benzenesulfonylindole RO4368554 acts as an antagonist at serotonin type 6 (5-HT_6) receptors.[2] Therefore, an efficient synthesis of these compounds is of current interest for organic chemists. However, it is difficult to synthesize 3-sulfonylindoles directly from the corresponding nonsubstituted indoles by electrophilic-substitution reactions, because the electrophilicity of sulfonyl groups is much lower than that of acyl groups and halogens; in general, 3-sulfonylindoles have been synthesized from nonsubstituted indoles by the electrophilic reaction of *N*-alkylthiosuccinimides with indoles, followed by oxidation [Eq. (1)].[1b] Recently, Yadav et al. reported the indium-catalyzed reaction of indoles with sulfonyl chlorides to produce 3-sulfonylindoles.[3] We repeated their reaction, but so far have not been able to obtain 3-sulfonylindoles in good yields.[4] Thus, development of an efficient and robust methodology to synthesize 3-sulfonylindoles, which could lead to the discovery of new biologically active compounds,[5] is still a challenging subject in organic synthesis.



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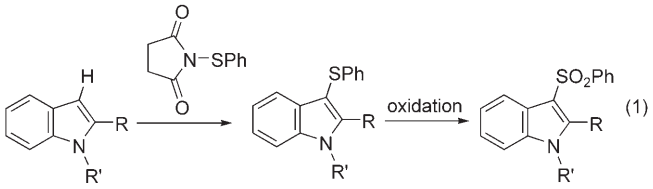
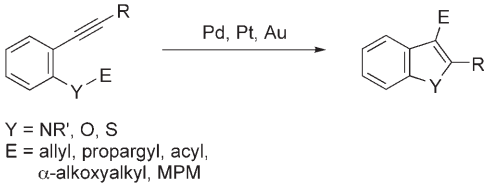


(1)

Several groups, including ours, have recently reported that the reaction of *ortho*-alkynylanilines,[6] *ortho*-alkynylphenyl ethers,[7] and *ortho*-alkynylphenyl sulfides[8] with a migrating functional group (E) on the heteroatom (Y), in the presence of transition-metal catalysts, gave the corresponding 2,3-disubstituted indoles, benzofurans, and benzothiophenes, respectively, in an efficient and atom-economical manner [Eq. (2)]. Strongly electrophilic substituents, such as an acyl group, and even relatively less electrophilic groups, such as allyl, α-alkoxyalkyl, and methoxyphenylmethyl (MPM) groups, have been employed as the migrating group. Recently, we reported that the reaction of *ortho*-alkynyl-*N*-sulfonylanilines **1** in the presence of a catalytic amount of $AuBr_3$ gave the corresponding 3-sulfonylindoles **2** in good to excellent yields [Eq. (3)].[9] Furthermore, we reported that the $InBr_3$-catalyzed cyclization of 2-alkynyl-5-methoxy-*N*-sulfonylanilines **1t–ad** proceeded by an unprecedented 1,7-migration of the sulfonyl group to produce 6-sulfonylindoles **3** as the major product in good to high yields [Eq. (4)]. In this article, we report a detailed study of these aminosulfonylation reactions.



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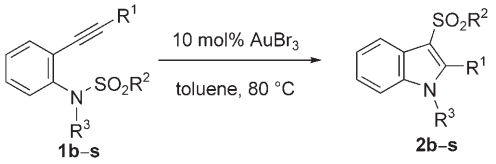

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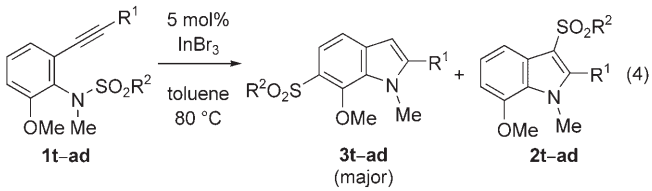
Abstract in Japanese:

金触媒によるオルトアルキニル-*N*-スルホアニリドの環化反応により 3-スルホニルインドールが高収率で得られることを見いだした。すなわち 10 モル%の三価臭化金の存在下、基質及びを 80°C で加熱攪拌した結果、対応する 3-メシルインドール高収率で生成した。更に、基質のアニリン部位の 6 位にメトキシ基が置換された基質においてはインジウム触媒を用いることにより 6-スルホニルインドールが主生成物として得られることを明らかにした。金触媒による反応においては [1,3] スルホニル転位を経て進行するのに対し、インジウム触媒反応は前例のない [1,7] スルホニル転位とそれに引き続く [1,5] プロトン移動を経て進行するものと考えられる。



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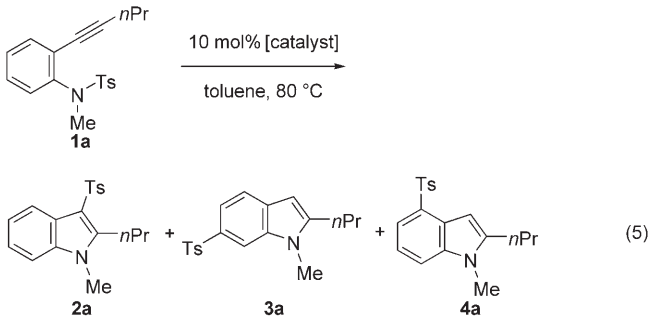
Results and Discussion

Screening of Metal Catalysts for Cyclization of *N*-Methyl-2-(1-pentynyl)-*N*-tosylaniline

First, the catalytic activity of transition-metal compounds was tested with *N*-methyl-2-(1-pentynyl)-*N*-tosylaniline (**1a**) as substrate (Equation (5); Ts = tosyl). The reaction of **1a** in



(5)

the presence of 10 mol% of $PtCl_2$ in toluene at 80°C for 1 h gave a 46:48:6 mixture of **2a**, *N*-methyl-2-propyl-6-tosylindole (**3a**), and *N*-methyl-2-propyl-4-tosylindole (**4a**) in 85% combined yield (Table 1, entry 1). 6-Sulfonylindole **3a** and 4-sulfonylindole **4a** were derived from an unprecedented sulfonyl migration to the benzene ring of the indole skele-

Table 1. Catalytic activity of metal complexes in the intramolecular aminosulfonylation of *N*-methyl-2-(1-pentynyl)-*N*-tosylaniline (**1a**).[a]

Entry	Catalyst	Combined yield [%][b]	**2a**/**3a**/**4a**[c]
1	$PtCl_2$	85	46:48:6
2	$PtCl_4$	94	54:45:>1
3	$PdCl_2$	>99	54:43:3
4	PdI_2	92	49:46:5
5	$Ba(OTf)_2$	52	38:48:14
6	$Sc(OTf)_3$	70	41:43:16
7	$Yb(OTf)_3$	75	29:47:24
8	$HfCl_4$	95	56:39:5
9	$Cu(OTf)_2$	64	41:43:16
10	AgOTf	79	39:53:8
11	$AuBr_3$	>99	68:19:13
12	$InBr_3$	>99	39:19:42
13	$InCl_3$	91	43:15:42
14	$In(OTf)_3$	75	39:39:22
15	$Sn(OTf)_2$	83	40:41:19
16	$Bi(OTf)_3$	88	38:48:14

[a] The reaction of **1a** (0.25 mmol) was carried out in the presence of 10 mol% of metal catalyst in toluene at 80°C for 1 h. [b] Determined by NMR spectroscopy with CH_2Cl_2 as an internal standard. [c] Determined by ^1H NMR spectroscopy. Tf = trifluoromethanesulfonyl.

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ton. In the previous metal-catalyzed migration of *ortho*-alkynylacetanilides,[6e] *ortho*-alkynylphenyl acetals,[7f] and *ortho*-alkynylphenyl α-alkoxyalkyl sulfides,[8a] we did not observe substitution of the benzene ring by the migrating groups. In contrast to aminoacylation,[6e] in which only platinum complexes showed good catalytic activity, the present reaction was promoted by a wide variety of metal catalysts such as platinum, palladium, barium, scandium, ytterbium, hafnium, copper, silver, gold, indium, tin, and bismuth salts (Table 1). Protic acids, such as triflic acid and acetic acid, did not promote the reaction at all. The structures of **2a**, **3a**, and **4a** were identified by spectroscopic methods. Furthermore, the structures of **2a** and **3a** were unambiguously determined by X-ray crystallography (Figure 1); the possibility that the products could be the sulfinyl esters was ruled out.[10,11]

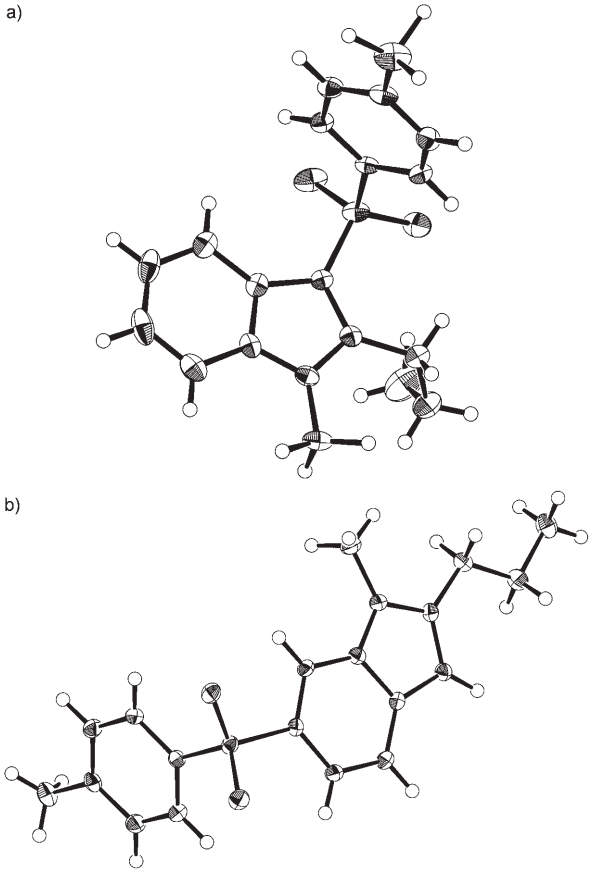


Figure 1. ORTEP drawings of a) **2a** and b) **3a**. Ellipsoids are drawn at the 50% probability level.

Synthesis of 3-Sulfonylindoles by $AuBr_3$-Catalyzed Cyclization

The test experiments with **1a** revealed that 1) the aromatic substitution reaction with the tosyl group took place together with C–N bond formation, thus leading to the formation of the unexpected by-products **3a** and **4a**; 2) the use of $AuBr_3$ gave **2a** as the major product, whereas the use of $InBr_3$ gave **2a** and **4a** as the major products (Table 1, entries 11–13). Next, we changed the tosyl group to the methanesulfonyl (mesyl) group. The results of the reaction of *ortho*-alkynylsulfoanilides **1b–1l** with $AuBr_3$ as catalyst [Eq. (3)] are summarized in Table 2. The reaction of *N*-mesyl-*N*-methyl-2-(1-pentynyl)aniline (**1b**) in the presence of 10 mol% of $AuBr_3$ in toluene at 80°C for 1 h gave 3-mesyl-1-methyl-2-propylindole (**2b**) in 95% yield (Table 2, entry 1). No other regioisomer derived from aromatic substitution was obtained. The reaction of **1b** with $AuCl_3$ or $PtCl_2$ instead of $AuBr_3$ gave **2b** in 85 or 93% yield, respectively. Substrate **1c**, which has a cyclohexyl group at R^1, was converted into **2c** in 62% yield (Table 2, entry 2). The reaction of **1d**, which bears a bulky *tert*-butyl group at R^1, afforded **2d** in 38% yield, along with 29% of the recovered **1d** and 10% of the aromatic-substitution products (Table 2, entry 3). The reaction of *N*-mesyl-*N*-methyl-2-(phenylethynyl)aniline (**1e**) proceeded smoothly to give **2e** in 92% yield, together with trace amounts of a mixture of **3e** and **4e** (Table 2, entry 4). The reactions of 2-(arylethynyl)-*N*-tosylanilines **1f** and **1g**, in which R^1 is an electron-donating aromatic ring, gave **2f** and **2g** in good yields, whereas the reaction with **1h**, which is substituted with an electron-withdrawing aromatic ring, produced **2h** in low yield, along with significant amounts of the other regioisomers (Table 2, entries 5–7). The ratio of **3h** to **4h** was approximately 1:1. Terminal alkyne **1i** was converted into 3-mesyl-substituted indole **2i** in 71% yield, whereas the reaction of ynoate **1j** led to a mixture of unidentified products of the starting material (Table 2, entries 9 and 10). The reaction of *N*-benzyl- (**1k**) and *N*-isopropylsulfoanilide (**1l**) afforded the corresponding indoles **2k** and **2l** in moderate yields (Table 2, entries 10 and 11). Besides the methanesulfonyl group, we tested other arenesulfonyl (**1m–q**), 2,2,2-trifluoroethanesulfonyl (**1r**), and trifluoromethanesulfonyl (**1s**) groups (Table 2, entries 12–18). The reactions of arenesulfonanilides **1m–q** proceeded smoothly to give **2m–q** in good to high yields, along with considerable amounts of the regioisomers (Table 2, entries 12–16). The reaction of 2,2,2-trifluoroethanesulfonanilide **1r** gave the product **2r** in 63% yield, along with 28% of the other regioisomers, whereas no reaction occurred at all with trifluoromethanesulfoanilide **1s** (Table 2, entries 17 and 18).

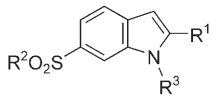
Synthesis of 6-Sulfonylindoles by $InBr_3$-Catalyzed Cyclization

With the selective synthesis of 3-sulfonylindoles achieved, our interest then focused on the selective synthesis of 4- or 6-sulfonylindoles through aromatic-ring-substitution reactions. Many attempts to synthesize the 4- or 6-sulfonylindole as the major product by varying the reaction conditions, such as solvent, ligand, additive, and temperature, only led to a mixture of **2**, **3**, and/or **4**. Thus, we modified the substrate by adding functional groups. Among the various substrates prepared, 2-alkynyl-6-methoxysulfonanilides **1t–ad**, which have a methoxy group at the 6-position of the aniline

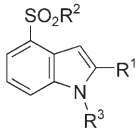
Table 2. $AuBr_3$-catalyzed cyclization of *ortho*-alkynyl-*N*-sulfonylanilines **1b–s**.[a]

Entry	1	R^1	R^2	R^3	2a	2 [%][b]	3 and 4 [%][c]
1	**1b**	*n*Pr	Me	Me	**2b**	95	>1
2	**1c**	Cy	Me	Me	**2c**	62	25
3	**1d**	*t*Bu	Me	Me	**2d**	38[d]	10
4	**1e**	Ph	Me	Me	**2e**	92	2
5	**1f**	*p*-MeC_6H_4	Me	Me	**2f**	87	>1
6	**1g**	*p*-$MeOC_6H_4$	Me	Me	**2g**	81	5
7	**1h**	*p*-$F_3CC_6H_4$	Me	Me	**2h**	51	20
8	**1i**	H	Me	Me	**2i**	71	>1
9	**1j**	CO_2Et	Me	Me	–	decomp.[e]	–
10	**1k**	*n*Pr	Me	Bn	**2k**	44	>1
11	**1l**	*n*Pr	Me	*i*Pr	**2l**	60	>1
12	**1m**	*n*Pr	Ph	Me	**2m**	52	22
13	**1n**	*n*Pr	*p*-$MeOC_6H_4$	Me	**2n**	85	7
14	**1o**	*n*Pr	*m*-$MeOC_6H_4$	Me	**2o**	90	4
15	**1p**	*n*Pr	*p*-$O_2NC_6H_4$	Me	**2p**	79	11
16	**1q**	*n*Pr	*p*-AcC_6H_4	Me	**2q**	80	5
17	**1r**	*n*Pr	CH_2CF_3	Me	**2r**	63	28
18	**1s**	*n*Pr	CF_3	Me	–	no reaction[f]	–

[a] The reaction of **1b–s** (0.25 mmol) was carried out in the presence of 10 mol% of $AuBr_3$ in toluene at 80°C for 1 h. [b] Yield of isolated product. [c] Yield of an inseparable mixture of **3** and **4** determined by GC. [d] Substrate **1d** was recovered in 29% yield. [e] A mixture of unidentified products was obtained. [f] **1s** was recovered quantitatively. Cy = cyclohexyl.



3b–s



4b–s

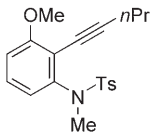
moiety, were mainly converted into the corresponding 6-sulfonylindoles **3t–ad** in the presence of catalytic amounts of $InBr_3$ [Eq. (4)]. The results are summarized in Table 3. The

Table 3. $InBr_3$-catalyzed cyclization of 2-alkynyl-6-methoxy-*N*-methyl-*N*-sulfonylanilines **1t–ad**.[a]

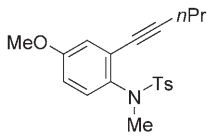
Entry	1	R^1	R^2	Catalyst	Yield [%][b]	3/2[c]
1	**1t**	*n*Pr	*p*-MeC_6H_4	$InBr_3$	95	87:13
2	**1t**	*n*Pr	*p*-MeC_6H_4	$AuBr_3$	60	72:28
3	**1t**	*n*Pr	*p*-MeC_6H_4	$PdBr_2$	97	60:40
4	**1u**	*n*Pr	*p*-$MeOC_6H_4$	$InBr_3$	99	84:16
5	**1v**	*n*Pr	Ph	$InBr_3$	98	78:22
6	**1w**	*n*Pr	*p*-$O_2NC_6H_4$	$InBr_3$	99	66:34
7	**1x**	*n*Pr	Me	$InBr_3$	decomp.[d]	–
8	**1y**	Cy	*p*-MeC_6H_4	$InBr_3$	97	87:13
9	**1z**	Ph	*p*-MeC_6H_4	$InBr_3$	99	90:10
10	**1aa**	*p*-$MeOC_6H_4$	*p*-MeC_6H_4	$InBr_3$	98	85:15
11	**1ab**	*p*-$F_3CC_6H_4$	*p*-MeC_6H_4	$InBr_3$	88	83:17
12	**1ac**	H	*p*-MeC_6H_4	$InBr_3$	73	54:46
13	**1ad**	Me_3Si	*p*-MeC_6H_4	$InBr_3$	no reaction[e]	–

[a] The reaction of **1t–ad** was carried out in the presence of 5 mol% of $InBr_3$ in toluene at 80°C. [b] Yield of an isolated mixture of **2** and **3**. [c] The ratio was determined by ^1H NMR spectroscopy. [d] A complex mixture of the regioisomers was obtained. [e] **1ad** was quantitatively recovered.

reaction of **1t** in the presence of 5 mol% of $InBr_3$ in toluene at 80°C for 2 h gave an 87:13 mixture of **3t** and **2t** in 95% combined yield (Table 3, entry 1). The reaction of **1t** with $AuBr_3$ or $PdBr_2$ instead of $InBr_3$ gave **3t** and **2t** with lower regioselectivities (Table 3, entries 2 and 3). The reaction of **1u**, which has an electron-donating methoxy group at the arenesulfonyl moiety, produced 6-sulfonylindole **3u** with higher regioselectivity than for **1w**, which has an electron-withdrawing nitro group (Table 3, entries 4 and 6). The reaction of the *N*-mesylaniline **1x** proceeded sluggishly to give a mixture of unidentified products (Table 3, entry 7). Substrate **1y**, which has a cyclohexyl group at R^1, was converted into **3y** with high regioselectivity (Table 3, entry 8). The ratio of **3** to **2** was not affected by the electronic properties of the R^1 substituent (Table 3, entries 9–11), although it was lower when terminal alkyne **1ac** was employed as substrate (Table 3, entry 12). A bulky trimethylsilyl group at the alkynyl moiety totally interfered with the cyclization (Table 3, entry 13). The reactions of **1ae**, **1af**, and **1ag**,



1ae



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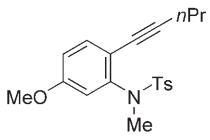

1ag

which have a methoxy group at the 3-, 4-, and 5-position, respectively, proceeded sluggishly to give an inseparable mixture of unidentified products.

Mechanism

To determine whether the migration of the sulfonyl group occurs in an intramolecular or intermolecular fashion, we performed cross-over experiments (Equations (6) and (7)). The reaction of a 1:1 mixture of **1e** and **1n** in the presence of a catalytic amount of $AuBr_3$ gave the corresponding products **2e** and **2n** in 66 and 65% yield, respectively; the cross-over products, such as **2b** and **2ah**, were not detected by GC–MS or NMR spectroscopic analysis [Eq. (6)]. Furthermore, the $InBr_3$-catalyzed reaction of a 1:1 mixture of **1u** and **1ab** afforded the products **3u** and **2u**, which were derived from **1u**, as well as **3ab** and **2ab**, which were derived from **1ab**; again, no cross-over products, such as **2t, 2ai, 3t**, and **3ai**, were obtained [Eq. (7)]. These results clearly indicate that the present reaction proceeds in an intramolecular manner.

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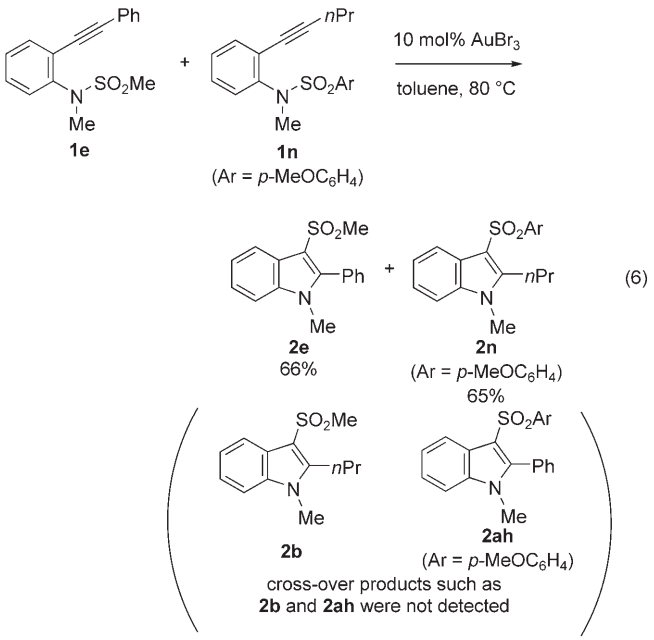
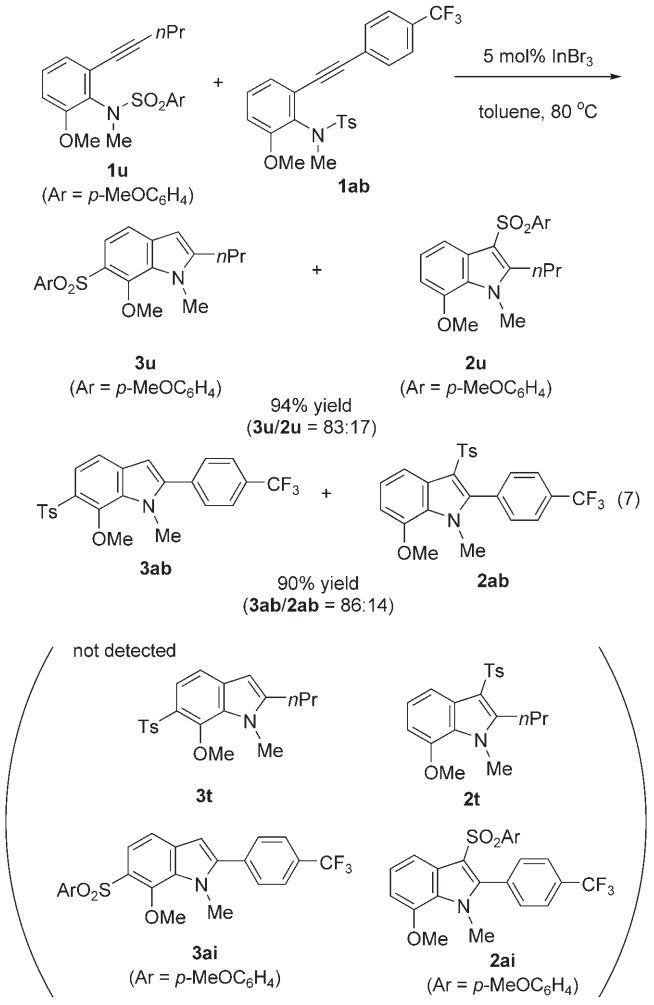
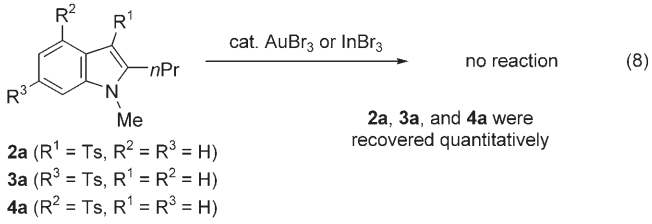
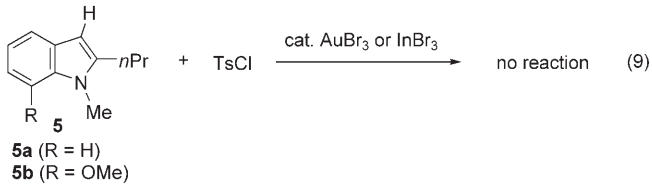




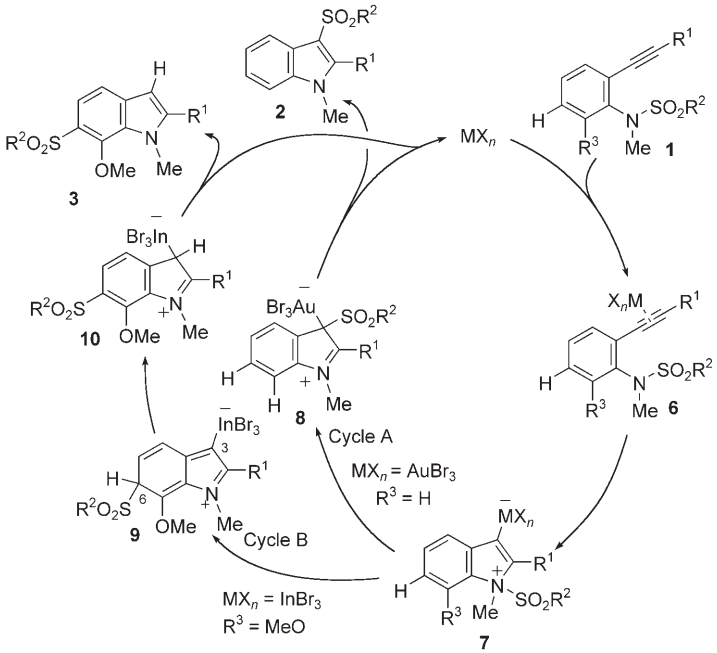
The isolated products **2a**, **3a**, and **4a** remained unchanged in the presence of $InBr_3$ or $AuBr_3$ in toluene at 80 °C for 2 h, thereby suggesting that interconversion between the products does not take place under the reaction conditions [Eq. (8)].



Mixing of indoles **5a** and **5b** with tosyl chloride in the presence of $AuBr_3$ or $InBr_3$ did not give sulfonylindoles **2**, **3**, or **4** [Eq. (9)]. Accordingly, it is unlikely that electrophilic substitution of the indole with tosyl halides occurs under the reaction conditions.



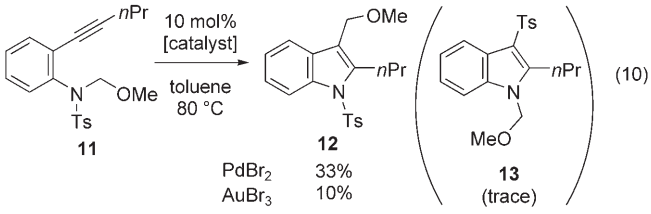
The above experimental results led us to propose the mechanism shown in Scheme 1 for the cyclization of **1**. The Lewis acid–transition-metal complex MX_n coordinates to the triple bond of substrate **1** to form the π complex **6**. Nu-



Scheme 1. Plausible mechanism for the cyclization of **1**.

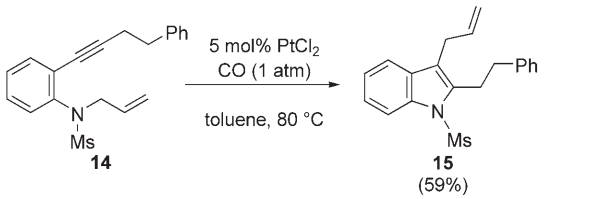
cleophilic attack of the nitrogen atom on the alkynyl moiety then leads to the cyclized intermediate **7**. For the gold-catalyzed reaction of **1a–s**, the sulfonyl group migrates to the 3-position of the indole skeleton (cycle A),[12] and elimination of $AuBr_3$ from **8** then gives 3-sulfonylindole **2**. In the indium-catalyzed reaction of substrates **1t–ad**, unprecedented consecutive [1,7] sulfonyl and [1,5] proton shifts take place (cycle B).[13] Elimination of $InBr_3$ from the resulting intermediate **10** then gives 6-sulfonylindoles **3**. An interaction between a benzene ring on the sulfonyl group and the indium catalyst might play a crucial role in the selective production of 6-sulfonylindoles **3**, as the $InBr_3$-catalyzed reaction of *N*-mesylaniline **1x** gives a complex mixture of unidentified products. Some unclarified points still remain in the proposed mechanism. For example, why does the Au-catalyzed reaction proceed by cycle A, but the In-catalyzed reaction proceeds by cycle B? Why does the 7-OMe substituent selectively deliver the sulfonyl group at the 6-position? Nevertheless, the present reaction provides a useful method for the synthesis of 2-substituted (or nonsubstituted) 3-sulfonylindoles and 7-methoxy-6-sulfonylindoles.

Recently, we reported that the reaction of *N*-methoxymethyl-2-(1-pentynyl)-*N*-tosylaniline (**11**) in the presence of catalytic amounts of $PdBr_2$ gave the product **12**, which derives from migration of the methoxymethyl group, in 33% yield; only trace amounts (>3%) of 3-tosylindole **13** were detected [Eq. (10)].[6f] The reaction of **11** with $AuBr_3$ as a catalyst instead of $PdBr_2$ gave only 3-methoxymethylindole **12** in 10% yield. These results suggest that the ability of the methoxymethyl group to migrate is higher than that of the tosyl group in the reaction of **11**, irrespective of the catalyst species. Recently, Fürstner and Davies reported that the reaction of *ortho*-alkynylaniline **14**, which bears both allyl and mesyl groups on the nitrogen atom, in the presence of catalytic amounts of $PtCl_2$ under CO atmosphere afforded 3-allylindole **15** (Equation (11); Ms = methanesulfonyl).[6b] This result also indicates that the ability of the mesyl group to migrate is much lower than that of the allyl group in the reaction of **14**.

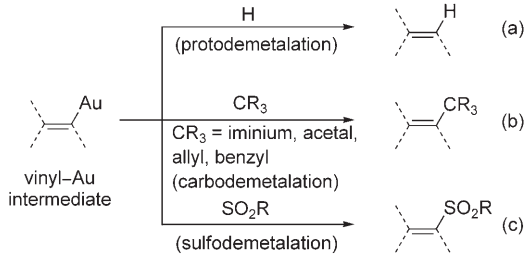


(10)

The classification of the termination step in gold-catalyzed reactions is shown in Scheme 2. The vinyl–Au intermediate is trapped by a proton, the so-called protodemetalation reaction (type a).[14] Recently, it was disclosed that such intermediates can also be captured by carbon electrophiles, such as iminium, α-alkoxyalkyl, allyl, and benzyl groups, in an intramolecular fashion (type b; carbodemetalation).[6–8a] To the best of our knowledge, the present result is the first example of sulfodemetalation, in which the vinyl–Au intermediate is captured intramolecularly by the sulfonyl group (type c; see also Scheme 1, **7**→**2**).



(11)



Scheme 2. Capture of the vinyl–Au intermediate by electrophiles. a) Protons (protodemetalation), b) carbon electrophiles (carbodemetalation), and c) sulfonyl groups (sulfodemetalation).

Conclusions

We are now in a position to synthesize 3-sulfonylindoles very smoothly by the gold-catalyzed reactions of *ortho*-alkynylsulfonanilides. This reaction proceeds through formal addition of a nitrogen–sulfur bond to a triple bond, the so-called aminosulfonylation.[16] Furthermore, we have demonstrated that selective [1,7] migration takes place in the indium-catalyzed reactions of 2-alkynyl-6-methoxysulfonanilides. To the best of our knowledge, the synthesis of 6-sulfonylindoles has been rarely investigated.[17] Therefore, it is expected that the present methodology is applicable to the synthesis of a wide variety of 3- and 6-sulfonylindoles in an atom-economical manner.

Experimental Section

General

^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM AL 400 (400 MHz), JEOL JNM α-500 (500 MHz), and BRUKER AVANCE-600 (600 MHz) spectrometers. ^{1}H NMR spectra are reported as follows: chemical shifts (δ) in ppm relative to that of $CHCl_3$ at 7.24 ppm, multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broadened), coupling constants (Hz), and integration. ^{13}C NMR chemical shifts (δ) are reported in ppm relative to the central line of the triplet for $CDCl_3$ at 77 ppm. IR spectra were recorded on a JASCO FT/IR-460 Plus spectrometer; absorptions are reported in cm^{-1}. High-resolution mass spectra were obtained on a HITACHI M-2500s spectrometer. X-ray crystallographic data were obtained by a Rigaku/MSC Saturn diffractometer with a Cu CCD device. Column chromatography was carried

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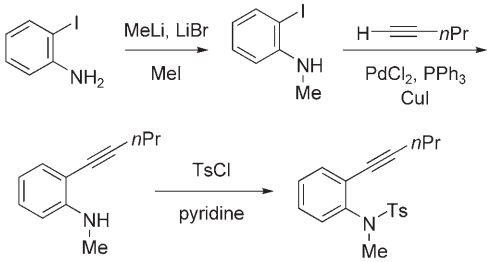
out with silica gel 60 N (spherical, neutral, 40–100 μm, KANTO Chemical Co.) or Florisil gel (75–150 μm, KANTO Chemical Co.). Analytical thin-layer chromatography (TLC) was performed on a 0.2-mm precoated plate Kieselgel 60 F_{254} (Merck). All manipulations were conducted under argon atmosphere with standard Schlenk techniques. $PdCl_2$ was purchased from Kawaken fine chemicals, and $AuBr_3$, $InBr_3$, and $PtCl_2$ were purchased from Aldrich. These metal salts were used as purchased. Toluene (WAKO) was stored with 4-Å molecular sieves (MS4Å) under Ar atmosphere. All the alkynylsulfonanilides **1** were prepared according to the following procedures. All other compounds were commercially available.

*Representative Procedure for the Preparation of 2-Alkynylsulfonanilides (**1a–s**)*



1a

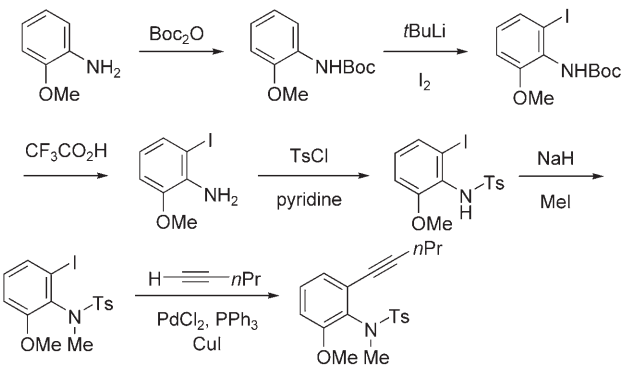
1) MeLi·LiBr complex (1.5 M in diethyl ether solution, 165 mL, 248 mmol) was added dropwise to a solution of 2-iodoaniline (50.0 g, 228 mmol) in THF (400 mL) at −78 °C over 1 h, and the mixture was stirred for another 30 min. Iodomethane (18.0 mL, 289 mmol) in THF (40.0 mL) was added dropwise to the reaction mixture, and the mixture was stirred further for 1 h. The resulting solution was then allowed to warm to room temperature and stirred for 2 h. After consumption of the starting material, as monitored by TLC, water was added to the reaction solution. The mixture was neutralized with hydrochloric acid (2 N) and extracted with diethyl ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was purified by silica-gel column chromatography with hexane/ethyl acetate (10:1) as eluent to give *N*-methyl-2-iodoaniline (45.9 g, 86 %).

2) A solution of *N*-methyl-2-iodoaniline (23.3 g, 100 mmol) in MeCN (100 mL), Et_3N (41.6 mL, 300 mmol), and 1-pentyne (14.8 mL, 150 mmol) were successively added to a solution of $PdCl_2$ (0.44 g, 2.5 mmol), CuI (0.68 g, 3.6 mmol), and PPh_3 (1.31 g, 5.0 mmol) in MeCN (100 mL) under argon atmosphere. The resulting solution was stirred overnight at room temperature. After the reaction was complete, saturated aqueous NH_4Cl/NH_3 was added, and the mixture was extracted with diethyl ether. The combined organic layers were washed with saturated aqueous NH_4Cl and brine and dried over Na_2SO_4. After the solvent was removed in vacuo, the crude product was purified by silica-gel column chromatography with hexane/ethyl acetate (15:1–4:1) as eluent to afford *N*-methyl-2-(1-pentynyl)aniline (15.3 g, 88 %).

3) Toluenesulfonyl chloride (1.05 g, 5.5 mmol) was added to a solution of *N*-methyl-2-(1-pentynyl)aniline (0.87 g, 5.0 mmol) in pyridine (8.0 mL). The reaction mixture was stirred at room temperature and monitored by TLC. After complete consumption of the starting material, saturated aqueous $CuSO_4$ was added, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was purified by silica-gel column chromatography with hexane/ethyl acetate (10:1) as eluent to give *N*-methyl-2-(1-pentynyl)-*N*-tosylaniline (**1a**; 1.55 g, 95 %).

*Representative Procedure for the Preparation of 2-Alkynyl-6-methoxysulfonanilides (**1t–ad**)*

1) Boc_2O (30.6 mL, 132 mmol; Boc = *tert*-butoxycarbonyl) was added to a solution of *o*-anisidine (14.8 g, 120 mmol) in THF (180 mL) under argon atmosphere, and the reaction was heated at reflux overnight. The solvent



1t

was removed in vacuo, then water (120 mL) was added to the residue. The mixture was extracted with diethyl ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was purified by silica-gel column chromatography with hexane/ethyl acetate (10:1) as eluent to give *N*-Boc-2-methoxyaniline quantitatively.

2) A 1000-mL round-bottomed flask and syringes were carefully flame-dried for the following procedure. *t*BuLi (1.6 M solution in pentane, 91.2 mL, 132 mmol) was added dropwise to a solution of *N*-Boc-2-methoxyaniline (13.4 g, 60 mmol) in diethyl ether (72 mL) at −20 °C under argon atmosphere, and the mixture was stirred for 3 h at the same temperature. The reaction mixture was then cooled to −90 °C, and a solution of iodine (19.0 g, 74.9 mmol) in diethyl ether (160 mL) was added dropwise. The reaction mixture was then allowed to warm to room temperature and kept stirred overnight. Saturated aqueous $Na_2S_2O_3$ was added to this reaction mixture, and the resulting mixture was then extracted with diethyl ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was purified by silica-gel column chromatography with hexane/ethyl acetate (50:1–20:1) as eluent to give *N*-Boc-2-iodo-6-methoxyaniline (9.9 g, 47 %).

3) CF_3COOH (9.4 mL, 127 mmol) was added dropwise to a solution of *N*-Boc-2-iodo-6-methoxyaniline (3.5 g, 10 mmol) in CH_2Cl_2 (50 mL) at 0 °C under argon atmosphere, and the mixture was stirred for 3 h at room temperature. After consumption of the starting material, as monitored by TLC, water was added to the reaction solution. The mixture was neutralized with aqueous NaOH (3 N) and extracted with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed in vacuo. The crude 2-iodo-6-methoxyaniline was used without further purification in the following step.

4) Toluenesulfonyl chloride (2.39 g, 1.25 mmol) was added to a solution of 2-iodo-6-methoxyaniline (crude, ≈10 mmol) in pyridine (10 mL). The reaction mixture was stirred at room temperature, and progress of the reaction was monitored by TLC. After complete consumption of the starting material, saturated aqueous $CuSO_4$ was added, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude material was purified by silica-gel column chromatography with hexane/ethyl acetate (10:1–4:1) as eluent to give 2-iodo-6-methoxy-*N*-methyl-*N*-tosylaniline (2.27 g, 56 % over two steps).

5) Iodomethane (0.42 mL, 6.25 mmol) was added dropwise to a solution of 2-iodo-6-methoxy-*N*-tosylaniline (2.07 g, 5.0 mmol) in DMF (10 mL) at 0 °C, then NaH (60 % in mineral oil, 0.25 g, 6.25 mmol) was added in several portions. The reaction mixture was stirred for 5 h at room temperature and then poured onto crushed ice. The resulting mixture was extracted with diethyl ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was purified by silica-gel column chromatography with hexane/ethyl acetate (3:1) as eluent to give 2-iodo-6-methoxy-*N*-methyl-*N*-tosylaniline (2.0 g, 96 %).

6) A solution of $[Pd(PPh_3)_4]$ (0.19 g, 0.16 mmol) and CuI (0.06 g, 0.32 mmol) in DMF (1.0 mL), 1-pentyne (0.59 mL, 6.0 mmol), and Et_2NH (4.0 mL) were successively added to a solution of 2-iodo-6-methoxy-*N*-methyl-*N*-tosylaniline (1.67 g, 4.0 mmol). The resulting solution was

stirred at room temperature. After the reaction was complete, saturated aqueous NH_4Cl/NH_3 was added, and the product was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. The concentrated crude product was purified by silica-gel column chromatography with hexane/ethyl acetate (4:1–2:1) as eluent to afford 2-methoxy-*N*-methyl-6-(1-pentynyl)-*N*-tosylaniline (**1t**; 1.87 g, 82%).

*Typical Procedure for the $AuBr_3$-Catalyzed Cyclization of **1a–s***

Toluene (0.5 mL, 0.5 M) was added to a mixture of $AuBr_3$ (10.9 mg, 0.025 mmol) and *N*-mesyl-*N*-methyl-2-(1-pentynyl)aniline (**1b**; 62.8 mg, 0.25 mmol) at room temperature, and the mixture was warmed immediately to 80 °C. After complete consumption of the starting material, as monitored by TLC, the reaction mixture was cooled to room temperature and filtered through a short SiO_2 pad, and the filtrate was concentrated. The residue was purified by silica-gel column chromatography with hexane/ethyl acetate (10:1) as eluent to afford 3-mesyl-1-methyl-2-propylindole (**2b**; 59.7 mg, 95%).

*Typical Procedure for the $InBr_3$-Catalyzed Cyclization of **1t–ad***

Toluene (1.0 mL, 0.25 M) was added to a mixture of $InBr_3$ (4.4 mg, 0.0125 mmol) and **1t** (71.4 mg, 0.25 mmol) at room temperature, and the mixture was warmed immediately to 80 °C. After complete consumption of the starting material was determined by TLC, the reaction mixture was cooled to room temperature and purified by Florisil column chromatography with hexane/ethyl acetate (10:1) as eluent to afford 7-methoxy-1-methyl-2-propyl-6-tosylindole (**3t**; 59.0 mg, 83%) and 7-methoxy-1-methyl-2-propyl-3-tosylindole (**2t**; 8.8 mg, 12%). Further purification was performed by gel permeation chromatography with an LC-918 (Japan Analytical Industry Co.) instrument.

Experimental Data

2a: 1-Methyl-2-propyl-3-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3044–2872, 1471, 1287 (S=O, sulfonyl), 1139, 1081 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.6 Hz, 3H), 1.59–1.69 (m, 2H), 2.36 (s, 3H), 3.12–3.16 (m, 2H), 3.69 (s, 3H), 7.20–7.30 (m, 5H), 7.85 (d, J = 8.4 Hz, 2H), 8.09–8.14 ppm (m, 1H); ^{13}C NMR (149.40 MHz, $CDCl_3$): δ = 14.2, 21.4, 23.1, 26.9, 29.9, 109.5, 110.9, 120.0, 122.2, 122.8, 125.0, 126.1, 129.5, 136.3, 141.8, 142.9, 146.0 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}NO_2SNa$: 350.1185 $[M+Na]^+$; found: 350.1184; elemental analysis: calcd (%) for $C_{19}H_{21}NO_2S$: C 69.69, H 6.46, N 4.28, S 9.79; found: C 69.02, H 6.47, N 4.28, S 9.78;

2b: 3-Mesyl-1-methyl-2-propyl-1*H*-indole: IR (KBr): $\tilde{\nu}$ = 3003–2962, 1514, 1468, 1340, 1314 (S=O, sulfonyl), 1294, 1160, 1132, 1016 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 0.99 (t, J = 7.1 Hz, 3H), 1.64 (tq, J = 7.8, 7.3 Hz, 2H), 3.01 (s, 3H), 3.05 (t, J = 7.3 Hz, 2H), 7.16–7.27 (m, 3H), 7.89 ppm (d, J = 7.6 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.2, 23.4, 26.5, 30.0, 45.9, 109.6, 110.0, 119.5, 122.2, 122.9, 124.8, 136.2, 146.0 ppm; HRMS (ESI): m/z calcd for $C_{13}H_{17}NO_2SNa$: 308.0716 $[M+Na]^+$; found: 308.0715.

2c: 2-Cyclohexyl-3-mesyl-1-methylindole: White solid. IR (neat): $\tilde{\nu}$ = 2917–2850, 1496, 1465, 1291, 1129, 1118, 1104, 975, 938 cm^{-1}; ^1H NMR (594.17 MHz, $CDCl_3$): δ = 1.33–1.50 (m, 4H), 1.81–2.04 (m, 7H), 3.10 (s, 3H), 3.90 (s, 3H), 7.25–7.34 (m, 3H), 8.08 ppm (d, J = 7.9 Hz, 1H); ^{13}C NMR (149.40 MHz, $CDCl_3$): δ = 26.0, 26.5, 26.7, 30.4, 32.9, 46.3, 109.4, 110.2, 120.1, 122.3, 123.0, 125.1, 136.7, 149.1 ppm; HRMS (ESI): m/z calcd for $C_{16}H_{21}NNaO_2S$: 314.1191 $[M+Na]^+$; found: 314.1184.

2d: 2-*tert*-Butyl-3-mesyl-1-methylindole: IR (KBr): $\tilde{\nu}$ = 3078–2928, 1481, 1470, 1308 (S=O, sulfonyl), 1286, 1147, 1113, 1024 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.69 (s, 9H), 3.15 (s, 3H), 3.88 (s, 3H), 7.14–7.26 (m, 3H), 8.09 ppm (d, J = 7.6 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 32.2, 35.4, 35.8, 46.0, 109.7, 113.4, 120.9, 122.2, 123.0, 126.5, 136.9, 152.3 ppm; HRMS (ESI): m/z calcd for $C_{14}H_{19}NO_2SNa$: 288.1029 $[M+Na]^+$; found: 288.1028.

2e: 3-Mesyl-1-methyl-2-phenyl-1*H*-indole: IR (KBr): $\tilde{\nu}$ = 3003–2853, 1607, 1581, 1467, 1319 (S=O, sulfonyl), 1142, 1105 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 2.91 (s, 3H), 3.56 (s, 3H), 7.32–7.44 (m, 4H), 7.46–7.53 (m, 4H), 8.17 ppm (d, J = 7.2 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 31.1, 45.7, 110.0, 112.5, 120.3, 122.5, 123.6, 124.8, 128.2, 128.8, 129.8, 130.6, 136.0, 143.9 ppm; HRMS (ESI): m/z calcd for $C_{16}H_{15}NO_2SNa$: 308.0716 $[M+Na]^+$; found: 308.0715.

2f: 3-Mesyl-1-methyl-2-(*p*-tolyl)-1*H*-indole: IR (KBr): $\tilde{\nu}$ = 3072–3020, 1487, 1466, 1319 (S=O, sulfonyl), 1290, 1130, 1107 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 2.44 (s, 3H), 2.90 (s, 3H), 3.56 (s, 3H), 7.32–7.40 (m, 7H), 8.17 ppm (d, J = 7.2 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 21.6, 31.0, 45.7, 110.0, 112.4, 120.4, 122.5, 123.5, 124.9, 125.8, 129.0, 130.5, 136.0, 139.9, 144.2 ppm; HRMS (ESI): m/z calcd for $C_{17}H_{17}NO_2SNa$: 322.0872 $[M+Na]^+$; found: 322.0871.

2g: 3-Mesyl-2-(4-methoxyphenyl)-1-methyl-1*H*-indole: IR (KBr): $\tilde{\nu}$ = 3071–2926, 1488, 1466, 1340, 1318 (S=O, sulfonyl), 1290, 1130, 1107 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 2.89 (s, 3H), 3.56 (s, 3H), 3.87 (s, 3H), 7.03 (d, J = 8.8 Hz, 2H) 7.31–7.39 (m, 5H), 8.17 ppm (d, J = 7.6 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 31.0, 45.5, 55.3, 110.0, 112.3, 113.7, 120.3, 120.6, 122.5, 123.5, 124.9, 132.0, 135.9, 144.0, 160.6 ppm; HRMS (ESI): m/z calcd for $C_{17}H_{17}NO_3SNa$: 338.0821 $[M+Na]^+$; found: 338.0821.

2h: 3-Mesyl-1-methyl-2-{4-(trifluoromethyl)phenyl}-1*H*-indole: White solid. IR (KBr): $\tilde{\nu}$ = 2928, 1468, 1325 (S=O, sulfonyl), 1302, 1072 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 2.93 (s, 3H), 3.54 (s, 3H), 7.32–7.42 (m, 3H), 7.57 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 8.12 ppm (d, J = 7.6 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 31.2, 45.9, 110.2, 113.1, 120.3, 122.4, 122.9, 124.1, 124.7, 125.1, 125.2, 131.3, 132.6, 136.3, 142.1 ppm; HRMS (ESI): m/z calcd for $C_{17}H_{14}F_3NO_2SNa$: 376.0590 $[M+Na]^+$; found: 376.0589.

2i: 3-Mesyl-1-methyl-1*H*-indole: IR (KBr): $\tilde{\nu}$ = 3121–2924, 1687, 1522, 1481, 1423, 1319 (S=O, sulfonyl), 1178, 1136, 1107 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 3.13 (s, 3H), 3.84 (s, 3H), 7.29–7.39 (m, 3H), 7.66 (s, 1H), 7.91 ppm (d, J = 7.6 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 33.6, 45.5, 110.3, 114.4, 119.4, 122.4, 123.6, 124.2, 133.34, 137.1 ppm; HRMS (ESI): m/z calcd for $C_{10}H_{11}NO_2SNa$: 232.0403 $[M+Na]^+$; found: 232.0402.

2k: 1-Benzyl-3-mesyl-2-propylindole: IR (neat): $\tilde{\nu}$ = 3030–2850, 1746, 1512, 1453, 1412, 1289, 1131, 1114 cm^{-1}; ^1H NMR (594.17 MHz, $CDCl_3$): δ = 1.01 (t, J = 7.4 Hz, 3H), 1.62 (m, 2H), 3.13 (m, 2H), 3.16 (s, 3H), 5.39 (s, 2H), 6.98 (d, J = 6.7 Hz, 2H), 7.22–7.31 (m, 6H), 8.09 ppm (d, J = 6.8 Hz, 1H); ^{13}C NMR (149.40 MHz, $CDCl_3$): δ = 14.2, 23.7, 26.6, 45.8, 46.9, 110.4, 110.7, 119.6, 122.5, 123.3, 125.1, 125.8, 127.9, 129.0, 135.9, 136.1, 146.2 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}NNaO_2S$: 350.1191 $[M+Na]^+$; found: 350.1185.

2l: 1-Isopropyl-3-mesyl-2-propylindole: IR (neat): $\tilde{\nu}$ = 2972–2871, 1514, 1456, 1405, 1296, 1136, 1112 cm^{-1}; ^1H NMR (270.05 MHz, $CDCl_3$): δ = 1.09 (t, J = 7.3 Hz, 3H), 1.69 (d, J = 7.0 Hz, 6H), 1.61–1.77 (m, 2H), 3.11 (s, 3H), 3.13–3.20 (m, 2H), 4.72 (m, 1H), 7.21–7.28 (m, 2H), 7.56–7.62 (m, 1H), 7.99–8.06 ppm (m, 1H); ^{13}C NMR δ = (67.80 MHz, $CDCl_3$): 14.2, 21.3, 23.7, 26.6, 45.8, 47.7, 109.6, 112.5, 119.0, 119.8, 121.6, 122.2, 125.9, 133.7, 145.1 ppm; HRMS (ESI): m/z calcd for $C_{15}H_{21}NNaO_2S$: 302.1191 $[M+Na]^+$; found: 302.1185.

2m: 3-Benzenesulfonyl-1-methyl-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3078–2870, 1295 (S=O, sulfonyl), 1143, 1082 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.2 Hz, 3H), 1.60–1.68 (m, 2H), 3.12–3.17 (m, 2H), 3.70 (s, 3H), 7.25–7.31 (m, 3H), 7.40–7.49 (m, 3H), 7.96–7.99 (m, 2H), 8.11–8.15 ppm (m, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 23.2, 27.0, 30.0, 109.5, 110.5, 120.0, 122.3, 122.8, 125.1, 126.0, 128.8, 132.1, 136.3, 144.6, 146.3 ppm; HRMS (ESI): m/z calcd for $C_{18}H_{19}NO_2SNa$: 336.1029 $[M+Na]^+$; found: 336.1028.

2n: 3-(4-Methoxybenzenesulfonyl)-1-methyl-2-propyl-1*H*-indole: White solid. IR (neat): $\tilde{\nu}$ = 3093–2845, 1593, 1291 (S=O, sulfonyl), 1260, 1133 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.2 Hz, 3H), 1.59–1.69 (m, 2H), 3.12–3.16 (m, 2H), 3.69 (s, 3H), 3.79, (s, 3H), 6.89 (d, J = 8.8 Hz, 2H), 7.23–7.30 (m, 3H), 7.90 (d, J = 8.8 Hz, 2H), 8.08–8.12 ppm (m, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 23.2, 26.9, 30.0, 55.5, 109.4, 111.3, 114.0, 120.0, 122.1, 122.7, 125.0, 128.2, 136.3, 136.6, 145.7, 162.5 ppm; HRMS (ESI) m/z calcd for $C_{19}H_{21}NO_3SNa$: 366.1134 $[M+Na]^+$; found: 366.1136.

2o: 3-(3-Methoxybenzenesulfonyl)-1-methyl-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3009–2849, 1592, 1470, 1281 (S=O, sulfonyl), 1131 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.2 Hz, 3H), 1.64 (tq, J = 7.2, 7.2 Hz, 2H), 3.12–3.16 (m, 2H), 3.69 (s, 3H), 3.80 (s, 3H), 6.98 (dd, J = 1.2, 8.0 Hz, 1H), 7.25–7.33 (m, 4H), 7.51–7.53 (m, 2H), 8.12–8.13 ppm (m, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 23.2, 26.9, 30.0, 55.6, 109.5, 110.5, 111.0, 118.3, 118.3, 119.9, 122.3, 122.8, 125.1, 129.9, 136.3, 145.8, 146.3, 159.6 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}NO_3SNa$: 366.1134 $[M+Na]^+$; found: 366.1134.

2p: 1-Methyl-3-(4-nitrobenzenesulfonyl)-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3110, 2967–2873, 1530, 1348 (S=O, sulfonyl), 1141 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.08 (t, J = 7.2 Hz, 3H), 1.67 (tq, J = 7.2, 7.2 Hz, 2H), 3.14 (t, J = 7.2 Hz, 2H), 3.73 (s, 3H), 7.24–7.34 (m, 3H), 8.07–8.13 (m, 3H), 8.24 ppm (d, J = 8.8 Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 23.3, 27.0, 30.2, 108.9, 109.9, 119.6, 122.9, 123.4, 124.2, 124.9, 127.2, 136.5, 147.3, 149.6, 150.1 ppm; HRMS (ESI): m/z calcd for $C_{18}H_{18}N_2O_4SNa$: 381.0879 $[M+Na]^+$; found: 381.0880.

2q: 3-(4-Acetylbenzenesulfonyl)-1-methyl-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3365, 3011–2869, 1692 (C=O, acyl), 1395, 1260 (S=O, sulfonyl), 1142, 1083 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.08 (t, J = 7.2 Hz, 3H), 1.62–1.70 (m, 2H), 2.58 (s, 3H), 3.13–3.17 (m, 2H), 3.71 (s, 3H), 7.26–7.32 (m, 3H), 7.97–8.11 ppm (m, 5H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 23.2, 26.8, 30.1, 109.7, 119.8, 122.6, 123.1, 124.9, 126.3, 128.7, 136.4, 139.5, 146.8, 148.2, 196.6 ppm (acyl); HRMS (ESI): m/z calcd for $C_{20}H_{21}NO_3SNa$: 378.1134 $[M+Na]^+$; found: 378.1136.

2r: 1-Methyl-2-propyl-3-(2,2,2-trifluoroethanesulfonyl)-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3011–2873, 1318 (S=O, sulfonyl), 1246, 1139, 1076 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.08, (t, J = 7.6 Hz, 3H), 1.69–1.77 (m, 2H), 3.09–3.13 (m, 2H), 3.76 (s, 3H), 7.26–7.38 (m, 3H), 7.90–7.95 ppm (m, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.1, 23.3, 26.6, 30.2, 58.1, 58.4, 58.7, 59.0, 107.6, 109.9, 119.2, 120.2, 122.8, 122.9, 123.4, 124.8, 136.4, 148.2 ppm; HRMS (ESI): m/z calcd for $C_{14}H_{16}F_3NO_2SNa$: 342.0746 $[M+Na]^+$; found: 342.0746.

2t: 7-Methoxy-1-methyl-2-propyl-3-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3067–2841, 1578, 1490, 1261 (S=O, sulfonyl), 1112 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.06 (t, J = 7.6 Hz, 3H), 1.56–1.66 (m, 2H), 2.33 (s, 3H), 3.08–3.12 (m, 2H), 3.89 (s, 3H), 3.97 (s, 3H), 6.65 (d, J = 8.0 Hz, 1H), 7.10 (dd, J = 8.0, 8.0 Hz, 1H), 7.20 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.84 ppm (d, J = 8.4 Hz, 2H); ^{13}C NMR (150.90 MHz, $CDCl_3$): δ = 14.2, 21.4, 22.9, 26.6, 33.2, 55.5, 103.9, 110.9, 112.5, 122.4, 125.9, 126.1, 127.1, 129.4, 141.8, 142.8, 146.1, 147.3 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{23}NO_3SNa$: 380.1291 $[M+Na]^+$; found: 380.1290.

2u: 7-Methoxy-3-(4-methoxybenzenesulfonyl)-1-methyl-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3040–2843, 1595, 1495, 1259 (S=O, sulfonyl), 1127 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.06 (t, J = 7.6 Hz, 3H), 1.61 (tq, J = 7.6, 7.6 Hz, 2H), 3.08–3.12 (m, 2H), 3.79 (s, 3H), 3.89 (s, 3H), 3.97 (s, 3H), 6.65 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 8.8 Hz, 2H), 7.10 (dd, J = 8.0, 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.88 ppm (d, J = 8.8 Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 22.9, 26.6, 33.2, 55.4, 103.7, 111.1, 112.4, 113.8, 122.2, 125.8, 126.9, 128.0, 128.0, 136.5, 145.7, 147.1, 162.3 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{23}NO_4SNa$: 396.1240 $[M+Na]^+$; found: 396.1241.

2v: 3-Benzenesulfonyl-7-methoxy-1-methyl-2-propyl-1*H*-indole: IR (KBr): $\tilde{\nu}$ = 2928–2833, 1609, 1582, 1331, 1267 (S=O, sulfonyl), 1186 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.06 (t, J = 7.6 Hz, 3H), 1.55–1.65 (m, 2H), 3.08–3.12 (m, 2H), 3.89 (s, 3H), 3.98 (s, 3H), 6.66 (d, J = 7.6 Hz, 1H), 7.11 (dd, J = 7.6, 7.6 Hz, 1H), 7.38–7.45 (m, 3H), 7.71 (d, J = 7.6 Hz, 1H), 7.93–7.96 ppm (m, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 22.9, 26.7, 33.3, 55.5, 103.9, 110.5, 112.5, 122.5, 125.9, 126.0, 127.1, 128.7, 132.0, 144.6, 146.4, 147.2 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}NO_3SNa$: 366.1134 $[M+Na]^+$; found: 366.1134.

2w: 7-Methoxy-1-methyl-3-(4-nitrobenzenesulfonyl)-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3107, 2960–2843, 1524, 1345 (S=O, sulfonyl), 1223, 1009 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.08 (t, J = 7.7 Hz, 3H), 1.63 (tq, J = 7.7, 7.7 Hz, 2H), 3.10–3.11 (m, 3H), 3.91 (s, 3H), 4.02 (s, 3H), 6.70 (d, J = 8.0 Hz, 1H), 7.15 (dd, J = 8.0, 8.0 Hz, 1H), 7.66 (dd, J = 0.8, 8.0 Hz, 1H), 8.09–8.12 (m, 2H), 8.22–8.26 ppm (m, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.3, 23.1, 26.8, 33.5, 55.6, 104.4, 108.8, 112.0, 123.2, 124.1, 126.08, 126.9, 127.1, 147.3, 147.4, 149.6, 150.1 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{20}N_2O_5SNa$: 411.0985 $[M+Na]^+$; found: 411.0986.

2y: 2-Cyclohexyl-7-methoxy-1-methyl-3-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 1576, 1489, 1255 (S=O, sulfonyl), 1145 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.21–1.88 (m, 10H), 2.34 (s, 3H), 3.88 (s, 3H), 4.06–4.12 (m, 4H), 6.65 (d, J = 8.0 Hz, 1H), 7.11 (dd, J = 8.0, 8.0 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.84 ppm (d, J = 8.0 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 21.4, 25.9, 26.9, 29.7, 35.8, 55.5, 103.9, 111.2, 113.0, 122.3, 125.9, 126.2, 127.3, 129.2, 142.0, 142.5, 147.2, 148.8 ppm; HRMS (ESI): m/z calcd for $C_{23}H_{27}NO_3SNa$: 420.1604 $[M+Na]^+$; found: 420.1606.

2z: 7-Methoxy-1-methyl-2-phenyl-3-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 2956, 1578, 1470, 1302 (S=O, sulfonyl), 1152 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 3.71 (s, 3H), 3.91 (s, 3H), 6.73 (d, J = 8.0 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 7.20 (dd, J = 8.0, 8.0 Hz, 1H), 7.27–7.28 (m, 2H), 7.44–7.54 (m, 5H), 7.91 ppm (d, J = 8.0 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 21.4, 34.5, 55.5, 104.1, 113.0, 113.6, 127.7, 125.9, 126.3, 126.9, 127.9, 128.9, 129.3, 129.4, 130.8, 141.2, 142.5, 144.3, 147.4 ppm; HRMS (ESI): m/z calcd for $C_{23}H_{21}NO_3SNa$: 414.1134 $[M+Na]^+$; found: 414.1136.

2aa: 7-Methoxy-2-(4-methoxyphenyl)-1-methyl-3-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3093–2840, 1901, 1610, 1482, 1308 (S=O, sulfonyl), 1245, 1150 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 3.71 (s, 3H), 3.90–3.91 (m, 6H), 6.72 (d, J = 8.0 Hz, 1H), 6.99 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 7.16–7.20 (m, 3H), 7.49 (d, J = 8.8 Hz, 2H), 7.90 ppm (d, J = 8.0 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 21.4, 34.4, 55.3, 55.5, 104.1, 113.0, 113.3, 113.4, 121.1, 122.6, 125.8, 126.3, 126.9, 128.9, 132.1, 141.3, 142.4, 144.4, 147.3, 160.3 ppm; HRMS (ESI): m/z calcd for $C_{24}H_{23}NO_4SNa$: 444.1240 $[M+Na]^+$; found: 444.1242.

2ab: 7-Methoxy-1-methyl-3-tosyl-2-[4-(trifluoromethyl)phenyl]-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3088–2836, 1577, 1453, 1314 (S=O, sulfonyl), 1262, 1121 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 2.25 (s, 3H), 3.65 (s, 3H), 3.85 (s, 3H), 6.68 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 8.4 Hz, 2H), 7.15 (dd, J = 8.0, 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.82 ppm (d, J = 8.0 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 21.4, 34.6, 55.5, 104.4, 113.0, 114.2, 123.1, 124.8, 124.8, 124.9, 124.9, 125.1, 126.1, 126.3, 126.7, 129.1, 131.3, 131.6, 133.1, 140.9, 142.2, 142.0, 147.5 ppm; HRMS (ESI): m/z calcd for $C_{24}H_{20}F_3NO_3SNa$: 482.1008 $[M+Na]^+$; found: 482.1008.

2ac: 7-Methoxy-1-methyl-3-tosyl-1*H*-indole: This compound was obtained as an inseparable mixture with an unidentified isomer (**3ac**) in the ratio **2ac**/**3ac** = 88:12. ^1H NMR (594.17 MHz, $CDCl_3$): δ = 2.35 (s, 3H), 3.89 (s, 3H), 4.06 (s, 3H), 6.66 (d, J = 8.0 Hz, 1H), 7.11 (dd, J = 8.0, 8.0 Hz, 1H), 7.22–7.24 (m, 2H), 7.48 (dd, J = 0.7, 8.0 Hz, 1H), 7.60 (s, 1H), 7.88 ppm (d, J = 8.3 Hz, 2H).

3a: 1-Methyl-2-propyl-6-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3060–2833, 1596, 1471, 1285 (S=O, sulfonyl), 1149 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 1.04 (t, J = 7.2 Hz, 3H), 1.75 (tq, J = 7.2, 7.2 Hz, 2H), 2.36 (s, 3H), 2.73 (t, J = 7.2 Hz, 2H), 3.73 (s, 3H), 6.30 (s, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.95 ppm (s, 1H); ^{13}C NMR (125.65 MHz, $CDCl_3$): δ = 13.9, 21.5, 21.7, 29.0, 30.0, 100.0, 109.2, 118.3, 120.2, 127.3, 129.6, 131.4, 132.8, 136.2, 140.2, 143.2, 146.0 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}NO_2SNa$: 350.1185 $[M+Na]^+$; found: 350.1185; elemental analysis: calcd (%) for $C_{19}H_{21}NO_2S$: C 69.69, H 6.46, N 4.28, S 9.79; found: C 69.81, H 6.55, N 4.24, S 9.62.

3t: 7-Methoxy-1-methyl-2-propyl-6-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3011–2837, 1596, 1462, 1282 (S=O, sulfonyl), 1141 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.6 Hz, 3H), 1.66 (tq, J = 7.6, 7.6 Hz, 2H), 2.29 (s, 3H), 2.57 (t, J = 7.6 Hz, 2H), 3.78 (s, 3H), 3.94 (s, 3H), 6.20 (s, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.76 ppm (d, J = 8.4 Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): δ = 14.0, 21.4, 21.6, 29.0, 31.5, 65.1, 100.4, 115.6, 119.9, 126.0, 127.5, 129.1, 129.4, 135.6, 140.5, 143.0, 145.0, 146.5 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{23}NO_3SNa$: 380.1291 $[M+Na]^+$; found: 380.1292.

3u: 7-Methoxy-6-(4-methoxyphenylsulfonyl)-1-methyl-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}$ = 3071–2840, 1592, 1461, 1287 (S=O, sulfonyl),

1151 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=1.04$ (t, $J=7.6$ Hz, 3H), 1.74 (tq, $J=7.6$, 7.6 Hz, 2H), 2.65 (t, $J=7.6$ Hz, 2H), 3.80 (s, 3H), 4.02 (s, 3H), 6.27 (s, 1H), 6.89 (d, $J=9.2$ Hz, 2H), 7.33 (d, $J=8.4$ Hz, 1H), 7.73 (d, $J=8.4$ Hz, 1H), 7.89 ppm (d, $J=9.2$ Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=14.0$, 21.4, 28.9, 31.4, 55.4, 65.0, 100.3, 113.6, 115.4, 119.7, 126.3, 129.3, 129.5, 135.1, 135.4, 144.8, 146.4, 162.6 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{23}NO_4SNa$: 396.1240 $[M+Na]^+$; found: 396.1239.

3v: 6-Benzenesulfonyl-7-methoxy-1-methyl-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}=3086$, 2988–2833, 1531, 1299 (S=O, sulfonyl), 1207, 1154 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=1.05$ (t, $J=7.8$ Hz, 3H), 1.74 (tq, $J=7.8$, 7.8 Hz, 2H), 2.65 (t, $J=7.8$ Hz, 2H), 3.86 (s, 3H), 4.02 (s, 3H), 6.29 (s, 1H), 7.35 (d, $J=8.4$ Hz, 1H), 7.41–7.52 (m, 3H), 7.76 (d, $J=8.4$ Hz, 1H) 7.96 ppm (d, $J=7.6$ Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=14.1$, 21.4, 29.0, 31.5, 65.1, 100.5, 115.6, 120.0, 125.7, 127.4, 128.4, 129.4, 132.3, 135.7, 143.3, 145.1, 146.6 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}NO_3SNa$: 366.1134 $[M+Na]^+$; found: 366.1135.

3w: 7-Methoxy-1-methyl-6-(4-nitrobenzenesulfonyl)-2-propyl-1*H*-indole: IR (neat): $\tilde{\nu}=3097$, 2962–2835, 1529, 1347 (S=O, sulfonyl), 1306, 1209, 1158, 1013 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=1.05$ (t, $J=7.4$ Hz, 3H), 1.75 (tq, $J=7.4$, 7.4 Hz, 2H), 2.67 (t, $J=7.4$ Hz, 2H), 3.86 (s, 3H), 4.08 (s, 3H), 6.31 (s, 1H), 7.39 (d, $J=8.4$ Hz, 1H), 7.74 (d, $J=8.4$ Hz, 1H), 8.10–8.13 (m, 2H), 8.25–8.28 ppm (m, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=14.0$, 21.4, 29.0, 31.6, 65.5, 100.8, 116.1, 119.9, 123.7, 124.1, 128.7, 129.2, 136.4, 145.1, 147.3, 148.9, 149.8 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{20}N_2O_5SNa$: 411.0985 $[M+Na]^+$; found: 411.0986.

3y: 2-Cyclohexyl-7-methoxy-1-methyl-6-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}=$ 2947–2844, 1448, 1281 (S=O, sulfonyl), 1138 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=1.19$–1.40 (m, 5H), 1.71 (d, $J=11.6$ Hz, 1H), 1.78–1.91 (m, 4H), 2.29 (s, 3H), 2.52–2.59 (m, 1H), 3.82 (s, 3H), 3.95 (s, 3H), 6.19 (s, 1H), 7.14 (d, $J=8.0$ Hz, 2H), 7.27 (d, $J=8.4$ Hz, 1H), 7.67 (d, $J=8.4$ Hz, 1H), 7.76 ppm (d, $J=8.0$ Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=$ 21.5, 26.0 26.5, 31.3, 32.9, 35.8, 65.0, 98.4, 115.6, 119.9, 126.0, 127.4, 129.0, 129.2, 135.6, 140.4, 142.9, 145.1, 151.7 ppm; HRMS (ESI): m/z calcd for $C_{23}H_{27}NO_3SNa$: 420.1604 $[M+Na]^+$; found: 420.1605.

3z: 7-Methoxy-1-methyl-2-phenyl-6-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}=3092$–2832, 1595, 1467, 1300 (S=O, sulfonyl), 1151 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=2.37$ (s, 3H), 3.87 (s, 3H), 4.09 (s, 3H), 6.56 (s, 1H), 7.23–7.25 (m, 2H), 7.41–7.47 (m, 6H), 7.83 (d, $J=8.4$ Hz, 1H), 7.87 ppm (d, $J=$ 8.4 Hz, 1H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=21.6$, 33.5, 65.3, 103.0, 116.3, 120.5, 127.2, 127.5, 128.6, 128.6, 129.1, 129.4, 130.8, 131.5, 135.5, 140.3, 143.1, 145.7, 146.6 ppm; HRMS (ESI): m/z calcd for $C_{23}H_{21}NO_3SNa$: 414.1134 $[M+Na]^+$; found: 414.1136.

3aa: 7-Methoxy-2-(4-methoxyphenyl)-1-methyl-6-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}=2942$, 2836, 1593, 1494, 1287 (S=O, sulfonyl), 1148 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=2.36$ (s, 3H), 3.85 (s, 3H), 4.07 (s, 3H), 6.50 (s, 1H), 6.99 (d, $J=8.8$ Hz, 2H), 7.23 (d, $J=8.8$ Hz, 2H), 7.38 (d, $J=8.8$ Hz, 2H), 7.42 (d, $J=8.8$ Hz, 1H), 7.81 (d, $J=8.8$ Hz, 1H), 7.86 ppm (d, $J=8.8$ Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=21.6$, 33.4, 55.4, 65.0, 102.4, 114.1, 116.1, 120.4, 123.8, 126.9, 127.5, 129.1, 130.6, 130.6, 135.6, 140.3, 143.1, 145.6, 146.6, 159.9 ppm; HRMS (ESI): m/z calcd for $C_{24}H_{23}NO_4SNa$: 444.1240 $[M+Na]^+$; found: 444.1242.

3ab: 7-Methoxy-1-methyl-6-tosyl-2-[4-(trifluoromethyl)phenyl]-1*H*-indole: IR (neat): $\tilde{\nu}=3102$–2833, 1594, 1459, 1322 (S=O, sulfonyl), 1150 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=2.38$ (s, 3H), 3.89 (s. 3H), 4.10 (s. 3H), 6.62 (s, 1H), 7.24 (d, $J=8.4$ Hz, 2H), 7.47 (d, $J=8.4$ Hz, 1H), 7.60 (d, $J=8.0$ Hz, 2H), 7.74 (d, $J=8.0$ Hz, 2H), 7.83–7.88 ppm (m, 3H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=21.5$, 33.5, 65.0, 104.0, 116.6, 120.7, 122.4, 125.1, 125.5, 125.5, 125.5, 125.6, 126.9, 127.5, 127.8, 127.9, 129.1, 129.4, 129.5, 129.8 ppm; HRMS (ESI): m/z calcd for $C_{24}H_{20}F_3NO_3SNa$: 482.1008 $[M+Na]^+$; found: 482.1010.

3ac: 7-Methoxy-1-methyl-6-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}=3095$–2836, 1598, 1479, 1349 (S=O, sulfonyl), 1301, 1155 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=2.37$ (s, 3H), 3.98 (s, 3H), 4.07 (s, 3H), 6.48 (d, $J=3.2$ Hz, 1H), 7.09 (d, $J=3.2$ Hz, 1H), 7.24 (d, $J=8.0$ Hz, 2H), 7.43 (d, $J=8.0$ Hz, 1H), 7.77 (d, $J=8.0$ Hz, 1H), 7.85 ppm (d, $J=8.0$ Hz, 2H); ^{13}C NMR (100.40 MHz, $CDCl_3$): $\delta=21.6$, 35.5, 65.6, 102.2, 116.8, 120.0, 127.1, 127.5, 129.2, 129.2, 134.0, 136.2, 140.2, 143.2, 145.8 ppm; HRMS (ESI): m/z calcd for $C_{17}H_{17}NO_3SNa$: 338.0821 $[M+Na]^+$; found: 338.0820.

4a: 1-Methyl-2-propyl-4-tosyl-1*H*-indole: IR (neat): $\tilde{\nu}=3060$, 2956–2871, 1532, 1277 (S=O, sulfonyl), 1144 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=1.05$ (t, $J=7.2$ Hz, 2H), 1.77 (tq, $J=7.2$, 7.2 Hz, 2H), 2.33 (s, 3H), 2.72 (t, $J=7.2$ Hz, 2H), 3.66 (s, 3H), 6.75 (s, 1H), 7.20–7.24 (m, 3H), 7.43 (d, $J=8.0$ Hz, 1H), 7.80 (d, $J=8.0$ Hz, 1H), 7.88 ppm (d, $J=8.4$ Hz, 2H); ^{13}C NMR (150.90 MHz, $CDCl_3$): $\delta=14.0$, 21.5, 21.7, 29.0, 29.7, 98.7, 113.9, 119.7, 120.6, 124.7, 127.2, 129.5, 130.3, 138.3, 139.6, 143.3, 144.5 ppm; HRMS (ESI): m/z calcd for $C_{19}H_{21}NO_2SNa$: 350.1185 $[M+Na]^+$; found: 350.1185; elemental analysis: calcd (%) for $C_{19}H_{21}NO_2S$: C 69.69, H 6.46, N 4.28, S 9.79; found: C 69.56, H 6.64, N 4.28, S 9.68.

12: 3-Methoxymethyl-2-propyl-1-tosylindole: IR (neat): $\tilde{\nu}=2961$–2854, 1519, 1458, 1300, 1260, 1113 cm^{-1}; ^1H NMR (399.65 MHz, $CDCl_3$): $\delta=$ 2.32 (s, 3H), 3.12 (s, 3H) 5.19 (s, 2H), 7.10 (d, $J=8.0$ Hz, 2H), 7.33–7.38 (m, 4H), 7.46–7.57 (m, 6H), 8.32–8.35 ppm (m, 1H); ^{13}C NMR (149.40 MHz, $CDCl_3$): $\delta=21.4$, 56.1, 74.8, 110.8, 115.5, 120.9, 123.1, 124.1, 125.1, 126.6, 127.6, 127.8, 127.9, 128.5, 129.2, 129.9, 131.2, 135.6, 140.8, 143.0, 144.1 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{23}NO_3S$: 380.1296 $[M+Na]^+$; found: 380.1291.

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[1] a) T. M. Williams, T. M. Ciccarone, S. C. MacTough, C. S. Rooney, S. K. Balani, J. H. Condra, E. A. Emini, M. E. Goldman, W. J. Greenlee, L. R. Kauffman, J. A. O'Brien, V. V. Sardana, W. A. Schleif, A. D. Theoharides, P. S. Anderson, *J. Med. Chem.* **1993**, *36*, 1291–1294; b) R. Silvestri, G. De Martino, G. La Regina, M. Artico, S. Massa, L. Vargiu, M. Mura, A. G. Loi, T. Marceddu, P. La Colla, *J. Med. Chem.* **2003**, *46*, 2482–2493; c) R. Silvestri, M. Artico, G. De Martino, G. La Regina, R. Loddo, M. La Colla, P. La Colla, *J. Med. Chem.* **2004**, *47*, 3892–3896; d) R. Ragno, A. Coluccia, G. La Regina, G. De Martino, F. Piscitelli, A. Lavecchia, E. Novellino, A. Bergamini, C. Ciaprini, A. Sinistro, G. Maga, E. Crespan, M. Artico, R. Silvestri, *J. Med. Chem.* **2006**, *49*, 3172–3184.

[2] C. K. Lieben, A. Blokland, A. Sik, E. Sung, P. van Nieuwenhuizen, R. Schreiber, *Neuropsychopharmacology* **2005**, *30*, 2169–2179.

[3] J. S. Yadav, B. V. S. Reddy, A. D. Krishna, T. Swamy, *Tetrahedron Lett.* **2003**, *44*, 6055–6058.

[4] We repeated their reaction several times, but so far we could not obtain 3-sulfonylindoles in good yields; the reaction of indole and tosyl chloride under the conditions mentioned in reference [3] gave 3-tosylindole in 16% yield in our hands.

[5] a) R. Ragno, M. Artico, G. De Martino, G. La Regina, A. Coluccia, A. Di Pasquali, R. Silvestri, *J. Med. Chem.* **2005**, *48*, 213–223; b) R. Bernotas, S. Lenicek, S. Antane, G. M. Zhang, D. Smith, J. Coupet, B. Harrison, L. E. Schechter, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5499–5502.

[6] Migration of allyl groups: a) S. Cacchi, G. Fabrizi, P. Pace, *J. Org. Chem.* **1998**, *63*, 1001–1011; b) A. Fürstner, P. W. Davies, *J. Am. Chem. Soc.* **2005**, *127*, 15024–15025; propargyl groups: c) S. Cacchi, G. Fabrizi, L. Moro, *Tetrahedron Lett.* **1998**, *39*, 5101–5104; d) F. M. Istrate, F. Gagosz, *Org. Lett.* **2007**, *9*, 3181; acyl groups: e) T. Shimada, I. Nakamura, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 10546–10547; α-alkoxyalkyl groups: f) I. Nakamura, Y. Mizushima, U. Yamagishi, Y. Yamamoto *Tetrahedron* **2007**, *63*, 8670–8676.

[7] Allyl groups: a) A. Arcadi, S. Cacchi, M. Del Rosario, G. Fabrizi, F. Marinelli, *J. Org. Chem.* **1996**, *61*, 9280–9288; b) S. Cacchi, G. Fabrizi, L. Moro, *Synlett* **1998**, 741–745; c) N. Monterio, G. Balme, *Synlett* **1998**, 746–747; d) A. Fürstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.* **2000**, *122*, 6785–6786; e) A. Fürstner, F. Stelzer, H. Szillat, *J. Am. Chem. Soc.* **2001**, *123*, 11863–11869; α-alkoxyalkyl groups: f) I. Nakamura, Y. Mizushima, Y. Yamamoto, *J. Am. Chem. Soc.* **2005**, *127*, 15022–15023; g) reference [6b]; h) A. Fürstner, E. K. Heil-

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mann, P. W. Davies, *Angew. Chem.* **2007**, *119*, 4844–4847; *Angew. Chem. Int. Ed.* **2007**, *46*, 4760–4763.

[8] a) I. Nakamura, T. Sato, Y. Yamamoto, *Angew. Chem.* **2006**, *118*, 4585–4587; *Angew. Chem. Int. Ed.* **2006**, *45*, 4473–4475; b) I. Nakamura, T. Sato, M. Terada, Y. Yamamoto, *Org. Lett.* **2007**, *9*, 4081–4083.

[9] I. Nakamura, U. Yamagishi, D. Song, S. Konta, Y. Yamamoto, *Angew. Chem.* **2007**, *119*, 2334–2337; *Angew. Chem. Int. Ed.* **2007**, *46*, 2284–2287.

[10] CCDC-659610 and -622538 contain the supplementary crystallographic data for **2a** and **3a**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

[11] P. M. T. Ferreira, H. L. S. Maia, L. S. Monteiro, *Tetrahedron Lett.* **2002**, *43*, 4495–4497.

[12] Migration of sulfonyl groups: a) S. Roy, I. Das, K. Bhanuprakash, B. D. Gupta, *Tetrahedron* **1994**, *50*, 1847–1858; b) J. J. Gonzáles, P. M. Nieto, P. Prados, A. M. Echavarren, J. de Mendoza, *J. Org. Chem.* **1995**, *60*, 7419–7423; c) K. Oda, R. Hiratsuka, M. Machida, *Heterocycles* **1996**, *43*, 463–470; d) Y. Horino, M. Kimura, Y. Wakamiya, T. Okajima, Y. Tamaru, *Angew. Chem.* **1999**, *111*, 123–126; *Angew. Chem. Int. Ed.* **1999**, *38*, 121–124; e) Y. Horino, M. Kimura, M. Naito, S. Tanaka, Y. Tamaru, *Tetrahedron Lett.* **2000**, *41*, 3427–3431.

[13] A review of Au-catalyzed reactions: a) D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395–403; b) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478–3519; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; c) A. S. K. Hashmi, G. J. Hutchings, *Angew. Chem.* **2006**, *118*, 8064–8105; *Angew. Chem. Int. Ed.* **2006**, *45*, 7896–7936; d) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271–2296; e) N. Asao, *Synlett* **2006**, 1645–1656; f) R. A. Widenhoefer, X. Han, *Eur. J. Org. Chem.* **2006**, 4555–4563; g) S. Ma, S. Yu, Z. Gu, *Angew. Chem.* **2006**, *118*, 206–209; *Angew. Chem. Int. Ed.* **2006**, *45*, 200–203; h) A. S. K. Hashmi, *Angew. Chem.* **2005**, *117*, 7150–7154; *Angew. Chem. Int. Ed.* **2005**, *44*, 6990–6993.

[14] K. K. Park, J. J. Lee, J. Ryu, *Tetrahedron* **2003**, *59*, 7651–7659.

[15] Examples: a) Y. Horino, M. R. Luzung, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 11364–11365; b) A. K. Buzas, F. M. Istrate, F. Gagosz, *Angew. Chem.* **2007**, *119*, 1159–1162; *Angew. Chem. Int. Ed.* **2007**, *46*, 1141–1144; c) J. H. Lee, F. D. Toste, *Angew. Chem.* **2007**, *119*, 930–932; *Angew. Chem. Int. Ed.* **2007**, *46*, 912–914; d) L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2005**, *127*, 6962–6963; e) S. Chang, M. Lee, D. Y. Jung, S. H. Cho, S. K. Han, *J. Am. Chem. Soc.* **2006**, *128*, 12366–12367.

[16] Z. Liu, R. C. Larock, *J. Am. Chem. Soc.* **2005**, *127*, 13112–13113.

[17] Synthesis of 6-sulfonylindoles: J. Caixach, R. Capell, C. Galvez, A. Gonzalez, N. Roca, *J. Heterocycl. Chem.* **1979**, *16*, 1631–1635.

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