(千葉大学審査学位論文)

Study on Novel C-N Bond Formation with Hypervalent Iodine Compounds

超原子価ヨウ素を用いた新規炭素–窒素結合形成反応の研究

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Contents

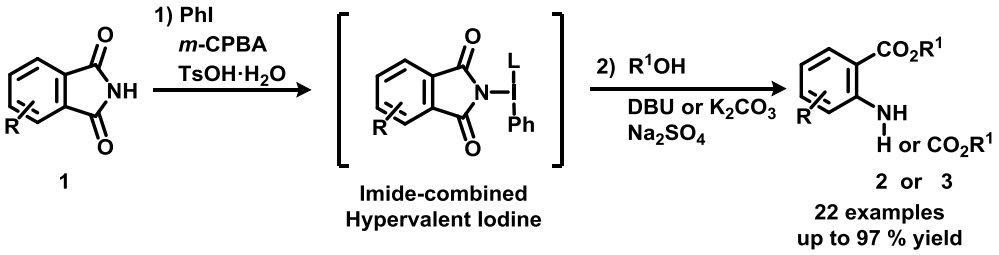
Abstract

Chapter 1

Hofmann-type Rearrangement of Imides by in-situ generaed Imide-combined Hypervalent Iodines

Aromatic amino acids (e.q., anthranilic acid) and aliphatic β, γ-amino acids were prepared from cyclic imides using hypervalent iodine generated in situ from iodoarene, TsOH, and *m*-CPBA. The Hofmann-type rearrangement was induced by nucleophilic attack of alcohol first followed by the Hofmann rearrangement. Here, imide-combined hypervalent iodine that was a key intermediate of the reaction, and played important role under basic conditions in alcohol.

Scheme 1: Hofmann-type Rearrangement of Cyclic Imides

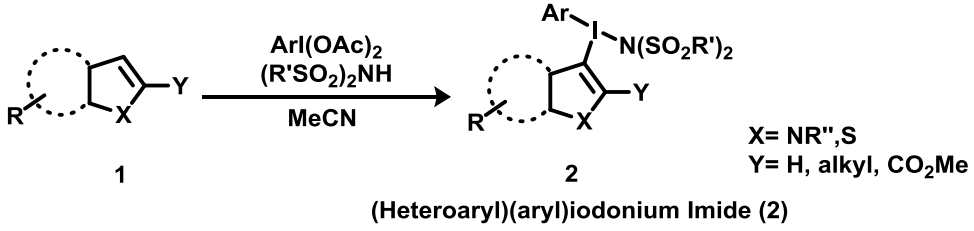


Chapter 2

Preparation of Novel Imide-combined Hypervalent Iodines: (Heteroaryl)(aryl)-iodonium Imides

(Heteroaryl)(aryl)iodonium imides were prepared from various heteroaromatics with (diacetoxyiodo)benzene (DIB) and bis(sulfonyl)imides. These novel hypervalent iodines were stable as white solid, and the unique structure was observed from two types of iodane (III), imide-combined λ^3-iodane and asymmetric diaryliodonium salt containing heterocycles.

Scheme 2: Preparation of (Heteroaryl)(aryl)iodonium Imides

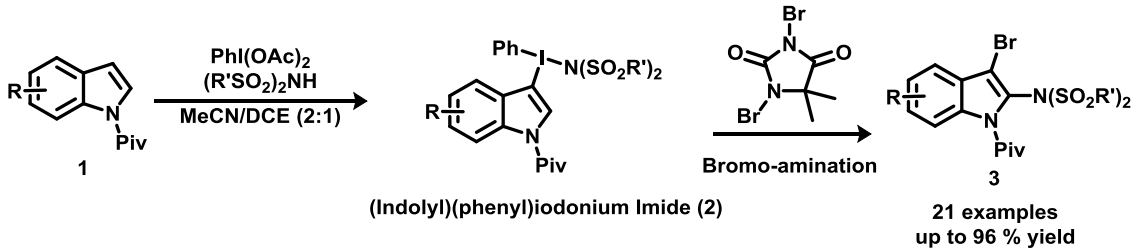


Chapter 3

Regioselective Bromo-amination of Indoles via (Indolyl)(aryl)iodonium Imides

N-(3'-Bromo-1'-pivaloyl-1'*H*-indol-2'-yl)-4-methyl-*N*-tosylbenzenesulfonamides were obtained by bromo-amination of (indolyl)(phenyl)iodonium imides using brominating reagents. This reaction is C-H dual-functionalization on one-step with complete regioselectivity.

Scheme 3: Regioselective Bromo-amination of Indoles

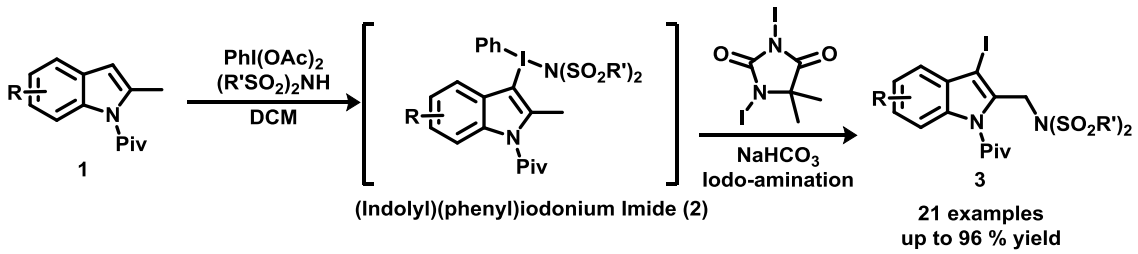


Chapter 4

Regioselective Iodo-amination of 2-Methylindoles via (Indolyl)(aryl)iodonium Imides

N-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)methyl)-*N*-(methanesulfonyl)methanesulfonamides were prepared by iodo-amination of 2-methylindole derivatives via (2-methylindolyl)(phenyl)iodonium imides using iodinating reagents. This reaction transformed both sp^2 C-H and non-activated sp^3 C-H bonds to C-I and C-N bonds, respectively.

Scheme 4: Regioselective Iodo-amination of Indoles

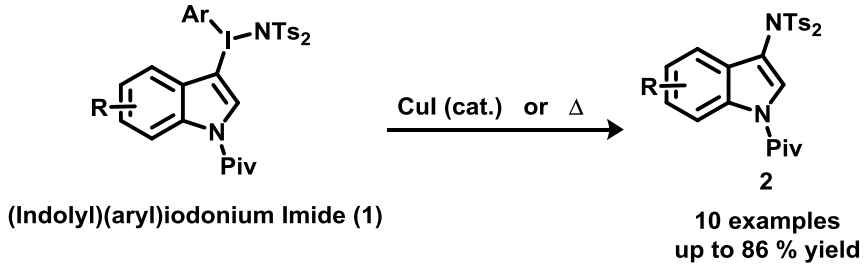


Chapter 5

Ligand Coupling Reaction of (Indolyl)(aryl)iodonium Imides to Form C-N Bond at 3-Position in Indole Group; Effect of Substitutents of Hypervalent Iodine for Reaction Selectivity

N-(1'-pivaloyl-1'*H*-indol-3'-yl)-4-methyl-*N*-tosylbenzenesulfonamides were generated by ligand coupling reaction of (indolyl)(aryl)iodonium imides using catalytic amount of cupper iodide (I) or under heat conditions. Substitutent on hypervalent iodines controlled the reaction with high regioselectivity.

Scheme 5: C-N Coupling Reaction of (Indolyl)(aryl)iodonium Imides

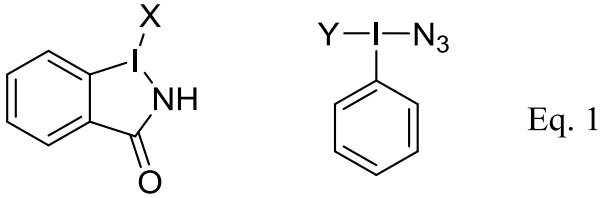


General Introduction:

C-N Bond Formation with I-N Bond-contained Hypervalent Iodines

The first hypervalent iodine compound, (dichloroiodo)benzene, was discovered by Willgerodt in 1886[1]. Since then, various hypervalent iodines were synthesized and a lot of unique reactions using iodanes were reported[2]. For example, iodosylbenzene and (diacetoxyiodo)benzene (DIB) were prepared in 1892[3], and 2-iodoxybenzoic acid was provided in 1893[4]. These compounds were used as low toxic and powerful oxidant instead of heavy metal reagents. Moreover, Dess and Martin developed a very useful pentavalent iodane in 1983[5], which is called Dess-Martin periodinane and widely used as an oxidatnt for synthesis of medicinal and biologically active compounds. Hydroxy(tosyloxy)iodobenzene reported by Neiland and Karele in 1970 was named Koser's reagent and known to oxidative C-O bond formation reagents[6].

All compounds exemplified above are I-O bond-combined polyvalent iodane. On the other hands, I-N bond contained hypervalent iodines are not so common. These species lack for stability and sensitive to air or moisture. Then, many scientists had studied to develop new hypervalent iodines possessing I-N bond and C-N bond formation reactions to utilize for synthesis of natural compounds. Since benziodazole (**1**) was released by Wolf and Steinberg in 1965[7], many types of I-N bond-combined hypervalent iodines were prepared and used for oxdative C-N bond formations. Thus in this section, the author studied I-N bond-contained hypervalent iodines and their application to the C-N bond formation reactions.

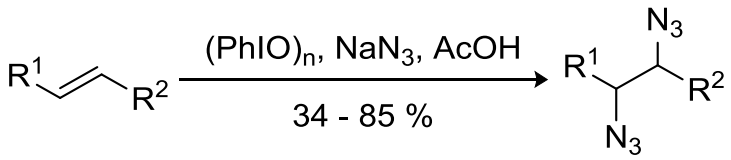


1 **2** Eq. 1

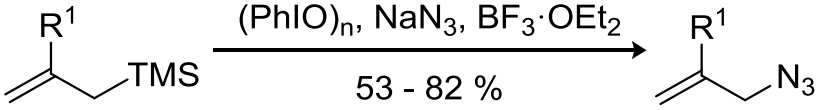
1-1 Azidoiodanes

Azidoiodanes (**2**) are useful reagents for azidation reactions, and prepared from iodoxybenzene or DIB with trimethylsilyl azide or sodium azide. However, azidoiodanes are not stable and usually generated in situ. In 1970, Zbiral group reported the first study about azidoiodanes generated with DIB and $TMSN_3$, and succeeded azidation of alkene (**3**) [Eq. 2][8]. In 1980s, Moriarty group[9], and Ochiai and Fujita group[10] obtained azide (**6**) from alkene (**5**) using iodosylbenzene, NaN_3, and acid [Eq. 3],

respectively.

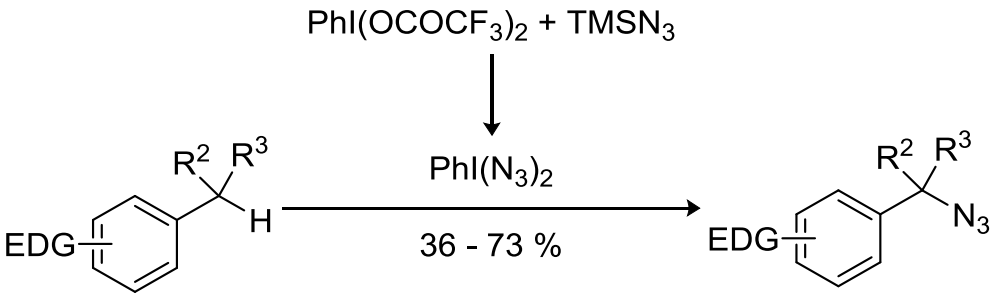


3 **4** Eq. 2



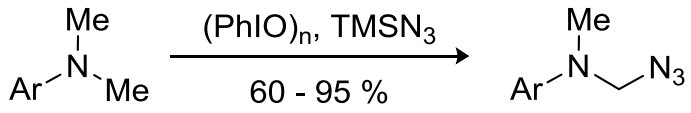
5 **6** Eq. 3

Kita group reported benzilic sp^3 C-H azidation of electron rich aromatics (**7**) with $PhI(N_3)_2$ generated in situ from [bis(trifluoroacetoxy)iodo]benzene (PIFA) and $TMSN_3$ [Eq. 4] [11].

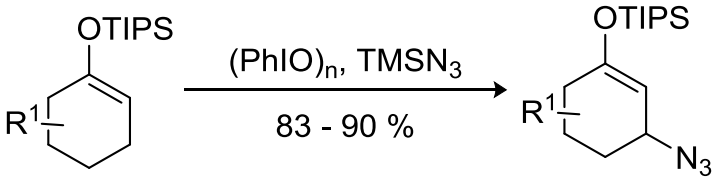


7 **8** Eq. 4

Magnus group studied metal-free sp^3 C-H azidation of *N*,*N*-dimethylaniline (**9**)[11a] and silyl enol ether (**11**)[11b] derivatives, respectively, using iodosylbenzene and $TMSN_3$ in high yields [Eq. 5, 6].

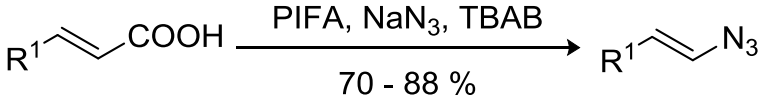


9 **10** Eq. 5

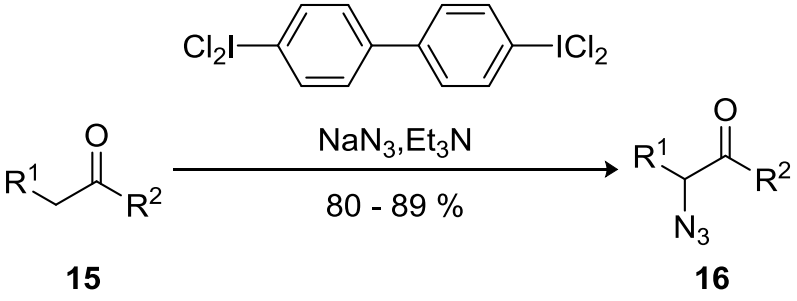


11 **12** Eq. 6

Telvekar group investigated synthesis of vinyl azide (**14**) and α-azide carbonyl compounds (**16**) with hypervalent iodine and sodium azide [Eq. 7, 8][12].

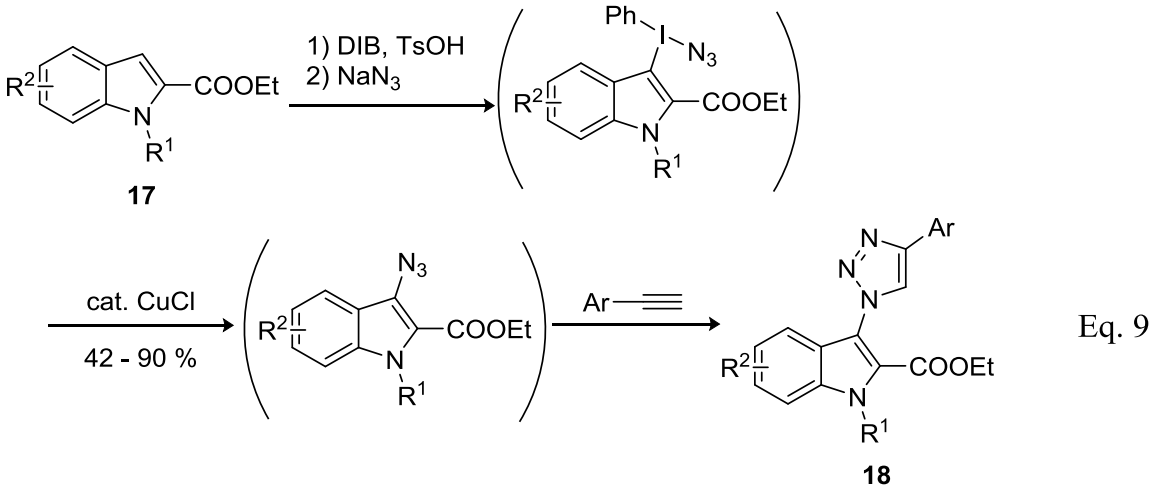


13 **14** Eq. 7



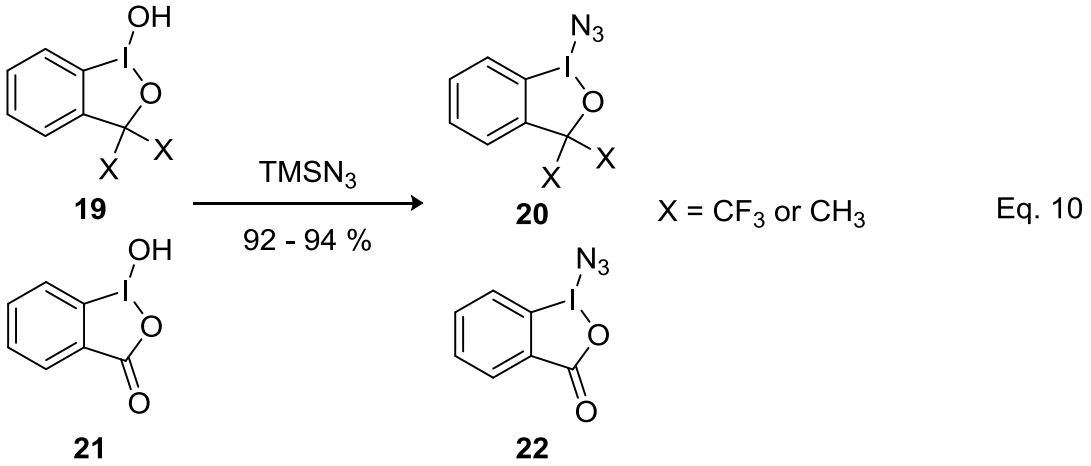
15 **16** Eq. 8

In 2012, Suna group reported azidation of indole-2-carboxylate derivatives (**17**) with DIB, TsOH, NaN_3, and copper catalyst [Eq. 9][13].



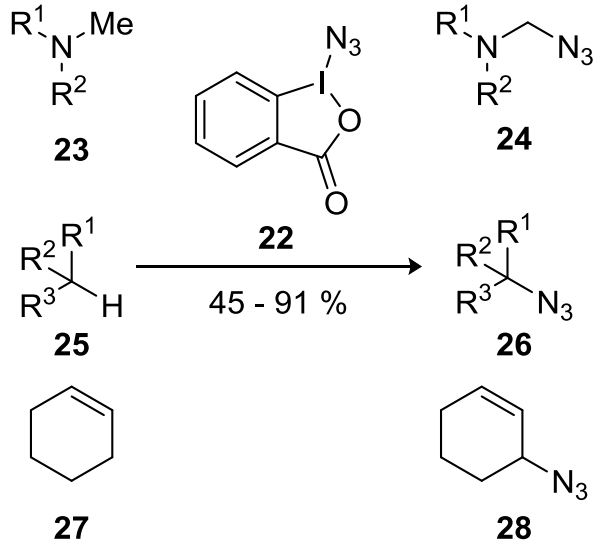
Eq. 9

To the focus on synthesis of novel azidoiodanes, Zhdankin group developed thermally stable and easily handling azidoiodanes (**20**, **22**) in 1994[14]. Compounds **20** and **22** are generated from iodoxole (**19**, **21**) with $TMSN_3$, and able to be isolated [Eq. 10].



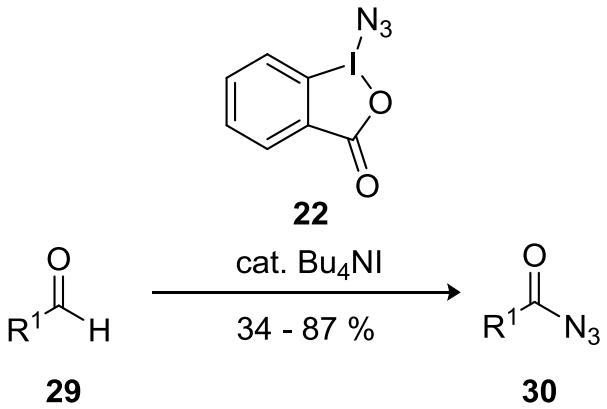
Eq. 10

Benziodoxole azides (**22**) are widely uesd for C-N bond formation. For example, Zhdankin group reported metal-free azidation of various sp^3 C-H bonds [Eq. 11][15].



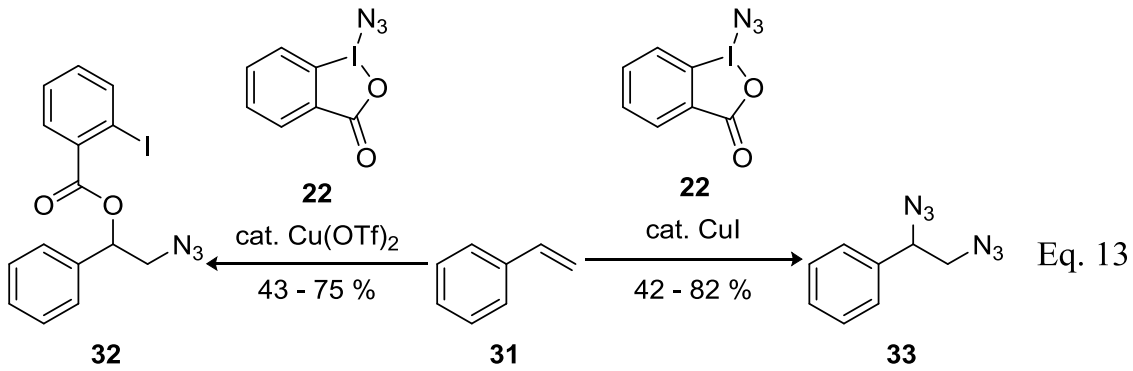
Eq. 11

Saito group succeeded metal-free azidation of aldehydes (**29**) with benziodoxole azides **22** [Eq. 12][16].



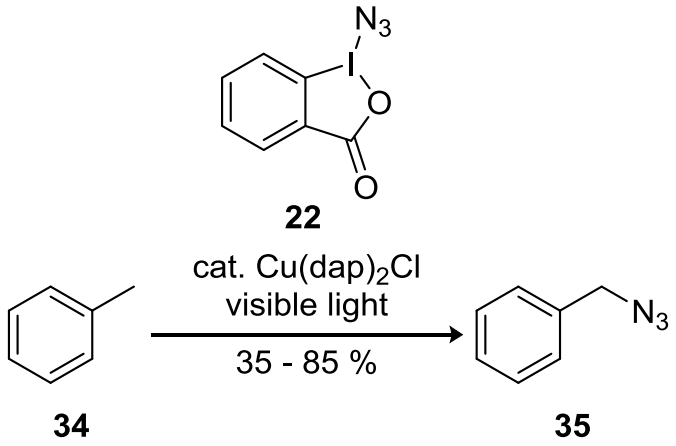
Eq. 12

Loh group studied vicinal difunctionalization of styrenes (**31**) with benziodoxole azides (**22)** and copper catalyst [Eq. 13][17].



Eq. 13

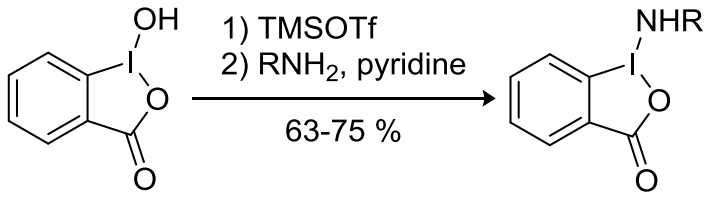
Recently, Greaney group reported direct benzylic C-H azidation with benziodoxole azides (**22)** and photoredox catalyst under irradiation with a visible light [Eq. 14][18].



Eq. 14

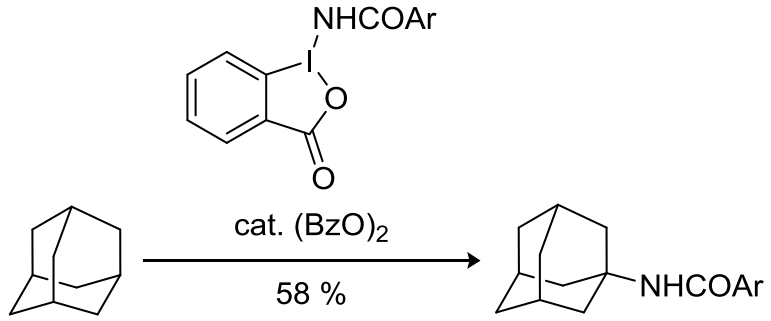
1-2 Amide and Iminoiodanes

Amideiodanes are unstable species and rapidly decompose and produce isocyanates by the Hofmann rearrangement[19]. However, in 1997, Zhdankin group succeeded in preparation of stable amideiodane (**37**) and demonstrated metal-free amination of sp^3 carbon of adamantane (**38**) and *N*,*N*-dimethylaniline derivatives (**40**), respectively, with aminoiodane (**37**) [Eq. 16, 17][20].



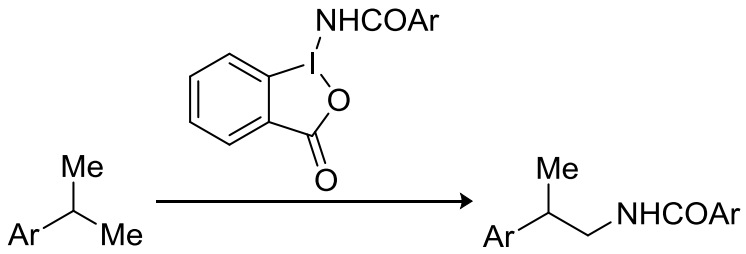
36 **37**

Eq. 15



38 **39**

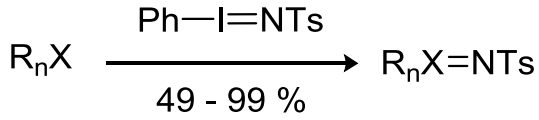
Eq. 16



40 **41**

Eq. 17

On the other hands, iminoiodanes (ArI=NR) which are polyvalent iodine possessing I=N double bond are excellent reagent for oxidative amination and nitrogen source with metal complex. The most popular iminoiodane is PhI=NTs, which is synthesized from DIB or PIFA, $TsNH_2$, and bases. In 1975, Yamada group reported preparation of iminoiodane and transformation of phosphine and sulfide (**42**) to phosphorane and surfurane (**43**), respectively [Eq. 18][21].

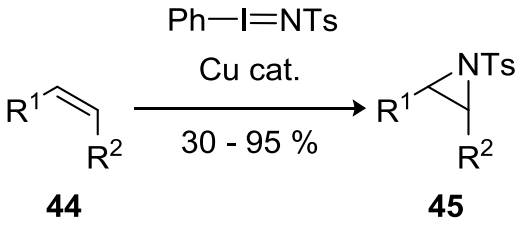


42 **43** n = 2, X = S, SO
n = 3, X = P

Eq. 18

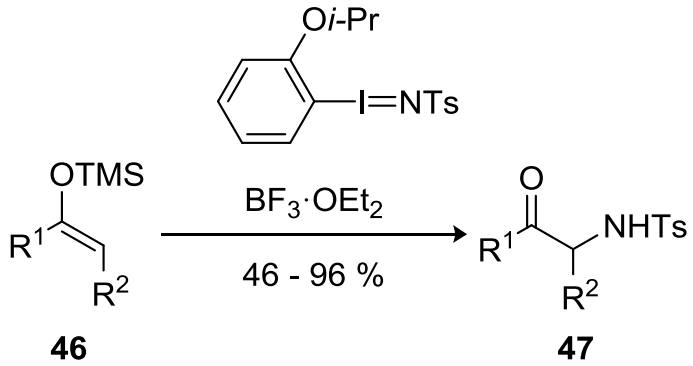
Since then, many reactions with iminoidanes were reported[22]. In particular, focusing on C-N bond formation, Jacobsen[23a] and Evans[23b] group developed asymmetric aziridation

of olefins (**44**) with PhINTs and copper catalysts [Eq. 19].



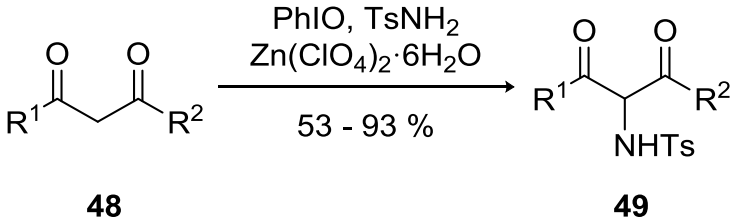
Eq. 19

Zhdankin group reported metal free C-N bond formation of silyl enol ethers (**46**) with iminoiodane [Eq. 20][24]. In this paper, they developed 2-alkoxyiminoiodanes and applied to amination reaction. Most iminoiodanes are less soluble in non-polar organic solvents, however, the hypervalent iodines which bear moderate solubility and high reactivity were developed.



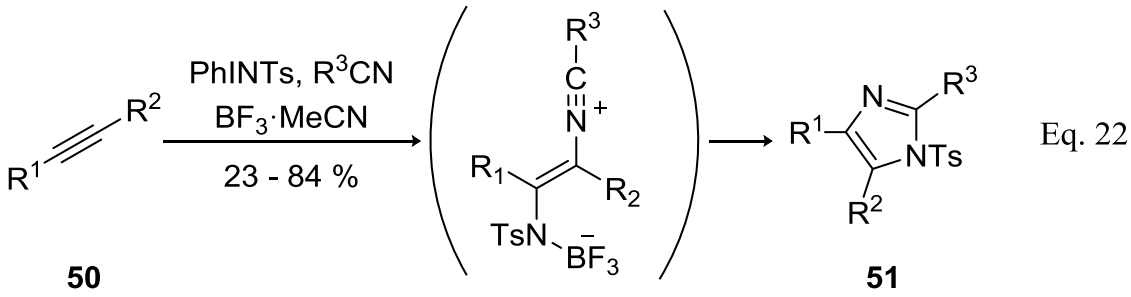
Eq. 20

In 2012, Zhang group succeeded in amination of 1,3-dicarbonyl compounds (**48**) with PhINTs generated in situ from iodosobenzene, $TsNH_2$, and Lewis acid [Eq. 21][25].



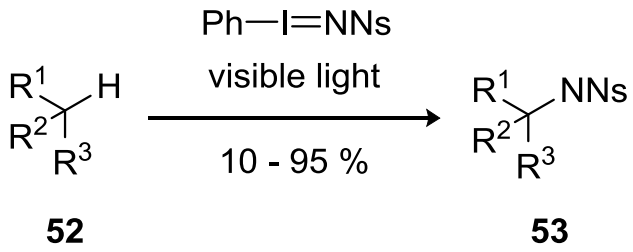
Eq. 21

Saito group investigated the reaction of alkynes (**50**) with iminoiodane and Lewis acid in nitriles, and obtained imidazoles (**51**) under metal-free conditions [Eq. 22][26].



Eq. 22

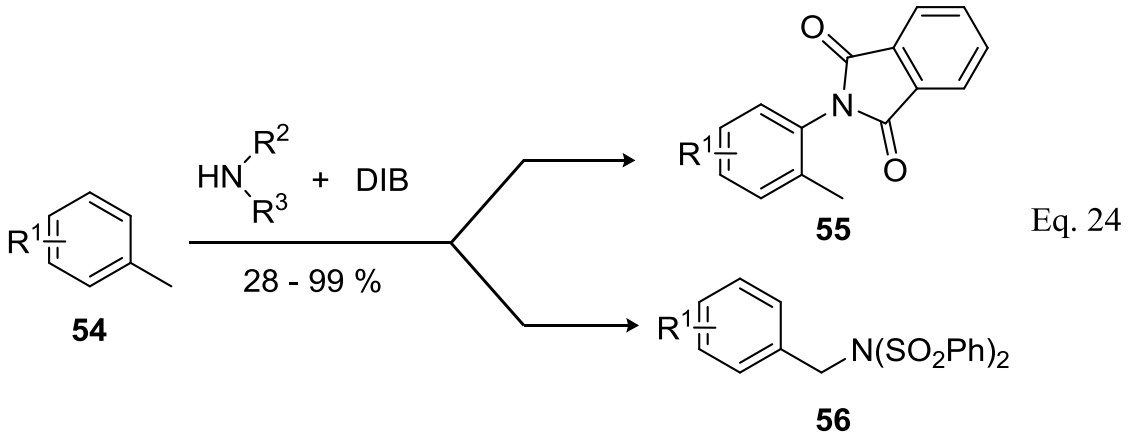
Recently, Lamar group reported metal-free C-N bond formation at sp^3 carbon with PhINNs (Ns : 4-nitrobenzenesulfonyl) under irradiation with a visible light [Eq. 23][27].



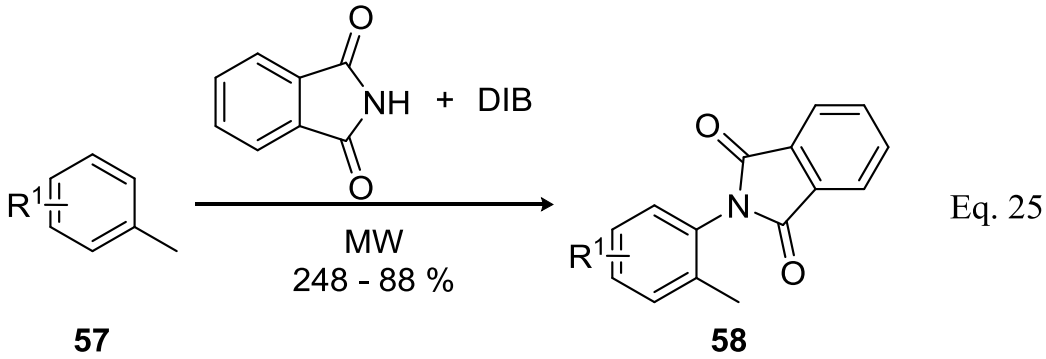
Eq. 23

1-3 Imide-combined Iodanes

Imides, such as phthalimide and succinimide, possess electron-deficient nitrogen atom, and can be used for ligand of hypervalent iodines. In 1983, Hadjiarapoglou group succeeded in synthesis of imide-combined hypervalent iodines possessing two phthalimide groups[28]. However, phenyliodane (III) bis(phthalimidate) is soluble in only high polar solvents, such as DMSO, and sensitive to moisture. In 2011, Chang[29a] group and DeBoef[29b,c] group reported metal-free intermolecular amination of methylarenes (**54**, **57**) with phthalimide-combined hypervalent iodine generated in situ from DIB and phthalimide under heating or MW irradiation conditions [Eq. 24, 25].

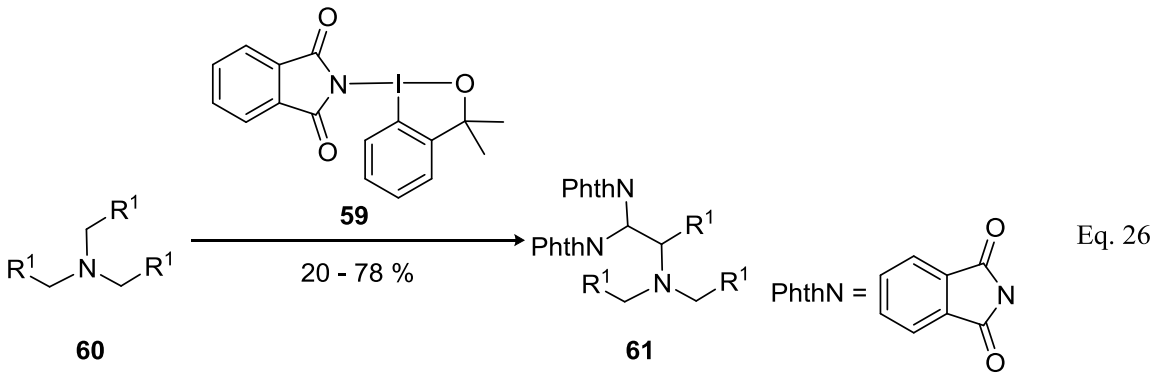


Eq. 24



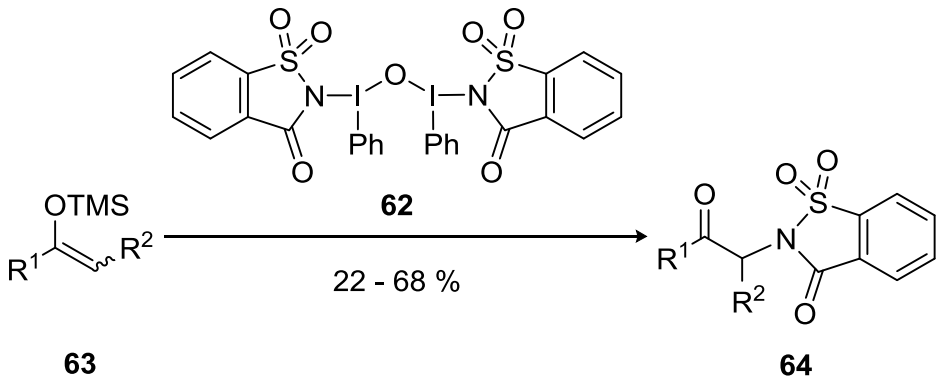
Eq. 25

Minakata group developed benziodoxole-type imide-combined iodane (**59**) (III), and applied to amination of tertiary alkylamine (**60**) [Eq. 26][30]. **59** is soluble in various organic solvents.



Eq. 26

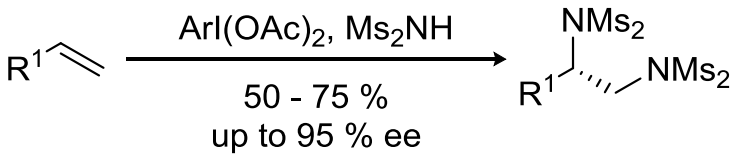
Zhdankin group succeeded in preparation of α-aminoketones with silyl enol ether (**63**) and saccharine-combined hypervalent iodine (**62**) [Eq. 27][31].



63 **64**

Eq. 27

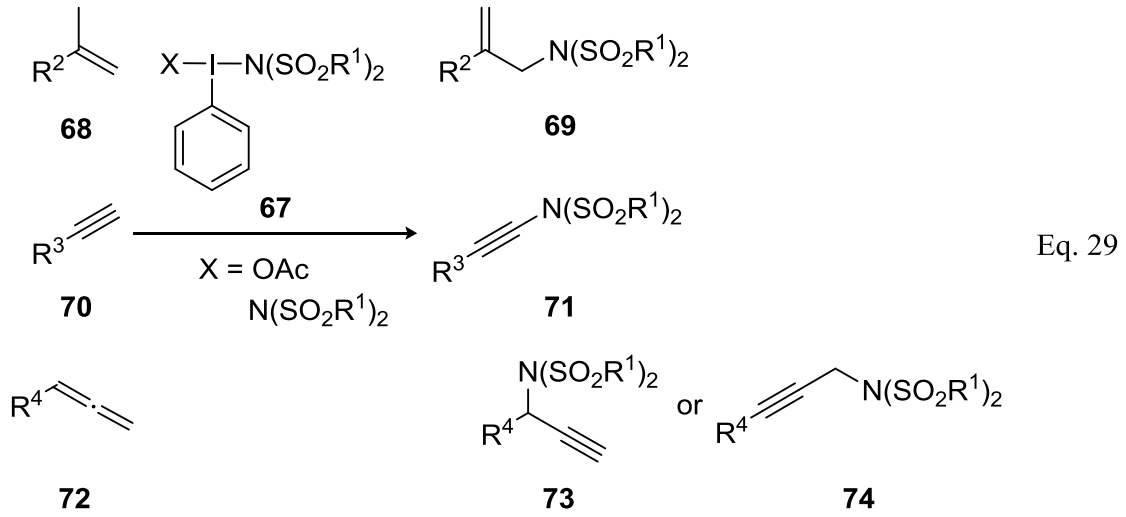
On the other hands, Muñis group reported enantioselective metal-free 1,2-diamination of styrenes (**65**) with ArI(OAc)NMs_2 which was generated in situ from (diacetoxyiodo)arene and bis(mesyl)imide [Eq. 28][32].



65 **66**

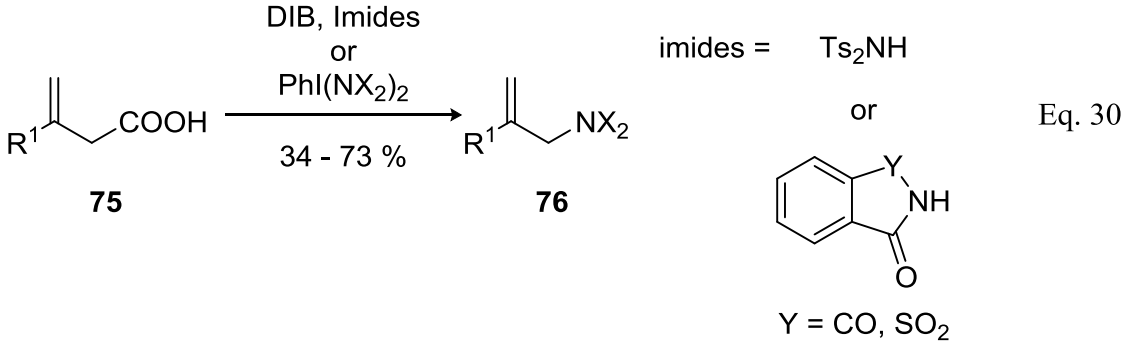
Eq. 28

Bis(sulfonyl)-type imide-combined hypervalent iodines (**67**) are easy to prepare from only (diacetoxyiodo)arene and bis(sulfonyl)imides at room tempareture, and are soluble in various organic solvents. Muñis group also investigated C-N bond formation reactions of allylic compounds (**68**)[33a], alkynes (**70**)[33b], allenes (**72**)[33c], and so on, with **67** [Eq. 29][33d,e].



Eq. 29

In 2014, Minakata group reported decarboxylation-amination of unsaturated carboxylic acids (**75**) with imide-combined hypervalent iodines [Eq. 30][34] .



Eq. 30

Conclusion

Various hypervalent iodines possessing I-N bond were prepared and applied to C-N bond formation. However, some of them are unstable and require careful treatment and operation. Moreover, their synthetic utilities to substrates are limited. Thus, the author studied about the following programs: development of new synthetic method for phthalimide-combined hypervalent iodines (chaper 1), preparation of novel imide-combined iodanes (chapter 2), and discovery of C-N bond formation reaction with novel trivalent iodanes (chapters 1, 3, 4, 5).

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Chapter 1

Hofmann-type Rearrangement of Imides by in-situ generated Imide-combined Hypervalent Iodines

Abstract

Aromatic amino acids (e.q., anthranilic acid) and aliphatic β, γ-amino acids were prepared from cyclic imides using hypervalent iodine generated in situ from iodoarene, TsOH, and *m*-CPBA. The Hofmann-type rearrangement was induced by nucleophilic attack of alcohol first followed by the Hofmann rearrangement. Here, imide-combined hypervalent iodine that was a key intermediate of the reaction, and played important role under basic conditions in alcohol.

Introduction

Amino acids are one of the most important compounds in living bodies, and some amino acid-like chemicals possess biological activity. Especially, aromatic amino acids are found in a lot of medicinal compounds[1]. However, synthetic methods of substituted anthranilic acids required many steps, with heavy metals[2]. On the other hands, Hofmann-type rearrangement of phthalimide is attractive strategy for preparation of anthranilic acid derivatives. Nevertheless, useful synthetic studies of anthranilic acid by Hofmann-type rearrangement have not been reported[3].

The Hofmann rearrangement is useful reaction to obtain amines from carboxyamides. Many types of haloganation reagents were used for the Hofmann rearrangement, and hypervalent iodines are also useful and efficient oxidants for the reaction[4]. The groups of Zhdankin[5] and Ochiai[6] reported that iodine (III) could be finitely employed for the Hofmann rearrangement of aliphatic amides.

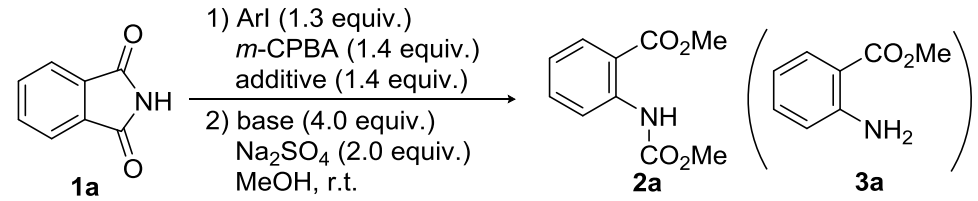
The author developed the first Hofmann-type rearrangement of cyclic imides by use of hypervalent iodine compounds generated in situ from iodoarenes, TsOH, and *m*-CPBA[7], and discovered imide-combined hypervalent iodine as the key intermediate of the reaction. This method transformed cyclic imides to aromatic and aliphatic β, γ-amino acids in high yields, respectively.

Results and Discussion

First, the author screened a series of bases, sulfonic acids, and substituted groups of iodoarenes on Hofmann-type rearrangement of phthalimide (Table 1). Trivalent iodines, HTIB analogue, were generated in situ from iodoarene, *m*-CPBA, and surfonic acid in chloroform. Then, the iodane (III), HTIB analogue, was treated with phthalimide, bases,

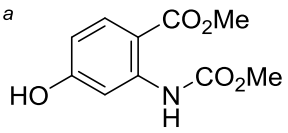
and Na_2SO_4 in methanol. The Hofmann-type rearrangement product was not obtained without base (entry 1), however, the yield was increased to 93 % by using K_2CO_3 (entry 2). Other bases were not effective for the reaction (entries 3-6). Although phthalimide was also transformed to the product with methansulfonic acid and *p*-chlorobenzenesulfonic acid instead of *p*-toluenesulfonic acid (entries 7, 8) under the same conditions, the yield of anthranilic acid derivative (**2a**) was decreased without sulfonilic acid (entry 9). In addition, *p*-chloroiodobenzene, which has an electron-withdrawing group on iodobenzene, reduced the yield of the product, as compared with iodobenzene and *t*-butyliodobenzene (entries 10, 11).

Table 1. Screening of Hofmann-type Rearrangement of Phthalimide



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

entry	Ar	additive	base	time (h)	yield (%)	ratio 1:2
1	Ph	$TsOH·H_2O$	-	24	trace	<1:>99
2	Ph	$TsOH·H_2O$	K_2CO_3	2	93	88:12
3	Ph	$TsOH·H_2O$	MeONa	4	trace	-
4	Ph	$TsOH·H_2O$	Et_3N	7	29	>99:<1
5	Ph	$TsOH·H_2O$	DBU	4	72[a]	99:1
6	Ph	$TsOH·H_2O$	TMG	4	15	>99:<1
7	Ph	$MeSO_3H$	K_2CO_3	4	84	91:9
8	Ph	*p*-$ClC_6H_4SO_3H$	K_2CO_3	4	89	94:6
9	Ph	-	K_2CO_3	5	66	95:5
10	*p*-ClC_6H_4	$TsOH·H_2O$	K_2CO_3	5	42	93:7
11	*p*-*t*-BuC_6H_4	$TsOH·H_2O$	K_2CO_3	4	92	92:8

[a] 

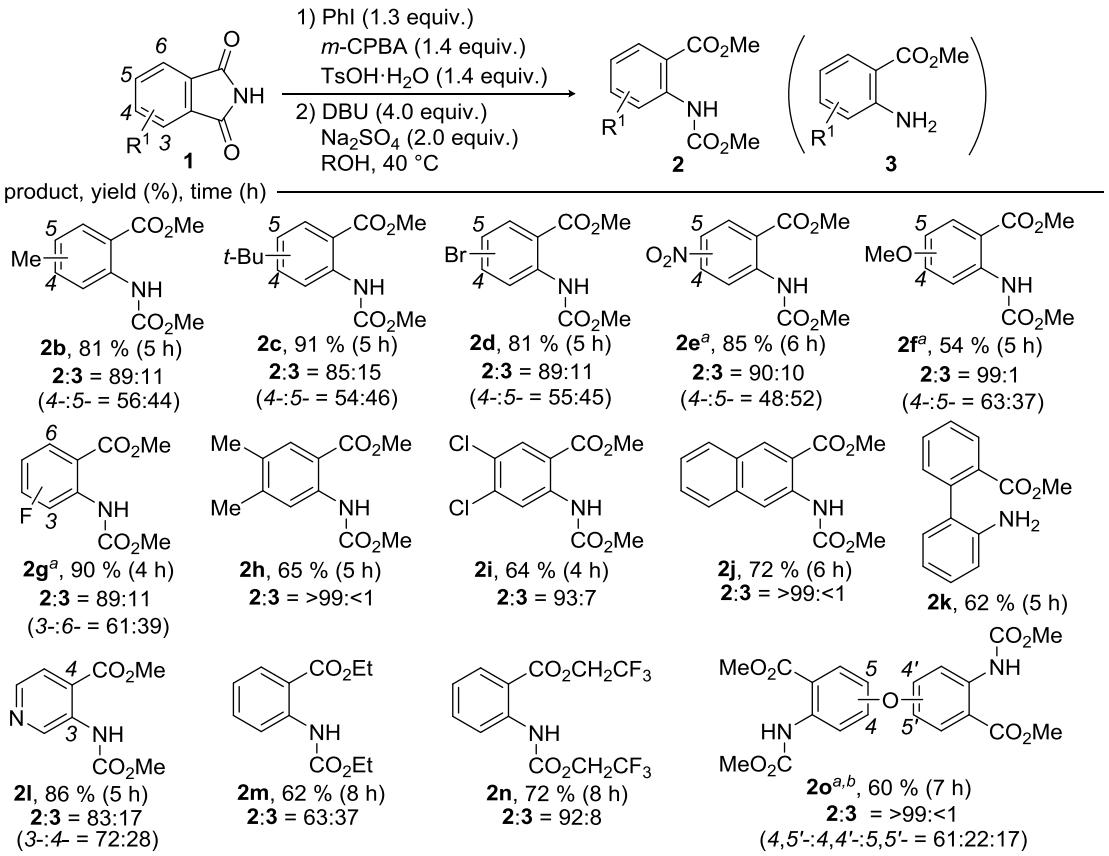
(20 % yield)

Next, the author examined Hofmann-type rearrangement of various phthalimides based on the optimized conditions, and DBU was used as a base instead of K_2CO_3 (Table 2). 4-Substituted phthalimides bearing Me (**1b**), *t*-Bu (**1c**), Br (**1d**), or NO_2 (**1e**) were transformed to the corresponding substituted anthranilic acid derivatives (**2b**-**2e**) in high yields, respectively. Strong electron-donating 4-methoxy phthalimide (**1f**) was converted into the product (**2f**) in good yield, and 3-fluoro phthalimide (**1g**) gave the

desired product (**2g**) in high yield.

4,5-Dimethylphenyl (**1h**), 4,5-dichlorophenyl (**1i**), naphthyl (**1j**), and biphenyl (**1k**) imides provided the corresponding di-substituted products (**2h-2k**) in high yields, respectively. Amino-isonicotinic acid derivative (**2l**) was obtained from 3,4-pyridine dicarboximide (**1l**) in excellent yield. In addition, treatment of **1a** with other alcohols, such as ethanol and 2,2,2-trifluoroethanol, instead of methanol for Hofmann-type rearrangement produced the anthranilic acid derivatives bearing ester and carbamate (**2m**, **2n**) in good yields, respectively. 4,4'-Oxybisphthalimide (**1o**) was transformed to an oxybisanthranilic acid derivative (**2o**) in 60% yield using double amount of each reagents. Almost all substrates provided the small amount of by-product (**3**, X=H), however, **3a** was easily converted to desired product (**2a**) with methylchloroformate in quantitative yield. Unfortunately, a mixture of two regioisomers was obtained with phthalimide (**1b-1g**, **1l**, **1o**) derivatives in law selectivity, and the ratios of regioselectivity were shown in experimental section.

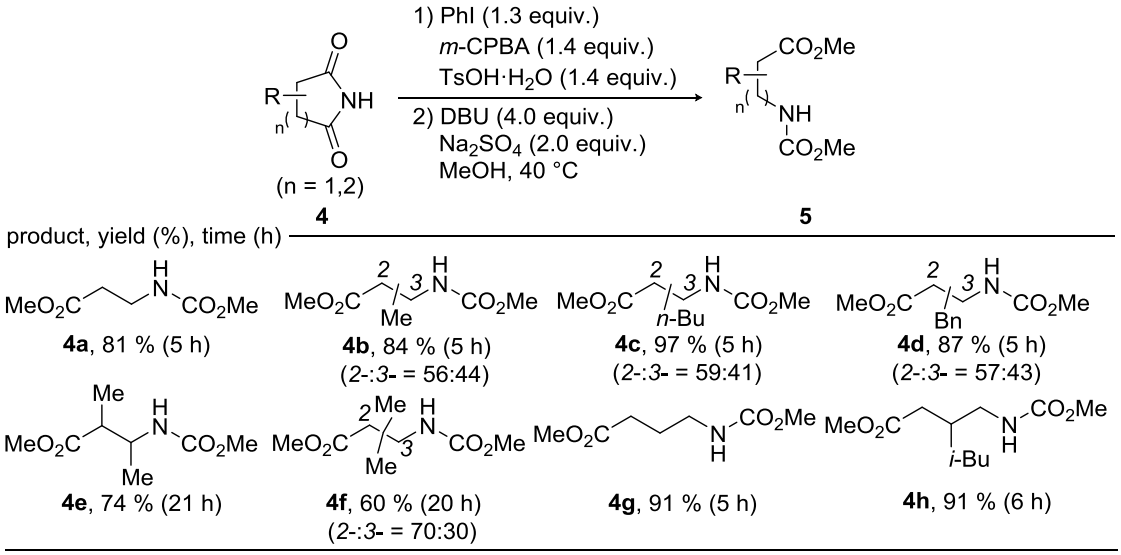
Table 2. Hofmann-type Rearrangement of Phthalimides **1** Using Hypervelent Iodine (III) Generated in Situ



[a] Reaction temperature was r.t.. [b] PhI (2.3 equiv.), *m*-CPBA (2.5 equiv.), $TsOH \cdot H_2O$ (2.5 equiv.), DBU (8.0 equiv.), and Na_2SO_4 (4.0 equiv.) were used.

The author also studied the application of Hofmann-type rearrangement to aliphatic cyclic imides to obtain β- and γ-amino acid derivatives (Table 3). Succinimide (**4a**) and mono-substituted succinimides (**4b-d**) produced β-amino acid derivatives in high yields, respectively, using the same reaction conditions as those of aromatic cyclic imides. 2,3- or 2,2- dimethylsuccinimide (**4e, f**) also provided desired products in good yields, respectively. Moreover, glutarimide (**4g**) gave γ-amino acid derivatives, and 3-isobutylglutarimide (**4i**) directly produced Pregabalin precursor. This precursor was easily transformed by hydrolysis to Pregabalin, which is used for neuropathic pain[8]. The result showed that Hofmann-type rearrangement is useful synthetic strategy for amino acid-like medicinal compounds.

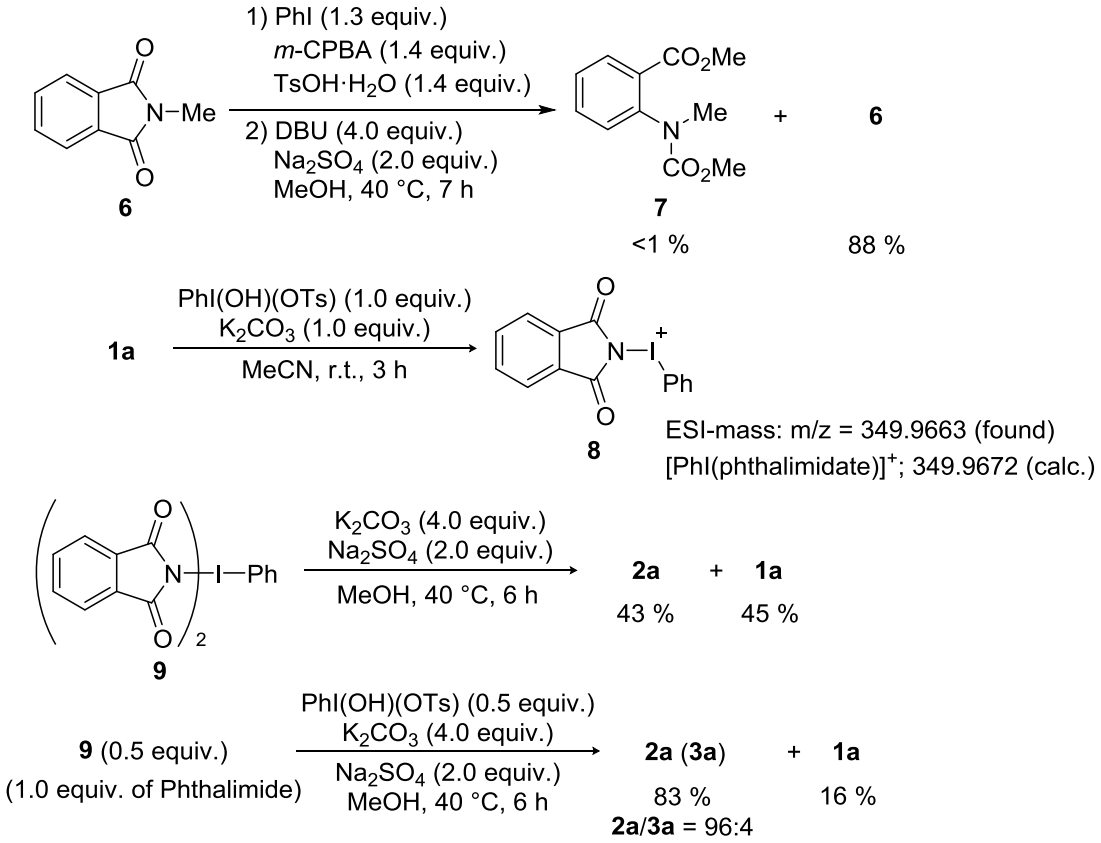
Table 3. Hofmann-type Rearrangement of Aliphatic Imides **4** Using Hypervelent Iodine (III) Generated in Situ



The author examined several reactions to clarify the mechanism of Hofmann-type rearrangement with hypervalent iodine (Scheme 2). *N*-methylphthalimide (**6**) was not converted into desired product (**7**) in optimized conditions, and the tratment of phthalimide with [hydroxy(tosyloxy)iodo]benzene (HTIB) and K_2CO_3 in methanol gave 349.9663 peak on high resolution ESI-MS analysis, which is assigned to $[PhI(phthalimidate)]^+$ (**8**)**,** calculated MS **:** 349.9672). These results suggested that first phthalimide-combined hypervalent iodine species was formed in the presence of base, and then methanol attacked carbonyl group. On the other hands, treatment of phenyliodine(III) bis[phthalimidate] (**9**)[9] in the presence of K_2CO_3 in methanol provided both 43 % yield of anthranilic acid derivatives (**2a**) and 45 % yield of phthalimide (**1a**).

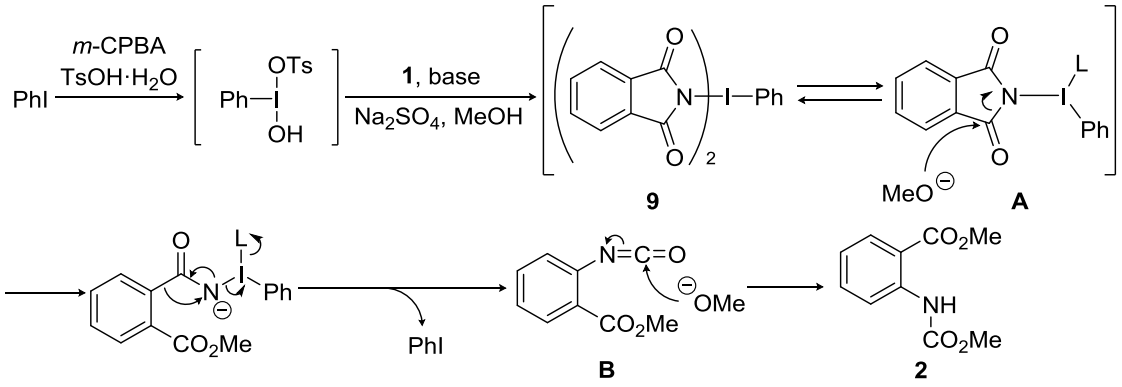
Moreover, addition of HTIB to the above methanol solution of **9** under the same reaction conditions increased the desired product (**2a** or **3a**) to 83 % yield and **1a** was decreased to 16 % yield. This result suggests that **9** was a key intermediate of the reaction, and re-oxidized phthalimide by HTIB was converted into the product.

Scheme 2. Mechanistic Study of Hofmann-Type Rearrangement of Phthalimide Derivatives



According to some blank experiments shown in Scheme 2, the author proposed the mechanism of Hofmann-type rearrangement, as shown in Scheme 3. HTIB is formed from PhI, *m*-CPBA, and TsOH•H_2O[7a]. This compound reacts with cyclic imide in the presence of base, and generates imide-combined hypervalent iodine intermediate (**9** or **A**). The intermediates **9** or **A** is attacked by methanol followed by the Hofmann rearrangement to give isocyanate (**B**). Finally, isocyanate **B** is transformed to carbamate product **2** by methanol.

Scheme 3. Plausible Reaction Mechanism for the Hofmann-Type Rearrangement of Imides



In conclusion, the author developed the new synthetic method of anthranilic acid and β- and γ-amino acid derivatives from cyclic imides with Hofmann-type rearrangement using hypervalent iodines. This reaction produces wide range of aromatic and aliphatic amino acid under mild conditions without any metal reagents. In addition, it is the first report to prepare imide-combined hypervalent iodine species in situ from iodoarene.

Experimental

1. General Methods. ^{1}H NMR spectra were measured on a JEOL ECS-400 (400 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; sep = septet; m = multiplet; br = broad), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on a JEOL ECS-400 (100 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm). High-resolution mass spectra were recorded by Thermo Fisher Scientific Exactive Orbitrap mass spectrometers. Infrared (IR) spectra were recorded on a JASCO FT/IR 4100 spectrometer. Single crystal X-ray diffraction data were collected at 173 K on a Bruker SMART APEX II CCD diffractometer with Mo Kα (λ = 0.71073) radiation and graphite monochromeater. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60GF254 0.25 mm) were used. The products were purified by column chromatography on neutral silica gel (Kanto Chemical Co., Inc. silica gel 60N, Prod. No. 37560-84; Merck silica gel 60, Prod. No. 1.09385.9929). Visualization was accomplished by UV light (254 nm), anisaldehyde, $KMnO_4$, and phosphomolybdic acid. In experiments that required dry solvents such as chloroform and methanol were distilled in prior to use.

2. General procedure for the Hofmann-type rearrangement of imides (1) using hypervalent iodine generated from iodoarene, *m*-CPBA, and *p*-toluenesulfonic acid in situ.

To prepare hypervalent iodines (0.33 mmol) were used iodobenzene (36.4 μL, 0.33 mmol), *m*-CPBA (94.9 mg, 0.36 mmol), and *p*-TsOH·H_2O (68.0 mg, 0.36 mmol) in $CHCl_3$ (1 mL), and the solution was stirred at room temperature for 2 h under argon atmosphere. The solvents were removed *in vacuo*, and the desired product was obtained in situ as a white solid. Then Na_2SO_4 (0.50 mmol, 71.0 mg) and MeOH (2 mL) was added, and the solution was stirred at 0 °C for 10 min. To the solution were added **1a** (36.8 mg, 0.25 mmol) and K_2CO_3 (138.2 mg, 1.0 mmol) at 0 °C, and the obtained mixture was stirred at room temperature for 2 h. Saturated $NaHCO_3$ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica-gel column chromatography (eluent: hexane/AcOEt = 5/1), to give the desired product **2a** (40.5 mg, 79% yield) and **3a** (5.0 mg, 14% yield).

Methyl 2-[(methoxycarbonyl)amino]benzoate (2a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.92 (s, 3H), 7.03 (td, *J* = 8.2, 1.2 Hz, 1H), 7.53 (td, *J* = 8.0, 1.2 Hz, 1H), 8.01 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.43 (dd, *J* = 8.2, 1.2 Hz, 1H), 10.51 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.2 (2C), 114.5, 118.8, 121.5, 130.8, 134.6, 141.7, 154.1, 168.5. IR (neat) 3299, 1740, 1690, 1600, 1535, 1459, 1272 cm^{-1}. MS (APCI) calcd for $C_{10}H_{12}NO_4$ $[M+H]^+$ 210.0761, found 210.0761.

Methyl anthranilate (3a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 5.71 (brs, 2H), 6.63 (t, *J* = 8.2 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 7.25 (td, *J* = 8.2, 1.6 Hz, 1H), 7.85 (dd, *J* = 8.2, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.4, 110.7, 116.2, 116.6, 131.2, 134.0, 150.4, 168.5. IR (neat) 3480, 3372, 1691, 1616, 1436, 1247 cm^{-1}. MS (APCI) calcd for $C_8H_{10}NO_2$ $[M+H]^+$ 152.0706, found 152.0702.

Methyl 2-[(methoxycarbonyl)amino]methylbenzoate (2b, 4- and 5-isomers): In Table 2, 4-:5- = 56:44. The 4-isomer and 5-isomer were separeted by recrystallization. 4-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.78 (s, 3H), 3.89 (s, 3H), 6.84 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 8.26 (s, 1H), 10.51 (brs, 1H). ^{13}C NMR (100 MHz, CDCl3) δ 22.1, 52.1, 52.2, 112.0, 119.1, 122.6, 130.8, 141.7, 145.7, 154.1, 168.5. 5-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.78 (s, 3H), 3.91 (s, 3H), 7.34 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.80 (d, *J* = 1.6 Hz, 1H), 8.30 (d, *J* = 8.7 Hz, 1H), 10.36 (brs, 1H). 13C NMR (100 MHz, CDCl3) δ 20.1, 52.2 (2C), 114.4, 118.8, 130.9, 131.0, 135.3, 139.3, 154.1, 168.5. IR (KBr) 3273, 1740, 1688, 1594, 1533, 1440, 1249 cm^{-1}. MS (APPI) calcd for $C_{11}H_{13}NO_4$ $[M]^+$ 223.0839, found 223.0841.

Methyl *tert*-butyl-2-[(methoxycarbonyl)amino]benzoate (2c, 4- and 5-isomers): In Table 2, 4-:5- = 54:46. 4-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.79 (s, 3H), 3.89 (s, 3H), 7.05 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.91 (t, *J* = 8.5 Hz, 1H), 8.54 (d, *J* = 1.8 Hz, 1H), 10.52 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8 (3C), 35.3, 52.1 (2C), 111.8, 115.7, 118.8, 130.5, 141.6, 154.1, 158.5, 168.3. 5-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 3.77 (s, 3H), 3.91 (s, 3H), 7.57 (dd, *J* = 9.1, 2.5 Hz, 1H), 8.00 (d, *J* = 2.5 Hz, 1H), 8.34 (d, *J* = 9.1 Hz, 1H), 10.39 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1 (3C), 34.1, 52.0 (2C), 114.1, 118.6, 127.1, 131.8, 139.2, 114.3, 154.1, 168.5. IR (neat) 3302, 1739, 1693, 1582, 1524, 1438, 1260 cm^{-1}. MS (APCI) calcd for $C_{14}H_{20}NO_4$ $[M+H]^+$ 266.1387, found 266.1377.

Methyl bromo-2-[(methoxycarbonyl)amino]benzoate (2d, 4- and 5-isomers): In

Table 2, 4-:5- = 55:45. 4-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.91 (s, 3H), 7.16 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 8.69 (d, *J* = 2.0 Hz, 1H), 10.53 (brs, 1H). ^{13}C NMR (100 MHz, CDCl3) δ 52.4, 52.5, 113.1, 121.7, 124.8, 129.6, 131.9, 142.6, 153.9, 168.0. 5-Isomer: ^{1}H NMR (400 MHz, CDCl3) δ 3.79 (s, 3H), 3.92 (s, 3H), 7.61 (dd, *J* = 9.1, 2.5 Hz, 1H), 8.12 (d, *J* = 2.5 Hz, 1H), 8.36 (d, *J* = 9.1 Hz, 1H), 10.42 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.40, 52.45, 113.8, 116.0, 120.5, 133.3, 137.3, 140.8, 153.8, 167.3. IR (KBr) 3259, 1739, 1689, 1593, 1519, 1433, 1249 cm^{-1}. MS (APPI) calcd for $C_{10}H_{10}BrNO_4$ $[M]^+$ 286.9788, found 286.9789.

Methyl 2-[(methoxycarbonyl)amino]nitrobenzoate (2e, 4- and 5-isomers): In Table 2, 4-:5- = 42:58. The 4-isomer and 5-isomer were separeted by column chromatography. 4-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 3.99 (s, 3H), 7.82 (dd, *J* = 8.9, 2.1 Hz, 1H), 8.17 (d, *J* = 8.9 Hz, 1H), 9.35 (d, *J* = 2.1 Hz, 1H), 10.57 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.7, 53.0, 113.8, 115.6, 118.7, 132.1, 142.7, 151.3, 153.7, 167.0. 5-Isomer: 1H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 3H), 4.00 (s, 3H), 8.37 (dd, *J* = 9.4, 2.8 Hz, 1H), 8.67 (d, *J* = 9.4 Hz, 1H), 8.91 (d, *J* = 2.8 Hz, 1H), 10.87 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.9, 53.0, 114.1, 118.8, 127.0, 129.3, 141.2, 146.9, 153.5, 167.0. IR (KBr) 3263, 1751, 1692, 1516, 1439, 1352, 1251 cm^{-1}. MS (APCI) calcd for $C_{10}H_9N_2O_6$ $[M–H]^-$ 253.0455, found 253.0463.

Methyl methoxy-2-[(methoxycarbonyl)amino]benzoate (2f, 4- and 5-isomers): In Table 2, 4-:5- = 63:37. The 4-isomer and 5-isomer were separeted by column chromatography. 4-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.869 (s, 3H), 3.873 (s, 3H), 6.55 (dd, *J* = 8.9, 2.7 Hz, 1H), 7.92 (d, *J* = 8.9 Hz, 1H), 8.06 (d, *J* = 2.7 Hz, 1H), 10.72 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.9, 52.2, 55.4, 102.3, 107.1, 109.0, 132.4, 143.9, 154.1, 164.5, 168.3. 5-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H), 3.81 (s, 3H), 3.92 (s, 3H), 7.12 (dd, *J* = 9.2, 3.2 Hz, 1H), 7.49 (d, *J* = 3.2 Hz, 1H), 8.33 (d, *J* = 9.2 Hz, 1H), 10.19 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.2, 52.3, 55.6, 114.4, 115.4, 120.4, 121.3, 135.4, 153.8, 154.2, 168.1. IR (KBr) 3258, 1740, 1687, 1598, 1533, 1431, 1278 cm^{-1}. MS (APPI) calcd for $C_{11}H_{13}NO_5$ $[M]^+$ 239.0788, found 239.0790.

Methyl fluoro-2-[(methoxycarbonyl)amino]benzoate (2g, 3- and 6-isomers): In Table 2, 3-:6- = 61:39. The 3-isomer and 6-isomer were separeted by column chromatography. 3-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.92 (s, 3H), 7.18 (td, *J* = 8.2, 5.0 Hz, 1H), 7.33 (t, *J* = 8.2 Hz, 1H), 7.73 (dd, *J* = 8.2, 1.2 Hz, 1H),

8.38 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.4, 52.7, 106.0 (d, *J*C–F = 14.4 Hz), 110.1 (d, *J*C–F = 24.0 Hz), 114.8 (d, *J*C–F = 3.8 Hz), 134.4 (d, *J*C–F = 10.5 Hz), 141.8 (d, *J*C–F = 2.9 Hz), 153.9, 162.2 (d, *J*C–F = 258.7 Hz), 167.1 (d, *J*C–F = 3.8 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -116.5. 6-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.96 (s, 3H), 6.79 (ddd, *J* = 11.0, 8.2, 1.2 Hz, 1H), 7.45 (td, *J* = 8.7, 6.1 Hz, 1H), 8.17 (d, *J* = 8.7 Hz, 1H), 9.96 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.5, 52.9, 120.9 (d, *J*C–F = 21.1 Hz), 123.7 (d, *J*C–F = 1.9 Hz), 125.1 (d, *J*C–F = 8.6 Hz), 125.9 (d, *J*C–F = 3.8 Hz), 127.5 (d, *J*C–F = 13.4 Hz), 154.0, 156.2 (d, *J*C–F = 252.9 Hz), 166.8 (d, *J*C–F = 3.8 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -105.4. IR (KBr) 3345, 1739, 1702, 1512, 1445, 1280, 1238 cm^{-1}. MS (APPI) calcd for $C_{10}H_{10}NO_4F$ $[M]^+$ 227.0588, found 227.0579.

Methyl 2-[(methoxycarbonyl)amino]-4,5-dimethylbenzoate (2h): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 2.30 (s, 3H), 3.77 (s, 3H), 3.89 (s, 3H), 7.74 (s, 1H), 8.21 (s, 1H), 10.36 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0, 20.5, 52.0, 52.1, 112.2, 119.7, 129.9, 131.3, 139.6, 144.4, 154.1, 168.5. IR (KBr) 3253, 1733, 1690, 1592, 1524, 1432, 1226 cm^{-1}. MS (APPI) calcd for $C_{12}H_{15}NO_4$ $[M]^+$ 237.0996, found 237.0096.

Methyl 4,5-dichloro-2-[(methoxycarbonyl)amino]benzoate (2i): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 3.93 (s, 3H), 8.07 (s, 1H), 8.66 (s, 1H), 10.43 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.6, 52.7, 114.0, 120.5, 125.1, 132.0, 139.0, 140.7, 153.7, 166.9. IR (KBr) 3256, 1736, 1694, 1580, 1503, 1311, 1220 cm^{-1}. MS (APPI) calcd for $C_{10}H_9NO_4$ $[M]^+$ 276.9903, found 276.9903.

Methyl 3-[(methoxycarbonyl)amino]2-naphthoate (2j): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82 (s, 3H), 3.97 (s, 3H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 2H), 8.59 (s, 1H), 8.79 (s, 1H), 10.42 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.2, 52.5, 115.4, 115.5, 125.1, 127.4, 127.9, 128.9, 129.2, 133.2, 136.4, 136.6, 154.3, 168.4. IR (KBr) 3295, 1733, 1696, 1547, 1448, 1292, 1213 cm^{-1}. MS (APPI) calcd for $C_{14}H_{13}NO_4$ $[M]^+$ 259.0839, found 259.0839.

Crystal data for 2j: Formula $C_{14}H_{13}NO_4$, colorless, crystal dimensions 0.30 × 0.30 × 0.20 mm^3, tetragonal, space group *P*4 (3), *a* = 8.0618(11) Å, *b* = 8.0618(11) Å, *c* = 37.917(5) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, *V* = 2464.4(6) Å3, *Z* = 8, ρ_{calc} = 1.398 g cm^{-3}, F(000) = 1088, μ(MoKα) = 0.103 mm^{-1}, *T* = 173 K. 13721 reflections collected, 5515 independent reflections with $I > 2\sigma(I)$ ($2\theta_{max}$ = 27.56°), and 347 parameters were used for the solution of the structure. The non-hydrogen atoms were refined

anisotropically. Flack x = 0.1643. *R*1 = 0.0481 and *wR*2 = 0.1060. GOF = 1.023. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-855556. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

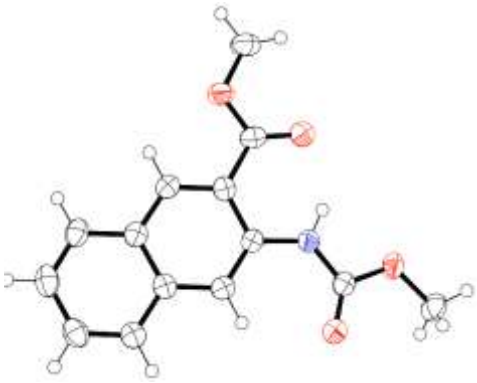


Figure S1. OPTEP drawing of **2j**.

Methyl 2'-amino-(1,1'-bipheyl)-2-carboxylate (3k): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.19 (s, 3H), 7.10 (d, *J* = 8.5 Hz, 1H), 7.35 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.49 (dd, *J* = 8.5, 7.4 Hz, 1H), 7.61 (dd, *J* = 8.2, 7.3 Hz, 1H), 7.81 (dd, *J* = 8.2, 7.6 Hz, 1H), 8.24-8.28 (m, 2H), 8.50 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.9, 114.9, 118.6, 122.0, 123.4, 123.7, 124.8, 128.4, 128.7, 129.7, 133.6, 134.0, 134.2, 153.9. IR (KBr) 3439, 1763, 1664, 1607, 1440, 1329, 1238 cm^{-1}. MS (APCI) calcd for $C_{14}H_{12}NO_4$ $[M–H]^+$ 226.0863, found 226.0862.

Methyl [(methoxycarbonyl)amino]nicotinate (2l, 3- and 4-isomers): In Table 2, 3-:4- = 83:17. The 3-isomer and 4-isomer were separeted by column chromatography. 3-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 3.97 (s, 3H), 8.35 (d, *J* = 6.0 Hz, 1H), 8.58 (d, *J* = 6.0 Hz, 1H), 9.12 (s, 1H), 10.59 (brs, 1H). 13C NMR (100 MHz, CDCl3) δ 52.5, 52.8, 110.3, 112.2, 148.1, 152.5, 153.4, 154.3, 167.8. 4-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82 (s, 3H), 3.97 (s, 3H), 7.76 (d, *J* = 5.2 Hz, 1H), 8.38 (d, *J* = 5.2 Hz, 1H), 9.78 (s, 1H), 10.05 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.7, 52.9, 120.3, 122.5, 136.3, 142.5, 143.0, 153.6, 167.2. IR (KBr) 3255, 1743, 1695, 1597, 1519, 1442, 1302, 1229 cm^{-1}. MS (APPI) calcd for $C_9H_{11}N_2O_4$ $[M+H]^+$ 211.0713, found 211.0712.

Ethyl 2-[(ethoxycarbonyl)amino]benzoate (2m): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.1 Hz, 3H), 1.41 (t, *J* = 7.1 Hz, 3H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 7.02 (td, *J* = 8.0, 1.2 Hz, 1H), 7.52 (td, *J* = 8.7, 1.6 Hz, 1H), 8.02 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.44 (dd, *J* = 8.7, 1.2 Hz, 1H), 10.51 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 61.1, 61.2, 114.7, 118.7, 121.3, 130.8, 134.4, 141.9, 153.7, 168.1. IR (neat) 3256, 1727, 1693, 1595, 1533, 1452, 1244 cm^{-1}. MS (APPI) calcd for $C_{12}H_{15}NO_4$ $[M]^+$ 237.0096, found 237.0096.

2”,2”,2”-Trifluoroethyl 2-{[(2’,2’,2’-trifluoroethoxy)carbonyl]amino}benzoate (2n): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.58 (q, *J* = 8.5 Hz, 2H), 4.70 (q, *J* = 8.5 Hz, 2H), 7.13 (td, *J* = 8.2, 1.2 Hz, 1H), 7.62 (td, *J* = 8.2, 1.6 Hz, 1H), 8.08 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.42 (dd, *J* = 8.2, 1.2 Hz, 1H), 10.41 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 60.9 (q, *J*C–F = 37.4 Hz), 61.0 (q, *J*C–F = 37.4 Hz), 113.4, 119.1, 122.6, 122.87 (q, *J*C–F = 278.8 Hz), 122.92 (q, *J*C–F = 278.8 Hz), 131.2, 135.8, 141.3, 151.4, 166.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ -73.9, -73.4. IR (KBr) 3289, 1752, 1704, 1599, 1535, 1452, 1285, 1178 cm^{-1}. MS (APPI) calcd for C12H8F6NO4 $[M–H]^-$ 344.0352, found 344.0365.

Dimethyl oxybis{2-[(methoxycarbonyl)amino]benzoate} (2o, 4,5’-, 4,4’-, and 5,5’-isomers): In Table 2, 4,5’-:4,4’-:5,5’- = 61:22:17. 4,5’-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.80 (s, 3H), 3.89 (s, 6H), 6.53 (dd, *J* = 8.9, 3.0 Hz, 1H), 7.29 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.73 (d, *J* = 3.0 Hz, 1H), 7.95 (d, *J* = 8.9 Hz, 1H), 8.06 (d, *J* = 2.5 Hz, 1H), 8.48 (d, *J* = 9.0 Hz, 1H), 10.42 (brs, 1H), 10.64 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.26 (2C), 52.29, 52.4, 106.8, 108.8, 110.1, 112.1, 120.5, 122.4, 127.0, 132.8, 138.6, 143.8, 148.7, 153.8 (2C), 162.9, 167.6, 168.0. 4,4’-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 6H), 3.90 (s, 6H), 6.69 (dd, *J* = 8.9, 2.3 Hz, 2H), 8.01 (d, *J* = 8.9 Hz, 2H), 8.16 (d, *J* = 2.3 Hz, 2H), 10.64 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.1 (2C), 52.4 (2C), 109.0 (2C), 110.1 (2C), 115.7 (2C), 132.9 (2C), 143.8 (2C), 154.0 (2C), 160.9 (2C), 168.0 (2C). 5,5’-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 6H), 3.88 (s, 6H), 7.21 (dd, *J* = 9.2, 3.0 Hz, 2H), 7.59 (d, *J* = 3.0 Hz, 2H), 8.41 (d, *J* = 9.2 Hz, 2H), 10.33 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.1 (2C), 52.3 (2C), 110.1 (2C), 120.2 (2C), 120.6 (2C), 125.2 (2C), 137.5 (2C), 151.0 (2C), 154.1 (2C), 167.7 (2C). IR (KBr) 3290, 1741, 1694, 1595, 1526, 1436, 1249 cm^{-1}. MS (APCI) calcd for $C_{20}H_{21}N_2O_9$ $[M+H]^+$ 433.1242, found 433.1239.

***N*-(Methoxycarbonyl)-β-alanine methyl ester (5a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ

2.55 (t, J = 6.1 Hz, 2H), 3.45 (q, J = 6.1 Hz, 2H), 3.66 (s, 3H), 3.70 (s, 3H), 5.23 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.2, 36.5, 51.8, 52.1, 156.9, 172.8. IR (neat) 3346, 1725, 1533, 1441, 1256 cm^{-1}. MS (ESI) calcd for $C_6H_{11}NO_4Na$ $[M+Na]^+$ 184.0580, found 184.0580.

Methyl [(methoxycarbonyl)amino]methylpropanoate (5b, 2- and 3-isomers): In Table 3, 2-:3- = 56:44. 2-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (d, J = 7.3 Hz, 3H), 2.67-2.75 (m, 1H), 3.26-3.42 (m, 2H), 3.66 (s, 3H), 3.70 (s, 3H), 5.24 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 39.8, 43.3, 51.7, 52.0, 157.0, 175.6. 3-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (d, J = 6.8 Hz, 3H), 2.48-2.58 (m, 2H), 3.66 (s, 3H), 3.69 (s, 3H), 4.01-4.18 (m, 1H), 5.07 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 40.2, 44.0, 51.5, 51.9, 156.1, 171.8. IR (neat) 3342, 1727, 1532, 1440, 1255 cm^{-1}. MS (ESI) calcd for $C_7H_{14}NO_4$ $[M+H]^+$ 176.0917, found 176.0920.

Methyl butyl-[(methoxycarbonyl)amino]propanoate (5c, 2- and 3-isomers): In Table 3, 2-:3- = 59:41. 2-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.0 Hz, 3H), 1.23-1.39 (m, 4H), 1.44-1.56 (m, 2H), 2.57-2.67 (m, 1H), 3.25-3.34 (m, 1H), 3.37-3.46 (m, 1H), 3.66 (s, 3H), 3.70 (s, 3H), 5.14 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.4, 28.2, 29.1, 42.0, 45.4, 51.7, 52.0, 157.0, 175.5. 3-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.0 Hz, 3H), 1.24-1.39 (m, 5H), 1.56-1.67 (m, 1H), 2.54 (t, J = 5.2 Hz, 2H), 3.66 (s, 3H), 3.68 (s, 3H), 3.89-4.00 (m, 1H), 5.19 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.3, 29.3, 34.0, 38.8, 48.0, 51.6, 51.9, 156.4, 172.0. IR (neat) 3342, 1729, 1533, 1441, 1254 cm^{-1}. MS (ESI) calcd for $C_{10}H_{20}NO_4$ $[M+H]^+$ 218.1387, found 218.1389.

Methyl benzyl-[(methoxycarbonyl)amino]propanoate (5d, 2- and 3-isomers): In Table 3, 2-:3- = 57:43. 2-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77-2.84 (m, 1H), 2.90-2.99 (m, 2H), 3.27-3.35 (m, 1H), 3.36-3.46 (m, 1H), 3.61 (s, 3H), 3.65 (s, 3H), 5.32 (brs, 1H), 7.12-7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6, 41.7, 47.0, 51.6, 51.9, 126.4, 128.3(2C), 128.6(2C), 138.0, 156.1, 174.4. 3-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42-2.55 (m, 2H), 2.77-2.84 (m, 1H), 2.90-2.99 (m, 1H), 3.61 (s, 3H), 3.63 (s, 3H), 4.16-4.25 (m, 1H), 5.43 (brs, 1H), 7.12-7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.2, 40.0, 49.2, 51.5, 51.8, 126.5, 128.3(2C), 129.1(2C), 137.4, 156.8, 171.8. IR (neat) 3341, 1728, 1532, 1442, 1259 cm^{-1}. MS (ESI) calcd for $C_{13}H_{18}NO_4$ $[M+H]^+$ 252.1230, found 252.1230.

Methyl 3-[(methoxycarbonyl)amino]-2-methylbutanoate (5e): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (d, *J* = 6.8 Hz, 3H), 1.20 (d, *J* = 7.3 Hz, 3H), 2.59-2.68 (m, 1H), 3.36 (s, 3H), 3.70 (s, 3H), 3.85-3.98 (m, 1H), 5.36 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 19.3, 43.9, 48.8, 51.6, 51.9, 156.6, 175.5. IR (neat) 3336, 1724, 1530, 1453, 1246 cm^{-1}. MS (ESI) calcd for $C_8H_{16}NO_4$ $[M+H]^+$ 190.1074, found 190.1075.

Methyl [(methoxycarbonyl)amino]dimethylpropanoate (5f, 2- and 3-isomers): In Table 3, 2-:3- = 70:30. 2-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 6H), 3.30 (d, *J* = 6.6 Hz, 2H), 3.66 (s, 3H), 3.69 (s, 3H), 5.21 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.9 (2C), 44.0, 48.7, 51.4, 51.9, 157.3, 177.4. 3-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (s, 6H), 2.69 (s, 2H), 3.62 (s, 3H), 3.68 (s, 3H), 5.21 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2 (2C), 43.5, 51.2, 51.4, 52.0, 155.5, 171.6. IR (neat) 3358, 1725, 1530, 1469, 1257 cm^{-1}. MS (ESI) calcd for $C_8H_{16}NO_4$ $[M+H]^+$ 190.1074, found 190.1076.

Methyl 4-[(methoxycarbonyl)amino]butanoate (5g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80-1.88 (m, 2H), 2.37 (t, *J* = 7.3 Hz, 2H), 3.23 (q, *J* = 6.5 Hz, 2H), 3.66 (s, 3H), 3.68 (s, 3H), 4.93 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.1, 31.2, 40.3, 51.6, 52.0, 157.1, 173.7. IR (neat) 3345, 1724, 1535, 1442, 1260 cm^{-1}. MS (ESI) calcd for $C_7H_{14}NO_4$ $[M+H]^+$ 176.0917, found 176.0917.

Methyl 3-{[(methoxycarbonyl)amino]methyl}-5-methylhexanoate (5h): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 1.07-1.23 (m, 2H), 1.65 (sep, *J* = 6.6 Hz, 1H), 2.08-2.19 (m, 1H), 2.29 (d, *J* = 6.6 Hz, 2H), 2.96-3.12 (m, 1H), 3.16-3.32 (m, 1H), 3.36 (s, 3H), 3.67 (s, 3H), 5.02 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.5(2C), 25.1, 33.5, 37.1, 41.4, 44.7, 51.5, 51.9, 157.2, 173.6. IR (neat) 3347, 1731, 1536, 1439, 1254 cm^{-1}. MS (ESI) calcd for $C_{11}H_{22}NO_4$ $[M+H]^+$ 232.1543, found 232.1543.

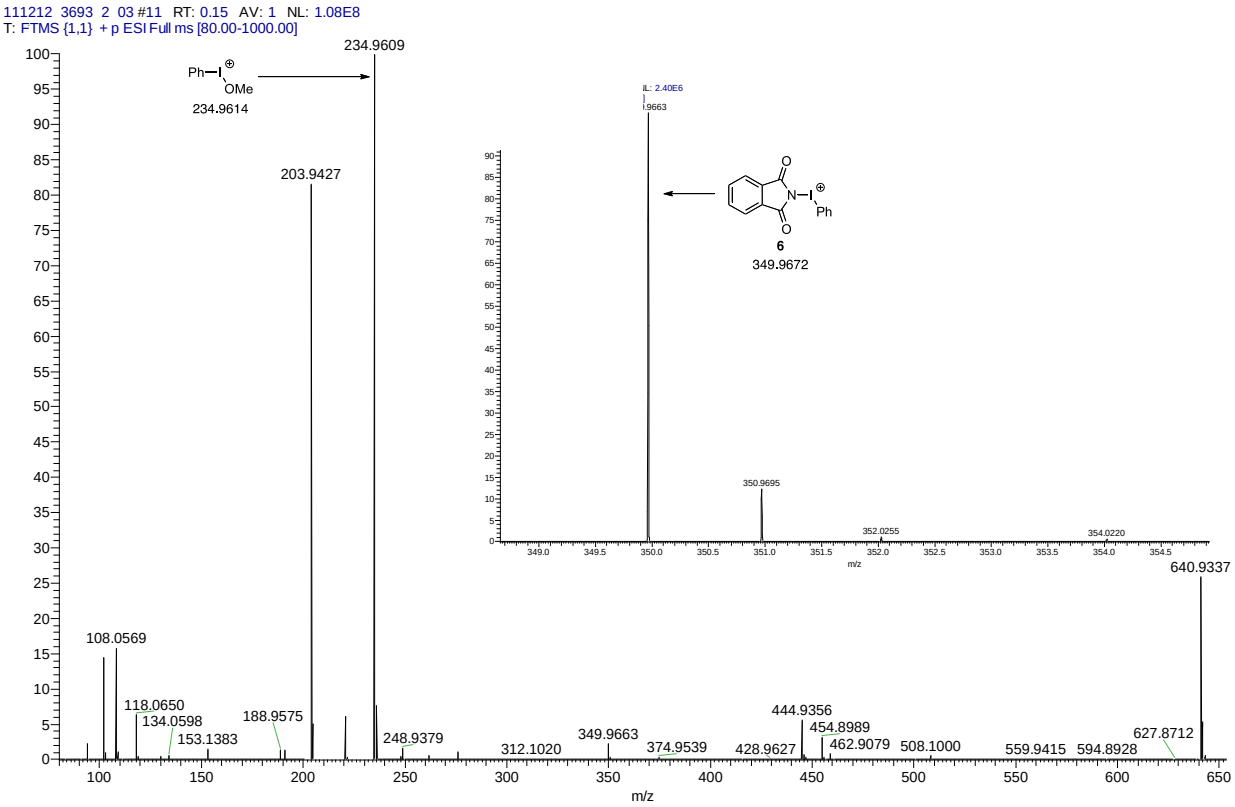
Phenyliodine (III) bis[phthalimidate] (7): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.23 (t, *J* = 8.0 Hz,2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.87 (s, 8H). ^{13}C NMR (100 MHz, DMSO) δ 122.9 (5C), 127.7, 130.7 (2C), 132.6 (4C), 134.3 (4C), 137.1 (2C), 169.2 (4C). IR (Nujol) 1736, 1692, 1670, 1611, 1279, 1117 cm^{-1}. MS (ESI) calcd for $C_{14}H_9INO_2$ $[M–Phthalimidate]^+$ 349.9668, found 349.9672.

3. General procedure for Methoxycarbonylation of Methyl anthranilate 3a.

To a solution of methyl anthranilate **3a** (37.8 mg, 0.25 mmol) in toluene (1 mL) was added methyl chloroformate (38.4 μL, 0.50 mmol) at room temperature under argon atomosphere, and the solution was refluxed for 8 h. After removal of the solvent under reduced pressure, the pure methyl 2-[(methoxycarbonyl)amino]benzoate **2a** was obtained as a colorless crystal (51.0 mg, >99% yield) without further purification by collumn chromatography.

4. In Situ HRMS-ESI Study.

To the solution of PhI(OH)(OTs) (39.1 mg, 0.10 mmol) and phthalimide **1a** (14.7 mg, 0.10 mmol) in MeCN (1 mL) was added K_2CO_3 (13.8 mg, 0.10 mmol), and the mixture stirred at room temperature for 3 h. The reaction mixture was diluted with MeCN/MeOH prior to the injection into the mass spectrometer.



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Chapter 2

Preparation of Novel Imide-combined Hypervalent Iodines: Heteroaryl(aryl)-iodonium Imides

Abstract

(Heteroaryl)(aryl)iodonium imides were prepared from various heteroaromatics with (diacetoxyiodo)benzene (DIB) and bis(sulfonyl)imides. These novel hypervalent iodines were stable as white solid, and the unique structure was observed from two types of iodane (III), imide-combined λ^3-iodane and asymmetric diaryliodonium salt containing heterocycles.

Introduction

Heteroaryl-contained hypervalent iodine is attractive reagent to obtain various heteroaryl substituted compounds[1,2]. In particular, C-N bond formation with hetroaryl hypervalent iodine is much important to use for synthesis of amino-heteroaryl rings, which are included in a lot of biological active and medicinal compounds[3]. Nevertheless, synthesis of heteroaryliodane containing I-N bond had been less studied. Recently, Suna group reported (indolyl)(phenyl)iodonium azide and azidation of indole[4], however, the iodonium azide was not stable and required heavy metal for C-N bond formation.

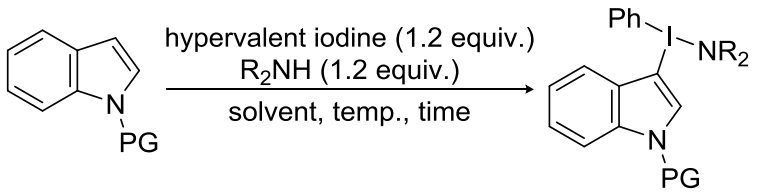
On the other hands, imide-combined hypervalent iodine was used as oxidative C-N bond formation. Muñis group reported useful C-N bond introduction to alkene, alkyne, and so on, using imide-combined hypervalent iodine[5], and the author also reported Hofmann-type rearrangement via imide-combined hypervalent iodine (Chapter 1)[6]. Here, the author reported preparation of novel imide-combined hypervalent iodines, heteroaryl(aryl)iodinum imides, which were stable as white solid and easily obtained from heteroaryl compounds.

Results and Discussion

First, the author used indole as a model compound, and screened the reaction conditions for preparation of (indolyl)(aryl)iodonium imide (**2**) (Table 1). MeCN and a mixture of MeCN/DCE(2:1) were effective solvents (entries 1-8), however, PhI(OAc)NR_2 generated in situ from hypervalent iodines and bis(sulfonyl)imids were sometimes precipitated in MeCN and the yield was not reproducible. DIB is the best hypervalent iodine reagent (entries 9, 10). Using *t*-butoxycalbonyl (Boc), benzoyl (Bz), and tosyl (Ts) as a *N*-protecting group, desired products (**2**) were obtained in good yield (entries 11-13). On the other hands, BzTsNH and PhTsNH instead of Ts_2NH did not give **2**

(entries 14, 15). From these results, the author believed that the active hypervalent iodine compound, $PhI(OAc)NR_2$, is not formed from the reaction with BzTsNH or PhTsNH, and treatment of *N*-Pivalpylindole (**1**) with DIB(1.2 equiv.) and Ts_2NH (1.2 equiv.) in MeCN/DCE(2:1) at 50 ˚C (entry 7) is the best conditions.

Table1. Screening for Preparation of Indolyl(phenyl)iodonium Imide **2**



1 **2**

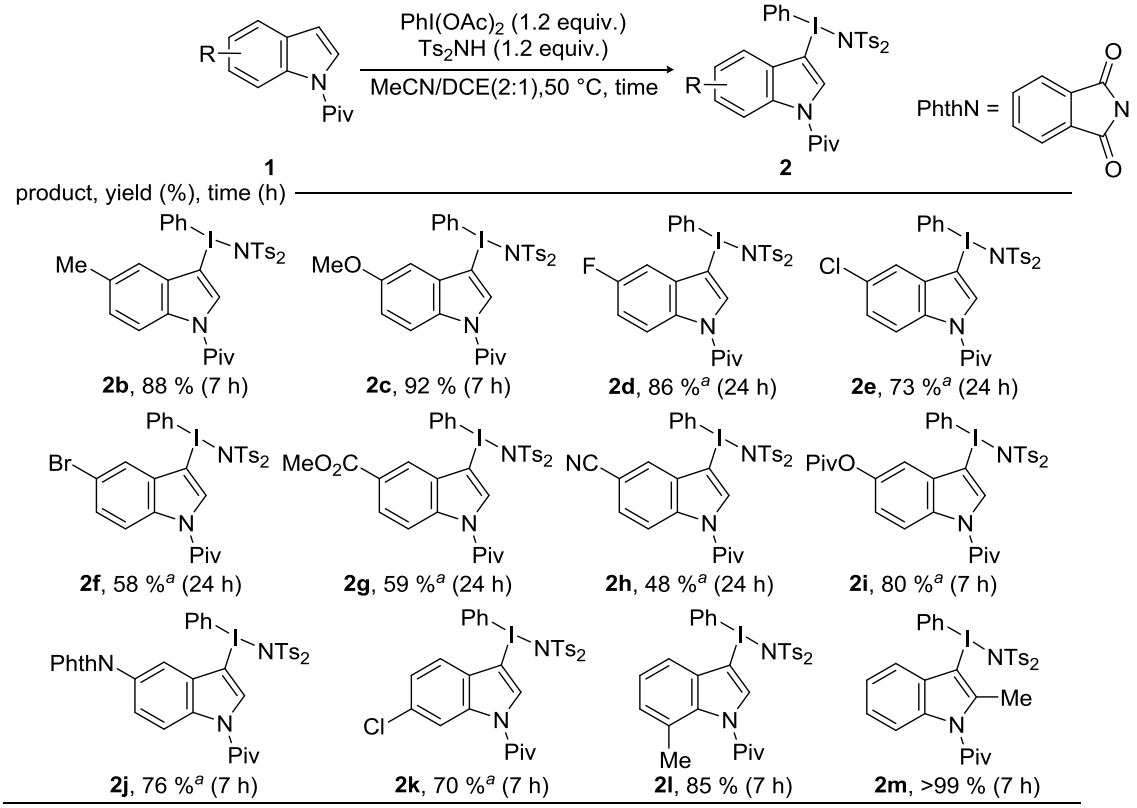
entry	PG	hypervalent iodine	R	solvent	temp. (°C)	time (h)	yield (%)
1	Piv	DIB	2Ts	MeCN	r.t.	3	95
2	Piv	DIB	2Ts	DCM	r.t.	7	83
3	Piv	DIB	2Ts	$CHCl_3$	r.t.	7	59
4	Piv	DIB	2Ts	toluene	r.t.	7	42
5	Piv	DIB	2Ts	THF	r.t.	7	0
6	Piv	DIB	2Ts	MeOH	r.t.	7	11
7	Piv	DIB	2Ts	MeCN/DCE(2:1)	50	7	90
8	Piv	DIB	2Ts	MeCN/TFE(2:1)	r.t.	7	65
9	Piv	BTI	2Ts	MeCN/DCE(2:1)	r.t.	7	43
10	Piv	HTIB	2Ts	MeCN/DCE(2:1)	r.t.	7	19
11	Boc	DIB	2Ts	MeCN/DCE(2:1)	50	7	26
12	Bz	DIB	2Ts	MeCN/DCE(2:1)	50	7	68
13	Ts	DIB	2Ts	MeCN/DCE(2:1)	50	7	66
14	Piv	DIB	Bz,Ts	MeCN	50	24	N.R.
15	Piv	DIB	Ph,Ts	MeCN	50	24	N.R.

N.R.= no reaction

Next, the author examined the preparation of (indolyl)(aryl)iodonium imides (**2**) from various substituted N-protected indoles (**1**) under optimized reaction conditions (Table 2). The reaction of 5-substituted indole bearing Me (**1b**), MeO (**1c**), F (**1d**), Cl (**1e**), PivO (**1i**), and PhthN (**1j**) groups gave the corresponding 5-substituted (indolyl)(aryl)iodonium imides (**2b**-**2e**, **2i**, **2j**) in high yields, respectively. (Indolyl)(aryl)iodonium imides bearing an electron-withdrawing group, such as Br (**1f**), CO_2Me (**1g**), and CN (**1h**), were also converted into desire products in good yields (**2f**-**2h**), respectively. (Indolyl)(aryl)iodonium imides bearing other monosubstituted indoles at different position were also transformed into the corresponding products in

good to high yields (**2k**-**2m**), respectively. In all substrates that the author examined, iodonium imides bonded at 3-position of indoles were observed and those imides bonded at 2-position of indoles were not observed at all.

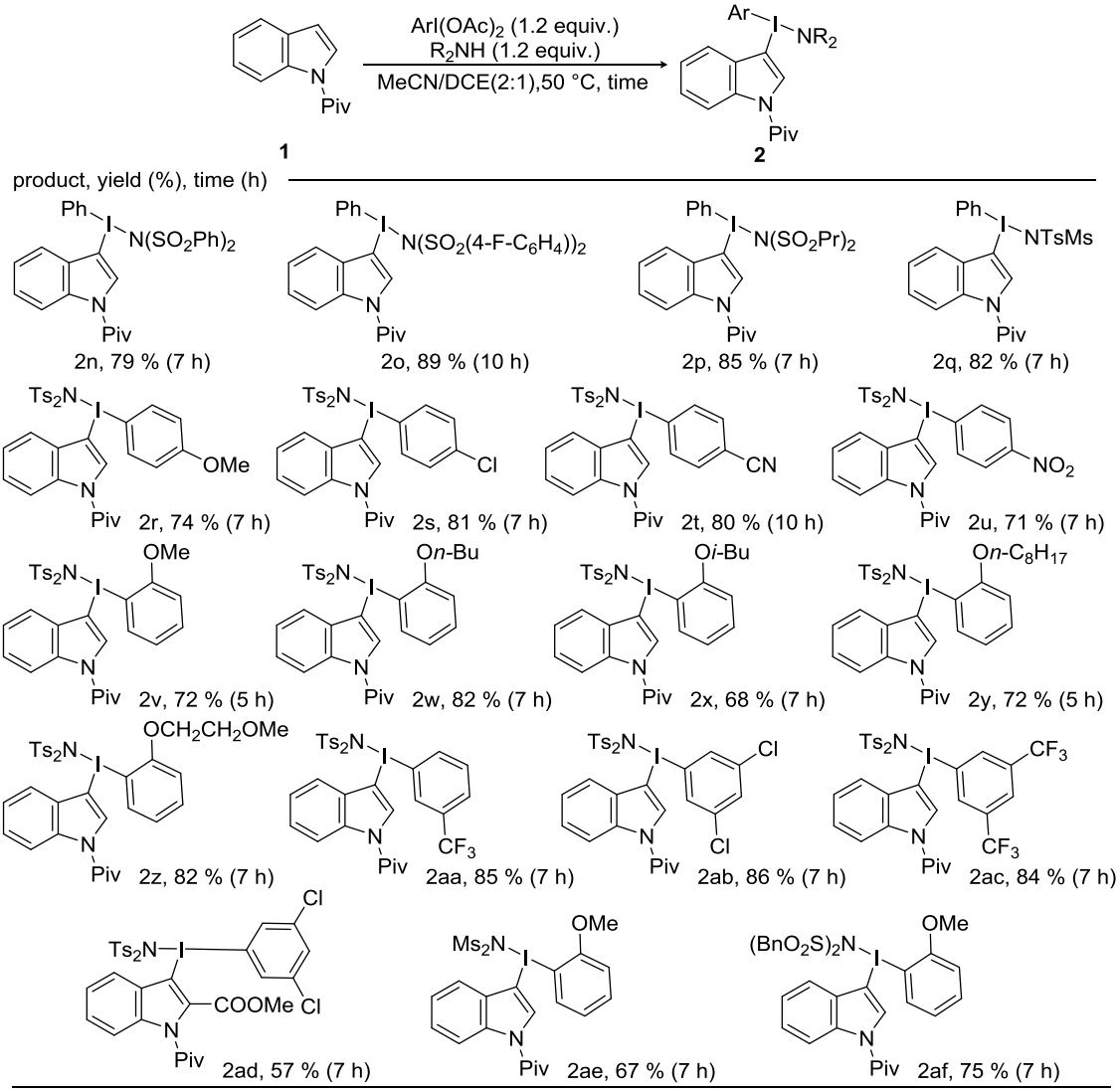
Table 2. Screening for Preparation of Indolyl(phenyl)iodonium Imides **2**



[a] DIB (1.5 equiv.) and Ts_2NH (1.5 equiv.) were used.

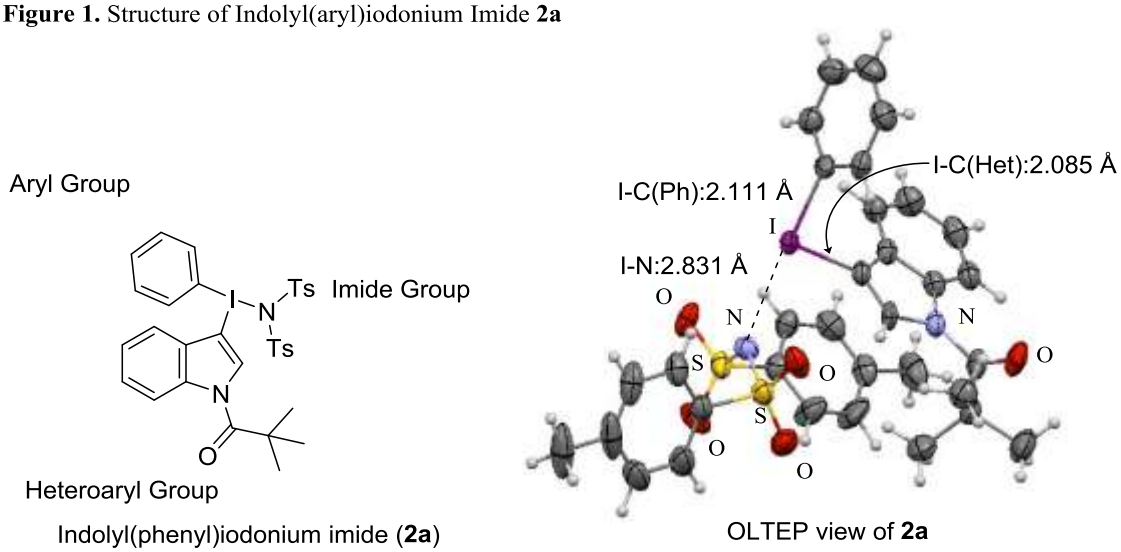
Then, the author also screened various bis(sulfonyl)imides and (diacetoxyiodo)arenes to optimized reaction conditions (Table 3). The formation of **2** proceeded with high conversion and the desired products were obtained in high yields (**2n**-**2ac**), respectively. In addition, the product **2** with methyl 1-pivaloylindole-2-carboxylate, Ms_2NH or $(BnSO_2)_2NH$ could be isolated using 1-(diaceetoxyiodo)-3,5-dichlorobenzene or 1-(diacetoxyiodo)-2-methoxybenzene instead of DIB, although **2** with DIB could not be isolated[7] (**2ae**-**af**).

Table 3. Screening for Preparation of Indolyl(aryl)iodonium Imides **2**



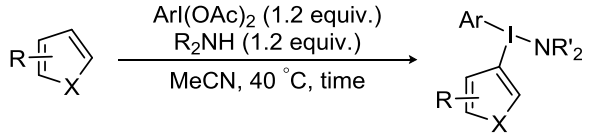
The crystal structure of (indolyl)(phenyl)iodonium imide (**2a)** is depicted in Figure 1. It displays that the bond distance of I-N, I-C (aryl) and I-C (het) are 2.831 Å, 2.111 Å, and 2.085 Å, respectively. Both I-C bond lengths are the same as I-C (aryl) bond length of the previously reported hypervalent iodines[4]. I-N bond length is similar to that of OTf, $OCOCF_3$, N_3 group in diaryliodonium salt[3h,8]. The author believes as follows, the above result suggest that Ts_2N group may be easily removable, electron density on iodine atom is extremely low, and therefore, nucleophilic attack to iodine atom followed by amination with imide may occur smoothly.

Figure 1. Structure of Indolyl(aryl)iodonium Imide **2a**



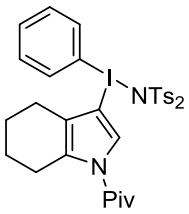
Moreover, the author succeeded in the preparation of heteroaryl(aryl)iodonium imide with heteroaromatic derivatives instead of indole derivatives (Table 4). The treatment of pyrrole derivatives, such as 4,5,6,7-tetrahydroindole (**3a**) and 3,5-dimethyl-1-ethoxycarbonylpyrrole (**3b**), with DIB and Ts_2NH gave desired products (**4a,b**) in high yields, respectively. The same treatment of 3,5-dimethylpyrrazole provided heteroaryl(aryl)iodonium imide (**4c**) in high yield using 1-(diacetioxyiodo)-2-methoxybenzene. Indazole (**3d**) was transformed to **4d** without any *N*-protection group. Sulfur-containing heteroaryl(aryl)iodonium imides (**4e,f**) were also obtained from thiophene derivatives (**3e,f**), respectively. In addition, the same treatment of 1,3,6-trimethyluracil (**3g**) and 2-methyl-4-quinolinol (**3h**) provided desired products (**4g,h**) in high yields, respectively.

Table 4. Screening for Preparation of Heteroaryl(aryl)iodonium Imides 4

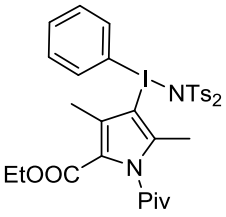


3 4

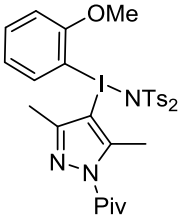
product, time, yield (%)



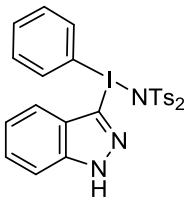
4a, 61 % (3 h)



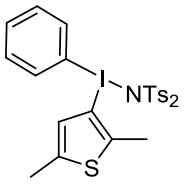
4b, 93 % (7 h)[a]



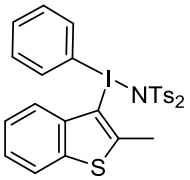
4c, 89 % (7 h)



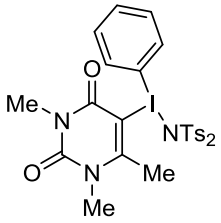
4d, 69 % (7 h)



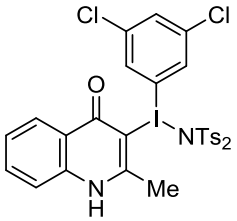
4e, 74 % (7 h)[a]



4f, 79 (7h)[a] %



4g, 87 (7 h) %



4h, 90 (7 h) %

Reaction scale was 1.0 mmol.

[a] Reaction temperature was r.t.

In conclusion, the author succeeded in the preparation of heteroaryl(aryl)iodonium imides from heteroaromatics, (diacetoxyiodo)arene, and bis(sulfonyl)imides. These novel imide-combined hypervalent iodines were easily prepared, isolated, and stable solid at room temperature in air. The author believes that those heteroaryl(aryl)iodonium imide possesses high reactivity for new C-N bond formation at the heteroaryl group.

Experimental

1. General Methods. ^{1}H NMR spectra were measured on a JEOL ECA-500 (500 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; sep = septet; m = multiplet; br = broad), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on a JEOL ECA-500 (125 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm). High-resolution mass spectra were recorded by Thermo Fisher Scientific Exactive Orbitrap mass spectrometers. Infrared (IR) spectra were recorded on a JASCO FT/IR 4100 spectrometer. Single crystal X-ray diffraction data were collected at 173 K on a Bruker SMART APEX II CCD diffractometer with Mo Kα (λ = 0.71073) radiation and graphite monochrometer. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60GF254 0.25 mm) were used. Visualization was accomplished by UV light (254 nm), anisaldehyde, $KMnO_4$, and phosphomolybdic acid.

2. 1 General Procedure Using Method A for Preparation of Indolyl(aryl)iodonium Imides (2)

To prepare PhI(OAc)NTs_2 were used DIB (96.6 mg, 0.30 mmol) and Ts_2NH (97.6 mg, 0.3 mmol) in MeCN (1.4 ml) and dichloroethane (0.7 ml). The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-pivaloylindole (50.3 mg, 0.25 mmol) was added, and the solution was stirred at 50 ˚C for 3 h. The solvent was removed under reduced pressure. Then, AcOEt (5 ml) and ether (3 ml) were added. The mixture was sonicated until precipitation occurred as the white solid, and ether (3 ml) was added to the mixture. The solid was filtrated and washed with AcOEt/ether (2:1) (15 ml), to give desired product **2a** (163.9 mg, 90 % yield).

2. 2 General Procedure Using Method B for Preparation of Indolyl(aryl)iodonium Imides (2)

To prepare PhI(OAc)NTs_2 were used DIB (96.6 mg, 0.30 mmol) and Ts_2NH (97.6 mg, 0.3 mmol) in MeCN (1.4 ml) and dichloroethane (0.7 ml). The mxture was stirred at room temperature for 30 min. under argon atmosphere. Then, 5-methoxy-*N*-pivaloylindole (57.8 mg, 0.25 mmol) was added, and the solution was stirred at 50 ˚C for 7 h. The solvent was removed under reduced pressure. Then, AcOEt (5 ml) and ether (3 ml) were added. The mixture was sonicated until precipitation

occurred as the white solid, and and ether (3 ml) was added to the mixture. The solid was filtrated and washed with AcOEt/ether (2:1) (15 ml). The crude product was purified by recrystalization from $CHCl_3$/AcOEt, to give desired product **2c** (174.5 mg, 92 % yield).

2. 3 General Procedure Method C for Preparation of Indolyl(aryl)iodonium Imides (2)

To prepare PhI(OAc)NTs_2 were used DIB (96.6 mg, 0.30 mmol) and Ts_2NH (97.6 mg, 0.3 mmol) in MeCN (1.4 ml) and dichloroethane (0.7 ml) The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, 6-chloro-*N*-pivaloylindole (58.9 mg, 0.25 mmol) was added, and the solution was stirred at 50 ˚C for 7 h. The solvent was removed under reduced pressure. Then, AcOEt (5 ml) and ether (3 ml) were added. The mixture was sonicated until precipitation occurred as the white solid, and ether (3 ml) was added to the mixture. The solid was filtrated and washed with AcOEt/ether (2:1) (15 ml). The crude product was purified by recrystalization from acetone/hexane, to give desired product **2k** (133.6 mg, 70 % yield).

2. 4 General Procedure Using Method D for Preparation of 4-Methyl-*N*-((4-methoxyphenyl)(1-pivaloyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2r)

To prepare ArI(OAc)NTs_2 were used 1-(diacetoxyiodo)-4-methoxybenzene (105.6 mg, 0.3 mmol) and Ts_2NH (97.6 mg, 0.3 mmol) in MeCN (1.4 ml) and dichloroethane (0.7 ml). The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-pivaloylindole (50.3 mg, 0.25 mmol) was added, and the solution was stirred at 50 ˚C for 7 h. The solvent was removed under reduced pressure. Then, AcOEt (3 ml) was added. The mixture was added dropwise to ether until the solvent changed clear solution to pale white, followed by sonication. Then, ether (1 ml) was added to the mixture. The solid was filtrated and washed with AcOEt/ether (1:1) (15 ml), to give desired product **2r** (141.2 mg, 74 % yield).

2. 5 General Procedure Using Method E for Preparation of *N*-((1-Benzoyl-1*H*-indol-3-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (2ah)

To prepare PhI(OAc)NTs_2 were used DIB (96.6 mg, 0.30 mmol) and Ts_2NH (97.6 mg, 0.3 mmol) in MeCN (1.4 ml) and dichloroethane (0.7 ml). The mixtue was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-benzoylindole (55.3 mg,

0.25 mmol) was added, and the solution was stirred at 50 ˚C for 7 h. The solvent was removed under reduced pressure. Then, AcOEt (3 ml) was added. The mixture was added dropwise to ether /hexane (1:1) until the solvent changed clear solution to pale white, followed by sonication. Then, ether (1 ml) was added to the mixture. The solid was filtrated and washed with AcOEt/hexane (2:1) (15 ml), to give desired product **2ah** (127.3 mg, 68 % yield).

2. 6 General Procedure Using Method F for Preparation of 4-Methyl-*N*-(1-pivaloyl-(3-trifluoromethylphenyl)-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2aa)

To prepare ArI(OAc)NTs_2 were used 1-(diacetoxyiodo)-3-trifluoromethylbenzene (117.0 mg, 0.3 mmol) and Ts_2NH (97.6 mg, 0.3 mmol) in MeCN (1.4 ml) and dichloroethane (0.7 ml). The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-pivaloylindole (50.3 mg, 0.25 mmol) was added, and the solution was stirred at 50 ˚C for 7 h. The solvent was removed under reduced pressure. Then, AcOEt (3 ml) was added. The mixture was added dropwise to ether /hexane (1:1) until the solvent changed clear solution to pale white. The solution was stored overnight at -10 ˚C. The solid was filtrated and washed with AcOEt/hexane (2:1) (15 ml), to give desired product **2aa** (159.1 mg, 85 % yield).

2. 7 General Procedure Using Method G for Preparation of *N*-((5-(1,3-Dioxyindolin-2-yl)-1-pivaloyl-1*H*-indol-3-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*tosylbenzenesulfonamide (2j)

To prepare ArI(OAc)NTs_2 were used DIB (96.6 mg, 0.30 mmol) and Ts_2NH (97.6 mg, 0.3 mmol) in MeCN (1.4 ml) and dichloroethane (0.7 ml). The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, 2-(*N*-pivaloyl-1*H*-indol-5-yl)isoindoline-1,3-dione (86.6 mg, 0.25 mmol) was added, and the solution was stirred at 50 ˚C for 7 h. The solvent was removed under reduced pressure. Then, AcOEt (5 ml) was added, and the mixture was filtrated and washed with AcOEt (5 ml). The filtrate was evaporated. Then AcOEt (3 ml) was added. The mixture was added dropwise to ether until the solvent changed clear solution to pale white, followed by sonicated. Then, ether (1 ml) was added to the mixture. The solid was filtrated and washed with AcOEt/ether (1:1) (15 ml), to give desired product **2j** (166.0 mg, 76 % yield).

4-Methyl-*N*-(phenyl(1-pivaloyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonam

ide (2a) (Isolated Method : A) **:** mp. 164 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ1.44 (s, 9H), 2.20 (s, 6H), 6.87 (d, *J*=8.0 Hz, 4H), 7.27 (t, *J*=7.5 Hz, 2H), 7.33 (t, *J*=7.5 Hz, 1H), 7.39-7.48 (m, 7H), 8.03 (d, *J*=7.5 Hz, 2H), 8.45 (d, *J*=8.3 Hz, 1H), 8.85(s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.4 (3C), 41.7, 86.0, 115.4, 117.6, 119.4, 125.1, 126.76 (4C), 126.81, 127.7, 128.5 (4C), 131.5 (3C), 134.9 (2C), 135.5, 136.3, 140.8 (2C), 141.0 (2C), 177.1. IR (neat) 1703, 1444, 1281, 1134, 1281, 1077, 1034 cm^{-1}. MS (ESI) calcd for $C_{33}H_{33}N_2O_5INaS_2$ $[M+Na]^+$ 751.0768, found 751.0754.

Crystal data for 2a: Formula $C_{33}H_{33}N_2O_5S_2 \cdot 2CHCl_3$, colorless, crystal dimensions 0.30 × 0.20 × 0.10 mm^3, prismatic, space group *P*2 (1), *a* = 18.254(3) Å, *b* = 9.5283(15) Å, *c* = 23.967(4) Å, α = 90.00 °, β = 97.187(2) °, γ = 90.00 °, *V* = 4157.7(11) Å3, *Z* = 4, ρ_{calc} = 1.545 g cm^{-3}, F(000) = 1944, μ(MoKα) = 1.298 mm^{-1}, *T* = 173 K. 22389 reflections collected, 9335 independent reflections with $I > 2\sigma(I)$ ($2\theta_{max}$ = 27.56°), and 539 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. *R*1 = 0.0678 and *wR*2 = 0.1797. GOF = 1.061. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1023214. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

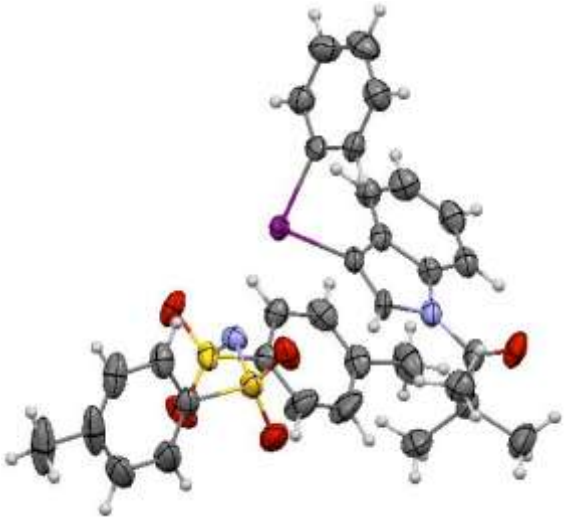


Figure 1. OPTEP drawing of **2a**.

4-Methyl-*N*-(phenyl(5'-methyl-1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenz

enesulfonamide (2b) (Isolated Method : A) **:** mp. 173 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 9H), 2.23 (s, 6H), 2.43 (s, 3H), 6.88 (d, *J*=8.0Hz,4H), 7.19 (s, 1H), 7.24 (d, *J*=8.6 Hz, 1H), 7.42-7.48 (m, 1H), 7.45 (d, *J*=8.0 Hz,4H), 8.06 (d, *J*=7.8 Hz, 2H), 8.32 (d, *J*=8.6 Hz, 1H), 8.78 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.26 (2C), 21.33, 28.4 (3C), 41.7, 85.4, 115.4, 117.4, 119.0, 126.8 (4C), 127.8, 128.4, 128.5 (4C), 131.6, 131.7 (2C), 134.5, 134.6 (2C), 135.2, 135.4, 140.7 (2C), 140.9 (2C), 176.9. IR (neat) 1699, 1489, 1294, 1131, 1078, 1037, 1014, 806, 760 cm^{-1}. MS (ESI) calcd for $C_{34}H_{35}N_2O_5INaS_2$ $[M+Na]^+$ 765.0924, found 765.0908.

***N*-((5'-Methoxy-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylb enzenesulfonamide (2c)** (Isolated Method : B) **:** mp. 199 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ1.43 (s, 9H), 2.20 (s, 6H), 3.80 (s, 3H), 6.86 (s, 5H), 6.87 (d, *J*=8.3 Hz,4H), 6.99 (dd, *J*=9.2, 2.3 Hz, 1H), 7.27 (t, *J*=7.7 Hz, 2H), 7.36-7.48 (m, 5H), 8.09 (d, *J*=7.7 Hz, 2H), 8.33(d, *J*=9.2 Hz, 1H), 8.79 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.4 (3C), 41.6, 55.9, 85.7, 101.6, 115.4, 115.8, 118.6, 126.7 (4C), 128.4 (4C), 128.8, 130.7, 131.50 (2C), 131.54, 134.9 (2C), 135.6, 140.8 (2C), 141.2 (2C), 176.8. IR (neat) 1711, 1471, 1434, 1260, 1201, 1128, 1075, 1039, 802, 737, 664 cm^{-1}. MS (ESI) calcd for $C_{34}H_{35}N_2O_5INaS_2$ $[M+Na]^+$ 781.0873, found 781.0867.

***N*-((5'-Fluoro-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylben zenesulfonamide (2d)** (Isolated Method : A) **:** mp. 178 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.22 (s, 6H), 6.90 (d, *J*=8.2 Hz, 4H), 7.05 (dd, *J*=9.2, 2.3 Hz, 1H), 7.13 (td, *J*=9.2, 2.3 Hz, 1H), 7.28 (t, *J*=7.5 Hz, 1H), 7.43 (d, *J*=8.2 Hz, 4H) 7.46 (t, *J*=7.5 Hz, 1H), 8.06 (d, *J*=7.5 Hz, 2H), 8.42 (dd, *J*=9.2, 4.6 Hz, 1H), 8.91 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.4 (3C), 41.7, 85.7, 105.2 (d, J_{C-F}=25.0 Hz), 114.7 (d, J_{C-F}=25.0 Hz), 115.6, 119.2, 126.7 (4C), 128.5 (4C), 129.1 (d, J_{C-F}=10.7 Hz), 131.56 (2C), 131.63, 132.6 135.1 (2C), 136.9, 141.06 (2C), 141.13 (2C), 160.2 (d, J_{C-F}=243.2 Hz), 177.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ -115.8. IR (neat) 1716, 1469, 1440, 1280, 1179, 1133, 1077, 1031, 1011, 813, 761, 738, 671 cm^{-1}. MS (ESI) calcd for $C_{33}H_{32}N_2O_5FINaS_2$ $[M+Na]^+$ 769.0674, found 769.0662.

***N*-((5'-Chloro-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*tosylben zenesulfonamide (2e)** (Isolated Method : A) **:** mp. 186 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.21 (s, 6H), 6.88 (d, *J*=8.1 Hz, 4H), 7.28 (t, *J*=7.8 Hz, 2H), 7.32-7.38 (m, 3H), 7.40 (d, *J*=8.1 Hz, 4H), 7.47 (t, *J*=7.8 Hz, 1H), 8.07 (d, *J*=9.8 Hz, 2H), 8.37 (d, *J*=9.8 Hz, 1H), 8.91 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C),

28.3 (3C), 41.7, 85.4, 115.8, 118.8, 118.9, 126.7 (4C), 126.9, 128.5 (4C), 129.2, 130.7, 131.5 (2C), 131.6, 134.6, 135.1 (2C), 136.7, 141.0 (2C), 141.1 (2C), 177.0. IR (neat) 1715, 14742, 1260, 1129, 1076, 1044, 810, 763, 735, 665 cm^{-1}. MS (ESI) calcd for $C_{32}H_{32}N_2O_5ClINaS_2$ $[M+Na]^+$ 785.0378, found 785.0367.

***N*-((5'-Bromo-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (2f)** (Isolated Method : A) **:** mp. 194 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.22 (s, 6H), 6.87 (d, *J*=8.1 Hz, 4H), 7.28(t, *J*=7.8 Hz, 2H), 7.41 (d, *J*=8.1 Hz, 4H), 7.46-7.62 (m, 3H), 8.06 (d, *J*=7.8 Hz, 2H), 8.30 (d, *J*=7.1 Hz, 1H), 8.89 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.8, 85.1, 115.7, 118.4, 119.1, 121.9, 126.7 (4C), 128.5 (4C), 129.5, 129.6, 131.6 (2C), 131.7, 135.1 (3C), 136.6, 140.87 (2C), 140.93 (2C), 177.0. IR (neat) 1714, 1441, 1281, 1163, 1133, 1081, 1040, 808, 763, 672 cm^{-1}. MS (ESI) calcd for $C_{35}H_{32}N_2O_5BrINaS_2$ $[M+Na]^+$ 828.9873, found 828.9861.

Methyl 3-(((4'-methyl-*N*-tosylphenyl)sulfonamido)(phenyl)-λ^3-iodanyl)-1-pivaloyl-1*H*-indole-5-carboxylate (2g) (Isolated Method : A) **:** mp. 189 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.23 (s, 6H), 3.95 (s, 3H), 6.91 (d, *J*=8.1 Hz, 4H), 7.30 (t, *J*=7.8 Hz, 2H), 7.44-7.50 (m, 1H), 7.46 (d, *J*=8.1 Hz,4H), 8.06-8.14 (m, 3H), 8.50 (d, *J*=7.5 Hz, 1H), 8.97 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 28.3 (3C), 41.9, 52.4, 86.5, 115.6, 117.6, 121.2, 126.8 (4C), 127.0, 127.7, 127.8, 128.6 (4C), 131.7 (2C), 131.8, 135.0 (2C), 137.0, 138.9, 140.7 (2C), 141.3 (2C), 166.4, 177.1. IR (neat) 1718, 1434, 1291, 1263, 1130, 1075, 1041, 764, 738, 665 cm^{-1}. MS (ESI) calcd for $C_{35}H_{35}N_2O_7INaS_2$ $[M+Na]^+$ 809.0823, found 809.0807.

3-(((4'-Methyl-*N*-tosylphenyl)sulfonamido)(phenyl)-λ^3-iodanyl)-1-pivaloyl-1*H*-indol-5-yl pivalate (2h) (Isolated Method : B) **:** mp. 195 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 1.37 (s, 9H), 1.45 (s, 9H), 2.21 (s, 6H), 6.90 (d, *J*=8.1 Hz, 4H), 7.11 (dd, *J*=9.2, 2.3 Hz, 1H), 7.16 (d, *J*=7.8 Hz, 1H), 7.31 (t, *J*=7.8 Hz, 2H), 7.44 (d, *J*=8.1 Hz, 4H), 7.48 (t, *J*=7.8 Hz, 1H), 8.08 (d, *J*=7.8 Hz, 2H), 8.45 (d, *J*=9.2 Hz, 1H), 8.83 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 27.2 (3C), 28.3 (3C), 39.1, 41.7, 85.8, 111.9, 115.8, 118.5, 120.9, 126.7 (4C), 128.5 (4C), 128.7, 129.7, 131.5 (2C), 133.7, 135.1 (2C), 136.5, 140.8 (2C), 141.3 (2C), 148.4, 176.97, 177.0. IR (neat) 1748, 1712, 1459, 1276, 1133, 1113, 1078, 1034, 822, 770, 741, 671 cm^{-1}. MS (ESI) calcd for $C_{38}H_{41}N_2O_7INaS_2$ $[M+Na]^+$ 851.1292, found 851.1279.

***N*-((5'-Cyano-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylben zenesulfonamide (2i)** (Isolated Method : A) **:** mp. 188 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.23 (s, 6H), 6.87 (d, *J*=8.0 Hz, 4H), 7.31 (t, *J*=7.8 Hz, 2H), 7.35 (d, *J*=8.0 Hz, 4H), 7.49 (t, *J*=7.8 Hz, 1H), 7.63 (dd, *J*=8.9,1.4 Hz,1H), 7.72 (d, *J*=1.4 Hz, 1H), 8.09 (d, *J*=7.8 Hz, 2H), 8.51 (d, *J*=8.9 Hz,1H), 9.02 (s,1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 28.2 (3C), 41.9, 86.3, 108.5, 115.8, 118.58, 118.62, 124.1, 126.6 (4C), 128.2, 128.5 (4C), 129.4, 131.7 (2C), 131.9, 135.3 (2C), 137.6, 138.1, 140.8 (2C), 141.0 (2C), 177.1. IR (neat) 2223, 1721, 1447, 1280, 1133, 1078, 1039, 821, 763, 672 cm^{-1}. MS (ESI) calcd for $C_{34}H_{32}N_3O_5INaS_2$ $[M+Na]^+$ 776.0720, found 776.0707.

***N*-((5'-(1",3"-dioxyindolin-2"-yl)-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4 -methyl-*N*-tosylbenzenesulfonamide (2j)** (Isolated Method : G) **:** mp. 190 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.19 (s, 6H), 6.85 (d, *J*=8.1 Hz, 4H), 7.29 (t, *J*=7.8 Hz, 2H), 7.38 (d, *J*=8.1 Hz, 4H), 7.41-7.50 (m, 2H), 7.62 (d, *J*=1.8 Hz, 1H), 7.76-7.82 (m, 2H), 7.86-7.94 (m, 2H) , 8.17 (d, *J*=7.8 Hz, 2H), 8.51 (d, *J*=8.9 Hz, 1H), 8.91 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.7, 86.6, 116.0, 117.7,118.3, 123.7 (2C), 125.0, 126.6 (4C), 128.3, 128.4 (4C), 128.6, 129.8, 131.6 (4C), 134.5 (2C), 135.2, 135.4 (2C), 136.3, 140.8 (2C), 141.3 (2C), 167.1 (2C), 177.0.. IR (neat) 1719, 1468, 1377, 1279, 1132, 1077, 1036, 814, 751, 716, 669 cm^{-1}. MS (ESI) calcd for $C_{27}H_{22}N_2O_3I$ $[M\text{-}Ts_2N^-]^+$ 549.0670, found 549.0657.

***N*-((6'-Chloro-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylben zenesulfonamide (2k)** (Isolated Method : C) **:** mp. 143 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.21 (s, 6H), 6.87 (d, *J*=8.2 Hz, 4H), 7.24-7.30 (m, 3H), 7.33 (d, *J*=8.3 Hz, 1H), 7.38 (d, *J*=8.2 Hz, 4H), 7.46 (t, *J*=7.5 Hz, 1H), 8.10 (d, *J*=7.5 Hz, 2H), 8.48 (d, *J*=1.7 Hz,1 H), 8.83 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.7, 86.3, 115.7, 117.8, 120.2, 125.6, 126.4, 126.6 (4C), 128.4 (4C), 131.5 (2C), 131.6, 133.0, 135.1 (2C), 135.9, 136.4, 141.0 (2C), 141.2 (2C), 177.0. IR (neat) 1714, 1421, 1265, 1161, 1131, 1077, 1042, 805, 766, 670 cm^{-1}. MS (ESI) calcd for $C_{33}H_{32}N_2O_5ClINaS_2$ $[M+Na]^+$ 785.0378, found 785.0364.

***N*-((7'-Methyl-1-pivaloyl-'1*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylben zenesulfonamide (2l)** (Isolated Method : A) **:** mp. 171 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.19 (s, 6H), 2.29 (s, 3H), 6.86 (d, *J*=8.1 Hz, 4H), 7.20 (d,

J=6.9 Hz, 1H), 7.21-7.31 (m, 5H), 8.04 (d, *J*=7.5 Hz, 2H), 8.63 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.2 (2C), 28.8 (3C), 42.7, 84.0, 115.8, 117.4, 124.8, 125.7, 126.8 (4C), 128.4 (4C), 128.7, 128.9, 131.4, 131.5 (2C), 134.6 (2C), 135.3, 135.6, 140.7 (2C), 141.3 (2C), 178.8. IR (neat) 1724, 1442, 1276, 1131, 1077, 1035, 811, 762, 738, 672 cm^{-1}. MS (ESI) calcd for $C_{34}H_{35}N_2O_5INaS_2$ $[M+Na]^+$ 765.0924, found 765.0913.

***N*-((2'-Methyl-1'-pivaloyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (2m)** (Isolated Method : D) **:** mp. 142 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.25 (s, 6H), 2.68 (s, 3H), 6.91 (d, *J*=8.0 Hz, 4H), 7.24 (d, *J*=7.6 Hz, 1H), 7.27-7.34 (m, 4H), 7.42-7.48 (m, 1H), 7.45 (d, *J*=8.2 Hz, 4H), 7.51 (d, *J*=7.6 Hz, 1H), 7.89 (d, *J*=8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.4, 21.3 (2C), 27.9 (3C), 44.8, 82.0, 112.2, 115.9, 119.4, 123.5, 124.5, 126.7 (4C), 127.6, 128.4 (4C), 131.4, 131.7 (2C), 133.5 (2C), 135.8, 140.5 (2C), 141.2 (2C), 143.1, 185.2. IR (neat) 1730, 1451, 1263, 1131, 1082, 1035 cm^{-1}. MS (ESI) calcd for $C_{34}H_{35}N_2O_5INaS_2$ $[M+Na]^+$ 765.0924, found 765.0908.

***N*-(Phenyl(1-pivaloyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-(phenylsulfonyl)benzenesulfonamide (2n)** (Isolated Method : A) **:** mp. 180 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 9H), 7.10 (t, *J*=8.0 Hz, 4H), 7.22 (t, *J*=7.7 Hz, 2H), 7.28 (t, *J*=8.0 Hz, 2H), 7.35 (t, *J*=7.7 Hz, 1H), 7.40-7.49 (m, 3H), 7.55 (d, *J*=8.0 Hz,4H), 8.07 (d, *J*=7.7 Hz, 2H), 8.46 (d, *J*=8.1 Hz, 1H), 8.84 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.3 (3C), 41.7, 85.9, 115.3, 117.7, 119.3, 125.2, 126.6 (4C), 126.9, 127.7, 127.9 (4C), 130.6 (3C), 131.6 (2C), 131.7, 134.9 (2C), 135.4, 136.3, 143.9 (2C), 177.1. IR (neat) 1712, 1444, 1279, 1131, 1078, 1038, 793, 744, 720, 688 cm^{-1}. MS (ESI) calcd for $C_{31}H_{29}N_2O_5INaS_2$ $[M+Na]^+$ 723.0455, found 723.0444.

4-Fluoro-*N*-((4'-fluorophenyl)sulfonyl)-*N*-(phenyl(1"-pivaloyl-1"*H*-indol-3"-yl)-λ^3-iodanyl)benzenesulfonamide (2o) (Isolated Method : E) **:** mp. 155 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 9H), 6.77 (dd, *J*=7.6, 7.2, Hz, 4H), 7.31 (t, *J*=8.1 Hz, 2H), 7.36 (t, *J*=8.1 Hz, 1H), 7.40-7.53 (m, 7H), 8.05 (d, *J*=8.1 Hz, 2H), 8.47 (d, *J*=8.3 Hz, 1H), 8.78 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.3 (3C), 41.7, 85.7, 114.9 (d, $J_{C\text{-}F}$=22.7 Hz, 4C), 115.0, 117.7, 119.2, 125.3, 127.1, 127.6, 129.2 (d, $J_{C\text{-}F}$=9.5 Hz, 4C), 131.7 (2C), 131.8, 134.8 (2C), 135.3, 136.3, 140.0 (2C), 163.9 (d, $J_{C\text{-}F}$=250.4 Hz, 2C), 176.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ -108.9. IR (neat) 1712, 1444, 1280, 1219, 1133, 1081, 1039 cm^{-1}. MS (ESI) calcd for $C_{31}H_{27}N_2O_5F_2INaS_2$ $[M+Na]^+$ 759.0266, found 759.0273.

***N*-(Phenyl(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-(propylsulfonyl)propane-1-sulfonamide (2p)** (Isolated Method : E) **:** mp. 97 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, *J*=7.5 Hz, 6H), 1.56 (s, 9H), 1.60-1.70 (m, 4H), 2.95-3.00 (m, 4H), 7.36-7.50 (m, 2H), 7.54 (t, *J*=7.5Hz, 1H), 8.11 (d, *J*=7.5 Hz, 2H), 8.49 (d, *J*=8.6 Hz, 1H), 8.65 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.0 (2C), 17.5 (2C), 28.5 (3C), 41.8, 56.1 (2C), 86.8, 115.3, 116.6, 117.8, 119.3, 125.4, 127.3 (4C), 127.5, 131.9 (2C), 132.0, 134.46 (2C), 134.53, 136.4, 176.7. IR (neat) 1706, 1442, 1303, 1270, 1095, 1046, 948, 822, 741, 608 cm^{-1}. MS (ESI) calcd for $C_{25}H_{33}N_2O_5INaS_2$ $[M+Na]^+$ 655.0768, found 655.0771.

4-Methyl-*N*-(methylsulfonyl)-*N*-(phenyl(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)benzenesulfonamide (2q) (Isolated Method : A) **:** mp. 150 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.23 (s, 3H), 2.80 (s, 3H), 6.99 (d, *J*=7.5 Hz, 2H), 7.30-7.38 (m, 3H), 7.40-7.52 (m, 3H), 7.56 (d, *J*=7.5 Hz, 2H), 8.07 (d, *J*=8.3 Hz, 2H), 8.47 (d, *J*=8.6 Hz, 1H), 8.75 (d, *J*=8.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 28.4 (3C), 41.7, 42.7, 86.2, 115.7, 117.7, 119.3, 125.2, 126.7 (2C), 127.0, 127.6, 128.7 (2C), 131.67 (2C), 131.73, 134.7 (2C), 135.1, 136.3, 141.2, 141.6, 177.0. IR (neat) 1710, 1443, 1267, 1120, 1080, 1051, 823, 747, 717 cm^{-1}. MS (ESI) calcd for $C_{27}H_{29}N_2O_5INaS_2$ $[M+Na]^+$ 675.0455, found 675.0450.

4-Methyl-*N*-((4"-methoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2r) (Isolated Method : D) **:** mp. 180 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.20 (s, 6H), 3.74 (s, 3H), 6.75 (d, *J*=9.2Hz, 2H), 6.88 (d, *J*=8.0Hz, 4H), 7.34 (t, *J*=7.5 Hz, 1H), 7.38-7.48 (m, 2H), 7.43 (d, *J*=8.0 Hz, 4H), 8.02 (d, *J*=9.2Hz, 2H), 8.45 (d, *J*=7.5 Hz, 1H), 8.83 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.4 (3C), 41.9, 55.5, 86.6, 103.9, 117.2 (2C), 117.7, 119.4, 125.0, 126.67, 126.71 (4C), 127.7, 128.4 (4C), 135.0, 136.2, 137.1 (2C), 140.8 (2C), 141.4 (2C), 162.2, 177.1. IR (neat) 1702, 1443, 1292, 1259, 1138, 1078, 1031, 1113, 814, 746, 671 cm^{-1}. MS (ESI) calcd for $C_{33}H_{34}N_2O_6INaS_2$ $[M+Na]^+$ 781.0873, found 781.0865.

4-Methyl-*N*-((4"-chlorphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2s) (Isolated Method : A) **:** mp. 190 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.20 (s, 6H), 6.87 (d, *J*=8.1 Hz, 4H), 7.17 (d, *J*=8.6 Hz, 2H), 7.31-7.40 (m, 5H), 8.04 (d, *J*=8.6 Hz, 2H), 8.45 (d, *J*=9.2 Hz, 1H), 8.87 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.7, 86.6, 112.7, 117.7 119.3, 125.1,

126.6 (4C), 126.8, 127.7, 128.5 (4C), 131.5 (2C), 135.6, 136.2, 136.6 (2C), 138.4, 141.0 (2C), 141.2 (2C), 177.1. IR (neat) 1703, 1443, 1281, 1136, 1077, 1029, 813, 754, 670 cm^{-1}. MS (ESI) calcd for $C_{33}H_{32}N_2O_5ClINaS_2$ $[M+Na]^+$ 785.0378, found 785.0361.

4-Methyl-*N*-((4"-cyanophenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2t) (Isolated Method : D) **:** mp. 167 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (s, 9H), 2.22 (s, 6H), 6.84 (d, *J*=8.3 Hz, 4H), 7.28 (d, *J*=8.3 Hz, 4H), 7.34 (t, *J*=8.5 Hz, 1H), 7.39-7.49 (m, 4H), 8.24 (d, *J*=8.6 Hz, 2H), 8.46 (d, *J*=8.5 Hz, 1H), 8.90 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.7, 86.5, 115.3, 117.0, 117.7, 119.2, 120.0, 125.3, 126.5 (4C), 127.0, 127.7, 128.5 (4C), 134.2 (2C), 135.7 (2C), 136.0, 136.2, 140.7 (2C), 141.2 (2C), 177.0. IR (neat) 2232, 1714, 1445, 1269, 1133, 1078, 1036, 814, 749, 671 cm^{-1}. MS (ESI) calcd for $C_{34}H_{32}N_3O_5INaS_2$ $[M+Na]^+$ 776.0720, found 776.0701.

4-Methyl-*N*-((4"-nitrophenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2u) (Isolated Method : A) **:** mp. 179 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 9H), 2.21 (s, 6H), 6.84 (d, *J*=8.1 Hz, 4H), 7.31 (d, *J*=8.1 Hz, 4H), 7.35 (t, *J*=7.5 Hz, 1H), 7.42-7.49 (m, 2H), 8.28 (dt, *J*=9.2, 2.0 Hz, 2H), 8.47 (d, *J*=7.5 Hz, 1H), 8.92 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.7, 86.5, 117.8, 119.2, 125.3, 125.8 (2C), 126.6 (4C), 127.0, 127.6, 128.5 (4C), 136.08, 136.14 (2C), 136.3, 140.7 (2C), 141.4 (2C), 149.3, 177.1. IR (neat) 1706, 1525, 1289, 1137, 1078, 1028, 1009, 819, 768, 671 cm^{-1}. MS (ESI) calcd for $C_{33}H_{32}N_3O_7INaS_2$ $[M+Na]^+$ 796.0619, found 796.0603.

4-Methyl-*N*-((2"-methoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2v) (Isolated Method : A) **:** mp. 204 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.25 (s, 6H), 3.97 (s, 3H), 6.85-6.93 (m, 5H), 6.99 (dd, *J*=8.3, 1.5 Hz, 1H), 7.38 (t, *J*=8.6 Hz, 1H), 7.40-7.52 (m, 7H), 7.59 (dd, *J*=8.3, 1.5 Hz, 1H), 8.51 (d, *J*=8.6 Hz, 1H), 8.87 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 28.4 (3C), 41.8, 57.0, 82.8, 103.9, 112.2, 117.7, 119.6, 124.0, 125.2, 126.6 (4C), 127.0, 127.6, 128.4 (4C), 133.8, 134.0, 136.3, 136.5, 140.7 (2C), 141.2 (2C), 156.3, 177.0. IR (neat) 1712, 1474, 1277, 1127, 1079, 1014, 751, 671 cm^{-1}. MS (ESI) calcd for $C_{34}H_{35}N_2O_6INaS_2$ $[M+Na]^+$ 781.0873, found 781.0853.

4-Methyl-*N*-((2"-*n*-butoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2w) (Isolated Method : E)**:** mp. 165 °C (decomp.) ^{1}H NMR (500

MHz, $CDCl_3$) δ 1.00 (t, *J*=7.5 Hz, 3H), 1.44 (s, 9H), 1.53 (sext, *J*=7.5 Hz, 2H), 1.87 (quin, *J*=7.5 Hz, 2H), 2.26 (s, 6H), 4.14 (t, *J*=7.5 Hz, 2H), 6.82-6.88 (m, 1H), 6.89 (d, *J*=8.0 Hz, 4H), 6.98 (d, *J*=7.5 Hz, 1H), 7.37 (t, *J*=7.5 Hz, 1H), 7.40-7.52 (m, 4H), 7.44 (d, *J*=8.0 Hz,4H), 8.52 (d, *J*=8.6 Hz, 1H), 8.88 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 19.1, 21.3 (2C), 28.4 (3C), 30.8, 41.8, 70.1, 82.4, 103.9, 113.0, 117.7, 119.5, 124.0, 125.2, 126.9 (4C), 127.0, 127.6, 128.3 (4C), 133.6 (3C), 136.3, 136.4 (2C), 140.6, 141.4, 155.8, 177.1. IR (neat) 1710, 1461, 1281, 1129, 1076, 1029, 1010 cm^{-1}. MS (ESI) calcd for $C_{37}H_{41}N_2O_6INaS_2$ $[M+Na]^+$ 823.1343, found 823.1335.

***N*-((2”-isobutoxyphenyl)(1’-pivaloyl-1’*H*-indol-3’-yl)-λ^3-iodanyl)-4-methyl-*N*-tosyl benzenesulfonamide (2x)** (Isolated Method : C) **:** mp. 156 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ1.12 (d, *J*=6.6 Hz, 6H), 1.44 (s, 9H), 2.19-2.32 (m, 7H), 3.94 (d, *J*=6.6 Hz, 1H), 6.87-6.94 (m, 5H), 7.01 (d, *J*=8.5 Hz, 1H), 7.36-7.48 (m, 8H), 7.51 (d, *J*=8.5 Hz, 1H), 8.55 (d, *J*=8.3 Hz, 1H), 8.92 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.4 (2C), 21.3 (2C), 28.1, 28.4 (3C), 41.8, 76.5, 82.2, 103.7, 113.1, 117.8, 119.4, 124.1, 125.3, 126.6 (4C), 127.1, 127.5, 128.4 (4C), 133.0, 133.5, 136.3, 136.3, 140.7 (2C), 141.5 (2C), 155.8, 177.1. IR (neat) 1712, 1446, 1281, 1132, 1078, 1012, 757, 669 cm^{-1}. MS (ESI) calcd for $C_{37}H_{41}N_2O_6INaS_2$ $[M+Na]^+$ 823.1343, found 823.1324.

***N*-((2”-(octyloxy)phenyl)(1’-pivaloyl-1’*H*-indol-3’-yl)-λ^3-iodanyl)-4-methyl-*N*-tosyl benzenesulfonamide (2y)** (Isolated Method : A) **:** mp. 136 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, *J*=7.2 Hz, 3H), 1.22-1.52 (m, 19H), 1.90 (quin, *J*=7.2 Hz, 2H), 2.27 (s, 6H), 4.14 (t, *J*=7.2 Hz, 2H), 6.86-6.94 (m, 5H), 6.99 (dd, *J*=8.3, 1.2 Hz, 1H), 7.38 (t, *J*=8.6 Hz, 1H), 7.41-7.53 (m, 8H), 8.54 (d, *J*=8.6 Hz, 1H), 8.89 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 21.3 (2C), 22.6, 25.8, 28.4 (3C), 28.8, 29.1, 29.3, 31.8, 41.7, 70.4, 82.6, 103.9, 113.0, 117.8, 119.5, 123.9, 125.2, 126.6 (4C), 127.0, 127.6, 128.4 (4C), 133.6 (2C), 136.3, 136.4, 140.7 (2C), 141.4 (2C), 155.8, 177.0. IR (neat) 1707, 1474, 1292, 1135, 1080, 1032, 759, 671 cm^{-1}. MS (ESI) calcd for $C_{41}H_{49}N_2O_6INaS_2$ $[M+Na]^+$ 879.1969, found 879.1974.

***N*-((2”-(2’”-methoxyethoxy)phenyl)(1’-pivaloyl-1’*H*-indol-3’-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (2z)** (Isolated Method : A) **:** mp. 78-82 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.26 (s, 6H), 3.47 (s, 3H), 3.82-3.92 (m, 2H), 4.28-4.40 (m, 2H), 6.84-6.96 (m, 5H), 7.07 (dd, *J*=8.3, 1.2 Hz, 1H), 7.38 (t, *J*=8.6 Hz, 1H), 7.41-7.52 (m, 7H), 7.58 (dd, *J*=8.3, 1.2 Hz, 1H), 8.51 (d, *J*=8.6 Hz, 1H), 8.89 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ21.3 (2C), 28.4 (3C), 41.7, 59.3, 70.2, 70.6, 83.4,

99.9, 105.6, 114.3, 117.7, 119.6, 124.5, 125.2, 126.6 (4C), 126.9, 127.7, 128.3 (4C), 133.7, 133.7, 134.0, 136.3, 140.7 (2C), 141.3 (2C), 156.0, 177.1. IR (neat) 1706, 1474, 1294, 1135, 1080, 1033, 759, 672 cm^{-1}. MS (ESI) calcd for $C_{36}H_{40}N_2O_7INaS_2$ $[M+Na]^+$ 825.1136, found 825.1121.

4-Methyl-*N*-(1'-pivaloyl-(3"-trifluoromethylphenyl)-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2aa) (Isolated Method : E)**:** mp. 139 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.20 (s, 6H), 6.85 (d, *J*=8.1 Hz, 4H), 7.31-7.42 (m, 2H), 7.42-7.48 (m, 2H), 7.67 (d, *J*=7.9 Hz, 1H), 8.34 (d, *J*=7.9 Hz, 1H), 8.38 (s,1H), 8.46 (d, *J*=8.3 Hz, 1H), 8.88 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.7, 87.1, 115.9, 117.7, 119.3, 120.3 (q, J_{C-F}=271.8 Hz, 1C), 125.2, 125.2, 126.6 (4C), 127.7, 128.2 (2C), 128.5 (4C), 131.7, 132.9 (q, J_{C-F}=33.4 Hz, 1C), 135.7, 136.2, 138.6, 140.9 (2C), 141.0 (2C), 177.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.6. IR (neat) 1706, 1443, 1292, 1136, 1077, 1033, 800, 748, 671 cm^{-1}. MS (ESI) calcd for $C_{34}H_{32}N_2O_5F_3INaS_2$ $[M+Na]^+$ 819.0642, found 819.0634.

4-Methyl-*N*-((3",5"-dichlorophenlyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2ab) (Isolated Method : A) **:** mp. 183 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 9H), 2.23 (s, 6H), 6.90 (d, *J*=8.0 Hz, 4H), 7.35-7.45 (m, 3H), 7.39 (d, *J*=8.6 Hz, 1H), 7.47 (td, *J*=8.6, 1.5 Hz, 1H), 7.95 (d, *J*=1.8 Hz, 2H), 8.48 (d, *J*=8.6, Hz, 1H), 8.87 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 28.4 (3C), 41.8, 87.1, 115.4, 117.7, 119.3, 125.3, 126.7 (4C), 127.0, 127.7, 128.6 (4C), 132.0, 132.7 (2C), 135.9, 136.3, 136.6 (2C), 140.8 (2C), 141.2 (2C), 177.1. IR (neat) 1714, 1444, 1283, 1135, 1077, 1031, 1012, 800, 745, 672 cm^{-1}. MS (ESI) calcd for $C_{33}H_{31}N_2O_5Cl_2INaS_2$ $[M+Na]^+$ 818.9988, found 818.9987.

4-Methyl-*N*-((3",5"-bis(trifluoromethyl)phenlyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2ac) (Isolated Method : E) **:** mp. 156 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.20 (s, 6H), 6.83 (d, *J*=8.0 Hz, 4H), 7.26 (d, *J*=8.0 Hz, 4H), 7.40 (t, *J*=7.8 Hz, 1H), 7.45-7.52 (m, 2H), 7.86 (s,1H), 8.47 (d, *J*=7.8 Hz,1H), 8.59 (s, 1H), 8.90 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.3 (3C), 41.7, 87.8, 116.9, 117.7, 119.2, 121.8 (q, J_{C-F}=271.9 Hz, 2C), 125.1, 125.3, 126.5 (4C), 127.1, 127.6, 128.5 (4C), 133.5 (q, J_{C-F}=34.6 Hz, 2C), 135.1 (2C), 136.0, 136.2, 140.4 (2C), 141.2 (2C), 177.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.8. IR (neat) 1715, 1342, 1273, 1152, 1129, 1077, 1038, 812, 753, 658 cm^{-1}. MS (ESI) calcd for $C_{35}H_{31}N_2O_5F_6INaS_2$ $[M+Na]^+$ 887.0515, found 887.0511.

Methyl 3-((3",5"-dichlorophenyl)((4'-methyl-*N*-tosylphenyl)sulfonamido)-λ^3-iodanyl)-1-pivaloyl-1*H*-indole-2-carboxylate (2ad) (Isolated Method : A) **:** mp. 178 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (s, 9H), 2.26 (s, 6H), 4.09 (s, 3H), 6.88 (d, *J*=8.1, Hz, 4H), 7.28 (d, *J*=8.1 Hz, 4H), 7.34 (d, *J*=8.3 Hz, 1H), 7.37-7.42 (m, 2H), 7.50 (t, *J*=8.3, Hz, 1H), 7.77 (d, *J*=8.3 Hz, 1H), 7.98 (d, *J*=2.0 Hz, 2H), 8.89 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ21.3 (2C), 27.9 (3C), 45.5, 53.9, 87.9, 112.6, 117.4, 122.1, 124.8, 126.7 (4C), 127.8, 128.2, 128.4 (4C), 130.2, 132.0, 132.5 (2C), 136.3, 136.6 (2C), 140.2 (2C), 140.8 (2C), 159.5, 182.7. IR (neat) 1739, 1710, 1510, 1273, 1156, 1134, 1079, 1030, 761, 652 cm^{-1}. MS (ESI) calcd for $C_{35}H_{33}N_2O_7INaS_2$ $[M+Na]^+$ 877.0043, found 877.0025.

***N*-((2"-methoxyphenlyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-mesylmethanesulfonamide (2ae)** (Isolated Method : F) **:** mp. 178 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.58 (s, 9H), 2.81 (s, 6H), 4.02 (s, 3H), 6.95 (t, *J*=8.3 Hz, 1H), 7.03 (d, *J*=8.3 Hz, 1H), 7.40 (t, *J*=8.0 Hz, 1H), 7.45-7.54 (m, 3H), 7.62 (d, *J*=8.3 Hz, 1H), 8.51 (d, *J*=8.0 Hz, 1H), 8.73 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 28.5 (3C), 41.8, 42.2 (2C), 57.0, 83.6, 104.6, 112.4, 117.7, 119.5, 124.0, 125.3, 127.2, 127.4, 134.2, 135.9, 136.2, 156.3, 176.8. IR (neat) 1710, 1474, 1284, 1105, 1037, 832, 756, 701 cm^{-1}. MS (ESI) calcd for $C_{22}H_{27}N_2O_6INaS_2$ $[M+Na]^+$ 629.0247, found 629.0263.

***N*-(benzylsulfonyl)-*N*-((2"-methoxyphenlyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)- 1-phenylmethanesulfonamide (2af)** (Isolated Method : E) **:** mp. 139 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (s, 9H), 4.37 (s, 4H), 6.80 (t, *J*=8.3 Hz, 1H), 6.90 (d, *J*=8.3 Hz, 1H), 6.95 (t, *J*=7.5 Hz, 2H), 7.10 (t, *J*=7.5 Hz, 4H), 7.21 (d, *J*=8.3 Hz, 1H), 7.32 (t, *J*=8.0 Hz, 1H), 7.36 (d, *J*=8.0 Hz, 1H), 7.38-7.49 (m, 6H), 8.39 (s, 1H), 8.45 (d, *J*=8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.5 (3C), 41.7, 56.7, 59.6 (2C), 83.8, 104.1, 112.1, 117.7, 119.6, 123.6, 124.9, 126.8, 127.1, 127.3 (2C), 127.8 (4C), 131.5 (4C), 132.0 (2C), 133.9, 134.7, 135.4, 136.1, 156.3, 176.6. IR (neat) 1712, 1474, 1442, 1281, 1106, 1027, 748, 697 cm^{-1}. MS (ESI) calcd for $C_{34}H_{35}N_2O_6INaS_2$ $[M+Na]^+$ 781.0873, found 781.0874.

***N*-((1'-*t*-butoxylcarbonyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (2ag)** (Isolated Method : A) **:** mp. 104 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.67 (s, 9H),2.26 (s, 6H),6.94 (d, *J*=8.0 Hz,4H), 7.30-7.39 (m, 3H), 7.40-7.55 (m, 7H), 8.07 (d, *J*=7.5 Hz, 2H), 8.20 (d, *J*=8.3 Hz, 1H), 8.42 (s, 1H). ^{13}C

NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 28.0 (3C), 84.7, 86.2, 115.8, 116.1, 119.8, 124.7, 126.5, 126.8 (4C), 128.5 (4C), 128.6, 131.6, 131.7 (2C), 134.5 (2C), 135.1, 135.3, 141.0 (4C), 147.8. IR (neat) 1743, 1450, 1255, 1134, 1080, 1036 cm^{-1}. MS (ESI) calcd for $C_{33}H_{33}N_2O_6INaS_2$ $[M+Na]^+$ 767.0717, found 767.0718.

***N*-((1'-Benzoyl-1'*H*-indol-3'-yl)(phenyl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (2ah)** (Isolated Method : E) **:** mp. 161 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 6H), 6.85 (d, *J*=8.1 Hz, 4H), 7.26 (t, *J*=7.7 Hz, 2H),7.37 (d, *J*=8.0 Hz,4H), 7.34-7.55 (m, 10H), 7.61 (t, *J*=7.5 Hz, 1H), 7.69 (d, *J*=7.2 Hz, 2H), 8.00 (d, *J*=7.7 Hz, 2H), 8.22 (s, 1H), 8.38 (d, *J*=8.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 86.7, 115.6, 116.7, 119.9, 125.5, 126.7 (4C), 128.4 (4C), 128.9, 129.2 (2C), 129.9 (2C), 131.5 (2C), 132.0, 133.2, 134.7 (2C), 135.7, 136.8, 140.7 (2C), 141.1 (2C), 167.9. IR (neat) 1695, 1445, 1282, 1133, 1081, 1029, 1010, 808, 761, 664 cm^{-1}.MS (ESI) calcd for $C_{35}H_{29}N_2O_5INaS_2$ $[M+Na]^+$ 771.0455, found 771.0448.

4-Methyl-*N*-(phenyl(1'-tosyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2ai) (Isolated Method : A) **:** mp. 151 °C (decomp.) ^1H NMR (500 MHz, DMSO-d6) δ2.29 (s,9H), 7.12 (d, *J*=8.0 Hz, 4H), 7.40 (t, *J*=8.0 Hz, 2H), 7.43-7.49 (m, 4H), 7.52 (d, *J*=8.0 Hz, 4H), 7.58 (d, *J*=7.2 Hz, 1H), 7.82 (d, *J*=8.0 Hz, 1H), 7.92 (d, *J*=8.0 Hz, 2H), 8.00 (d, *J*=8.4 Hz, 1H), 8.26 (d, *J*=7.8 Hz, 2H), 9.03 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8 (2C), 21.1, 90.3, 113.7, 117.3, 120.8, 125.2, 126.1 (4C), 126.9, 127.1 (2C), 128.2 (4C), 128.6, 130.6 (2C), 131.7 (2C), 132.0, 133.1, 133.4, 134.7 (2C), 135.0, 139.5 (2C), 143.8 (2C), 146.6. IR (neat) 1384, 1283, 1136, 1081, 1030, 1010, 812, 762, 672 cm^{-1}. MS (ESI) calcd for $C_{35}H_{31}N_2O_6INaS_3$ $[M+Na]^+$ 821.0267, found 821.0267.

4-Methyl-*N*-(phenyl(1-pivaloyl-4',5',6',7'-tetrahydro-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (4a) (Isolated Method : E) **:** mp. 129 °C (decomp.) ^1H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.63-1.73 (m, 4H), 2.24-2.29 (m, 2H), 2.28 (s, 6H), 2.77-2.83 (m, 2H), 6.97 (d, *J*=8.0 Hz, 4H), 7.36 (t, *J*=7.8 Hz, 2H),7.49 (d, *J*=8.0 Hz, 4H), 7.52 (t, *J*=7.8 Hz, 1H), 7.95 (d, *J*=7.8 Hz, 2H), 8.17 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 22.0, 22.6, 22.9, 25.4, 28.4 (3C), 41.8, 89.3, 122.4, 126.8 (4C), 128.2, 128.4 (4C), 131.5, 131.6 (2C), 134.3, 134.4 (2C), 140.6 (2C), 141.6 (2C), 177.1. IR (neat) 1709, 1279, 1139, 1079, 1032, 1012 cm^{-1}. MS (ESI) calcd for $C_{33}H_{37}N_2O_5INaS_2$ $[M+Na]^+$ 755.1081, found 755.1060.

Ethyl 4-(((4'-methyl-*N*-tosylphenyl)sulfonamido)(phenyl)-λ^3-iodanyl)-3,5-dimethyl-1-pivaloyl-pyrrole-2-carboxylate (4b) (Isolated Method : F) **:** mp. 144-147 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (s, 9H), 1.34 (t, *J*=7.2 Hz, 3H), 2.27 (s, 6H), 2.46 (s, 2H), 6.97 (br, 2H), 6.95 (d, *J*=8.0 Hz, 4H), 7.34 (t, *J*=7.5 Hz, 2H), 7.45-7.52 (m, 5H), 7.81 (d, *J*= 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 14.3, 21.3 (2C), 27.9 (3C), 45.3, 61.5, 93.4, 115.5, 122.3, 126.8 (4C), 128.4 (4C), 130.5, 131.4, 133.5 (2C), 139.2, 140.6 (2C), 141.0 (2C), 160.9, 183.5. IR (neat) 1754, 1697, 1408, 1283, 1130, 1039, 822, 750, 665 cm^{-1}. MS (ESI) calcd for $C_{34}H_{39}N_2O_7INaS_2$ $[M+Na]^+$ 801.1136, found 801.1133.

4-Methyl-*N*-((3',5'-dimethyl-1'-pivaloyl-pyrrazol-4'-yl)(phenyl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (4c) (Isolated Method : F) **:** mp. 91-95 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.29 (s, 6H), 2.40 (s, 3H), 2.74 (s, 3H), 3.93 (s, 3H), 6.93-6.99 (m, 5H), 7.01 (d, *J*=8.0 Hz, 1H), 7.47 (d, *J*=8.3 Hz, 4H), 7.52 (t, *J*=8.0 Hz, 1H), 7.71 (d, *J*= 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 15.9, 21.3 (2C), 27.7 (3C), 42.6, 57.0, 89.6, 104.5, 112.5, 123.8, 126.7 (4C), 128.4 (4C), 134.3, 134.9, 140.7 (2C), 141.0 (2C), 151.3 (2C), 156.4, 177.8. IR (neat) 1727, 1476, 1266, 1126, 1078, 812, 771, 665 cm^{-1}. MS (ESI) calcd for $C_{31}H_{36}N_2O_6INaS_2$ $[M+Na]^+$ 760.0982, found 760.0981.

4-Methyl-*N*-((indazol-3'-yl)(phenyl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (4d) (Isolated Method : E) **:** mp. 175 °C (decomp.) ^{1}H NMR (500 MHz, DMSO-d6) δ 2.31 (s, 6H), 3.46 (br, 1H), 7.49 (d, *J*=8.0 Hz, 2H), 7.50-7.57 (m, 5H), 7.61 (t, *J*=8.0 Hz, 1H), 7.72 (t, *J*=7.8 Hz, 1H), 7.99 (d, *J*= 8.3 Hz, 1H), 8.26 (d, *J*= 8.0 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d6) δ 20.9 (2C), 111.5, 114.7, 117.1, 119.6, 123.4, 124.4 (4C), 126.1 (4C), 131.8 (2C), 132.0, 135.0 (2C), 140.5 (2C), 143.9. IR (neat) 3174, 1259, 1126, 1077, 1037, 763, 677, 556 cm^{-1}. MS (ESI) calcd for $C_{27}H_{24}N_3O_4INaS_2$ $[M+Na]^+$ 668.0145, found 668.0128.

4-Methyl-*N*-((2',5'-dimethylthiophen-3'-yl)(phenyl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (4e) (Isolated Method : A) **:** 188 °C (decomp.) ^{1}H NMR (500 MHz, DMSO-d6) δ 2.31 (s, 6H), 2.40 (s, 3H), 2.62 (s, 3H), 7.15 (d, *J*=8.0 Hz, 4H), 7.26 (s, 1H), 7.48-7.56 (m, 6H), 7.66 (t, *J*=7.4 Hz, 1H), 8.16 (d, *J*= 7.4 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d6) δ 14.9, 16.5, 20.8 (2C), 101.5, 116.8, 126.1 (4C), 128.2 (4C), 129.3, 131.8 (2C), 131.9, 134.8 (2C), 139.5, 141.1, 143.9 (2C), 144.4 (2C). IR (neat) 1279, 1133, 1079, 1032, 810, 766, 742, 663 cm^{-1}. MS (ESI) calcd for $C_{26}H_{26}NO_4INaS_3$ $[M+Na]^+$ 661.9961, found 661.9971.

4-Methyl-*N*-((2'-methylbenzo[b]thiophen-3'-yl)(phenyl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (4f) (Isolated Method : A) **:** 181-184 °C ^{1}H NMR (500 MHz, DMSO-d6) δ 2.31 (s, 6H), 2.94 (s, 3H), 7.14 (d, *J*=8.0 Hz, 4H), 7.44-7.57 (m, 8H), 7.61 (t, *J*=7.5 Hz, 1H), 8.02-8.09 (m, 2H), 8.21 (d, *J*= 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d6) δ 17.8, 20.8 (2C), 102.0, 116.5, 123.1, 123.4, 126.0, 126.1 (4C), 126.5, 128.1 (4C), 131.8 (2C), 132.0, 134.8 (2C), 137.7, 137.9, 139.5 (2C), 143.9 (2C), 149.9. IR (neat) 1429, 1276, 1129, 1078, 1010, 758, 664 cm^{-1}. MS (ESI) calcd for $C_{29}H_{27}NO_4INaS_3$ $[M+Na]^+$ 697.9961, found 697.9966.

4-Methyl-*N*-(phenyl(1',3',6'-trimethyl-uracil-5'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (4g) (Isolated Method : E)**:** 172 °C (decomp.) ^{1}H NMR (500 MHz, DMSO-d6) δ 2.31 (s, 6H), 2.87 (s, 3H), 3.24 (s, 3H), 3.50 (s, 3H), 7.14 (d, *J*=8.0 Hz, 4H), 7.47-7.56 (m, 6H), 7.65 (t, *J*=8.0 Hz, 1H), 8.09 (d, *J*=8.0 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d6) δ 20.8 (2C), 24.4, 30.0, 34.1, 95.4, 116.4, 126.1 (4C), 128.1 (4C), 131.5 (2C), 131.9, 134.7 (2C), 139.5 (2C), 143.8 (2C), 150.7, 158.7, 161.4. IR (neat) 1706, 1651, 1583, 1281, 1230, 1149, 1084, 814, 743, 684 cm^{-1}. MS (ESI) calcd for $C_{27}H_{27}N_3O_6INaS_2$ $[M+Na]^+$ 704.0341, found 704.0356.

***N*-((3",5"-dichlorophenyl)(2'-methyl-4'-oxo-1',4'-dihydroquinolin-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (4h)** (Isolated Method : A) **:** 162 °C (decomp.) ^{1}H NMR (500 MHz, DMSO-d6) δ 2.30 (s, 6H), 2.92 (s, 3H), 3.51 (br, 1H), 7.14 (d, *J*=7.7 Hz, 4H), 7.44-7.56 (m, 5H), 7.68 (t, *J*=8.0 Hz, 1H), 7.81 (t, *J*= 8.0 Hz, 1H), 7.91 (br, 1H), 8.25 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d6) δ 20.8 (2C), 24.1, 105.4, 115.6, 118.7, 121.9, 126.1 (4C), 128.2 (4C), 131.7, 133.0 (2C), 133.7, 135.3 (2C), 139.3 (2C), 139.6 (2C), 143.8, 156.8, 171.5. IR (neat) 3114, 1276, 1129, 1073, 1031, 1010, 796, 763, 677 cm^{-1}. MS (ESI) calcd for $C_{30}H_{25}N_2O_5Cl_2INaS_2$ $[M+Na]^+$ 776.9519, found 776.9515.

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Chapter 3-5

Regio-controlled aminations of Indoles via (Indolyl)(aryl)iodonium Imide

Abstract

Three different aminations were performed by one hypervalent iodine, (indolyl)(aryl)iodonium imide. These reactions induced transformation of C-H bond to C-N bond regioselectively, and gave 2-, 3- or benzylic aminoindoles from indole derivatives.

Introduction

Amino indole is very important structure for medicinal or biologically active compounds[1]. Therefore, direct C-N bond formation of indoles is attractive for synthetic organic chemists, and various types of reactions using heavy metals[2] and without metals[3], were reported. Direct nitrogen introduction requires high regioselectivity, however, some reports were applied to limited indoles where reactive positions are blocked by substituents, such as 2-,3-alkyl, and carboxylindoles, or requires complex ligands. On the other hands, halo-amination is useful strategy for regioselective and direct C-N bond formation. Nicholas group reported 3,2-bromo-amination of indoles with benzophenone *O*-acetyloxime and $CuBr$[4], and Liu group succeeded in chloro-amination of indoles with Chloramine-T® and Cu/Pd catalysts[5]. However, both methods require stoichiometric amount of heavy metal reagents.

On the other hands, hypervalent iodine is effective reagent for functionalization of indoles. Recently, Suna group reported azidation of indole derivatives via (indolyl)(phenyl)iodonium azide with copper catalyst[2g]. However, the reaction was applied to only methyl indole-2-carboxylate derivatives, and the azidoiodane intermediate was unstable and careful experimental operation was required. Similarly, imide-combined hypervalent iodines are also useful reagents for C-N bond formation[6].

The author also developed novel imide and indole-combined hypervalent iodine, (indolyl)(aryl)iodonium imide[7]. This reagent is stable solid and easily prepared and able to isolate. Here, the author reported the new synthetic strategy for C-N bond formation of indole from (indolyl)(aryl)iodonium imide as substrate. This methodology contains three different atom-economy amination reactions, and the controled introduction of imide group by designing structures of the hypervalent iodines can be achieved.

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Chapter 3

Regioselective Bromo-amination of Indoles via (Indolyl)(aryl)iodonium Imides

N-(3'-Bromo-1'-pivaloyl-1'*H*-indol-2'-yl)-4-methyl-*N*-tosylbenzenesulfonamides were obtained by bromo-amination of (indolyl)(phenyl)iodonium imides using brominating reagents. This reaction is C-H dual-functionalization on one-step with complete regioselectivity.

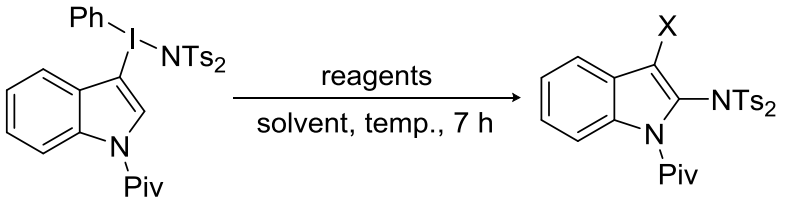
Introduction

Direct oxidative transformation of C-H bond to C-N bond is attractive on organic chemistry[1]. Moreover, direct and regioselective C-H dual-functionalization[2] is greatly ambitious, and possesses much possibility to reduce synthetic step, and therefore environmental load. Nevertheless, the study of regioselective C-H dual-functionalization of indole is lacked. On the best of the author's knowledge, Nicholas[3] group and Liu group[4] reported regioselective intermolecular 2,3-halo-amination of indoles. However, these methods required stoichiometric amount of heavy metal reagents. Recently, Yuan and Liu group[5] reported metal-free 3,3-dichloro-2-amination of indole with Chloramine-B®. However, the products require reduction process of halogen to give indole structure. Here, the author showed first metal-free 3,2-bromo-amination of indoles via (indolyl)(aryl)iodonium imide[6] with bromination reagent. This reaction forms both C-N and C-Br bonds regioselectively without any metal reagents.

Results and Discussion

First, the author screened a series of bromination reagents and solvent for the 3,2-bromo-amination of (indolyl)(phenyl)iodonium imides **2a** (Table 1). The treatment with *N*-Bromosuccinimide (NBS) and *N*-bromoacetamide transformed **2a** into 2-bis(tosyl)imidyl-3- bromoindole derivative (**3a**) in good yields (entries 1, 2), however, treatment with pyrridinium tribromide provided desired product (**3a**) in low yield (entry 3). Use of 1,3-dibromo-5,5-dimethylhydantin (DBH) increased the yield of **3a** (entry 4). On the other hands, both 1,3-dichloro-5,5-dimethylhydantin (DCH) and 1,3-diiodo-5,5-dimethylhydantin (DIH) were not effective at all (entries 4, 5). Then, other solvents were screened with DBH (entries 6-8). Solvents, such as $CHCl_3$, THF, and DMF, were not effective. Warming reaction temperature to 40 ˚C improved the yield of **3a** (entry 10).

Table 1. Regioselective 3,2-Halo-amination of Indolyl(phenyl)Iodonium Imide with Halogenation Reagents



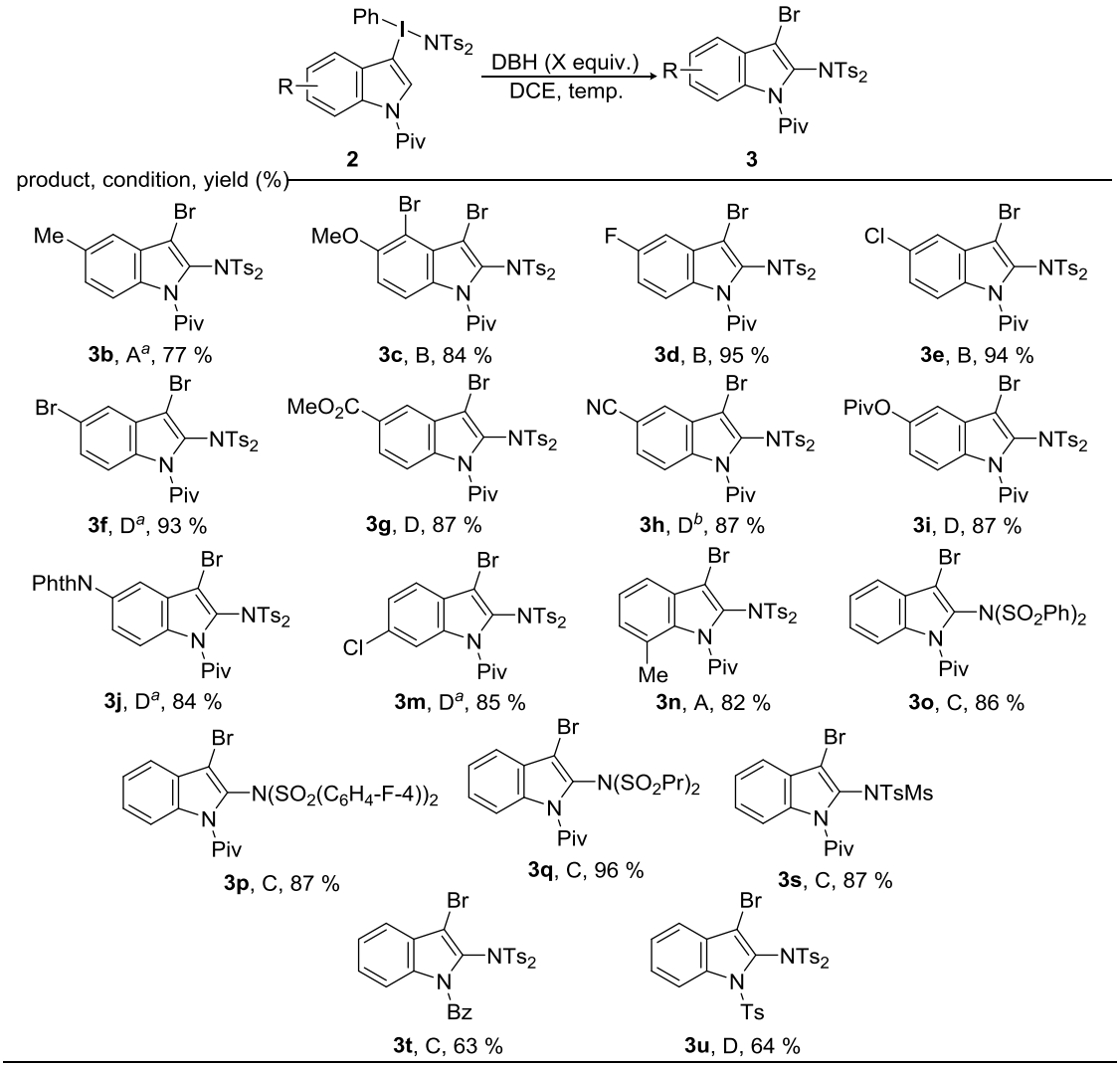
2 **3** X= Cl,Br,I

entry	reagents	solvent	temp. (°C)	yield (%)
1	NBS (1.2 equiv.)	DCM	r.t.	59
2	AcNHBr (1.2 equiv.)	DCM	r.t.	70
3	Pyridinium tribromide (1.2 equiv.)	DCM	r.t.	11
4	DBH (0.6 equiv.)	DCM	r.t.	80
5	DIH (0.6 equiv.)	DCM	r.t.	0
6	DCH (0.6 equiv.)	DCM	r.t.	N.R.
7	DBH (0.6 equiv.)	$CHCl_3$	r.t.	75
8	DBH (0.6 equiv.)	THF	r.t.	>1
9	DBH (0.6 equiv.)	DMF	r.t.	14
10	DBH (0.6 equiv.)	DCE	40	92

DBH:1,3-dibromo-5,5-dimethylhydantoin
DIH:1,3-diiodo-5,5-dimethylhydantoin
DCH:1,3-dichloro-5,5-dimethylhydantoin

To research the scope of substrate on redioselective 3,2-bromo-amination of (indolyl)(aryl)iodonium imides, various indoles and bis(sulfonyl)imides were examined (Table 2). The conditions for equivalent of DBH, solvent, and temperature had to be changed by the substituent group on indole group (Table 5, conditions A-E). The reaction of 5-substituted indoles bearing Me (**2b**), F (**2d**), Cl (**2e**), Br (**2f**), CO_2Me (**2g**), CN (**2h**), PivO (**2i**), and PhthN (**2j**) groups gave the corresponding monosubstituted *N*-(3-bromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (**3b, 3d-3j**) in high yields, respectively. The substrate bearing strong electron-donating group, such as MeO (**2c**), was converted into 3,4-dibromo product in high yield (**3c**). Other (indolyl)(aryl)iodonium imides bearing mono-substituted indole at other position were also transformed into the corresponding products in high yields (**3m**, **3n**), respectively. The same reaction of (indolyl)(aryl)iodonium imides having various bis(sulfonyl)imides **2** was carried out with high conversion and the desired products were obtained in high yields (**3p**-**3s**), respectively. Moreover, (indolyl)(aryl)iodonium imides bearing *N*-Ts or *N*-Bz groups instead of *N*-Piv group as a protecting group were also transformed into desired products in good yields (**3t**, and **3u**), respectively.

Table 2. Regioselective 3,2-Bromo-amination from Indolyl(aryl)iodonium Imides **2**



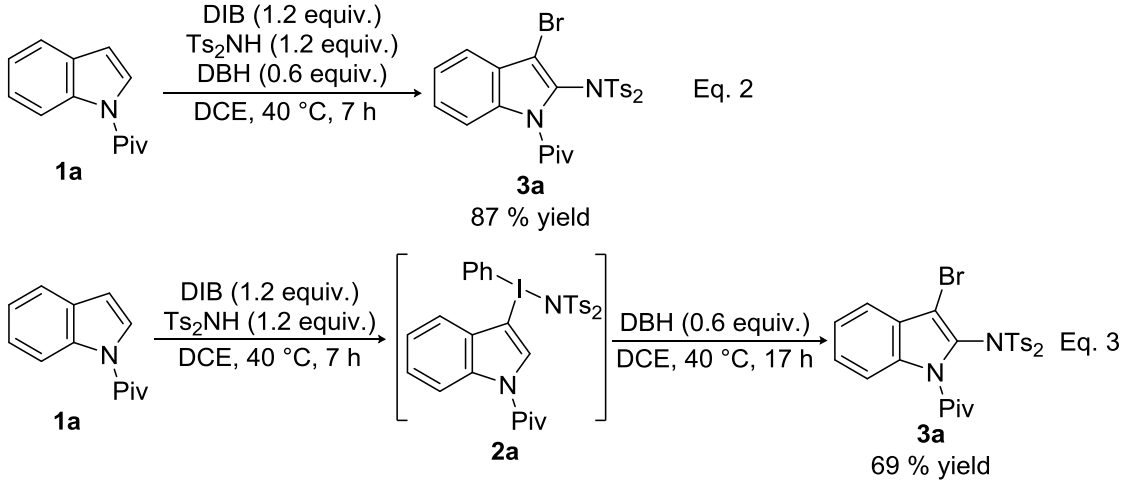
[a] First, a mixture of Ts_2NH (1.0 equiv.) and DBH was stirred at r.t. for 30 min. [b] Solvent was $MeCN/CH_3Cl$(2:1) .

conditions	DBH (equiv.)	solvent	temp. (°C)	time (h)	conditions	DBH (equiv.)	solvent	temp. (°C)	time (h)
condition A	0.6	DCM	r.t.	7	condition D	1.2	DCE	40	7
condition B	2.0	DCM	r.t.	7	condition E	1.2	DCE	40	24
condition C	0.6	DCE	40	7					

The author also searched direct conversion of 1-pivaloylindole **1** into *N*-(3-bromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (**3**) (Scheme 1). 3,2-Bromo-amination of (indolyl)(aryl)iodonium imide was carried out in high yield, however, isolation of **2** reduced the total yield of **3** from **1**. In addition, this method could not be used when (indolyl)(aryl)iodonium imides could not be isolated. The author examined two methods for one-pot synthesis of **3** from **1** (Scheme 2). Addition of DBH and **1a** at the same time (eq. 2) proceeded smoothly to give the the product in higher yield than that in addition of DBH after preparation of compound **2a**

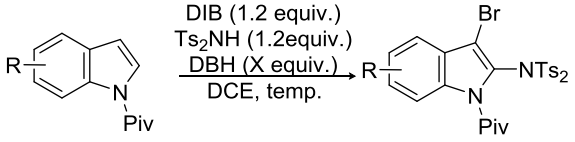
(eq. 3).

Scheme 1. One-pot 3,2-Bromo-amination from Indole **1a**



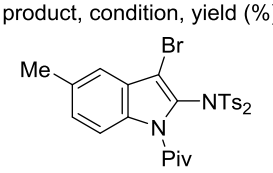
Then, the author examined direct conversion of various indoles into (indolyl)(aryl)iodonium imide (**2**) with bis(sulfonyl)imides, DIB, and DBH (Table 3). The conditions for equivalent of DBH, solvent, and temperature had to be changed by substituent groups on indoles, respectively (Table 6, conditions A-E). Treatment of monosubstuted indole **1**(**2b**-**2n**) and *N*-Ts or *N*-Bz protected indole (**2t**, **2u**) with various bis(sulfonyl)imides (**2o**-**2s**) gave the corresponding 2-bis(sulfonyl)imidyl-3-bromoindoles (**2b**-**2u**) in high yields, respectively. Direct conversion procedure improved the yield of the most products **3**, as compound with isolation method of (indolyl)(aryl)iodonium imide **2**. Especially, indoles, such as 5-NO_2 (**1l**), 4-Br (**1m**), and Ms_2NH (**1r**), where the isolation of **2** was impossible, were also transformed into compounds **3** bearing 5-NO_2 (**3l**), 4-Br (**3m**), and Ms_2NH (**3r**) in high yields using one-pot method.

Table 3. Regioselective 3,2-Bromo-amination of Indoles **1**

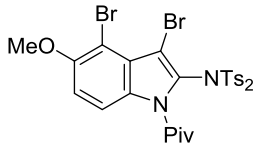


1 **3**

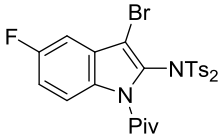
product, condition, yield (%)



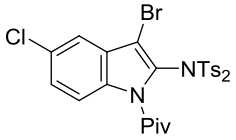
3b, A[a], 75 %



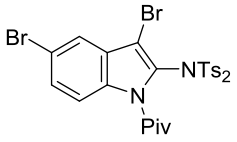
3c, B, 48 %



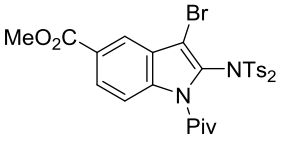
3d, B, 97 %



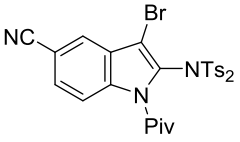
3e, B, 91 %



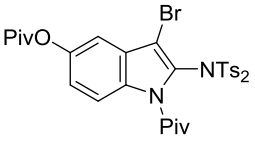
3f, D[a], 94 %



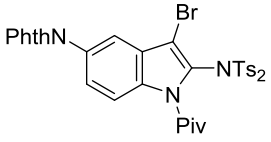
3g, D, 96 %



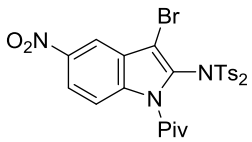
3h, D, 94 %



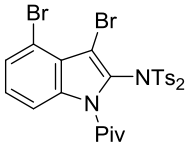
3i, D, 94 %



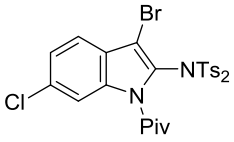
3j, D, 88 %



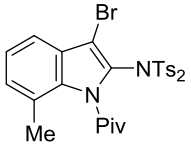
3l, E[a], 70 %



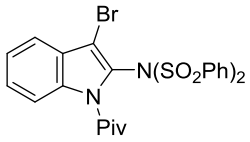
3l, B, 81 %



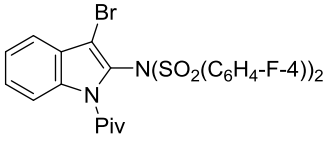
3m, B, 74 %



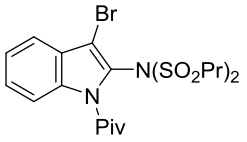
3n, D, 93 %



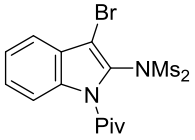
3o, A, 81 %



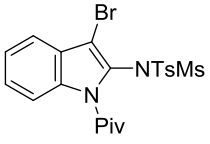
3p, A, 70 %



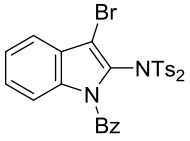
3q, A, 93 %



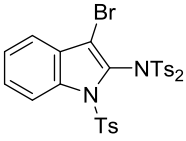
3r, C, 96 %



3s, A, 92 %



3t, B, 73 %



3u, D[a], 74 %

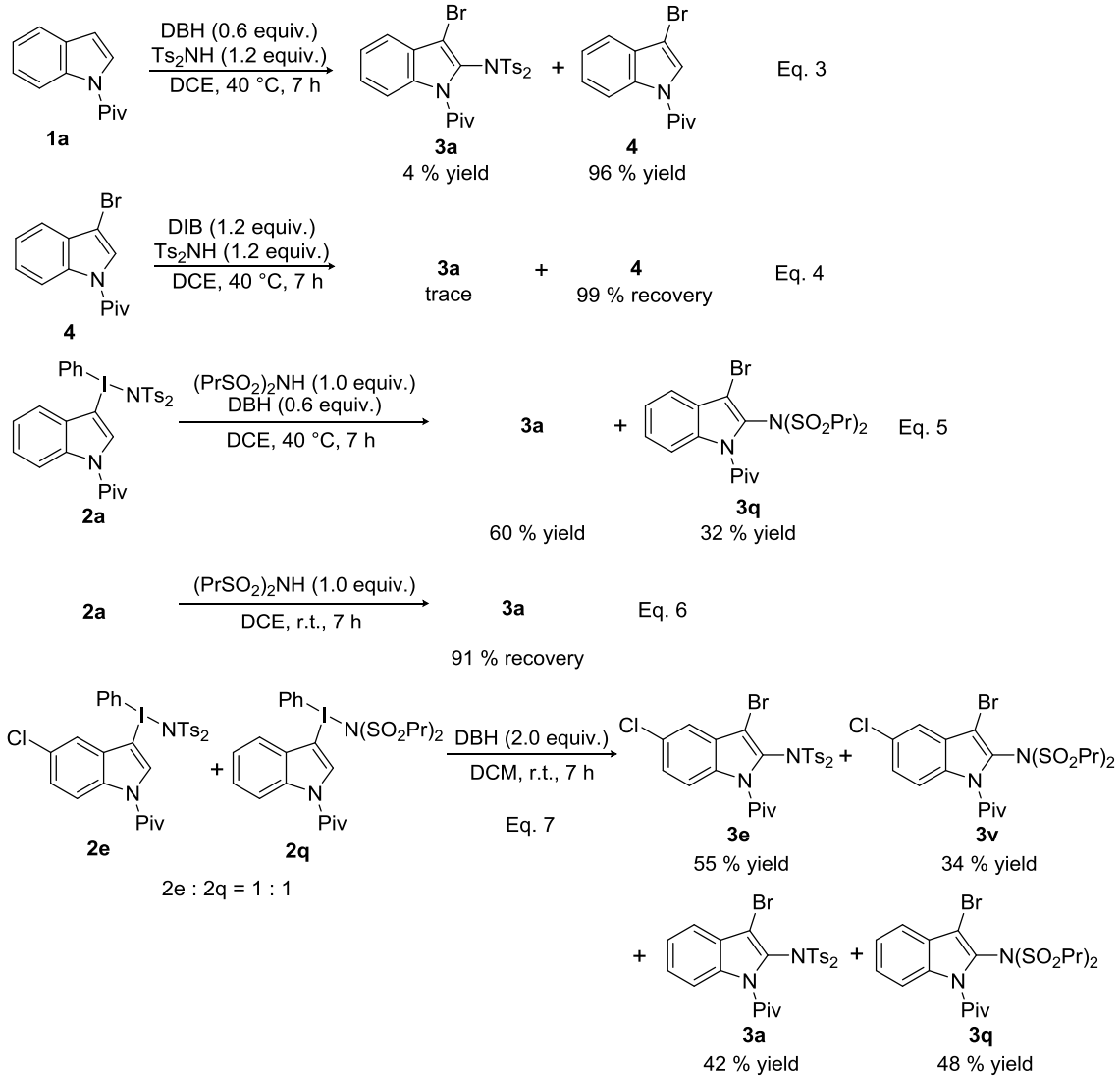
[a] First, a mixture of Ts_2NH (1.0 equiv.) and DBH was stirred at r.t. for 30 min.

conditions	DBH (equiv.)	solvent	temp. (°C)	time (h)	conditions	DBH (equiv.)	solvent	temp. (°C)	time (h)
condition A	0.6	DCM	r.t.	7	condition D	1.2	DCE	40	7
condition B	2.0	DCM	r.t.	7	condition E	1.2	DCE	40	24
condition C	0.6	DCE	40	7					

Next, the author investigated the reaction mechanism of the regioselective 3,2-bromo-amination of indole via (indolyl)(aryl)iodonium imide (Scheme 2). The reaction with 1-pivaloylindole (**1a**), bis(sulfonyl)imide, and DBH, without DIB proceeded to generate desired product (**3a**) in 4 % yield, and 3-bromo indole derivative **4** in 96 % yield, respectively. Moreover, **4** did not react with DIB and Ts_2NH under the present reaction conditions. These results suggested that generation of (indolyl)(aryl)iodonium imide **2** was necessary for the formation of **3**. In addition, the

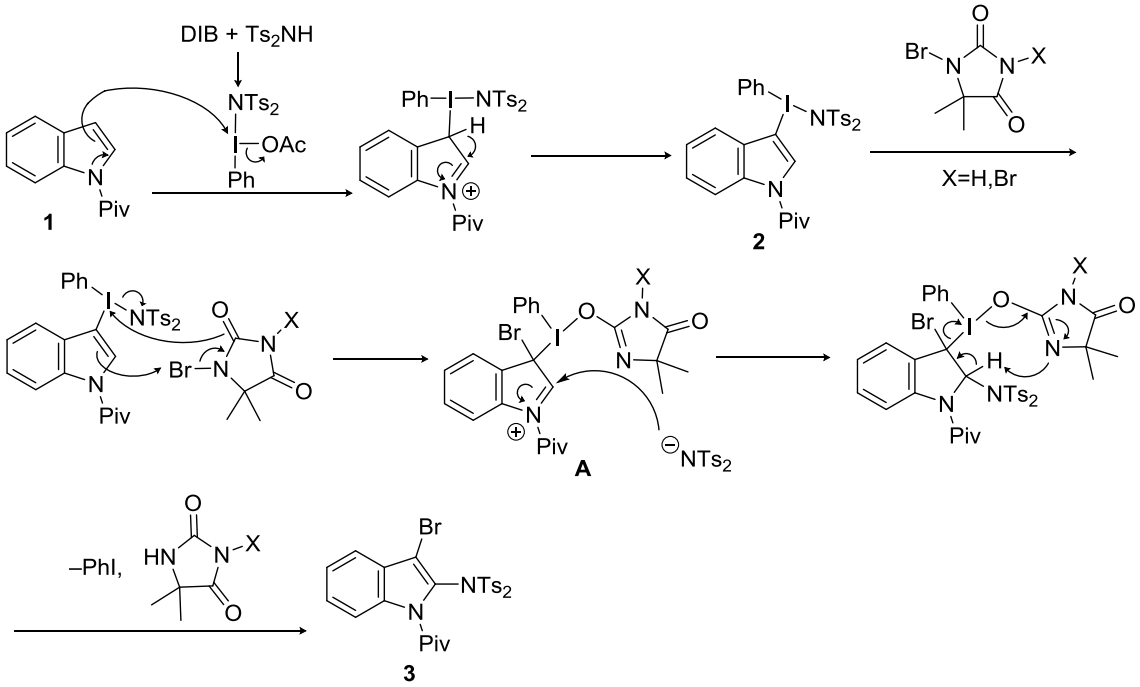
reaction of **2a** with DBH (0.6 equiv.) and $(PrSO_2)NH$ (1.0 equiv.) gave *N*-(3-bromo-1-pivaloyl-1*H*-indol-2-yl)- 4-methyl-*N*-tosylbenzenesulfonamide **(3a)** (60 % yield) and *N*-(3-bromo-1-pivaloyl-1*H*-indol-2-yl)-*N*-(propanesulfonyl)-propanesulfonamide (**3q**) (32 % yield), respectively. However, ligand exchange on the iodine atom was not observed by the treatment of **2a** with $(PrSO_2)_2NH$ in DCE. The treatment of 1:1 mixture of **2e** and **2q** with DBH (0.6 equiv.) provided four 3,2-bromo-amination products (**3a**, **3e**, **3q**, **3v**). These observations indicate that 3,2-bromo-amination of indole derivatives with DBH is intermolecular reaction via exchange for bis(sulfonyl)imide group on the iodine atom.

Scheme 2. Study for Reaction Mechanism of 3,2-Bromo-amination of **1a**



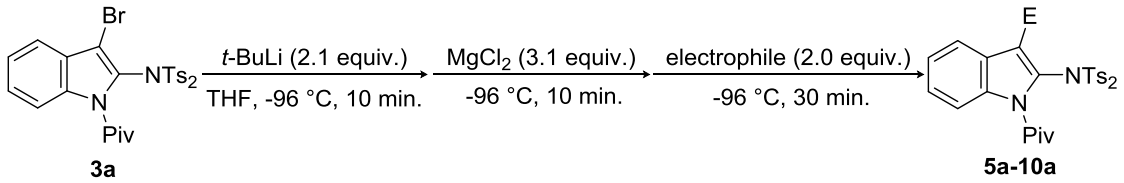
The proposed reaction mechanism is showed in Scheme 3. *N*-pivaloylndole **1** reacts with PhI(OAc)NTs_2 generated in situ from DIB and Ts_2NH, to give (indolyl)(aryl)iodonium imide **2** via deprotonation. Then, treatment of **2** with DBH gives intermediate **A**. At this step, reactivity of DBH is promoted by Lewis acidity of hypervalent iodine, and the Ts_2N group on the hypervalent iodine is substituted by 5,5-dimethylhydantoin derived from DBH to form **A**. Then, **A** is attacked by Ts_2N anion followed by aromatization to produce dual-functionalized indole **3** together with iodobenzene and 5,5-dimethylhydantoin.

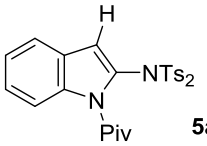
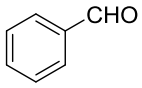
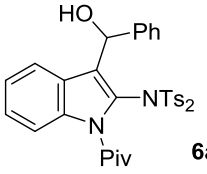
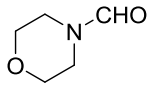
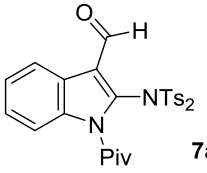
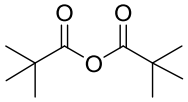
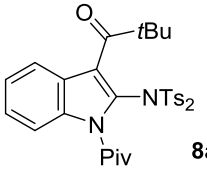
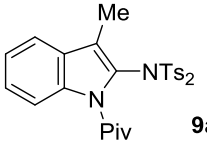
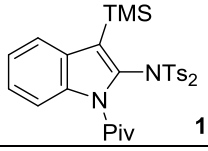
Scheme 3. Reaction Mechanism for 3,2-Bromo-amination of **1**



Then, the author demonstrated derivatization of 3,2-bromo-amination product **3a** (Table 4). Various 3-functionalized indoles (**5a-10a**) were obtained by halogen-lithium and -magnesium exchange of **3** with *t*BuLi and $MgCl_2$, followed by reaction with electrophiles, respectively.

Table 4. Functionalization of **3a** with *t*-BuLi



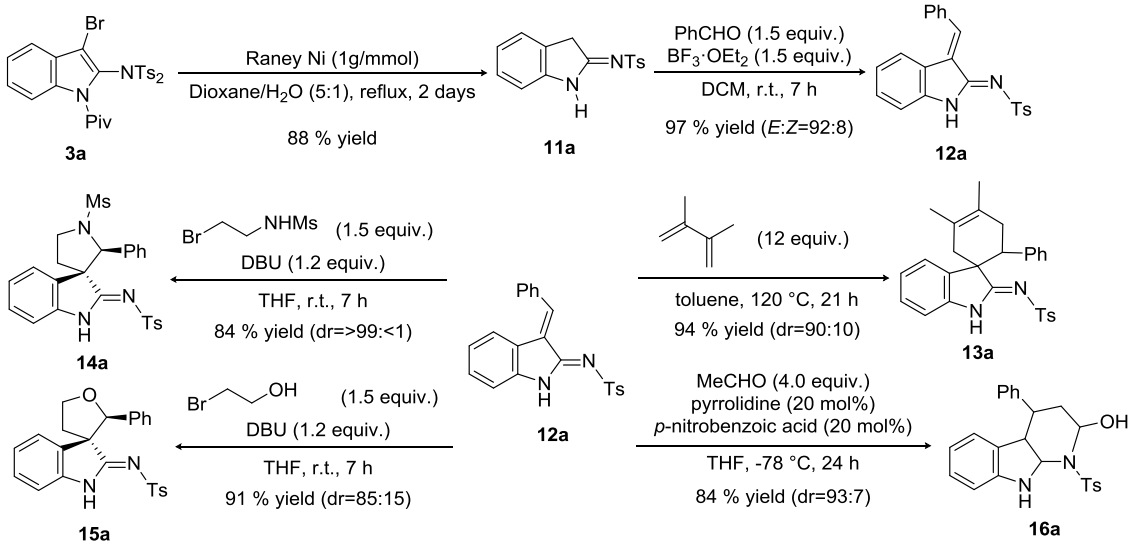
Electrophile	Product	Yield
H_2O	 **5a**	85[a]
	 **6a**	72
	 **7a**	70[b]
	 **8a**	66[b]
Me_2SO_4	 **9a**	75[b]
TMSOTf	 **10a**	58

[a] without $MgCl_2$
[b] Reaction temperature was -60 °C at 3rd step.

Moreover, the author also succeeded in synthesis of polycyclic indole derivatives from **3a** (Scheme 4). Thus, α,β-unsaturated imine (**12a**) was generated by reduction of **3a** with Raney Ni, followed by condensation with benzaldehyde (Scheme 4). **12a** is useful compounds for forming a part of medicinally important indoline derivatives. Treatment **12a** with 2,3-dimethylbutadiene under heating conditions gave Diels-Alder adduct **13a**, and with *N*-(2-bromoethyl)methansulfonamide and 2-bromoethanol with base provided spiro-hetero cyclic compounds **14a** and **15a**, respectively. New ionic 6-membered ring

formation by reaction of **12a** with benzaldehyde, pyrroridine, and 4-nitrobenzoic acid was also successfully obtained. These transformations showed easy preparation of various indole derivatives from **12a**, and with synthetic utility of **12a** for application to medicinally important indole derivatives.

Scheme 4. Derivation to Various Cyclic Compounds from **3a**



In conclusion, the author succeeded in regioselective 3,2-bromo-amination of indoles using indolyl(aryl)iodonium imides and bromination reagent. This is the first metal-free regioselective dual-functionalization of indoles, and it was applied to direct functionalization of *N*-pivaloylindole. The 3,2-bromo-amination product was easily transformed to various 3-substituted 2-aminoindole derivatives, and tricyclic compounds.

Experimental

1. General Methods. ^{1}H NMR spectra were measured on a JEOL ECA-500 (500 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; sep = septet; m = multiplet; br = broad), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on a JEOL ECA-500 (125 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm). High-resolution mass spectra were recorded by Thermo Fisher Scientific Exactive Orbitrap mass spectrometers. Infrared (IR) spectra were recorded on a JASCO FT/IR 4100 spectrometer. Single crystal X-ray diffraction data were collected at 173 K on a Bruker SMART APEX II CCD diffractometer with Mo Kα (λ = 0.71073) radiation and graphite monochrometer. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60GF254 0.25 mm) were used. The products were purified by column chromatography on neutral silica-gel (Kanto Chemical Co., Inc. silica gel 60N, Prod. No. 37560-84; Merck silica gel 60, Prod. No. 1.09385.9929). Visualization was accomplished by UV light (254 nm), anisaldehyde, $KMnO_4$, and phosphomolybdic acid.

1. General Procedure for Preparation of *N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3a) from 4-Methyl-*N*-(phenyl(1-pivaloyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (2a) (Table 4, entry 10)

To a solution of 4-methyl-*N*-(phenyl(1-pivaloyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide **2a** (72.9 mg, 0.10 mmol) in 1,2-dichloroethane (1mL) was added 1,3-dibromo-5,5-dimethylhydantoin (17.2 mg, 0.060 mmol). The mixture was stirred at 40 ºC for 7 h under argon atmosphere. Saturated Na_2SO_3 aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by water (10 mL) and brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 5/1), to give the desired product **3a** (55.4 mg, 92 % yield).

2. General Procedure for Preparation of *N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3a) from 1-Pivaloylindole (1a) (scheme 2)

To prepare PhI(OAc)NTs_2 were used DIB (38.7 mg, 0.12 mmol), Ts_2NH (39.1 mg, 0.12 mmol) in 1,2-dichloroethane (1mL. The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-pivaloylindole (**1a**) (20.1 mg, 0.10 mmol) and 1,3-dibromo-5,5-dimethylhydantoin (17.2 mg, 0.060 mmol) were added, and the solution was stirred at 40 ºC for 7 h. Saturated Na_2SO_3 aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by water (10 mL), brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 5/1), to give the desired product **3a** (52.4 mg, 87 % yield).

***N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3a):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (s, 9H), 2.48 (s, 6H), 7.24-7.30 (m, 1H), 7.33 (d, *J*=8.0 Hz, 4H), 7.41 (t, *J*=7.5 Hz, 1H), 7.52 (d, *J*=7.5 Hz, 1H), 7.55 (d, *J*=7.5 Hz, 1H), 7.98 (d, *J*=8.0 Hz, 4H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.2, 103.4, 113.8, 121.0, 122.2, 125.6, 125.9, 126.1, 129.1 (4C), 130.4 (4C), 133.7, 135.5 (2C), 145.4 (2C), 181.2. IR (neat) 1716, 1373, 1295, 1167, 660 cm^{-1}. MS (ESI) calcd for $C_{27}H_{27}N_2O_5BrNaS_2$ $[M+Na]^+$ 625.0437, found 625.0428.

Crystal data for 3a: Formula $C_{27}H_{27}BrN_2O_5S_2$, colorless, crystal dimensions 0.40 × 0.30 × 0.30 mm^3, prismatic, space group *P*bca, *a* = 11.3613(5) Å, *b* = 15.8902(15) Å, *c* = 29.9856(4) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, *V* = 5413.74(4) Å3, *Z* = 8, ρ_{calc} = 1.481 g cm^{-3}, F(000) = 2480, μ(MoKα) = 1.713 mm^{-1}, *T* = 173 K. 28834 reflections collected, 5143 independent reflections with $I > 2\sigma(I)$ ($2\theta_{max}$ = 27.51°), and 539 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. *R*1 = 0.0292 and *wR*2 = 0.0767. GOF = 1.105. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1023213. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

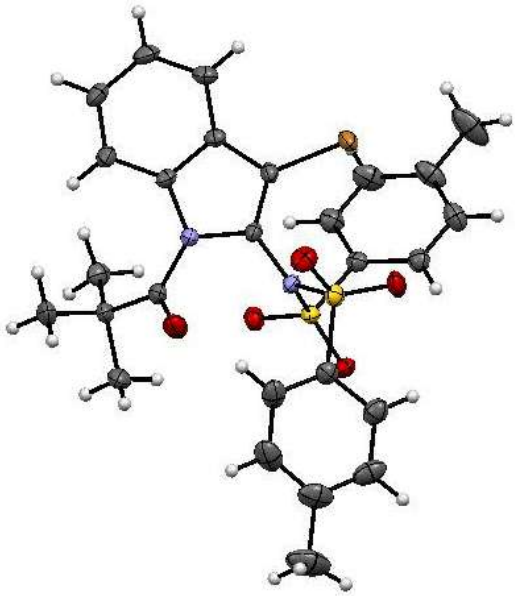


Figure 2. OPTEP drawing of **3a**.

***N*-(3-Bromo-5-methyl-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3b):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 9H), 2.46 (s, 3H), 2.47 (s, 6H), 7.23 (d, *J*=8.6 Hz, 1H), 7.29 (s, 1H), 7.32 (d, *J*=8.3 Hz, 4H), 7.45 (d, *J*=8.6 Hz, 1H), 7.96 (d, *J*=8.3 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 21.8 (2C), 28.1 (3C), 43.1, 103.2, 113.7, 120.4, 125.7, 125.9, 127.5, 129.2 (4C), 130.4 (5C), 132.0, 135.5 (2C), 145.4 (2C), 181.0. IR (neat) 1712, 1374, 1282, 1164, 662 cm^{-1}. MS (ESI) calcd for $C_{27}H_{25}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 678.9577, found 678.9586.

***N*-(3,4-Dibromo-5-methoxy-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3c):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.48 (s, 6H), 3.94 (s, 3H), 7.09 (d, *J*=9.2 Hz, 1H), 7.33 (d, *J*=8.3 Hz, 4H), 7.43 (d, *J*=9.2 Hz, 1H), 7.98 (d, *J*=8.3 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.2 (3C), 43.4, 57.7, 102.3, 104.2, 112.1, 113.3, 122.9, 128.6, 129.2 (4C), 129.9, 130.6 (4C), 135.6 (2C), 145.6 (2C), 151.9, 181.0. IR (neat) 1723, 1382, 1277, 1175, 1084, 648 cm^{-1}. MS (ESI) calcd for $C_{28}H_{28}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 615.0628, found 615.0639.

***N*-(3-Bromo-5-fluoro-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3d):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.48 (s, 6H), 7.12-7.21 (m, 2H), 7.33 (d, *J*=8.2 Hz, 4H), 7.49 (dd, *J*=8.5, 3.8 Hz, 1H), 7.96 (d, *J*=8.2 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.2, 102.8 (d, $J_{C\text{-}F}$=9.5 Hz), 106.0 (d, $J_{C\text{-}F}$=25.0 Hz), 114.5 (d, $J_{C\text{-}F}$=26.2 Hz), 115.2 (d, $J_{C\text{-}F}$=8.3 Hz), 126.5 (d, $J_{C\text{-}F}$=9.5 Hz),

127.5, 129.2 (4C), 130.1, 130.4 (5C), 135.3 (2C), 145.6 (2C), 158.7 (d, J_{C-F}=239.7 Hz), 180.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -119.8. IR (neat) 1723, 1373, 1300, 1171, 662 cm^{-1}. MS (ESI) calcd for $C_{27}H_{25}N_2O_5BrFS_2$ $[M-H^+]^-$ 619.0378, found 619.0392.

***N*-(3-Bromo-5-chloro-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3e):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.48 (s, 6H), 7.33 (d, *J*=8.1 Hz, 4H), 7.36 (dd, *J*=8.9, 2.3 Hz, 1H), 7.47 (d, *J*=8.9 Hz, 1H), 7.50 (d, *J*=2.3 Hz, 1H), 7.95 (d, *J*=8.1 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.2, 102.4, 115.1, 120.4, 126.3, 126.7, 127.3, 128.2, 129.3 (4C), 130.4 (4C), 131.9, 135.3 (2C), 145.6 (2C), 180.7. IR (neat) 1721, 1373, 1297, 1164, 1130, 661 cm^{-1}. MS (ESI) calcd for $C_{27}H_{25}N_2O_5BrClS_2$ $[M-H^+]^-$ 635.0082, found 635.0097.

***N*-(3,5-Dibromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3f):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (s, 9H), 2.48 (s, 6H), 7.33 (d, *J*=8.3 Hz, 4H), 7.42 (d, *J*=8.9 Hz, 1H), 7.50 (dd, *J*=8.9, 1.8 Hz, 1H), 7.66 (d, *J*=1.8 Hz, 1H), 7.95 (d, *J*=8.3 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.2, 102.2, 115.3, 123.5, 127.2, 128.8 (2C), 129.3, 130.4 (4C), 132.2, 135.3 (2C), 145.6 (2C), 180.7. IR (neat) 1725, 1373, 1299, 1165, 661 cm^{-1}. MS (ESI) calcd for $C_{27}H_{25}N_2O_5Br_2S_2$ $[M-H^+]^-$ 678.9577, found 678.9586.

Methyl 3-bromo-2-((4-methyl-*N*-tosylphenyl)sulfonamido)-1-pivaloyl-1*H*-indole-5-carboxylate (3g): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (s, 9H), 2.48 (s, 6H), 3.96 (s, 3H), 7.33 (d, *J*=8.4 Hz, 4H), 7.57 (dd, *J*=8.9, 0.60 Hz, 1H), 7.96 (d, *J*=8.4 Hz, 4H), 8.10 (dd, *J*=8.9, 1.7 Hz, 1H), 8.25 (dd, *J*=1.7, 0.60 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.3, 104.1, 113.6, 123.6, 124.3, 125.3, 126.8, 127.5, 129.3 (4C), 130.4 (4C), 135.2 (2C), 135.8, 145.7 (2C), 166.7, 180.7. IR (neat) 1720, 1379, 1289, 1166, 650 cm^{-1}. MS (ESI) calcd for $C_{29}H_{28}N_2O_5BrS_2$ $[M-H^+]^-$ 659.0527, found 659.0530.

***N*-(3-Bromo-5-cyano-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3h):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.49 (s, 6H), 7.34 (d, *J*=8.3 Hz, 4H), 7.60 (d, *J*=8.6 Hz, 1H), 7.64 (dd, *J*=8.6, 1.7 Hz, 1H), 7.88 (d, *J*=1.7 Hz, 1H), 7.95 (d, *J*=8.3 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.0 (3C), 43.4, 102.8, 105.9, 114.6, 118.9, 125.4, 126.4, 128.2, 128.6, 129.3 (4C), 130.4 (4C), 134.9, 135.0 (2C), 145.9 (2C), 180.6. IR (neat) 2225, 1728, 1372, 1308, 1165, 664 cm^{-1}. MS (ESI) calcd for $C_{28}H_{25}N_3O_5BrS_2$ $[M-H^+]^-$ 626.0424, found 626.0411.

3-Bromo-2-((4-methyl-*N*-tosylphenyl)sulfonamido)-1-pivaloyl-1*H*-indol-5-yl pivalate (3i): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 1.48 (s, 9H), 2.47 (s, 6H), 7.10 (dd, *J*=8.9, 2,8 Hz, 1H), 7.21 (d, *J*=2.8 Hz, 1H), 7.33 (d, *J*=8.2 Hz, 4H), 7.53 (d, *J*=8.9 Hz, 1H), 7.96 (d, *J*=8.2 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 27.2 (3C), 28.1 (3C), 39.1, 43.2, 103.1, 113.1, 114.6, 120.3, 126.2, 127.1, 129.2 (4C), 130.4 (4C), 131.2, 135.4 (2C), 145.5 (2C), 146.3, 177.5, 180.9. IR (neat) 1744, 1723, 1384, 1272, 1166, 652 cm^{-1}. MS (ESI) calcd for $C_{32}H_{34}N_2O_7BrS_2$ $[M\text{-}H^+]^-$ 701.0996, found 701.1014.

***N*-(3-Bromo-5-(1,3-dioxoisoindolin-2-yl)-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3J):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 9H), 2.48 (s, 6H), 7.34 (d, *J*=8.3 Hz, 4H), 7.45 (dd, *J*=8.9, 2.0 Hz, 1H), 7.60 (d, *J*=2.0 Hz, 1H), 7.67 (d, *J*=8.9 Hz, 1H), 7.79-7.85 (m, 2H), 7.94-8.03 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.2, 103.4, 114.5, 119.7, 123.8 (2C), 124.7, 126.1, 126.2, 127.5, 129.5 (4C), 130.5 (4C), 131.7 (2C) 132.8, 134.5 (2C), 135.4 (2C), 145.4 (2C), 167.5 (2C), 180.8. IR (neat) 1718, 1479, 1376, 1307, 1166, 1079, 661 cm^{-1}. MS (ESI) calcd for $C_{35}H_{29}N_3O_7BrS_2$ $[M\text{-}H^+]^-$ 746.0641, found 746.0641.

***N*-(3-Bromo-5-nitro-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3k):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (s, 9H), 2.50 (s, 6H), 7.35 (d, *J*=8.3 Hz, 4H), 7.61 (d, *J*=9.3 Hz, 1H), 7.95 (d, *J*=8.3 Hz, 4H), 8.30 (dd, *J*=9.3, 2.3 Hz, 1H), 8.48 (d, *J*=2.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.5, 104.0, 114.1, 118.0, 120.8, 125.3, 129.4 (4C), 130.4 (5C), 135.0 (2C), 136.0, 143.1, 146.0 (2C), 180.6. IR (neat) 1730, 1523, 1348, 1308, 1166, 873, 650 cm^{-1}. MS (ESI) calcd for $C_{27}H_{25}N_3O_7BrS_2$ $[M\text{-}H^+]^-$ 646.0323, found 646.0328.

***N*-(3,4-Dibromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3l):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.48 (s, 6H), 7.20 (dd, *J*=8.3, 7.8 Hz, 1H), 7.34 (d, *J*=8.5 Hz, 4H), 7.44 (d, *J*=7.8 Hz, 1H), 7.46 (d, *J*=8.3 Hz, 1H), 7.99 (d, *J*=8.5, Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.2 (3C), 43.6, 102.2, 113.0, 115.6, 121.9, 125.9, 127.4, 127.9, 129.2 (4C), 130.6 (5C), 134.7, 135.6 (2C), 145.6 (2C), 181.4. IR (neat) 1718, 1377, 1310, 1165, 662 cm^{-1}. MS (ESI) calcd for $C_{27}H_{25}N_2O_5Br_2S_2$ $[M\text{-}H^+]^-$ 678.9577, found 678.9598.

***N*-(3-Bromo-6-chloro-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonami**

de (3m): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 9H), 2.47 (s, 6H), 7.25 (dd, *J*=8.6, 1.5 Hz, 1H), 7.33 (d, *J*=8.2 Hz, 4H), 7.44 (d, *J*=8.6 Hz, 1H), 7.54 (d, *J*=1.5 Hz, 1H), 7.96 (d, *J*=8.2 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.1 (3C), 43.2, 103.1, 113.7, 122.0, 123.1, 124.1, 126.7, 129.3 (4C), 130.4 (4C), 132.0, 133.6, 135.3 (2C), 145.6 (2C), 180.7. IR (neat) 1726, 1374, 1292, 1165, 1072, 648 cm^{-1}. MS (ESI) calcd for $C_{27}H_{25}N_2O_5BrClS_2$ $[M\text{-}H^+]^-$ 635.0082, found 635.0094.

***N*-(3-Bromo-7-methyl-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3n):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.36 (s, 3H), 2.48 (brs, 6H), 7.14-7.21 (m, 2H), 7.22-7.46 (m, 5H), 7.76 (br, 2H), 8.14 (br, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 21.8 (2C), 28.6 (3C), 44.7, 102.7, 118.7, 122.3, 122.4, 125.4, 127.6, 128.9, 129.3 (4C), 130.5 (br, 4C), 131.3 (br, 2C), 136.1, 145.9 (br, 2C), 181.2. IR (neat) 1736, 1379, 1264, 1173 662 cm^{-1}. MS (ESI) calcd for $C_{28}H_{28}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 615.0628, found 615.0644.

***N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-*N*-(benzenesulfonyl)benzenesulfonamide (3o):** ^{1}H NMR (500 MHz, $CDCl_3$) δ1.49 (s, 9H), 7.27 (t, *J*=7.7 Hz, 1H), 7.42 (t, *J*=7.7 Hz, 1H), 7.49-7.59 (m, 6H), 7.68 (tt, *J*=7.5, 1.2 Hz, 2H), 8.09 (d, *J*=8.6, 1.2 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0 (3C), 43.2, 103.7, 113.9, 121.0, 122.3, 125.5, 125.8, 126.1, 128.6 (4C), 130.4 (4C), 133.6, 133.4 (2C), 138.3 (2C), 181.1. IR (neat) 1714, 1379, 1298, 1168, 685 cm^{-1}. MS (ESI) calcd for $C_{25}H_{22}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 573.0159, found 573.0175.

***N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-*N*-(4-fluorobenzenelsulfonyl)-4-fluorobenzenesulfonamide (3p):** ^{1}H NMR (500 MHz, $CDCl_3$) δ1.48 (s, 9H), 7.19-7.27 (m, 4H), 7.30 (t, *J*=7.7 Hz, 1H), 7.44 (t, *J*=7.7 Hz, 1H), 7.52-7.59 (m, 2H), 8.14 (dd, *J*=8.9, 5.2 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0 (3C), 43.2, 103.7, 113.9, 115.9 (d, $J_{C\text{-}F}$=9.5 Hz, 4C), 121.2, 122.5, 125.5, 125.6, 126.2, 133.5 (d, $J_{C\text{-}F}$=9.5 Hz, 4C), 133.6, 134.1 (d, $J_{C\text{-}F}$=2.4 Hz, 2C), 166.4 (d, $J_{C\text{-}F}$=256.3 Hz, 2C), 181.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ -102.0. IR (neat) 1712, 1387, 1285, 1238, 1176, 1154 cm^{-1}. MS (ESI) calcd for $C_{25}H_{20}N_2O_5BrF_2S_2$ $[M\text{-}H^+]^-$ 608.9971, found 608.9988.

***N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-*N*-(propanesulfonyl)propanesulfonamide (3q):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (t, *J*=7.4 Hz, 6H), 1.52 (s, 9H), 1.93-1.99 (m, 4H), 3.68-3.80 (m, 2H), 3.92-4.06 (m, 2H), 7.31 (t, *J*=8.0 Hz, 1H), 7.42 (t, *J*=8.0 Hz, 1H), 7.51 (d, *J*=8.0 Hz, 1H), 7.63 (d, *J*=7.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ

13.1 (2C), 16.9 (2C), 28.0 (3C), 43.4, 58.5 (2C), 102.8, 113.9, 120.9, 122.7, 125.36, 125.41, 126.1, 133.4, 182.7. IR (neat) 1712, 1374, 1299, 1163, 619 cm^{-1}. MS (ESI) calcd for $C_{19}H_{26}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 505.0472, found 505.0487.

***N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-*N*-(methanesulfonyl)methanesulfonamide (3r):** ^1H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 9H), 3.63 (s, 6H), 7.32 (t, *J*=7.8 Hz, 1H), 7.43 (t, *J*=7.8 Hz, 1H), 7.51 (d, *J*=7.8 Hz, 1H), 7.63 (d, *J*=7.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0 (3C), 43.4, 43.8 (2C), 102.5, 121.0, 122.8, 125.0, 125.4, 126.3, 133.4, 182.7. IR (neat) 1714, 1357, 1290, 1161, 621 cm^{-1}. MS (ESI) calcd for $C_{15}H_{18}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 448.9846, found 448.9858.

***N*-(3-Bromo-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-(methanesulfonyl)benzenesulfonamide (3s):** ^1H NMR (500 MHz, $CDCl_3$) δ1.60 (s, 9H), 2.44 (s, 3H), 3.83 (s, 3H), 7.27 (t, *J*=8.0 Hz, 1H), 7.30 (d, *J*=8.1 Hz, 2H), 7.41 (t, *J*=8.0 Hz, 1H), 7.50 (d, *J*=8.0 Hz, 1H), 7.56 (d, *J*=8.0 Hz,1H), 7.82 (d, *J*=8.1 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 28.1 (3C), 43.3, 44.0, 103.8, 114.0, 121.0, 122.5, 125.4, 125.6, 126.1, 129.7 (2C), 129.8 (2C), 133.4, 134.5, 146.0, 182.3. IR (neat) , 1718, 1361, 1300, 1171, 663 cm^{-1}. MS (ESI) calcd for $C_{21}H_{22}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 525.0159, found 525.0170.

***N*-(1-Benzoyl-3-bromo-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3t):** ^1H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 6H), 6.47 (d, *J*=8.6 Hz, 1H), 7.10 (t, *J*=8.6 Hz, 1H), 7.23 (t, *J*=7.7 Hz, 1H), 7.30 (d, *J*=8.0 Hz, 4H), 7.44 (t, *J*=7.7 Hz, 2H), 7.55 (d, *J*=8.6 Hz, 1H), 7.61 (t, *J*=8.6 Hz, 1H), 7.68 (d, *J*=7.7 Hz, 2H), 8.01 (d, *J*=8.0 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 105.8, 114.4, 120.8, 123.0, 126.0, 126.1, 126.4, 128.6 (2C), 129.2 (4C), 130.2 (4C), 130.5 (2C), 133.4, 133.9, 134.7, 135.7 (2C), 145.4(2C), 166.4. IR (neat) 1702, 1381, 1302, 1168 cm^{-1}. MS (ESI) calcd for $C_{29}H_{22}N_2O_5BrS_2$ $[M\text{-}H^+]^-$ 621.0148, found 621.0155.

***N*-(3-Bromo-1-tosyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (3u):** ^1H NMR (500 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.47 (s, 6H), 7.20 (d, *J*=8.2 Hz, 2H), 7.29 (t, *J*=7.6 Hz, 1H), 7.31-7.38 (m, 5H), 7.53 (d, *J*=7.7 Hz, 1H), 7.65 (d, *J*=7.7 Hz, 1H), 7.92 (d, *J*=8.2 Hz, 2H), 8.02 (d, *J*=8.3 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 21.8 (2C), 114.4, 121.1, 123.9, 126.5, 126.9, 127.4, 128.1 (2C), 129.3 (4C), 129.6 (2C), 130.4 (4C), 134.3, 135.99, 136.02 (2C), 145.0, 145.6 (2C). IR (neat) 1595, 1378, 1176, 1161, 1082, 658 cm^{-1}. MS (ESI) calcd for $C_{29}H_{24}N_2O_6BrS_3$ $[M\text{-}H^+]^-$ 670.9974, found 670.9990.

***N*-(3-Bromo-5-chloro-1-pivaloyl-1*H*-indol-2-yl)-*N*-(propanesulfonyl)propanesulfonamide (3v):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (t, *J*=7.4 Hz, 6H), 1.50 (s, 9H), 1.93-2.08 (m, 4H), 3.64-3.79 (m, 2H), 3.92-4.04 (m, 2H), 7.36 (dd, *J*=8.9, 2.3 Hz, 1H), 7.43 (d, *J*=8.9 Hz, 1H), 7.61 (d, *J*=2.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.1 (2C), 16.9 (2C), 28.1 (3C), 43.4, 58.6 (2C), 101.7, 115.1, 120.4, 126.47, 126.54, 126.63, 128.7, 131.6, 182.3. IR (neat) 1714, 1375, 1302, 1158, 862, 802 cm^{-1}. MS (ESI) calcd for $C_{19}H_{27}N_2O_5BrClS_2$ $[M+Na]^+$ 563.0047, found 563.0052.

3. Transformation of 2a into Various 2-Amino Indole Derivatives.

3.1. General Procedure for Electrophilic Addition of 3a with *t*-BuLi.

To a solution of **2a** (60.2 mg, 0.10 mmol) in THF (1.0 mL) was added dropwise the cooled *t*-BuLi (0.12 mL, 0.21 mmol, 1.8 M in pentane) at -96 ºC over 10 min. The solution was stirred at –96 ºC for 20 min. under argon atmosphere. Then, dried $MgCl_2$ (20.0 mg, 0.21 mmol) was added. After the obtained mixture was stirred at –96 ºC for 20 min, electrophiles were added and the reaction solution was kept at –96 ºC (electrophile: PhCHO, TMSOTf) or –60 ºC (electrophile: Piv_2O, 1-formylmorphorine, Me_2SO_4) for 1-2 h. Saturated NH_4Cl aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica-gel column chromatography (eluent: hexane/AcOEt = 8/1), to give the desired product **5a-10a**.

4-Methyl-*N*-(1-pivaloyl-1*H*-indol-2-yl)-*N*-tosylbenzenesulfonamide (5a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 9H), 2.48 (s, 6H), 6.15 (s, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.29-7.37 (m, 5H), 7.47-7.53 (m, 2H), 7.91 (d, *J* = 8.6 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 28.0 (3C), 43.4, 110.3, 113.6, 121.6, 121.8, 124.7, 125.5, 127.2, 129.1 (4C), 130.0 (4C), 134.6, 134.8 (2C), 145.4 (2C), 182.3. IR (neat) 1713, 1370, 1294, 1171 cm^{-1}. MS (ESI) calcd for $C_{27}H_{29}N_2O_5S_2$ $[M+H]^+$ 525.1512, found 525.1508.

***N*-(3-(Hydroxy(phenyl)methyl)-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (6a):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.22 (s, 3H), 2.50 (s, 3H), 2.86 (d, *J* = 2.3 Hz, 1H), 5.45 (d, *J* = 2.3 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 7.6 Hz, 1H), 7.19-7.28 (m, 6H), 7.28-7.33 (m, 1H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.86 (d, *J* = 8.5 Hz, 2H), 8.03 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 21.8, 28.3 (3C), 43.3, 66.6, 113.8, 121.4, 123.1, 124.2, 124.3, 124.9,

126.2, 127.0, 127.1 (2C), 127.6 (2C), 129.1 (2C), 129.4 (2C), 129.5 (2C), 130.5 (2C), 134.7, 135.1, 135.2, 140.1, 145.55, 145.64, 181.7. IR (neat) 2928, 1711, 1377, 1291, 1163 cm^{-1}. MS (ESI) calcd for $C_{34}H_{34}N_2NaO_6S_2$ $[M+Na]^+$ 653.1750, found 653.1739.

***N*-(3-Formyl-1-pivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (7a):** ^1H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.50 (s, 6H), 7.30-7.41 (m, 1H), 7.37 (d, *J* = 8.4 Hz, 4H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 4H), 8.37 (d, *J* = 7.8 Hz, 1H), 8.97 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9 (2C), 28.0 (3C), 43.7, 113.3, 119.3, 123.1, 123.2, 123.9, 126.0, 129.5 (4C), 130.3 (4C), 133.5 (2C), 134.1, 134.2, 146.4 (2C), 181.9, 185.4. IR (neat) 1724, 1674, 1381, 1311, 1166 cm^{-1}. MS (ESI) calcd for $C_{28}H_{28}N_2NaO_6S_2$ $[M+Na]^+$ 575.1281, found 575.1267.

***N*-(1,3-Dipivaloyl-1*H*-indol-2-yl)-4-methyl-*N*-tosylbenzenesulfonamide (8a):** ^1H NMR (500 MHz, $CDCl_3$) δ 1.27 (s, 9H), 1.43 (s, 9H), 2.48 (s, 6H), 7.25-7.30 (m, 1H), 7.32 (d, *J* = 8.4 Hz, 4H), 7.35-7.40 (m, 1H), 7.52 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8 (2C), 27.4 (3C), 28.3 (3C), 43.6, 44.1, 113.6, 121.9, 122.5, 123.3, 123.6, 124.6, 126.3, 128.7 (4C), 130.8 (4C), 132.9, 135.7 (2C), 145.0 (2C), 181.6, 205.6. IR (neat) 2930, 1718, 1672, 1379, 1289, 1165 cm^{-1}. MS (ESI) calcd for $C_{32}H_{36}N_2NaO_6S_2$ $[M+Na]^+$ 631.1907, found 631.1896.

4-Methyl-*N*-(3-methyl-1-pivaloyl-1*H*-indol-2-yl)-*N*-tosylbenzenesulfonamide (9a): ^1H NMR (500 MHz, $CDCl_3$) δ 1.50 (s, 9H), 1.51 (s, 3H), 2.47 (s, 6H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.30-7.39 (m, 1H), 7.33 (d, *J* = 7.8 Hz, 4H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.2, 21.8 (2C), 28.1 (3C), 43.0, 113.8, 120.2, 120.5, 121.1, 124.6, 124.9, 126.9, 129.1 (4C), 130.2 (4C), 134.2, 135.4 (2C), 145.2 (2C), 181.9. IR (neat) 1719, 1374, 1292, 1163 cm^{-1}. MS (ESI) calcd for $C_{28}H_{30}N_2NaO_5S_2$ $[M+Na]^+$ 561.1488, found 561.1484.

4-Methyl-*N*-(1-pivaloyl-3-(trimethylsilyl)-1*H*-indol-2-yl)-*N*-tosylbenzenesulfonamide (10a): ^1H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 9H), 1.39 (s, 9H), 2.47 (s, 6H), 7.21 (t, *J* = 7.9 Hz, 1H), 7.30-7.37 (m, 1H), 7.32 (d, *J* = 8.3 Hz, 4H), 7.54 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.11 (3C), 21.7 (2C), 28.3 (3C), 43.3, 113.8, 120.4, 120.9, 123.2, 124.0, 129.0 (4C), 130.4 (4C), 130.9, 131.2, 135.4, 136.2 (2C), 144.9 (2C), 181.4. IR (neat) 2922, 1715, 1447, 1375, 1294, 1170, 658 cm^{-1}. MS (ESI) calcd for $C_{30}H_{36}N_2NaO_5S_2Si$ $[M+Na]^+$ 619.1727, found 619.1711.

3.2. Transformation of 3a into 2-Amino-indole Derivatives 11a-15a.

3.2.1. Transformation of 3a into 11a.

To a solution of Raney Nickel (300 mg) in 1,4-dioxiane (4.0 mL) and H_2O (0.8 mL) was added **3a** (120.4 mg, 0.20 mmol). The solution was refluxed for 48 h under argon atmosphere. Then, the mixture was filtrated and washed with $CHCl_3$ (10 mL). The solution was removed under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 2/1), to give the desired product **11a** (64.3 mg, 88 % yield).

(*Z*)-*N*-(Indolin-2-ylidene)-4-methylbenzenesulfonamide (11a): ^{1}H NMR (500 MHz, $CDCl_3/CF_3CO_2H$) δ 2.44 (s, 3H), 4.24 (s, 2H), 7.21-7.29 (m, 2H), 7.33-7.43 (m, 4H), 7.88 (d, *J* = 8.3 Hz, 2H), 11.8 (brs, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 37.6, 113.1, 124.6, 125.9, 127.3 (2C), 129.1, 130.3 (2C), 135.3, 140.6, 146.2, 170.7. IR (neat) 2952, 1590, 1486, 1302, 1144 cm^{-1}. MS (ESI) calcd for $C_{15}H_{15}N_2O_2S$ $[M+H]^+$ 287.0849, found 287.0845.

3.2.3. Transformation of 11a into 12a.

To a solution of **11a** (36.3 mg, 0.10 mmol) in CH_2Cl_2 (1.0 mL) were added BF_3•Et_2O (18.5 μL, 0.15 mmol) and PhCHO (15.3 μL, 0.15 mmol). The mixture was stirred at room temperature for 7 h under argon atmosphere. Then, saturated $NaHCO_3$ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica-gel column chromatography (eluent: hexane/AcOEt = 2/1), to give the desired product **12a** (36.3 mg, 97 % yield, *E*:*Z* = 92:8).

***N*-((*Z*)-3-((*E*)-Benzylidene)indolin-2-ylidene)-4-methylbenzenesulfonamide (12a):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 6.92 (t, *J* = 7.8 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 7.21-7.28 (m, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.41-7.49 (m, 3H), 7.58-7.63 (m, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 2H), 8.11 (s, 1H), 10.12 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.5, 111.3, 121.3, 122.8, 123.1, 126.5 (2C), 128.7 (2C), 129.4 (4C), 129.5, 130.1, 130.2, 134.3, 139.1, 140.2, 141.8, 143.1, 160.6. IR (neat) 3280, 1571, 1461, 1312, 1280, 1134, 1085 cm^{-1}. MS (ESI) calcd for $C_{22}H_{19}N_2O_2S$ $[M+H]^+$ 375.1162, found 375.1154.

Crystal data for 12a: Formula $C_{22}H_{18}N_2O_2S$, yellow, crystal dimensions 0.30 × 0.10 × 0.10 mm^3, triclinic, space group P-1, *a* = 9.9285(7) Å, *b* = 10.1079(7) Å, *c* = 10.4705(7)

Å, α = S23 66.6900(10) °, β = 76.0070(10) °, γ = 89.8540(10) °, *V* = 931.25(11) Å3, *Z* = 2, ρ_{calc} = 1.335 g cm^{-3}, F(000) = 392, μ(MoKα) = 0.193 mm–1, *T* = 173 K. 5301 reflections collected, 4050 independent reflections with $I > 2\sigma(I)$ ($2\theta_{max}$ = 28.43°), and 245 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. *R*1 = 0.0458 and *wR*2 = 0.1094. GOF = 1.040. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1023215. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code +44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

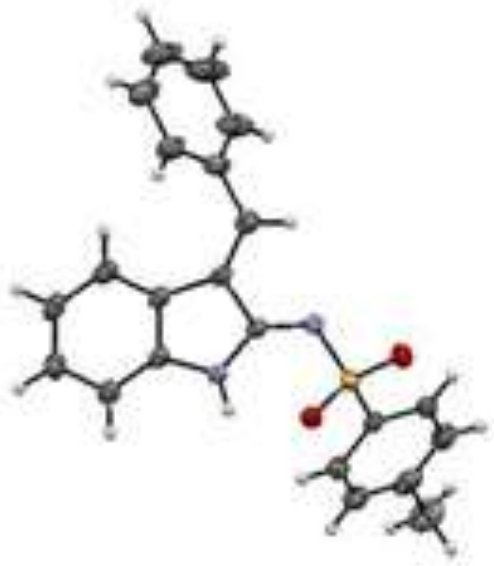


Figure 3. ORTEP drawing of **12a**.

3.2.4. Transformation of 12a into 13a.

To the solution of **12a** (37.4 mg, 0.1 mmol) in toluene (2 ml) was added 2,3-dimethyl-1,3-butadiene (15.3μl, 0.15 mmol). The solution was stirred at 120 ºC for 24 h. Then, the solvent was removed under reduced pressure to give the desired product **13a (**42.9 mg, 94 % yield, E/Z = 90:10) without any purifications.

4,5-Dimethyl-2-phenylspiro[cyclohex-4-ene-1,3'-indoline] (13a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.71 (s, 3H), 2.78 (s, 3H), 1.98 (d, *J*=17.2 Hz, 1H), 2.23 (dd, *J*=17.8, 5.5 Hz, 1H), 2.58 (t, *J*=17.8 Hz, 1H), 2.97 (d, *J*=17.2 Hz, 1H), 3.31 (dd, *J*=17.8, 5.5 Hz, 1H), 6.34 (d, *J*=7.7 Hz, 2H), 6.77 (t, *J*=7.7 Hz, 2H), 6.81 (d, *J*=7.5 Hz, 1H), 6.99 (t, *J*=7.5 Hz, 1H), 7.13 (t, *J*=7.5 Hz, 1H), 7.22-7.37 (m, 4H), 7.78 (d, *J*=8.3 Hz, 2H), 9.51 (brs, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 18.6, 18.9, 21.6, 36.5, 41.5, 47.1, 55.6, 110.6, 123.3, 123.5, 124.7, 125.4, 126.7, 126.8 (2C), 127.6 (2C), 127.9 (2C), 128.4, 129.3 (2C), 132.2, 140.9, 143.0, 173.0. IR (neat) 3289, 1606, 1282, 1141, 1090 cm^{-1}. MS (ESI) calcd for $C_{28}H_{27}N_2O_3S$ $[M\text{-}H^+]^-$ 455.1799, found 455.1812.

3.2.5. Transformation of 12a into 14a.

To a solution of **12a** (37.4 mg, 0.10 mmol) and 2-methanesulfonylethylamine (24.3 mg, 0.12 mmol) in THF (1.0 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (15.6 μL, 0.105 mmol. The mixture was stirred at room temperature for 7 h under argon atmosphere. Then, saturated NH_4Cl aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica-gel column chromatography (eluent: hexane/AcOEt = 3/1), to give the desired product **13a** (42.6 mg, 86% yield, *E*:*Z* = >99:<1).

(*Z*)-4-Methyl-*N*-(1'-(methanesulfonyl)-2'-phenylspiro[indoline-3,3'-pyrrolidin]-2-ylidene)benzenesulfonamide (14a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.20-2.28 (m, 1H), 2.41- 2.50 (m, 1H), 2.45 (s, 3H), 2.83 (s, 3H), 3.90-3.98 (m, 2H), 4.89 (s, 1H), 5.82 (d, *J* = 7.8 Hz, 1H), 6.68 (td, *J* = 7.8, 1.0 Hz, 1H), 6.71-7.30 (br, 2H), 6.93 (d, *J* = 7.8 Hz, 1H), 7.10-7.25 (m, 3H), 7.13 (td, *J* = 7.8, 1.0 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 8.2 Hz, 2H), 10.0 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 35.2, 35.9, 46.8, 62.1, 69.3, 110.7 (2C), 123.4, 125.4, 126.4 (2C), 127.2 (2C), 128.1, 128.2, 129.0, 129.8 (2C), 138.2, 139.1, 140.3 (2C), 144.0, 172.0. IR (neat) 3282, 1589, 1322, 1145, 1085 cm^{-1}. MS (ESI) calcd for $C_{25}H_{26}N_3O_4S_2$ $[M+H]^+$ 496.1359, found 496.1353.

Crystal data for 14a: Formula $C_{25}H_{25}N_3O_4S_2 \bullet C_4H_8O_2$, colorless, crystal dimensions 0.20 × 0.10 × 0.10 mm^3, triclinic, space group P-1, *a* = 9.5145(9) Å, *b* = 11.3505(10) Å, *c* = 12.4229(11) Å, α = 79.1933(10) °, β = 86.0059(12) °, γ = 82.6050(12) °, *V* = 1305.4(2) Å3, *Z* = 2, ρ_{calc} = 1.375 g cm^{-3}, F(000) = 570, μ(MoKα) = 0.247 mm^{-1}, *T* = 173 K. 7744 reflections collected, 5883 independent reflections with $I > 2\sigma(I)$ ($2\theta_{max}$ = 28.74°), and 364 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. *R*1 = 0.0528 and *wR*2 = 0.1411. GOF = 1.044. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1023217. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int.

code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

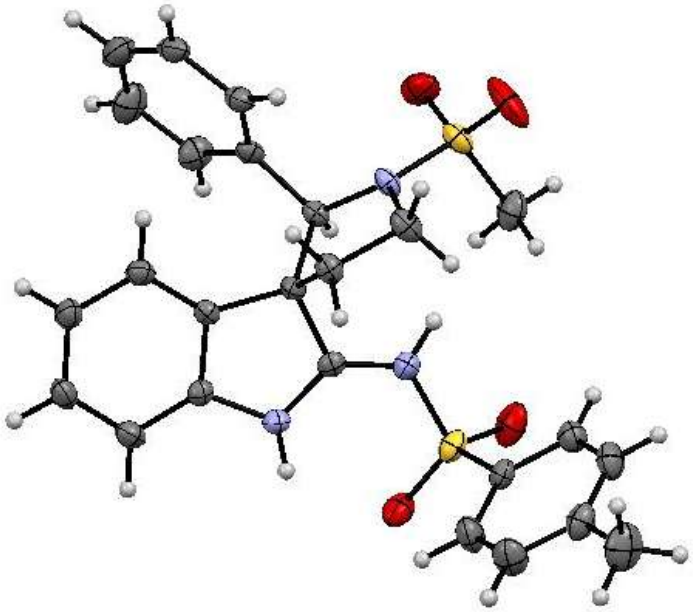


Figure 4. ORTEP drawing of **14a**.

3.2.6. Transformation of 12a into 15a.

To a solution of **12a** (37.4 mg, 0.10 mmol) in THF (1.0 mL) were added 2-bromoethanol (15.3 μL, 0.15 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (15.3 μL, 0.15 mmol). The mixture was stirred at room temperature for 7 h under argon atmosphere. Then, saturated NH_4Cl aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica-gel column chromatography (eluent: hexane/AcOEt = 2/1), to give the desired product **14a** (38.1 mg, 91% yield, *E*:*Z* = 85:15).

(*Z*)-4-Methyl-*N*-(2-phenyl-4,5-dihydro-2*H*-spiro[furan-3,3'-indolin]-2'-ylidene)benzenesulfonamide (15a): 1H NMR (500 MHz, CDCl3) □ 2.37 (ddd, *J* = 12.6, 8.3, 5.2 Hz, 1H), 2.46 (s, 3H), 2.89 (ddd, *J* = 12.6, 9.8, 7.2 Hz, 1H), 4.35 (td, *J* = 9.8, 5.2 Hz, 1H), 4.44 (td, *J* = 8.3, 7.2 Hz, 1H), 5.09 (s, 1H), 6.71 (d, *J* = 7.5 Hz, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 2H), 6.94-7.01 (m, 2H), 7.07 (t, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.96 (d, *J* = 8.0 Hz, 2H), 9.86 (s, 1H). 13C NMR (125 MHz, CDCl3) □ 21.6, 39.2, 62.9, 67.1, 89.1, 110.5, 123.5, 124.6, 125.2 (2C), 126.7 (2C), 127.49 (2C), 127.53, 128.2, 129.6 (2C), 131.2, 135.5, 138.5,

139.6, 143.6, 170.1. IR (neat) 3060, 1657, 1446, 1275, 1149 cm–1. MS (ESI) calcd for C24H23N2O3S [M+H]+ 419.1424, found 419.1416.

Crystal data for 15a: Formula $C_{24}H_{22}N_2O_3S$, colorless, crystal dimensions 0.20 × 0.10 × 0.10 mm^3, triclinic, space group P-1, *a* = 6.8453(4) Å, *b* = 11.1232(7) Å, *c* = 14.3467(9) Å, α = 95.8640(10) °, β = 94.6170(2) °, γ = 106.1630(10) °, *V* = 1036.91(11) Å3, *Z* = 2, ρ_{calc} = 1.340 g cm^{-3}, F(000) = 440, μ(MoKα) = 0.185 mm^{-1}, *T* = 173 K. 5925 reflections collected, 4519 independent reflections with $I > 2\sigma(I)$ ($2\theta_{max}$ = 28.44°), and 272 parameters were used for the solution of the structure. The non-hydrogen atoms were refined anisotropically. *R*1 = 0.0437 and *wR*2 = 0.1124. GOF = 1.079. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1023216. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

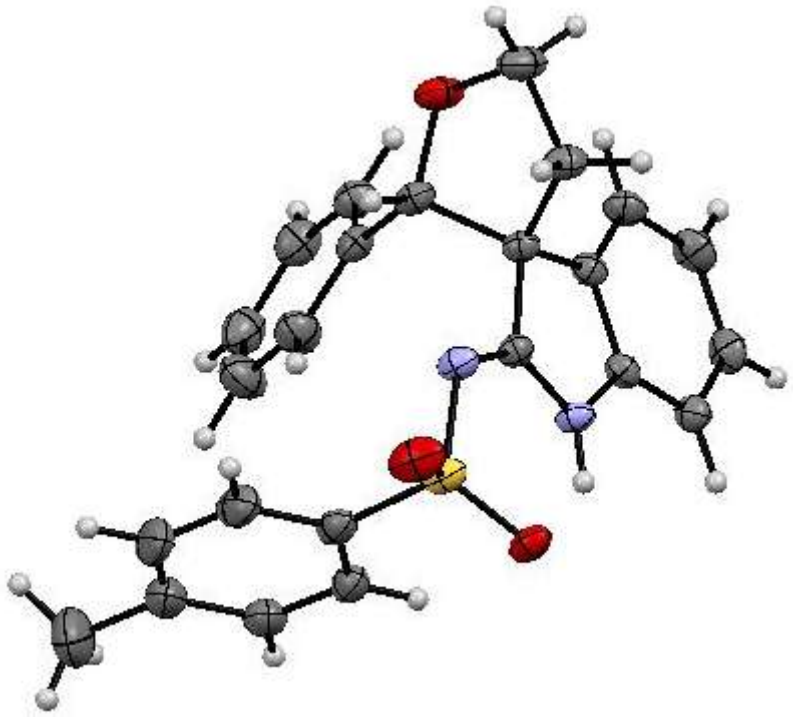


Figure 5. ORTEP drawing of **15a**.

3.2.7. Transformation of 12a into 16a.

To a solution of **12a** (37.4 mg, 0.10 mmol), 4-nitrobenzoic acid (3.3 mg, 0.02 mmol), and pyrrolidine (1.7 μL, 0.02 mol) in THF (1.0 mL) was added acetaldehyde (24.9 μL,

0.40 mmol, ca. 90% aq.) at -78 ºC. The mixture was stirred at -78 ºC for 24 h under argon atmosphere. Then, saturated $NaHCO_3$ aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica-gel column chromatography (eluent: hexane/AcOEt = 2/1), to give the desired product **16a** (35.2 mg, 82% yield).

4-Phenyl-1-tosyl-2,3,4,9-tetrahydro-1*H*-pyrido[2,3-*b*]indol-2-ol (16a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03-1,09 (m, 1H), 2.21 (ddd, *J* = 14.5, 6.0, 3.0 Hz, 1H), 2.38 (s. 3H), 2.94 (brs, 1H), 4.18 (dd, *J* = 11.5, 6.0 Hz, 1H), 5.74 (s, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 6.85 (t, *J* = 7.8 Hz, 1H), 6.87-6.93 (m, 2H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.14-7.20 (m, 3H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 9.04 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 34.0, 37.3, 79.8, 101.9, 110.7, 119.4, 119.7, 121.5, 125.6, 126.6, 126.9 (2C), 127.8 (2C), 128.4 (2C), 129.1, 130.1 (2C), 133.5, 134.0, 143.3, 144.8. IR (neat) 3480, 1593, 1468, 1362, 1162 cm^{-1}. MS (ESI) calcd for $C_{24}H_{23}N_2O_3S$ $[M+H]^+$ 419.1424, found 419.1424.

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(6) See chapter 2

Chapter 4

Regioselective Iodo-amination of 2-Methylindoles via (Indolyl)(aryl)iodonium Imides

N-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)methyl)-*N*-(methanesulfonyl)methanesulfonamides were prepared by iodo-amination of 2-methylindole derivatives via (2-methylindolyl)(phenyl)iodonium imides using iodinating reagents. This reaction transformed both sp^2 C-H and non-activated sp^3 C-H bonds to C-I and C-N bonds, respectively.

Introduction

Direct intermolecular C-H amination at non-activated sp^3 carbon is attractive as functionalization of commercially available and cheep compounds, and is useful for synthetic chemistry[1]. Although oxidative C-H functionalization of alkylindole is also noticed by a lot of organic chemists to construct new synthetic process of medicinal and bioactive compounds[2], direct intermolecular sp^3 carbon amination of alkylindoles required azide compounds or heavy metal reagents[2a,c]. On the other hands, halogenation reagents are useful compounds for direct and metal-free C-N bond formation at benzylic carbon atom[3], and some reports showed that hypervalent iodine is also effective for direct carbon-nitrogen bond construction reaction at non-activated sp^3 carbon atom[4].

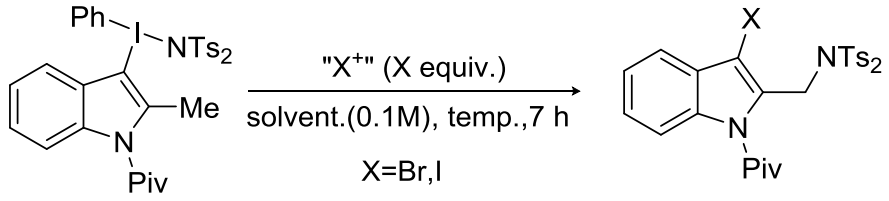
On chapter 2, the author developed novel imide-combined hypervalent iodine, (indolyl)(aryl)iodonium imide, and succeeded in C-H dual-functionalization of indole via (indolyl)(aryl)iodonium imide with bromination reagent in chapter 3[5]. These methods regioselectively transformed two C-H bonds to C-Br and C-N bond, respectively. Here, the author reports new regioselective dual-functionalization of 2-methylindole derivatives via (indolyl)(aryl)iodonium imide generated in situ with iodination reagent. This reaction provided 2-aminomethyl-3-iodoindole derivatives through oxidative C-N bond formation of non-activated sp^3 C-H bond.

Results and Discussion

First, the author screened haloganation reagents and solvents in halo-amination of (2-methylindolyl)(aryl)iodonium imide (Table 1). The same treatment as 3,2-bromo-amination of (indolyl)(aryl)iodonium imide with DBH gave *N*-((3'-bromo-1'-pivaloyl-1'*H*-indol-2'-yl)methyl)-4-methyl-*N*-tosylbenzenesulfonamide in moderate yield (entry 1). Use of 1.2 equivalents DBH decreased the product yield (entry 2), however, dark conditions and use of Ts_2NH (1.2 equiv.) improved the yield of

3a (entries 3,4). Although the author examined halo-amination with various solvents and bromination reagents, desire product was not obtained in high yield (entries 5-11). Amazingly, **3a** was produced in high yield by use of NIS or DIH instead of DBH (entries 12,13). Those iodination reagents were not effective for dual-functionalization of indole derivatives (see chapter 3), however, DIH was the best reagent for C-N bond formation of 2-methylindole derivatives.

Table 1. Regioselective Halo-amination of (2-MethylIndolyl)(phenyl)iodonium Imide with Halogenation Reagents



2a **3a**

entry	"X^+" (equiv.)	solvent	temp(°C)	yield (%)
1	DBH (0.6)	DCM	r.t.	54
2	DBH (1.2)	DCE	40	26
3[a]	DBH (0.6)	DCM	r.t.	60
4[a,b]	DBH (0.6)	DCM	r.t.	67
5[a,b]	DBH (0.6)	THF	r.t.	7
6[a,b]	DBH (0.6)	MeCN	r.t.	50
7[a,b]	DBH (0.6)	$CHCl_3$	r.t.	33
8[a,b]	NBS (1.2)	DCM	r.t.	70
9[a,b]	AcNHBr (1.2)	DCM	r.t.	12
10[a]	*N*-Bromophthalimide (1.2)	DCM	r.t.	74
11[a,b]	$PyHBr_3$ (1.2)	DCM	r.t.	0
12[a,b]	NIS (1.2)	DCM	r.t.	83
13[a,b]	**DIH (0.6)**	**DCM**	**r.t.**	**92**
14[a]	DIH (0.6)	DCM	r.t.	85

[a] under the dark conditions

[b] First, a mixture of Ts_2NH (1.0 equiv.) and "X^+" was stirred at r.t. for 30 min.

DBH:1,3-dibromo-5,5-dimethylhydantoin
DIH:1,3-diiodo-5,5-dimethylhydantoin

Although the desire product (**3a**) was obtained in high yield from **2a**, various (alkylindolyl)(aryl)iodonium imides **2** generated from substituted 2-alkylindole derivatives (**1**) could not be isolated from the reaction mixture of **1** with DIB and Ts_2NH. Then, the author studied one-pot preparation method for iodo-amination of **1a** (Scheme

1). The yield of product was 78 %, when DIB, Ts_2NH and DIH were added at same time. The condition of DIH and additional Ts_2NH adde after 1st step, generation of (indolyl)(aryl)iodonium imide intermediate, did not improve the yield of **3a**. Then, the author examined addition of bases after 1st step, followed by stirring for 10 minutes (Table 2). Use of 1.2 equivalent of $NaHCO_3$ was not affected in the yield of **3a** (entry 2), however, the product was formed in 96 % yield by using $NaHCO_3$ (2.4 equiv.) (entry 3). Other bases were not effective for iodo-amination of 2-methylindole derivatives (entries 4-7).

Scheme 1. One-pot Procedure of Regioselective Iodo-amination of **1a** with Halogenation Reagents

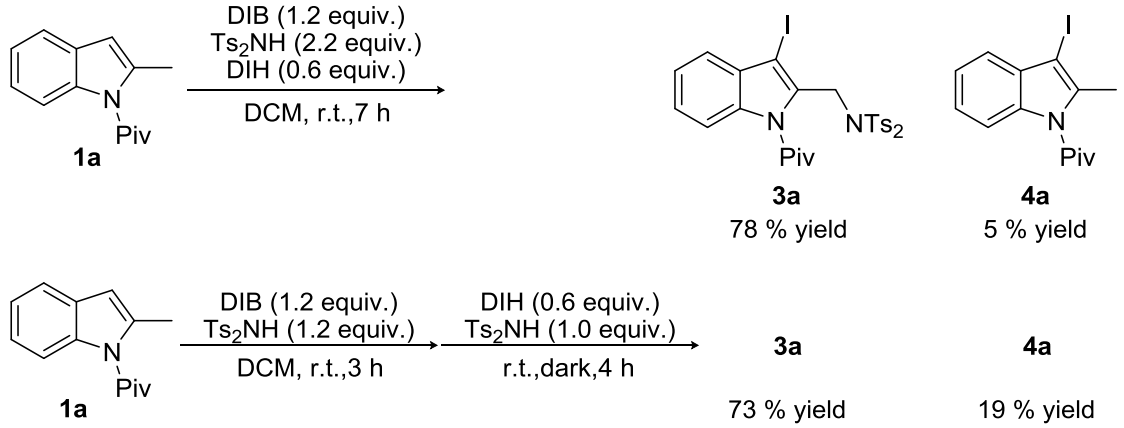
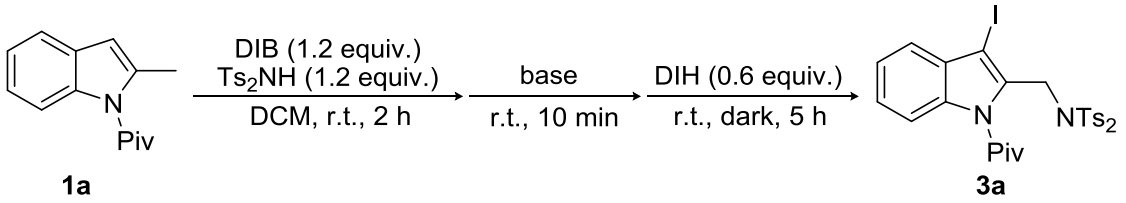


Table 2. Screening Bases for One-pot Procedure of Regioselective Iodo-amination of **1a**

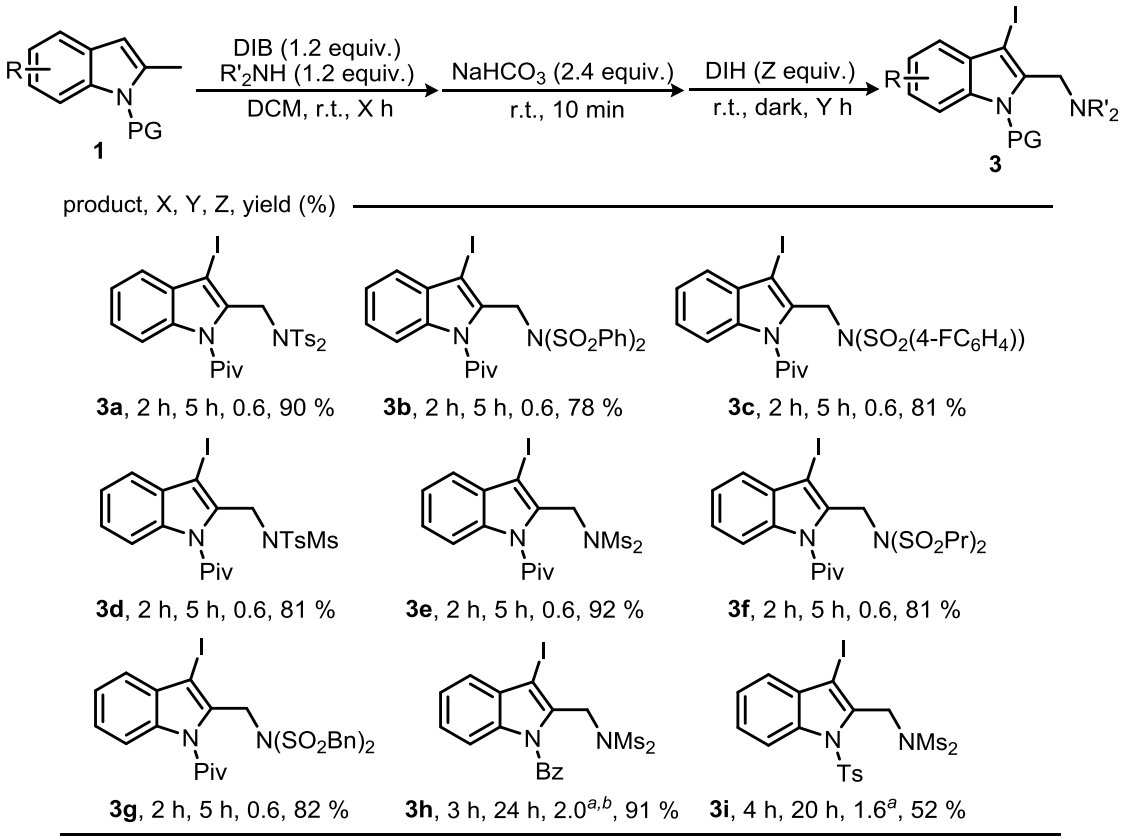


entry	base (equiv.)	yield
1	-	73 %
2	$NaHCO_3$ (1.2)	77 %
3	$NaHCO_3$ (2.4)	96 %
4	K_2CO_3 (2.4)	43 %
5	Na_2HPO_4 (2.4)	63 %
6	Et_3N (2.4)	messy
7	DBU (2.4)	messy

Next, the author examined screening various bis(sulfonyl)imides and *N*-protecting groups of 2-methylindole for iodo-amination (Table 3). Although both arene- and bis(alkanesulfonyl)imide gave α-amino-3-iodoindole derivatives (**3a-3f**) in high yield,

use of Ms_2NH was the best conditions for dual-functionalization of 2-methylindole with DIH. In addition, indole bearing Bz (**1h**) and Ts (**1g**) groups were also applied for effective to give desire products in 91 % and 52 % yields, respectively.

Table 3: Regioselective Iodo-amination of **1** with Various Bis(sulfonyl)imides and Protecting Groups



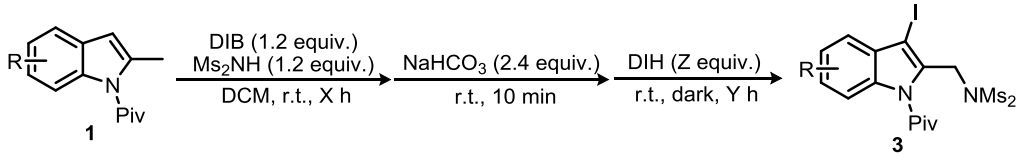
[a] R'_2NH (1.7 equiv.) was used.

[b] NIS (Z equiv.) was used instead of DIH.

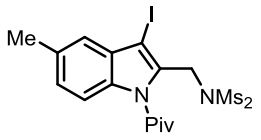
To research the range of substrates for redioselective iodo-amination of 2-methylindole, various 2-methylindoles were examined (Table 4). NIS was used instead of DIH for some substrates, and equivalent of iodination reagent depended on substitutent of 2-methylindole derivatives. 3,5-dimethylindole (**2j**) derivative gave *N*-((3'-bromo-5'-methyl-1'-pivaloyl-1'*H*-indol-2'-yl)methyl)-4-methyl-*N*-tosylbenzenes ulfonamide (**3j**) in high yield. The substrate bearing strong electron-donating group, MeO (**2q**), was converted into 3,6-diiodo product (**3k**) in high yield by using 2.4 equivalent of NIS. The reaction of 5 or 6-monosubstituted indoles bearing 5-F (**2k**), 5-Cl (**2l**), 5-Br (**2m**), 5-CO_2Me (**2n**), 5-CN (**2o**), 6-Me (**2r**), 6-MeO (**2s**), 6-Cl (**2t**), and

6-CO_2Ne (**2u**) groups, gave the corresponding monosubstituted products (**3k-3o, 3r-3u**) in high yields, respectively. 5- or 6-NO_2 indole derivative were also transformed to desire products in high yield in the presence of Na_2SO_4 (2.0 equiv.) without base. 4-Me (**1w**) indole derivative was also converted into 2-Ms_2NCH_2-3-iodo indole derivative (**3w**) in high yields, respectively. In addition, the same treatment of di-substituted indoles (**1x**, **1y**) and 3*H*-benzo[e]indole derivatives (**1z**) gave corresponding products in good to high yields, respectively. Unfortunately, 3-ethylindole derivative was not transformed to iodo-amination product.

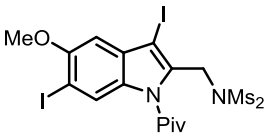
Table 4: Regioselective Iodo-amination of **1** with Various Substituted 2-Methylindole Derivatives



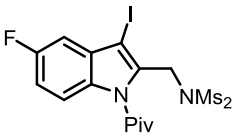
product, X, Y, Z, yield (%)



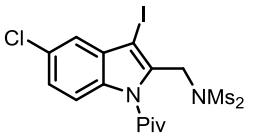
3j, 2 h, 5 h, 0.6, 72 %



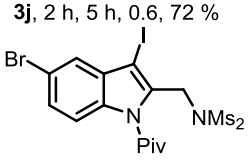
3k, 3 h, 4 h, 2.4[c], 95 %



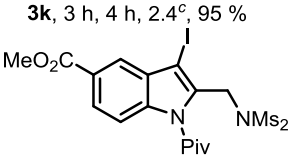
3l, 4 h, 2 h, 0.6[a], 82 %



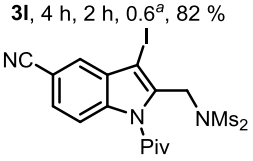
3m, 4 h, 17 h, 2.0[a,c], 91 %



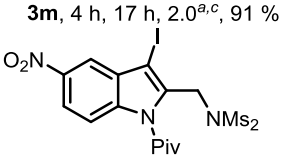
3n, 4 h, 17 h, 2.0[a,c], 96 %



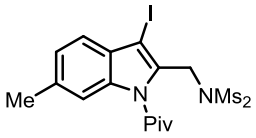
3o,4 h, 20 h, 2.0[a,c], 90 %



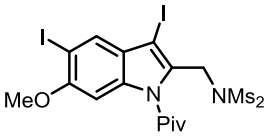
3p, 5 h, 18 h, 1.6[b,d], 82 %



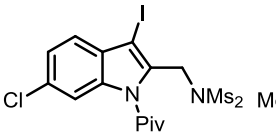
3q, 5 h, 21 h, 1.6[b,d,e], 77 %



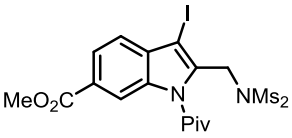
3r, 3 h, 3 h, 0.6[a], 89 %



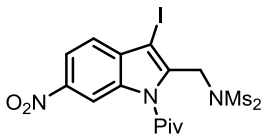
3s, 3 h, 4 h, 1.0, 89 %



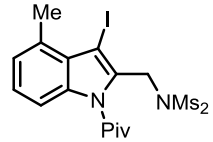
3t, 3 h, 20 h, 2.0[a,c], 95 %



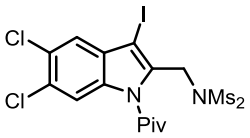
3u, 4 h, 3 h, 0.6[a], 87 %



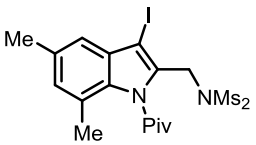
3v, 5 h, 25 h, 1.6[b,d,e], 77 %



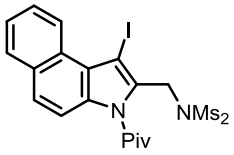
3w, 2 h, 4 h, 0.5, 81 %



3x, 5 h, 21 h, 3.0[a,c], 95 %



3y, 3 h, 4 h, 1.6[a], 56 %



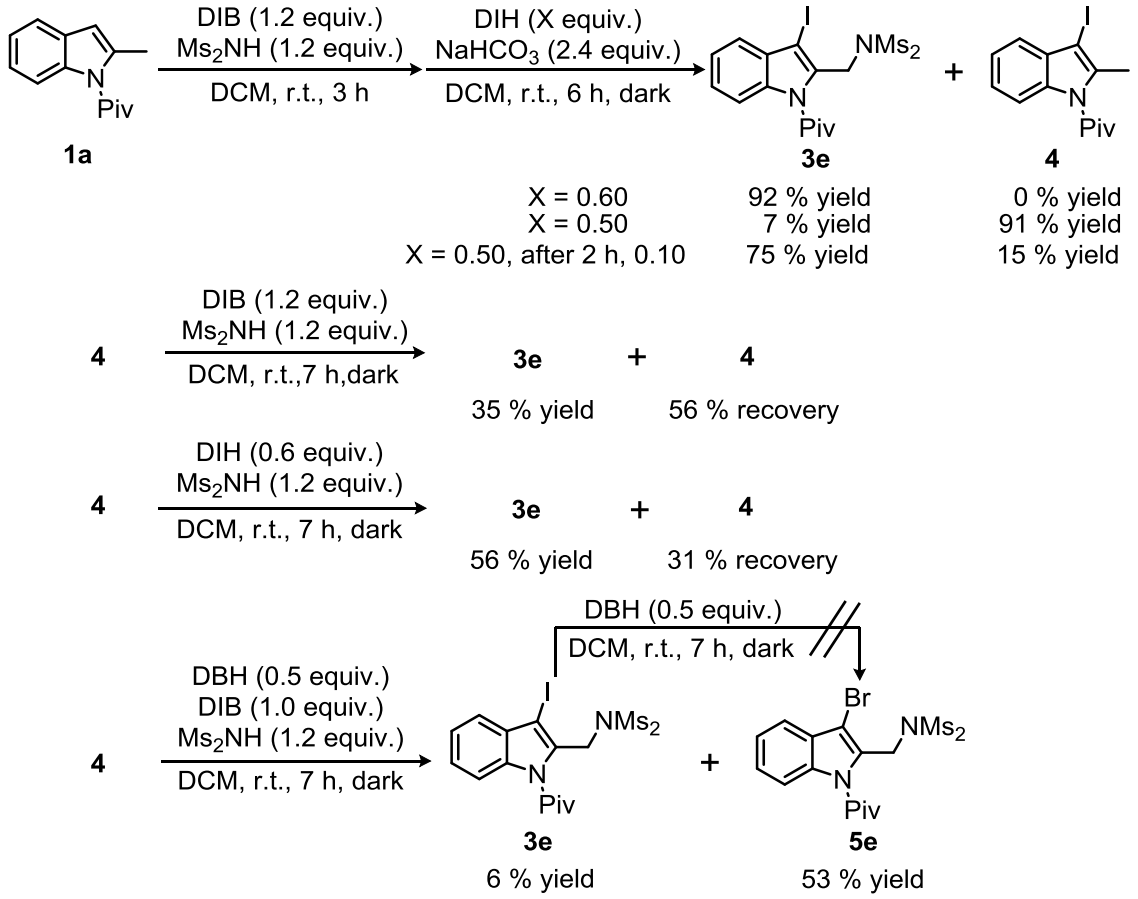
3z, 2 h, 5 h, 1.2[c], 83 %

[a] R'$_2$NH (1.7 equiv.) was used. [b] R'$_2$NH (2.4 equiv.) was used. [c] NIS (Z equiv.) was used instead of DIH.

[d] $NaHCO_3$ was not added. [e] Na_2SO_4 (2.0 equiv.) was added.

The author then examined some experimental studies to determine reaction mechanism for iodo-amination of 2-methylindole derivatives (Scheme 2). Reducing equivalent of DIH from 0.6 to 0.5, the desired product **3e** was obtained in only 7 % yield and 3-iodoindole derivative was formed in 91 % as a byproduct. Moreover, when DIH (0.1 equiv.) was added to the reaction mixture of (indolyl)(aryl)iodonium imide (**2e**) generated in situ from **1a** with DIH (0.5equiv.) stirring for 2h, the yield of **3e** was increased to 75 %. These results suggested that **4** is one of the intermediates for dual-functionalization of 2-methylindole derivatives. In addition, reaction of **4** with DIB (1.2 equiv.) and Ms_2NH (1.2 equiv.) in DCM for 7 h under dark conditions gave **3e** in 35 %, together with recovered **4** in 56 %. Surprisingly, the treatment of **1a** with only DIH (0.6 equiv.) and Ms_2NH (1.2 equiv.) also gave **3e** in 56 % yield. However, both methods provided **3e** in moderate yield less than that in the optimized conditions. On the other hands, treatment of **4** with DBH (0.5 equiv.), DIB (1.0 equiv.), and Ms_2NH (1.2 equiv.) provided 3-iodo-product **3e** and 3-bromo-product **5e** in 6 % and 53 % yields, respectively. Since **5a** was not produced by the reaction of **3e** with DBH (0.5 equiv.), **5e** was directly transformed from **4** with DBH. These observations suggest that both DIB and DIH separately gave iodo-amination product **3e**.

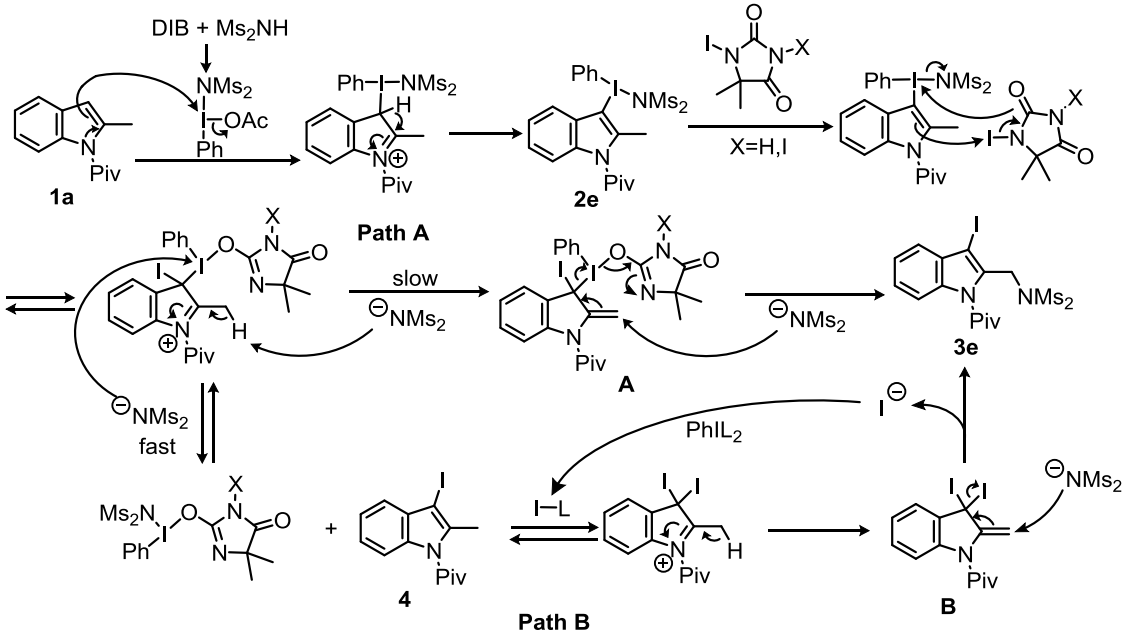
Scheme2: Experimental Study for Regioselective Iodo-amination of **1**



The proposed mechanism for iodo-amination is shown in Scheme 3. First, 2-methylindole derivative **1a** reacts with $PhI(OAc)NMs_2$ generated in situ from DIB and Ms_2NH to form (indolyl)(phenyl)iodonium imide **2e**.

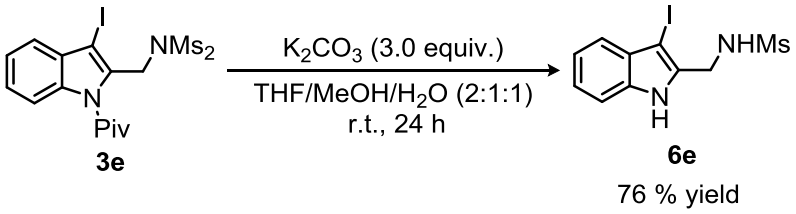
2e generates 2-methyl-3-iodoindole derivative **4** and hypervalent iodine species by using DIH. **4** is transformed to **3e** via two pathways. In the first pathway, **4** is re-oxidized with hypervalent iodine compound and enamine intermediate **A** is formed via dehydrogenation. Then, Ms_2N anion attacks intermediate **A** to give **3e** (Path A). In the second pathway, **4** reacts with iodination reagent again followed by dehydrogenation, and enamine intermediate **B** is formed. Intermediate **B** is converted into **3e** by the reaction with Ms_2N anion and the subsequent elimination of iodide ion. Iodide ion is re-oxidized by hypervalent iodine to regenerate iodination species (Path B). The author believed that both pathways are included under the optimized conditions.

Scheme 3: Proposed Reaction Mechanism on Regioselective Iodo-amination of **1**



The author also found removal of one methanesulfonyl group from the product **3e** by using K_2CO_3 (Scheme 4). The deprotection proceeded under mild conditions to give **6e**, which can be converted into various medicinal compounds via nucleophilic reactions.

Scheme 4: Transformation of **3e** to **6e**



In conclusion, the author developed first regioselective dual-fuctionalization of 2-methylindole derivatives via (indolyl)(aryl)iodonium imides with DIH or NIS. This reaction directly converted non-activated sp^3 C-H bond into C-N bond, and the product possesses synthetic utility for medicinal and biologically active compounds.

Experimental

1. General Methods. ^{1}H NMR spectra were measured on a JEOL ECA-400 (400 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; sep = septet; m = multiplet; br = broad), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on a JEOL ECA-400 (100 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm). High-resolution mass spectra were recorded by Thermo Fisher Scientific Exactive Orbitrap mass spectrometers. Infrared (IR) spectra were recorded on a JASCO FT/IR 4100 spectrometer. Single crystal X-ray diffraction data were collected at 173 K on a Bruker SMART APEX II CCD diffractometer with Mo Kα (λ = 0.71073) radiation and graphite monochrometer. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60GF254 0.25 mm) were used. The products were purified by column chromatography on neutral silica-gel (Kanto Chemical Co., Inc. silica gel 60N, Prod. No. 37560-84; Merck silica gel 60, Prod. No. 1.09385.9929). Visualization was accomplished by UV light (254 nm), anisaldehyde, $KMnO_4$, and phosphomolybdic acid.

1. General Procedure for Preparation of *N*-((3'-iodo-1'-pivaloyl-1'H-indol-2'-yl)-methyl)-4-methyl-N-tosylbenzenesulfonamide (3a) from 4-Methyl-*N*-(phenyl(1'-pivaloyl-2'-methyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide 2a (Table 1, entry 13)

To a solution of 4-methyl-*N*-(phenyl(1-pivaloyl-2-methyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide **2a** (74.3 mg, 0.10 mmol) in dichloromethane (1mL) was added 1,3-diiodo-5,5-dimethylhydantoin (22.2 mg, 0.060 mmol). The mixture was stirred at room temperature for 7 h under argon atmosphere. Then, saturated Na_2SO_3 aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by water (10 mL), brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 5/1), to give the desired product **3a** (61.1 mg, 92 % yield).

2. General Procedure for One-pot Preparation of *N*-((3'-iodo-1'-pivaloyl-1'*H*-indol-2'-yl)-methyl)-4-methyl-*N*-tosylbenzenesulfonam

ide (3a) from 1-Pivaloyl-2-methylindole 1a (Table 2, entry 3)

To prepare PhI(OAc)NTs_2 were used DIB (38.7 mg, 0.12 mmol), and Ts_2NH (39.1 mg, 0.12 mmol) in dichloromethane (1mL). The solution was stirred at room temperature for 30 min. under argon atmosphere. Then, 1-pivaloyl-2-methylindole (**1a**) (22.2 mg, 0.10 mmol) was added, and the obtained mixture was stirred at room temperature for 2 h. Then, $NaHCO_3$ (22.1 mg, 0.24 mmol) was added, and the obtained mixture was stirred at room temperature for 10 min, followed by addition of 1,3-diiodo-5,5-dimethylhydantoin (22.2 mg, 0.060 mmol). The mixture was stirred at room temperature for 5 h under argon atmosphere. Then, saturated Na_2SO_3 aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by water (10 mL), brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 5/1), to give the desired product **3a** (63.8 mg, 96 % yield).

***N*-((3'-iodo-1'-pivaloyl-1'*H*-indol-2'-yl)-methyl)-4-methyl-*N*-tosylbenzenesulfonamide (3a):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.31 (s, 6H), 5.27 (s, 2H), 7.05 (d, *J*=8.2 Hz, 4H), 7.17-7.32 (m, 4H), 7.63 (d, *J*=8.2 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5 (2C), 28.1 (3C), 44.5, 46.8, 72.1, 112.7, 121.7, 122.1, 124.9, 127.8 (4C), 129.1 (4C), 130.2, 130.7, 135.7, 136.8, 136.8 (2C), 144.5 (2C), 183.6. IR (neat) 1715, 1378, 1166, 832, 750 cm^{-1}. MS (ESI) calcd for $C_{28}H_{30}N_2O_5IS_2$ $[M+H]^+$ 665.0635, found 665.0641.

***N*-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(benzenesulfonyl)benzenesulfonamide (3b):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (s, 9H), 5.30 (s, 2H), 7.17-7.34 (m, 9H), 7.46 (t, *J*=7.6 Hz, 2H), 7.75 (dd, *J*=8.4, 1.2 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1 (3C), 44.4, 46.9, 72.5, 112.8, 121.9, 122.2, 125.0, 127.9 (4C), 128.5 (4C), 130.1, 130.7, 130.7, 135.5 (2C), 135.6, 139.6 (2C), 183.7. IR (neat) 1731, 1374, 1167, 999, 806, 741 cm^{-1}. MS (ESI) calcd for $C_{26}H_{27}N_2O_5IS_2$ $[M+H]^+$ 637.0333, found 637.0334.

4-Fluoro-*N*-(4"-fluorobenzenesulfonyl)-*N*-((3'-iodo-1'-pivaloyl-1'*H*-indol-2'-yl)-methyl)benzenesulfonamide (3c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (s, 9H), 5.27 (s, 2H), 6.90-7.00 (m, 4H), 7.20-7.37 (m, 4H), 7.72-7.81 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0 (3C), 44.5, 47.0, 72.3, 112.7, 115.8 (d, J_{C-F}=23.0 Hz, 4C), 121.8, 122.5, 125.2, 130.0, 130.2, 130.9 (d, J_{C-F}=9.6 Hz, 4C), 135.5 (d, J_{C-F}=3.8 Hz, 2C), 135.7, 165.6 (d, J_{C-F}=257.7 Hz, 2C), 183.7. ^{19}F NMR (390 MHz, $CDCl_3$) δ -102.9. IR (neat) 1745,

1590, 1492, 1384, 1240, 1173, 837 cm^{-1}. MS (ESI) calcd for $C_{26}H_{25}N_2O_5F_2IS_2$ $[M\text{-}H^+]^-$ 673.0130, found 673.0132.

***N*-((3'-iodo-1'-pivaloyl-1'*H*-indol-2'-yl)-methyl)-4-methyl-*N*-(methanesulfonyl)benzenesulfonamide (3d):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.27 (s, 3H), 3.36 (s, 3H), 5.19 (s, 2H), 6.97 (d, *J*=8.8 Hz, 2H), 7.20-7.27 (m, 1H), 7.29-7.33 (m, 2H), 7.34 (d, *J*=8.0 Hz, 1H), 7.55 (d, *J*=8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 28.1 (3C), 44.4, 44.6, 46.1, 76.7, 113.0, 121.9, 122.3, 124.9, 128.1 (2C), 129.0 (2C), 130.2, 131.5, 135.5, 135.6, 144.8, 184.0. IR (neat) 1686, 1364, 1163, 962, 841, 734 cm^{-1}. MS (ESI) calcd for $C_{22}H_{26}IN_2O_5S_2$ $[M+H]^+$ 589.0322, found 589.0326.

***N*-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3e):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 3.23 (s, 6H), 5.18 (s, 2H), 7.28 (t, *J*=8.0 Hz, 1H), 7.34 (t, *J*=8.0 Hz, 1H), 7.42 (d, *J*=8.0 Hz, 1H), 7.49 (d, *J*=8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.7 (2C), 44.2, 45.6, 70.6, 113.4, 122.2, 122.5, 125.0, 130.2, 132.7, 135.6, 184.4. IR (neat) 1692, 1363, 1154, 967, 753 cm^{-1}. MS (ESI) calcd for $C_{16}H_{21}N_2O_5ClIS_2$ $[M+Cl]^-$ 546.9631, found 546.9641.

***N*-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(propanesulfonyl)propanesulfonamide (3f):** ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, *J*=7.5 Hz, 6H), 1.47 (s, 9H), 1.82 (sext, *J*=7.5 Hz, 1H), 3.21-3.31 (m, 4H), 5.17 (s, 2H), 7.27 (t, *J*=8.0 Hz, 1H), 7.34 (t, *J*=8.0 Hz, 1H), 7.41 (d, *J*=8.0 Hz, 1H), 7.50 (d, *J*=8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7 (2C), 16.6 (2C), 28.1 (3C), 44.2, 46.2, 58.5 (2C), 70.8, 113.2, 122.2, 122.4, 125.1, 130.1, 132.9, 135.7, 184.2. IR (neat) 1703, 1370, 1151, 999, 805, 741 cm^{-1}. MS (ESI) calcd for $C_{20}H_{31}N_2O_5IS_2$ $[M+H]^+$ 569.0635, found 569.0641.

***N*-(benzylsulfonyl)-*N*-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-1-phenylmethanesulfonamide (3g):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 9H), 4.28 (br, 2H), 4.52 (s, 4H), 7.21-7.42 (m, 13H), 7.46 (d, *J*=7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0 (3C), 44.0, 47.3, 62.9 (4C), 113.0, 122.1, 122.4, 125.1, 126.7 (2C), 128.9 (4C), 129.4 (2C), 130.0, 131.2 (4C), 132.6, 135.5, 183.9. IR (neat) 1691, 1377, 1158, 744, 694 cm^{-1}. MS (ESI) calcd for $C_{28}H_{30}N_2O_5IS_2$ $[M+H]^+$ 665.0635, found 665.0644.

***N*-((1-benzoyl-3-iodo-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3h):** ^1H NMR (400 MHz, $CDCl_3$) δ 3.28 (s, 6H), 5.53 (s, 2H), 6.46 (d, *J*=7.6 Hz, 1H), 7.06 (td, *J*=8.0, 1.4 Hz, 1H), 7.23 (t, *J*=7.6 Hz, 1H), 7.47 (d, *J*=7.6 Hz, 1H), 7.53 (d,

J=8.0 Hz, 2H), 7.69 (t, *J*=7.6 Hz, 1H), 7.83 (dd, *J*=8.0, 1.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.7 (2C), 44.9, 75.2, 114.1, 122.1, 123.3, 125.3, 129.0 (2C), 130.46 (2C), 130.54, 133.8, 134.1, 134.9, 136.7, 169.5. IR (neat) 1685, 1375, 1158, 817, 745 cm^{-1}. MS (ESI) calcd for $C_{18}H_{18}N_2O_5INaS_2$ $[M+Na]^+$ 554.9516, found 554.9519.

***N*-((3-iodo-1-tosyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3i):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.49 (s, 6H), 5.46 (s, 2H), 7.20 (d, *J*=8.2 Hz, 2H), 7.28-7.35 (m, 1H), 7.326-7.43(m, 2H), 7.65 (d, *J*=8.2 Hz, 2H), 8.06 (d, *J*=8.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 42.8 (2C), 45.5, 80.8, 115.3, 122.5, 124.7, 126.5 (2C), 126.9, 130.1 (2C), 131.5, 132.8, 134.8, 136.7, 145.5. IR (neat) 1359, 1154, 996, 798, 754 cm^{-1}. MS (ESI) calcd for $C_{28}H_{20}N_2O_5IS_2Na$ $[M+Na]^+$ 604.9342, found 604.9348.

***N*-((3-iodo-5-methyl-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3j):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.47 (s, 3H), 3.22 (s, 6H), 5.17 (s, 2H), 7.15 (dd, *J*=8.5, 1.4 Hz, 1H), 7.26 (m, 1H), 7.32 (d, *J*=8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 28.2 (3C), 43.7 (2C), 43.9, 45.6, 70.6, 113.3, 121.8, 126.6, 130.4, 132.3, 132.7, 133.8, 184.2. IR (neat) 1728, 1362, 1157, 957, 761 cm^{-1}. MS (ESI) calcd for $C_{17}H_{23}N_2O_5ClIS_2$ $[M+Cl]^-$ 560.9787, found 560.9801.

***N*-((3,6-diiodo-5-methyoxy-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3k):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 3.23 (s, 6H), 3.97 (s, 3H), 5.14 (s, 2H), 6.83 (s, 1H), 7.84 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3 (3C), 43.7 (2C), 44.1, 45.5, 56.7, 70.0, 83.8, 102.2, 124.2, 131.1, 131.4, 134.5, 154.1, 183.6. IR (neat) 1694, 1365, 1161, 1036, 840 cm^{-1}. MS (ESI) calcd for $C_{17}H_{22}N_2O_6ClIS_2$ $[M+Cl]^-$ 702.8703, found 702.8722.

***N*-((5-fluoro-3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3l):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 3.24 (s, 6H), 5.15 (s, 2H), 7.07 (ddd, *J*=9.2, 9.0, 2.5 Hz, 1H), 7.17 (dd, *J*=8.7, 2.5 Hz, 1H), 7.35 (dd, *J*=9.2, 4.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.7 (2C), 44.2, 45.5, 69.5, 107.5 (d, $J_{C\text{-}F}$=24.9 Hz), 113.4 (d, $J_{C\text{-}F}$=25.9 Hz), 114.5 (d, $J_{C\text{-}F}$=8.6 Hz), 131.4 (d, $J_{C\text{-}F}$=10.5 Hz), 132.0, 134.4, 159.1 (d, $J_{C\text{-}F}$=241.4 Hz), 184.0. ^{19}F NMR (390 MHz, $CDCl_3$) δ -120.1. IR (neat) 1698, 1366, 1160, 979, 762 cm^{-1}. MS (ESI) calcd for $C_{16}H_{20}N_2O_5FClIS_2$ $[M+Cl]^-$ 564.9536, found 564.9548.

***N*-((5-chloro-3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3m):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 3.24 (s, 6H), 5.15 (s, 2H), 7.28 (dd, *J*=9.2, 2.0 Hz, 1H), 7.33 (dd, *J*=9.2, 0.48 Hz, 1H), 7.48 (dd, *J*=2.0. 0.48 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.7 (2C), 44.3, 45.4, 68.9, 114.4, 121.7, 125.3, 128.5, 131.5, 134.0, 134.1, 183.9. IR (neat) 1730, 1362, 1159, 947, 846 cm^{-1}. MS (ESI) calcd for $C_{16}H_{20}N_2O_5Cl_2IS_2$ $[M+Cl]^-$ 580.9241, found 580.9254.

***N*-((5-bromo-3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3n):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H), 3.24 (s, 6H), 5.15 (s, 2H), 7.27 (d, *J*=8.9 Hz, 1H), 7.42 (dd, *J*=8.9, 2.0 Hz, 1H), 7.64 (d, *J*=2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.7 (2C), 44.3, 45.4, 68.7, 114.7, 115.9, 124.8, 127.9, 132.0, 133.9, 134.3, 183.9. IR (neat) 1729, 1362, 1159, 938, 846 cm^{-1}. MS (ESI) calcd for $C_{16}H_{20}N_2O_5ClBrIS_2$ $[M+Cl]^-$ 624.8736, found 624.8746.

Methyl 3-iodo-2-((N-(methanesulfonyl)methylsulfonamido)methyl)-1-pivaloyl-1*H*-indole-5-carboxylate (3o): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (s, 9H), 3.26 (s, 6H), 3.96 (s, 3H), 5.18 (s, 2H), 7.73 (d, *J*=8.4 Hz, 1H), 7.94 (dd, *J*=8.4, 1.2 Hz, 1H), 8.19 (d, *J*=1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3 (3C), 43.6 (2C), 44.3, 45.3, 52.4, 69.5, 115.3, 121.9, 123.3, 126.7, 133.6, 135.0, 135.8, 167.0, 184.0. IR (neat) 1719, 1343, 1236, 1155, 979, 756 cm^{-1}. MS (APCI) calcd for $C_{18}H_{23}N_2O_7ClIS_2$ $[M+Cl]^-$ 604.9685, found 604.9692.

***N*-((5-cyano-3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3p):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 3.26 (s, 6H), 5.15 (s, 2H), 7.44 (d, *J*=8.7 Hz, 1H), 7.57 (dd, *J*=8.7, 1.6 Hz, 1H), 7.86 (d, *J*=1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1 (3C), 43.6 (2C), 44.7, 45.2, 68.9, 106.1, 114.0, 119.1, 127.56, 127.59, 130.3, 135.1, 137.3, 183.7. IR (neat) 2230, 1709, 1347, 1156, 1067, 1005, 843 cm^{-1}. MS (ESI) calcd for $C_{17}H_{20}N_3O_5ClIS_2$ $[M+Cl]^-$ 571.9583, found 571.9599.

***N*-((3-iodo-5-nitro-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3q):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 3.27 (s, 6H), 5.15 (s, 2H), 7.45 (d, *J*=9.2 Hz, 1H), 8.23 (dd, *J*=9.2, 2.0 Hz, 1H), 8.46 (d, *J*=2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1 (3C), 43.6 (2C), 44.8, 45.2, 69.9, 113.3, 119.1, 120.0, 130.2, 136.0, 138.4, 143.5, 183.6. IR (neat) 1714, 1520, 1361, 1154, 974, 836 cm^{-1}. MS (ESI)

calcd for $C_{16}H_{20}N_3O_7ClIS_2$ $[M+Cl]^-$ 591.9481, found 591.9485.

***N*-((3-iodo-6-methyl-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3r):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 2.49 (s, 3H), 3.21 (s, 6H), 5.16 (s, 2H), 7.09 (d, *J*=8.2 Hz, 1H), 7.19 (s, 1H), 7.35 (d, *J*=8.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 28.2 (3C), 43.7 (2C), 44.2, 45.7, 70.6, 113.3, 121.7, 124.2, 128.1, 131.7, 135.2, 136.0, 184.4. IR (neat) 1706, 1358, 1153, 965, 761 cm^{-1}. MS (ESI) calcd for $C_{17}H_{23}N_2O_5ClIS_2$ $[M+Cl]^-$ 560.9787, found 560.9794.

***N*-((3,5-diiodo-6-methoxyl-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3s):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H), 3.20 (s, 6H), 3.91 (s, 3H), 5.13 (s, 2H), 6.83 (s, 1H), 7.87 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.7 (2C), 44.6, 45.7, 56.7, 68.8, 80.9, 95.5, 126.1, 131.6, 132.4, 136.3, 155.9, 183.9. IR (neat) 1702, 1360, 1151, 1041, 824, 763 cm^{-1}. MS (ESI) calcd for $C_{17}H_{22}N_2O_6ClIS_2$ $[M+Cl]^-$ 702.8703, found 702.8712.

***N*-((6-chloro-3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3t):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 3.23 (s, 6H), 5.14 (s, 2H), 7.24 (dd, *J*=8.5, 1.8 Hz, 1H), 7.37-7.44 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.7 (2C), 44.3, 45.5, 69.8, 113.2, 123.1, 123.2, 128.8, 131.1, 133.3, 135.7, 183.8. IR (neat) 1712, 1358, 1153, 1072 962, 804, 760 cm^{-1}. MS (ESI) calcd for $C_{16}H_{20}N_2O_5Cl_2IS_2$ $[M+Cl]^-$ 580.9241, found 580.9251.

Methyl 3-iodo-2-((N-(methanesulfonyl)methylsulfonamido)methyl)-1-pivaloyl-1*H*-indole-6-carboxylate (3u): ^1H NMR (400 MHz, $CDCl_3$) δ 1.51 (s, 9H), 3.19 (s, 6H), 3.94 (s, 3H), 5.10 (s, 2H), 7.49 (d, *J*=8.5 Hz, 1H), 7.87 (d, *J*=1.4 Hz, 1H), 7.92 (dd, *J*=8.5, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2 (3C), 39.3, 43.9 (2C), 44.5, 52.3, 63.0, 110.8, 122.3, 123.1, 127.0, 130.2, 134.5, 134.8, 166.9, 176.5. IR (neat) 1781, 1716, 1351, 1248, 1159, 1072, 966, 825 cm^{-1}. MS (APCI) calcd for $C_{18}H_{23}N_2O_7IS_2$ $[M]^+$ 569.9986, found 569.9991.

***N*-((3-iodo-6-nitro-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3v):** ^1H NMR (400 MHz, $CDCl_3$) δ 1.53 (s, 9H), 3.22 (s, 6H), 5.11 (s, 2H), 7.58 (d, *J*=8.9 Hz, 1H), 8.08 (d, *J*=1.8 Hz, 1H), 8.14 (dd, *J*=8.9, 1.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2 (3C), 39.4, 43.8 (2C), 44.3, 62.4, 105.3, 117.4, 123.1, 131.1,

133.7, 136.8, 145.4, 176.3. IR (neat) 1793, 1514, 1335, 1159, 1050, 802, 747 cm^{-1}.

***N*-((3-iodo-4-methyl-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3w):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.23 (s, 6H), 5.18 (s, 2H), 6.96 (d, *J*=7.3 Hz, 1H), 7.15 (t, *J*=7.3 Hz, 1H), 7.25 (d, *J*=7.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 28.3 (3C), 43.6 (2C), 44.9, 46.3, 66.8, 111.3, 124.0, 125.8, 131.3, 132.0, 136.1, 184.7. IR (neat) 1732, 1366, 1158, 961, 729 cm^{-1}. MS (ESI) calcd for $C_{17}H_{24}N_2O_5IClS_2$ $[M+Cl]^-$ 560.9787, found 560.9762.

***N*-((5,6-dichloro-3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3x):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 3.24 (s, 6H), 5.12 (s, 2H), 7.52 (s, 1H), 7.58 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.6 (2C), 44.3, 45.4, 68.3, 114.8, 123.2, 127.1, 129.3, 130.1, 134.0, 134.7 183.4 IR (neat) 1712, 1353, 1156, 970, 844, 765 cm^{-1}. MS (ESI) calcd for $C_{16}H_{19}N_2O_5Cl_3IS_2$ $[M+Cl]^-$ 614.8851, found 614.8857.

***N*-((5,7-dimethyl-3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (3y):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (s, 9H), 2.39 (s, 3H), 2.43 (s, 3H), 3.20 (s, 6H), 5.12 (s, 2H), 6.92 (s, 1H), 7.12 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3, 21.1, 27.7 (3C), 43.6 (2C), 46.0, 47.1, 61.2, 119.8, 122.5 (2C), 129.3, 130.6, 132.4, 141.1, 189.0. IR (neat) 1740, 1368, 1157, 958, 838, 764 cm^{-1}. MS (ESI) calcd for $C_{18}H_{25}N_2O_5ClIS_2$ $[M+Cl]^-$ 574.9944, found 574.9950.

***N*-((1-iodo-3-pivaloyl-3*H*-benzo[e]indol-2-yl)methyl)-*N*-(methanesulfonyl)methanesulfonamide (3z):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.19 (s, 6H), 5.28 (s, 2H), 7.42 (d, *J*=9.1 Hz, 1H), 7.52 (t, *J*=8.2 Hz, 1H), 7.64-7.74 (m, 2H), 7.92 (d, *J*=8.2 Hz, 1H), 9.61 (d, *J*=8.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.8 (2C), 45.5, 46.5, 66.7, 112.9, 120.2, 121.4, 124.8, 125.9, 126.2, 127.9, 128.8, 129.2, 130.2, 133.3, 184.6. IR (neat) 1731, 1361, 1154, 960, 795 cm^{-1}. MS (ESI) calcd for $C_{20}H_{24}N_2O_5IClS_2$ $[M+Cl]^-$ 596.9787, found 596.9794.

***N*-((3-bromo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide (5e):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (s, 9H), 3.23 (s, 6H), 5.16 (s, 2H), 7.28 (t, *J*=8.5 Hz, 1H), 7.35 (t, *J*=8.5 Hz, 1H), 7.47 (d, *J*=8.5 Hz, 1H), 7.59 (d, *J*=8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (3C), 43.6 (2C), 43.9, 44.1, 100.1, 113.6, 120.0, 122.5, 125.0, 137.3, 130.2, 134.7, 184.2. IR (neat) 1697, 1366, 1159, 1048, 841, 762

cm^{-1}. MS (ESI) calcd for $C_{16}H_{21}N_2O_5INaS_2$ $[M+Na]^+$ 486.9967, found 486.9963.

3. General Procedure for Preparation of *N*-((3-iodo-1*H*-indol-2-yl)methyl)methanesulfonamide (6e) from *N*-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methylsulfonyl)methanesulfonamide (3e) (Scheme 4)

To a solution of *N*-((3-iodo-1-pivaloyl-1*H*-indol-2-yl)-methyl)-*N*-(methanesulfonyl)methanesulfonamide **3e** (51.24 mg, 0.10 mmol) in THF (1mL), MeOH (0.5 ml), and H_2O (0.5 ml) was added K_2CO_3 (41.5 mg, 3.0 mmol). The mixture was stirred at room temperature for 24 h. Then, saturated NH_4Cl aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 5/1), to give the desired product **6e** (26.7 mg, 76 % yield).

***N*-((3-iodo-1*H*-indol-2-yl)methyl)methanesulfonamide (6e):** ^1H NMR (400 MHz, $CDCl_3$) δ 3.42 (s, 3H), 4.67 (s, 2H), 7.13-7,27 (m, 2H), 7.30 (d, *J*=8.0 Hz, 1H), 7.42 (d, *J*=8.0 Hz, 1H), 8.79 (br, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.2, 59.0, 67.7, 111.2, 120.7, 120.9, 123.3, 130.2, 135.6, 136.1. IR (neat) 3291, 1450, 1220, 1078, 908, 741 cm^{-1}.

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Chapter 5

Abstract

Ligand Coupling Reaction of (Indolyl)(aryl)iodonium Imides to Form C-N Bond at 3-Position in Indole Group; Effect of Substitutents of Hypervalent Iodine for Reaction Selectivity

N-(1'-pivaloyl-1'*H*-indol-3'-yl)-4-methyl-*N*-tosylbenzenesulfonamides were generated by ligand coupling reaction of (indolyl)(aryl)iodonium imides using catalytic amount of cupper iodide (I) or under heat conditions. Substitutent on hypervalent iodines controlled the reaction with high regioselectivity.

Introduction

Diaryliodonium salt is very useful aryl source for ligand of metal catalysts and arylation of carbon or heteroatoms by nucleophilic or radical reaction[1]. In particular, copper catalysts have been used for ligand coupling reaction between various compounds with diaryliodonium salts[2]. However, coupling reaction with unsymmetric diaryliodonium salts usually gives three products with low selectivity. To solve the problem, mesitylene(aryl)iodonium salt has been used to control regioselectivity by steric barrier of mesitylene group[3].

The author developed (indolyl)(aryl)iodonium imide, which is not only imide-combined hypervalent iodine but also heteroaryl(aryl)iodonium compounds[4]. To expand the synthetic utility of the imide-combined hypervalent iodines, study of intramolecular C-N ligand coupling reaction of (indolyl)(aryl)iodonium imide is very important. However, (indolyl)(mesityl)iodonium imide could not be isolated by the previous method in chapter 2[5]. Ever if it works, the yield is not so good. Then, the author studied designing hypervalent iodine to control selectivity of ligand coupling reaction. Here, the author reported regioselective C-N ligamd coupling reaction of (indolyl)(aryl)iodonium imides bearing ortho-alkoxyaryl group.

Results and discussion

First, the author examined C-N ligamd coupling reaction of (indolyl)(phenyl)iodonium imide with CuCl (10 mol %) at room temperature in dichloromethane (Scheme 1). However, the yield of coupling product indole (**2a**) was only 11 %, and that of coupling with a phenyl group (**4a**) and 3-iodoindole group (**3a**) were 41 % and 66 % yield, respectively. Then, the author studied screening reaction conditions for ligand coupling

reaction (Table 1). The addition of BF_3•OEt_2 or 1,10-phenanthroline was not much effective for the reaction (entries 2, 3). Heating conditions improved the selectivity (entries 4, 5), however, other cupper catalyst did not give good effect for yield of **2a** (entries 6, 7).

Scheme 1. C-N Ligand Coupling Reaction with Cu Catalyst

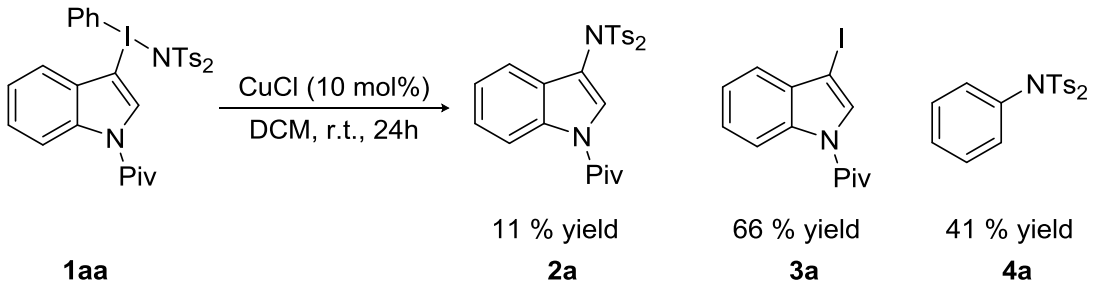
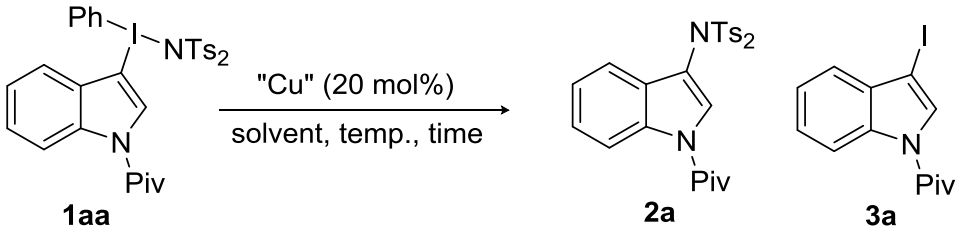


Table 1. Screening Reaction Conditions for C-N Ligand Coupling Reaction of **1aa**



entry	"Cu"	solvent	temp. (°C)	time	yield (%) 2a	3a
1	CuCl	DCM	r.t.	6 h	6	70
2[a]	CuCl	DCM	r.t.	7 h	17	47
3[b]	CuCl	DCM	r.t.	6 h	7	88
4	CuCl	DCE	60	2 h	8	64
5	CuCl	toluene	100	3 h	20	80
6	$(mecn)_4CuBF_4$	toluene	100	3 h	18	81
7	CuOAc	toluene	100	3 h	19	79

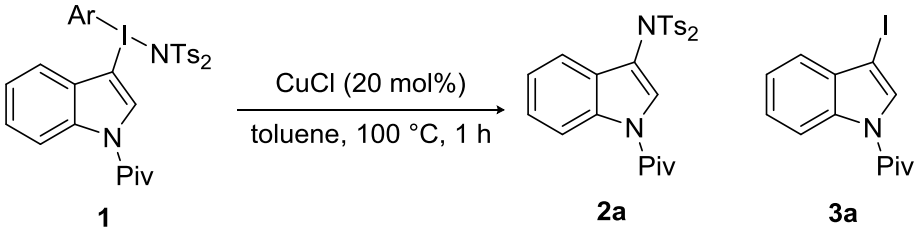
[a] BF_3·OEt_2 (1.0 equiv.) was added.

[b] 1,10-phen·H_2O (20 mol%) was added.

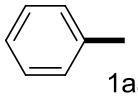
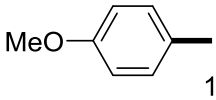
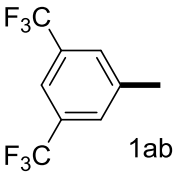
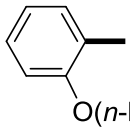
Next, the author searched C-N ligand coupling reaction of (indolyl)(aryl)iodonium imide bearing various substituent (Table 2). Use of **1** bearing 3,5-bis(trifluoromethyl)phenyl (**1ab**) or 4-methoxyphenyl (**1ac**) group gave **2a** in low yield using CuCl (20 mol%) at 100 ˚C in toluene. These results suggested that electronic

effect does not affect the reaction selectivity of C-N ligand coupling reaction. On the other hand, **1** bearing 2-*n*-butoxyphenyl group (**1ad**) extremely improved the yield of **2a**. Zhdankin group reported that 2-alkoxyphenyl group improved solubility of ArNTs[6]. However, it is the first application of 2-alkoxyphenyl-combined hypervalent iodine to control selectivity of C-N ligand couplig reaction.

Table 2. Study on Effect of Substituents for C-N Lingand Coupling Reaction

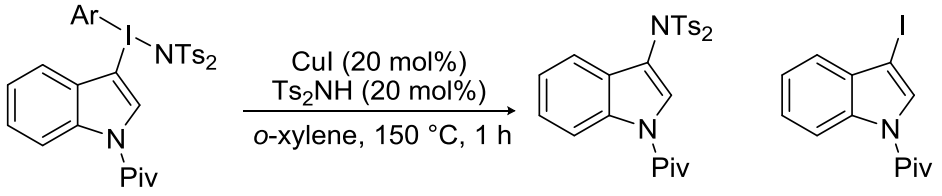


1 **2a** **3a**

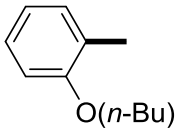
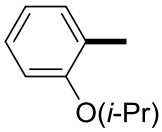
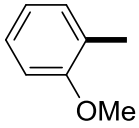
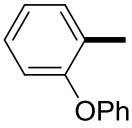
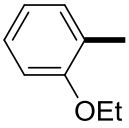
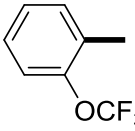
Entry	Ar	Yields (%) 2a	3a	Entry	Ar	Yields (%) 2a	3a
1	 1aa	14	76	3	 1ac	19	81
2	 1ab	22	69	4	 1ad	74	20

To study the effect of 2-alkoxyphenyl group in **1** for regioselective C-N ligand coupling reaction, the author examined amination at 3-position of indole with (indolyl)(aryl)iodonium imide bearing various 2-alkoxy groups (Table 3). The reaction was carried out in the presence of a catalytic amount of CuI and Ts_2NH at 150 ˚C, as shown in Table 3. 2-MeO (**1ae**) and 2-EtO (**1af**) phenyl groups gave **2a** in good yields, respectively, and sterically hindered groups, such as 2-*i*-PrO (**1ag**) and 2-PhO (**1ah**) phenyl groups, also provided the desired products in high yields. Moreover, **2a** was obtained with **1ai** bearing electron-withdrawing group, 2-CF_3Ophenyl group (**1ai**).

Table 3. Study on Effect of Substituents for C-N Lingand Coupling Reaction



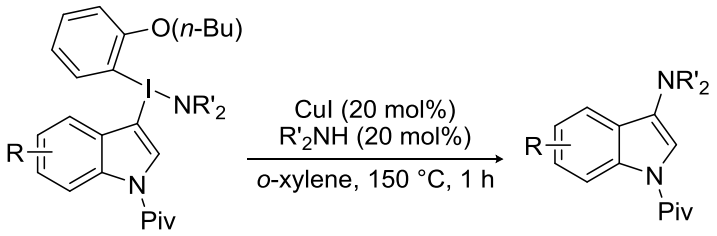
1 **2a** **3a**

Entry	Ar		Yields (%) 2a	3a	Entry	Ar		Yields (%) 2a	3a
1		1ad	88	11	4		1ag	82	11
2		1ae	77	23	5		1ah	81	18
3		1af	78	18	6		1ai	86	5

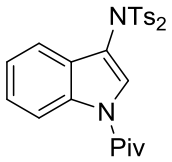
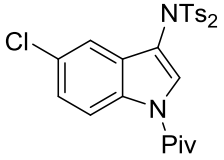
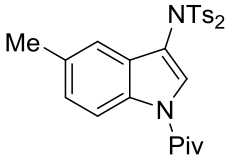
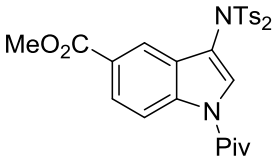
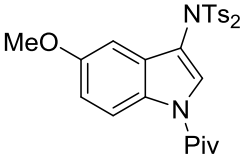
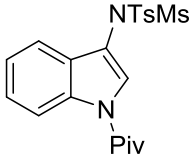
The author examined the coupling reaction of various substituted (indolyl)(2-butoxyphenyl)iodonium imides (**1**) with under optimized reaction conditions (Table 4).

Electron-donating groups, such as 5-Me (**1bd**) and 5-MeO (**1cd**), on indole group promoted the reaction to give 3-aminoindole derivatives (**2a,b**) in high yields, and the products (**2**) bearing 5-Cl (**2d**) and 5-COOMe (**2e**) groups were obtained from hypervalent iodoine (**1**) in high yields, respectively. In addition, use of unsymmetrical imide-combined hypervalent iodine (**1fd**) gave desired product **2f** in high yield.

Table 4. Selective C-N Ligand Coupling Reaction of Indolyl(aryl)iodonium Imide **1**

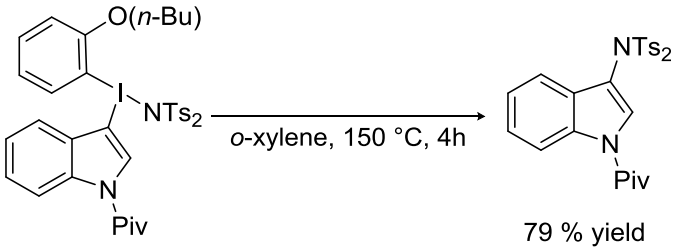


1 **2**

Entry	Product		Yield (%)	Entry	Product		Yield (%)
1		**2a**	88	4		**2d**	86
2		**2b**	87	5		**2e**	86
3		**2c**	85	6		**2f**	86

The author also succeeded in C-N ligand coupling of (indolyl)(aryl)iodonium imide (**1ad**) without any catalysts (Scheme 2). This reaction was carried out at 150 ˚C for 4h under metal-free conditions and the yield of **2a** was almost the same as that in C-N ligand coupling reaction with Cu catalyst.

Scheme 2. C-N Ligand Coupling Reaction without Any Catalysts



1ad **2a**

In conclusion, the author developed cupper-catalyzed C-N ligand coupling reaction of

(indolyl)(aryl)iodonium imide and regioselective coupling reaction was carried out by design of hypervalent iodine ligand. The reaction provided 3-imide substututed indole derivatives, and proceeds without metal catalysts. The author believed that the present regioselective coupling reaction of hypervalent iodine bearing 2-alkoxyphenyl group can be used for functionalization of indoles and hypervalent iodine chemistry.

Experimental

1. General Methods. ^{1}H NMR spectra were measured on a JEOL ECA-500 (500 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; sep = septet; m = multiplet; br = broad), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on a JEOL ECA-500 (125 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm). High-resolution mass spectra were recorded by Thermo Fisher Scientific Exactive Orbitrap mass spectrometers. Infrared (IR) spectra were recorded on a JASCO FT/IR 4100 spectrometer. Single crystal X-ray diffraction data were collected at 173 K on a Bruker SMART APEX II CCD diffractometer with Mo Kα (λ = 0.71073) radiation and graphite monochrometer. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60GF254 0.25 mm) were used. The products were purified by column chromatography on neutral silica-gel (Kanto Chemical Co., Inc. silica gel 60N, Prod. No. 37560-84; Merck silica gel 60, Prod. No. 1.09385.9929). Visualization was accomplished by UV light (254 nm), anisaldehyde, $KMnO_4$, and phosphomolybdic acid.

2. 1 General Procedure Using Method A for Preparation of Indolyl(aryl)iodonium Imides (1)

To prepare PhI(OAc)NTs_2 were used DIB (386.5 mg, 1.2 mmol) and Ts_2NH (390.5 mg, 1.2 mmol) in MeCN (10 ml). The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-pivaloylindole (201.3 mg, 1.0 mmol) was added, and the solution was stirred at 40 ˚C for 7 h. The solvent was removed under reduced pressure. Then AcOEt (10 ml) and ether (5 ml) were added. The mixture was sonicated until precipitation occurred as the white solid, and ether (5 ml) was added to the mixture. The solid was filtrated and washed with AcOEt/ether (2:1) (15 ml), to give desired product **2a** (597.5 mg, 82 % yield).

2. 2 General Procedure Using Method B for Preparation of 4-Methyl-*N*-((2"-phenoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (1ah)

To prepare PhI(OAc)NTs_2 were used 1-(diacetoxyiodo)-2-phenoxybenzene (497.0 mg, 1.2 mmol) and Ts_2NH (390.5 mg, 1.2 mmol) in MeCN (10 ml). The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-pivaloylindole (201.3

mg, 1.0 mmol) was added, and the solution was stirred at room temperature for 5 h. The solvent was removed under reduced pressure. Then, AcOEt (6 ml) was added. The mixture was added dropwise to ether /hexane (1:1) until the solvent changed clear solution to pale white, followed by sonication and addition of ether (2 ml). The solid was filtrated and washed with AcOEt/hexane (2:1) (15 ml), to give desired product **1ah** (566.3 mg, 69 % yield).

2. 3 General Procedure Using Method C for Preparation of *N*-((2"-isopropoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (1ag)

To prepare ArI(OAc)NTs_2 were used 1-(diacetoxyiodo)-2-isopropoxybenzene (456.2 mg, 1.2 mmol) and Ts_2NH (390.5 mg, 1.2 mmol) in MeCN (10 ml). The mixture was stirred at room temperature for 30 min. under argon atmosphere. Then, *N*-pivaloylindole (201.3 mg, 1.0 mmol) was added, and the solution was stirred at 40 ˚C for 5 h. The solvent was removed under reduced pressure. Then, AcOEt (6 ml) was added. The mixture was added dropwise to ether /hexane (1:1) until the solvent changed clear solution to pale white. The solution was stored overnight at -10 ˚C. The solid was filtrated and washed with AcOEt/hexane (2:1) (15 ml), to give desired product **1ag** (566.5 mg, 72 % yield).

The experimental data of compound **1aa**-**1ae** : see chapter 2

***N*-((2"-etoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (1af)** (Isolated Method : A, 71 % yield) **:** mp. 161 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (s, 9H), 1.54 (t, *J*=7.2 Hz, 3H), 2.27 (s, 6H), 4.25 (q, *J*=7.2 Hz, 2H), 6.87-6.95 (m, 5H), 6.99 (dd, *J*=8.3, 0.85 Hz, 1H), 7.39 (td, *J*=8.3, 0.85 Hz, 1H), 7.42-7.55 (m, 8H), 8.54 (d, *J*=8.6 Hz, 1H), 8.88 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 21.3 (2C), 28.4 (3C), 41.8, 66.1, 82.5, 104.0, 113.0, 117.8, 119.5, 124.0, 125.2, 126.6 (4C), 127.1, 127.6, 128.4 (4C), 133.6, 133.7, 136.3, 136.4, 140.8 (2C), 141.3 (2C), 155.6, 177.0. IR (neat) 1712, 1467, 1278, 1127, 1079, 1046, 750, 671 cm^{-1}. MS (ESI) calcd for $C_{35}H_{37}N_2O_6INaS_2$ $[M+Na]^+$ 795.1030, found 795.1021.

***N*-((2"-isopropoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (1ag)** (Isolated Method : C, 72 % yield) **:** mp. 172 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.46 (d, *J*=6.0 Hz, 6H), 2.26 (s, 6H), 4.74 (sep, *J*=6.0 Hz, 1H), 6.83-6.93 (m, 5H), 6.99 (d, *J*=8.0 Hz, 1H), 7.35-7.47 (m, 8H), 7.50 (d, *J*=8.0 Hz, 1H), 8.55 (d, *J*=8.3 Hz, 1H), 8.89 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ

21.2 (2C), 21.8 (2C), 28.4 (3C), 41.7, 73.6, 82.1, 104.7, 114.0, 117.8, 119.5, 123.9, 125.2, 126.5 (4C), 127.0, 127.5, 128.4 (4C), 133.1, 133.4, 136.3, 136.5, 140.7 (2C), 141.5 (2C), 154.6, 177.1. IR (neat) 1719, 1442, 1290, 1124, 1082, 1053, 751, 670 cm^{-1}. MS (ESI) calcd for $C_{36}H_{39}N_2O_6INaS_2$ $[M+Na]^+$ 809.1186, found 809.1174.

4-Methyl-*N*-((2"-phenoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (1ah) (Isolated Method : B, 69 % yield) **:** mp. 196 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 9H), 2.23 (s, 6H), 6.74 (dd, *J*=8.3, 1.2 Hz, 1H), 6.83-6.92 (m, 6H), 6.99 (td, *J*=8.3, 1.2 Hz, 1H), 7.21 (t, *J*=7.5 Hz, 1H), 7.28-7.37 (m, 4H), 7.42-7.48 (m, 5H), 7.51 (d, *J*=8.0 Hz, 1H), 8.10 (dd, *J*=8.3, 1.2 Hz, 1H), 8.48 (d, *J*=8.0 Hz, 1H), 8.75 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3 (2C), 28.3 (3C), 41.7, 84.8, 105.8, 117.3, 117.6, 119.8, 120.3 (2C), 125.1, 125.4, 125.6, 126.7 (4C), 126.8, 127.7, 128.4 (4C), 130.2 (2C), 133.9, 136.1, 136.2, 136.5, 140.8 (2C), 141.2 (2C), 154.6, 156.1, 177.0. IR (neat) 1706, 1444, 1294, 1135, 1076, 1031, 747, 670 cm^{-1}. MS (ESI) calcd for $C_{39}H_{37}N_2O_6INaS_2$ $[M+Na]^+$ 843.1030, found 843.1013.

4-Methyl-*N*-((2"-(trifluoromethoxy)phenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (1ai) (Isolated Method : B, 60 % yield) **:** mp. 155 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.23 (s, 6H), 6.86 (q, *J*=8.0 Hz, 4H), 7.20 (t, *J*=8.0 Hz, 1H), 7.30 (d, *J*=8.6 Hz, 1H), 7.32-7.47 (m, 7H), 7.49 (d, *J*=8.0 Hz, 1H), 8.30 (d, *J*=8.0 Hz, 1H), 8.46 (d, *J*=8.6 Hz, 1H), 8.79 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2 (2C), 28.2 (3C), 41.6, 86.3, 107.6, 117.1, 117.5, 119.4, 124.2 (q, J_{C-F}=261.1 Hz), 125.0, 126.59 (4C), 126.64, 127.6, 128.4 (4C), 128.9, 134.0, 135.9, 136.0, 138.7, 140.76 (2C), 140.82 (2C), 147.6, 177.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ -56.6. IR (neat) 1715, 1446, 1247, 1134, 1079, 1011, 762, 672 cm^{-1}. MS (ESI) calcd for $C_{34}H_{32}N_2O_6F_3INaS_2$ $[M+Na]^+$ 835.0591, found 835.0591.

***N*-((2"-butoxyphenyl)(5'-methyl-1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (1bd)** (Isolated Method : C, 70 % yield) **:** mp.102-104 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (t, *J*=7.2 Hz, 3H), 1.43 (s, 9H), 1.56 (sext, *J*=7.2 Hz, 2H), 1.92 (quin, *J*=7.2 Hz, 2H), 2.27 (s, 6H), 2.45 (s, 3H), 4.19 (t, *J*=7.2 Hz, 2H), 6.87-6.94 (m, 5H), 7.02 (dd, *J*=8.3, 0.90 Hz, 1H), 7.20 (s, 1H), 7.33 (d, *J*=8.6 Hz, 1H), 7.37 (dd, *J*=8.3, 1.2 Hz, 1H), 7.40-7.50 (m, 5H), 8.42 (d, *J*=8.6 Hz, 1H), 8.84 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 19.2, 21.3 (2C), 21.4, 28.4 (3C), 30.8, 41.7, 70.1, 81.7, 103.8, 113.0, 117.5, 119.1, 124.1, 126.6 (4C), 127.7, 128.4 (4C), 128.6, 132.7, 133.5, 134.5, 135.3, 136.5, 140.6 (2C), 141.6 (2C), 155.6, 177.0. IR (neat) 1712, 1465,

1279, 1133, 1079, 805, 763, 672 cm^{-1}. MS (ESI) calcd for $C_{38}H_{43}N_2O_6INaS_2$ $[M+Na]^+$ 837.1499, found 837.1488.

***N*-((2"-butoxyphenyl)(5'-methoxy-1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (1cd)** (Isolated Method : B, 69 % yield) **:** mp. 156 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.01 (t, *J*=7.5 Hz, 3H), 1.43 (s, 9H), 1.54 (sext, *J*=7.5 Hz, 2H), 1.90 (quin, *J*=7.5 Hz, 2H), 2.27 (s, 6H), 3.81 (s, 3H), 4.18 (t, *J*=7.5 Hz, 2H), 6.84 (d, *J*=7.5 Hz, 1H), 6.88-6.96 (m, 5H), 7.02 (dd, *J*=8.0, 1.2 Hz, 1H), 7.09 (dd, *J*=8.0, 1.2 Hz, 1H), 7.09 (dd, *J*=9.2, 2.3 Hz, 1H), 7.40 (dd, *J*=8.3, 1.5 Hz, 1H), 7.42-7.51 (m, 5H), 8.45 (d, *J*=9.2 Hz, 1H), 8.81 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 19.1, 21.3 (2C), 28.5 (3C), 30.8, 41.6, 55.8, 70.2, 81.8, 101.8, 103.7, 113.1, 115.9, 118.8, 124.0, 126.5 (4C), 128.3 (4C), 128.6, 130.8, 132.8, 133.5, 136.6, 140.6 (2C), 141.6 (2C), 155.7, 157.6, 176.8. IR (neat) 1701, 1469, 1280, 1127, 1077, 803, 749, 664 cm^{-1}. MS (ESI) calcd for $C_{38}H_{44}N_2O_7INaS_2$ $[M+Na]^+$ 853.1449, found 853.1434.

***N*-((2"-butoxyphenyl)(5'-chloro-1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-tosylbenzenesulfonamide (1dd)** (Isolated Method : B, 54 % yield) **:** mp. 182 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (t, *J*=7.2 Hz, 3H), 1.45 (s, 9H), 1.55 (sext, *J*=7.2 Hz, 2H), 1.91 (quin, *J*=7.2 Hz, 2H), 2.27 (s, 6H), 4.16 (t, *J*=7.2 Hz, 2H), 6.87-6.95 (m, 5H), 7.00 (d, *J*=8.0 Hz, 1H), 7.38-7.50 (m, 7H), 7.63 (d, *J*=8.0 Hz, 1H), 8.44 (d, *J*=9.5 Hz, 1H), 8.95 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 19.2, 21.3 (2C), 28.3 (3C), 30.8, 41.8, 70.1, 82.2, 104.2, 113.0, 118.9, 119.2, 124.0, 126.6 (4C), 127.1, 128.4 (4C), 129.0, 130.9, 134.0, 134.6, 137.5, 140.8 (2C), 141.4 (2C), 155.9, 177.0. IR (neat) 1712, 1443, 1280, 1129, 1078, 805, 756, 665 cm^{-1}. MS (ESI) calcd for $C_{37}H_{40}N_2O_6ClINaS_2$ $[M+Na]^+$ 857.0953, found 857.0943.

Methyl 3-(((4"-methyl-*N*-tosylbenzene)sulfonamido)(2'-*n*-butoxyphenyl)-λ^3-iodanyl)-1-pivaloyl-1*H*-indole-5-carboxylate (1ed) (Isolated Method : C, 49 % yield) **:** mp. 182 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (t, *J*=7.2 Hz, 3H), 1.46 (s, 9H), 1.54 (sext, *J*=7.2 Hz, 2H), 1.91 (quin, *J*=7.2 Hz, 2H), 2.26 (s, 6H), 3.94 (s, 3H), 4.19 (t, *J*=7.2 Hz, 2H), 6.86-6.94 (m, 5H), 7.00 (dd, *J*=8.3, 1.2 Hz, 1H), 7.42-7.50 (m, 5H), 7.60 (dd, *J*=8.3, 1.2 Hz, 1H), 8.12 (d, *J*=1.7 Hz, 1H), 8.15 (dd, *J*=8.9, 1.7 Hz, 1H), 8.56 (d, *J*=8.9 Hz, 1H), 9.02 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 19.1, 21.2 (2C), 28.3 (3C), 30.7, 41.8, 52.3, 70.1, 83.4, 104.2, 113.0, 117.6, 121.4, 124.0, 126.6 (4C), 127.0, 127.6, 127.9, 128.4 (4C), 134.0, 134.3, 137.7, 138.8, 140.7 (2C), 141.6 (2C), 155.9, 166.3,

177.1. IR (neat) 1717, 1469, 1279, 1127, 1076, 817, 748, 664 cm^{-1}. MS (ESI) calcd for $C_{39}H_{43}N_2O_8INaS_2$ $[M+Na]^+$ 881.1398, found 881.1403.

***N*-((2"-butoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-4-methyl-*N*-(methanesulfonyl)benzenesulfonamide (1fd)** (Isolated Method : C, 51 % yield) **:** mp.72-75 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (t, *J*=7.2 Hz, 3H), 1.48 (s, 9H), 1.56 (sext, *J*=7.2 Hz, 2H), 1.90 (quin, *J*=7.2 Hz, 2H), 2.26 (s, 3H), 2.86 (s, 3H), 4.17 (t, *J*=7.2 Hz, 2H), 6.90 (d, *J*=8.1 Hz, 1H), 6.95 (d, *J*=8.0 Hz, 2H), 7.01 (d, *J*=8.1 Hz, 1H), 7.38 (t, *J*=8.3 Hz, 1H), 7.41-7.53 (m, 7H), 8.53 (d, *J*=8.3 Hz, 2H), 8.79 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 19.1, 21.3, 28.4 (3C), 30.8, 41.8, 42.8, 70.1, 82.7, 104.0, 113.1, 117.7, 119.4, 123.9, 125.2, 126.5 (2C), 127.0, 127.5, 128.5 (2C), 133.5, 133.7, 136.1, 136.2, 140.8, 141.7, 155.8, 177.0. IR (neat) 1708, 1443, 1276, 1120, 1083, 808, 758, 658 cm^{-1}. MS (ESI) calcd for $C_{31}H_{37}N_2O_6INaS_2$ $[M+Na]^+$ 747.1030, found 747.1017.

3. General Procedure for C-N Ligand Coupling Reaction of 4-Methyl-*N*-((2"-*n*-butoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (1ad) with Cupper Catalyst (Table 3, entry 1)

To a solution of 4-methyl-*N*-((2-*n*-butoxyphenyl)(1-pivaloyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzene sulfonamide **1ad** (80.1 mg, 0.10 mmol) in *o*-xylene (1mL) were added CuI (3.81 mg, 0.020 mmol) and Ts_2NH (6.51 mg, 0.020 mmol). The mixture was stirred at 150 ºC for 1 h under argon atmosphere. Then, saturated NH_4Cl aqueous solution (10 mL) was added to the reaction mixture, and the product was extracted with AcOEt (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 5/1), to give the desired product **3a** (46.2 mg, 88 % yield).

4-Methyl-*N*-(1'-pivaloyl-1'*H*-indol-3'-yl)-*N*-tosylbenzenesulfonamide (2a) : mp. 207 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.46 (s, 6H), 7.07 (d, *J*=7.9 Hz, 1H), 7.17 (t, *J*=7.9 Hz, 1H), 7.30-7.36 (m, 5H), 7.46 (s, 1H), 7.87 (d, *J*=8.3 Hz, 4H), 8.46 (d, *J*=7.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7 (2C), 28.5 (3C), 41.3, 115.8, 117.3, 118.6, 124.1, 126.0, 126.8, 127.7, 128.6 (4C), 129.6 (4C), 135.7, 136.2 (2C), 145.2 (2C), 176.7. IR (neat) 1702, 1374, 1316, 1165 cm^{-1}. MS (ESI) calcd for $C_{27}H_{28}N_2O_5S_2Na$ $[M+Na^+]^+$ 547.1332, found 547.1316.

4-Methyl-*N*-(5'-methyl-1'-pivaloyl-1'*H*-indol-3'-yl)-*N*-tosylbenzenesulfonamide (2a) : mp. 214 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 2.28 (s, 3H), 2.47 (s, 6H), 6.71 (s, 1H), 7.14 (d, *J*=8.6 Hz, 1H), 7.32 (d, *J*=8.3 Hz, 4H), 7.42 (s, 1H), 7.87 (d, *J*=8.3 Hz, 4H), 8.31 (d, *J*=8.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 21.7 (2C), 28.5 (3C), 41.2, 115.6, 116.9, 118.4, 126.9, 127.4, 127.6, 128.7 (4C), 129.5 (4C), 133.8, 133.9, 136.3 (2C), 145.2 (2C), 176.6. IR (neat) 1701, 1379, 1308, 1156, 901, 811, 658 cm^{-1}. MS (ESI) calcd for $C_{28}H_{30}N_2O_5S_2Na$ $[M+Na^+]^+$ 561.1448, found 561.1488.

***N*-(5'-methoxy-1'-pivaloyl-1'*H*-indol-3'-yl)-4-methyl-*N*-tosylbenzenesulfonamide (2b) :** mp. 224 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 2.46 (s, 6H), 3.62 (s, 3H), 6.37 (d, *J*=2.6 Hz, 1H), 6.92 (dd, *J*=9.2, 2.6 Hz, 1H), 7.32 (d, *J*=8.3 Hz, 4H), 7.43 (s, 1H), 7.88 (d, *J*=8.3 Hz, 4H), 8.34 (d, *J*=9.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7 (2C), 28.6 (3C), 41.2, 55.2, 115.4, 115.6, 118.3, 127.8, 128.0, 128.6 (4C), 129.6 (4C), 130.2, 136.4 (2C), 145.2 (2C), 156.7, 176.4. IR (neat) 1701, 1380, 1312, 1162, 904, 814, 658 cm^{-1}. MS (ESI) calcd for $C_{28}H_{30}N_2O_6S_2Na$ $[M+Na^+]^+$ 577.1437, found 577.1437.

***N*-(5'-chloro-1'-pivaloyl-1'*H*-indol-3'-yl)-4-methyl-*N*-tosylbenzenesulfonamide (2c) :** mp. 201-204 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 9H), 2.48 (s, 6H), 6.81 (d, *J*=2.0 Hz, 1H), 7.27 (dd, *J*=8.9, 2.0 Hz, 1H), 7.33 (d, *J*=8.3 Hz, 4H), 7.52 (s, 1H), 7.85 (d, *J*=8.3 Hz, 4H), 8.38 (d, *J*=8.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7 (2C), 28.4 (3C), 41.3, 115.2, 118.2, 126.2, 128.0, 128.6 (4C), 128.7, 129.7 (4C), 130.0, 133.9, 136.0 (2C), 145.6 (2C), 176.6. IR (neat) 1708, 1379, 1307, 1163, 903, 815, 660 cm^{-1}. MS (ESI) calcd for $C_{27}H_{27}N_2ClO_5S_2Na$ $[M+Na^+]^+$ 581.0492, found 581.0944.

Methyl 3-((4'-methyl-*N*-tosylbenzene)sulfonamido)-1-pivaloyl-1*H*-indole-5-carboxylate (2d) : mp. 224 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 9H), 2.46 (s, 6H), 3.89 (s, 3H), 7.33 (d, *J*=8.3 Hz, 4H), 7.54 (s, 1H), 7.63 (d, *J*=1.5 Hz, 1H), 7.86 (d, *J*=8.3 Hz, 4H), 8.02 (dd, *J*=8.9, 1.5 Hz, 1H), 8.50 (d, *J*=8.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7 (2C), 28.4 (3C), 41.4, 52.0, 116.2, 117.1, 126.1, 126.6, 127.2, 128.6 (4C), 128.8, 129.7 (4C), 136.0 (2C), 138.1, 145.5 (2C), 166.7, 176.7. IR (neat) 1717, 1389, 1313, 1165, 817, 658 cm^{-1}. MS (ESI) calcd for $C_{29}H_{30}N_2O_7S_2Na$ $[M+Na^+]^+$ 605.1387, found 605.1388.

4-Methyl-*N*-(5'-methyl-1'-pivaloyl-1'*H*-indol-3'-yl)-*N*-(methanesulfonyl)benzenesulfonamide (2e) : mp. 217 °C (decomp.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 9H), 2.43 (s, 3H), 3.56 (s, 3H), 7.25-7.30 (m, 3H), 7.32 (d, *J*=8.0 Hz, 1H), 7.37 (d, *J*=8.0 Hz, 1H), 7.62 (s, 1H), 7.79 (d, *J*=8.3 Hz, 2H), 8.48 (d, *J*=8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 28.5 (3C), 41.4, 44.0, 115.2, 117.4, 118.2, 124.4, 126.2, 126.7, 127.2, 128.8 (2C), 129.6 (2C), 135.1, 136.7, 145.6, 176.7. IR (neat) 1704, 1366, 1157, 900, 749, 660 cm^{-1}. MS (ESI) calcd for $C_{21}H_{25}N_2O_5S_2Na$ $[M+Na^+]^+$ 471.1019, found 471.1020.

4. General Procedure for C-N Ligand Coupling Reaction of 4-Methyl-*N*-((2"-*n*-butoxyphenyl)(1'-pivaloyl-1'*H*-indol-3'-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide (1ad) without Any Catalists (Scheme 2)

To a solution of 4-methyl-*N*-((2-*n*-butoxyphenyl)(1-pivaloyl-1*H*-indol-3-yl)-λ^3-iodanyl)-*N*-tosylbenzenesulfonamide **1ad** (80.1 mg, 0.10 mmol) in *o*-xylene (1mL) was stirred at 150 ºC for 4 h under argon atmosphere. Then, the organic solvent was concentrated under reduced pressure and the crude product was purified by column chromatography on silica-gel (eluent: hexane/AcOEt = 5/1), to give the desired product **3a** (41.5 mg, 79 % yield).

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List of Publications

Papers

1. Hofmann-Type Rearrangement of Imides by in Situ Generation of Imide-Hypervalent Iodines(III) from Iodoarenes
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Patent

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