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HALOGENATION OF DIMETHYL INDOLE-2,3-DICARBOXYLATES USING PhI(OAc)$_2$ AND ALKALI METAL HALIDE

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Abstract – We studied selective bromination and iodination of dimethyl indole-2,3-dicarboxylates using phenyliodine diacetate (PIDA), LiBr, and LiI in the presence of Lewis acid. The protective group on the nitrogen of indole is important for selectivity of the halogenation position, and the use of a benzenesulfonyl group as a protective group resulted in preferential halogenation of indole at the 6-position.

INTRODUCTION

Many bioactive natural products and pharmaceutical agents possess an indole skeleton.[1] Halogenated indoles with novel biological activities have also been found as secondary metabolites of marine organisms.[2] We examined the utility of dimethyl indole-2,3-dicarboxylates and indole-2,3-dicarboxylic anhydrides, which were shown to be useful synthons for the synthesis of various indole alkaloids, such as pratosine,[3] hippadine,[3] murrayaquinone-A,[4] elipticine,[5] olivacine,[6] caulersin,[7] cryptosanguinolentine,[8] and kalbretorine.[9] We have also studied the reactivity of dimethyl indole-2,3-dicarboxylates toward electrophilic reagents, such as brominating agents[10] and nitrating agents.[11] Most bromoindole alkaloids have a bromine atom at the 5- or 6-position. Normally, bromination of the indole skeleton occurs preferentially at the 5-position compared to the 6-position because the electron density at the former is higher than that at the latter. Chae and co-workers reported the selective bromination of dimethyl indole-2,3-dicarboxylate using bromine in the presence of sodium acetate in acetic acid to give dimethyl

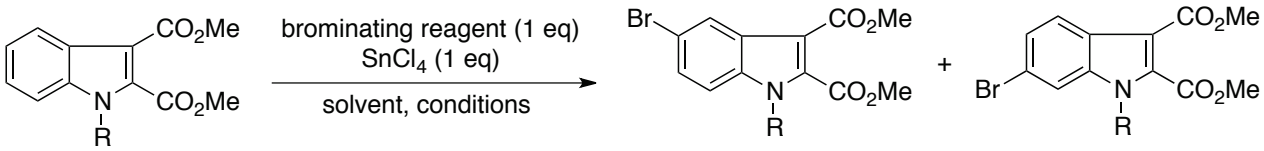
5-bromoindole-2,3-dicarboxylate as the sole product.[12] However, preferential bromination of the 5-position is unsurprising, as mentioned above, and they did not examine the effects of the protecting group on the indole nitrogen in bromination. We then investigated the bromination of various *N*-protected dimethyl indole-2,3-dicarboxylates using pyridinium hydrobromide perbromide (PHPB) and bromine in the presence of Lewis acid.[10] Interestingly, the introduction of a protective group on the indole nitrogen affected the selectivity of bromination position, and an electron-withdrawing group resulted in preferential bromination of the 6-position.

Here, we investigated bromination and iodination with other halogenation conditions and protective groups on indole nitrogen to examine the effects on the selectivity of the bromination and iodination position of *N*-protected dimethyl indole-2,3-dicarboxylates.

RESULTS AND DISCUSSION

In our previous study, three types of functional group—benzyl, benzenesulfonyl, and trifluoromethanesulfonyl groups—were used as the protective group of the indole nitrogen in bromination of dimethyl indole-2,3-dicarboxylate,[10] and selected results are shown in Table 1. The best conditions to preferentially obtain brominated product at the 6-position are indicated for each protective group. Preferential bromination at the 6-position was achieved using an electron-withdrawing group as the protective group for nitrogen (Entries 3 and 4), whereas non-substituent and electron-donating groups as a protective group for nitrogen resulted in preferential bromination at the 5-position (Entries 1 and 2).

Table 1. Preferential bromination at 6-position of dimethyl indole-2,3-carboxylates with various *N*-protective group using Br_2 and PHPB as brominating reagents



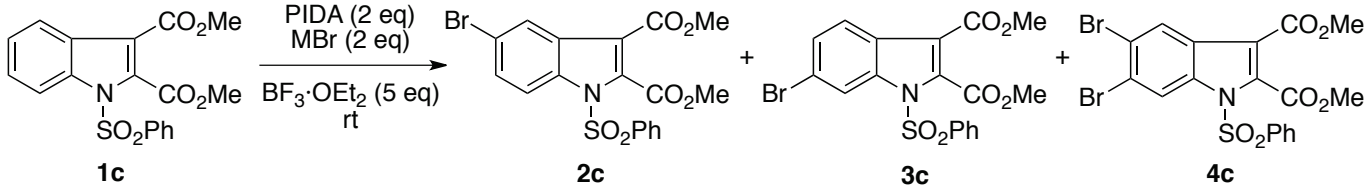
1 **2** (5-brominated product) **3** (6-brominated product)

Entry	R	Reagent	Solvent	Conditions		Yield (%)[b]	
				Temp (°C)	Time (h)	**2**	**3**
1	H (**1a**)	Br_2	CH_2Cl_2	rt	1	77 (**2a**)	0 (**3a**)
2	Bn (**1b**)	PHPB	CH_2Cl_2	rt	3	70 (**2b**)	23 (**3b**)
3[a]	SO_2Ph (**1c**)	PHPB	CH_2Cl_2	rt	2	40 (**2c**)	51 (**3c**)
4	SO_2CF_3 (**1d**)	Br_2	$(CH_2Cl)_2$	reflux	9	23 (**2d**)	45 (**3d**)

a) 5 eq of PHPB and $SnCl_4$ were used. b) The yields were determined by ^{1}H NMR.

In this study, we focused on the bromination reagent and employed a combination of hypervalent iodine reagent and alkali metal halide for selective bromination at the 6-position. Hypervalent iodine reagents are known as easy to handle reagents that act as mild and low-toxicity oxidants, and are used widely in organic synthesis.[13] The combination of phenyliodine diacetate (PIDA) and alkali metal halide was reported to act as a halogenating reagent[14] and we have also applied these combinations to decarboxylative halogenation reaction.[9,15] The advantage of these methods can easily arrange the kind of halogenation by changing alkali metal halide. First, we investigated the solvent effect for bromination of dimethyl 1-benzenesulfonylindole-2,3-dicarboxylate using a combination of PIDA and LiBr. However, no reaction proceeded using 2 equivalents of PIDA and 2 equivalents of LiBr in THF, MeCN, CH_2Cl_2, and CF_3CH_2OH. We then added $BF_3{\cdot}OEt_2$ for activation of PIDA and found that the bromination reaction proceeded in each solvent (Table 2). In THF, 5-bromoindole derivative (**2c**) and 6-bromoindole derivative (**3c**) were obtained in yields of 22% and 48%, respectively, and **1c** was recovered in 23% yield (Entry 1). A slight decrease in the yield of **3c** was observed in MeCN and 5,6-dibromoindole (**4c**) was obtained with a yield of 33% (Entry 2). The use of CH_2Cl_2 and CF_3CH_2OH gave **3c** with the same yield (55%), but **2c** was obtained with a yield of 35% in CH_2Cl_2 (Entry 3), and **2c** (14%) in addition to **4c** (23%) were obtained in CF_3CH_2OH (Entry 4). We examined several alkali metal bromides, all of which showed similar reactivity (Entries 5 and 6), but the yield of **3c** was lower than in the case of LiBr (Entry 4). Therefore, LiBr was used for further investigations.

Table 2. Effects of solvent and alkali metal bromide used for bromination



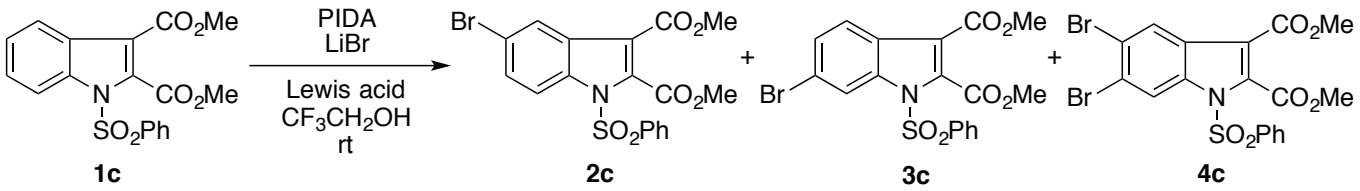
1c **2c** **3c** **4c**

Entry	Solvent	MBr	Time (h)	Yield (%)[a]		
				2c	**3c**	**4c**
1	THF	LiBr	2	22	48	- (23)[b]
2	MeCN	LiBr	1	20	39	33
3	CH_2Cl_2	LiBr	0.5	35	55	8
4	CF_3CH_2OH	LiBr	4	14	55	23
5	CF_3CH_2OH	NaBr	4	15	46	36
6	CF_3CH_2OH	KBr	4	16	48	27

a) The yields were determined by ^{1}H NMR. b) The yields in the parenthesis indicated the recovery of starting material.

Next, the effects of Lewis acid and the amounts of reagents were examined (Table 3). We first employed 5 equivalents of $BF_3{\cdot}OEt_2$ as an activating reagent for PIDA (Entry 1), and then examined the effects of reducing the amount of $BF_3{\cdot}OEt_2$. The reaction was performed in the presence of 1 equivalent of $BF_3{\cdot}Et_2O$ affording **2c** (27%), **3c** (58%), and **4c** (9%). The yield of **3c** was almost the same as that obtained using 5 equivalents of $BF_3{\cdot}OEt_2$ (Entry 1), and the yield of **4c** was decreased to 9% although that of **2c** was increased to 27% (Entry 2). $ZnCl_2$ as a weaker Lewis acid was then chosen as an activator. The addition of 5 equivalents of $ZnCl_2$ provided similar results to those seen with 1 equivalent of $BF_3{\cdot}OEt_2$ (Entry 3). Further decreasing the amounts of each reagent (1.5 equivalents of PIDA, 1.5 equivalents of LiBr, and 2 equivalents of $ZnCl_2$) afforded the best result (65% yield of **3c**) (Entry 4). Changing the solvent from CF_3CH_2OH to $(CF_3)_2CHOH$ was less effective for the reaction (Entry 5).

Table 3. Optimization of the amounts of reagents and effect of Lewis acid



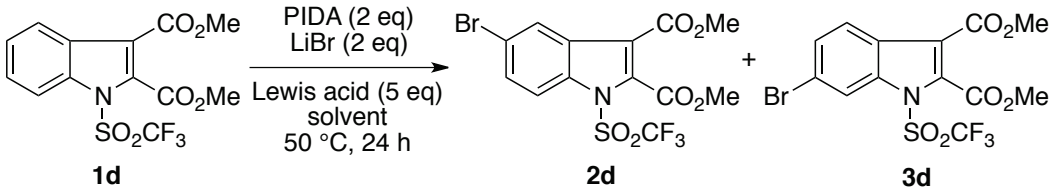
1c **2c** **3c** **4c**

Entry	PIDA (eq)	LiBr (eq)	Lewis acid (eq)	Time (h)	Yield (%)[b]		
					2c	**3c**	**4c**
1	2.0	2.0	$BF_3{\cdot}OEt_2$ (5.0)	4.0	14	55	23
2	2.0	2.0	$BF_3{\cdot}OEt_2$ (1.0)	0.5	27	58	9
3	2.0	2.0	$ZnCl_2$ (5.0)	0.5	21	59	18
4	1.5	1.5	$ZnCl_2$ (2.0)	0.5	28	65	7
5[a]	1.5	1.5	$ZnCl_2$ (2.0)	24	16	37	- (29)[c]

a) The reaction was performed in $(CF_3)_2CHOH$. b) The yields were determined by ^1H NMR. c) The yields in the parenthesis indicated the recovery of starting material.

We expected that using a stronger electron-withdrawing group as a protective group for nitrogen of indole would increase the yield of **3**. Therefore, a trifluoromethanesulfonyl group was used for the reaction (Table 4). The reaction was conducted using 2 equivalents of PIDA and 2 equivalents of LiBr in the presence of 5 equivalents of $ZnCl_2$, which gave **2d** in 8% yield and **3d** in 20% yield (Entry 1). Use of $BF_3{\cdot}OEt_2$ instead of $ZnCl_2$ afforded similar results (Entry 2). Changing the solvent to $(CH_2Cl)_2$ also gave similar results (Entry 3), and use of MeCN as a solvent enhanced bromination; however, preferential bromination at the 6-position was not observed, and **2d** was obtained in a yield of 32% and **3d** was obtained in a yield of 37% (Entry 4).

Table 4. Bromination of dimethyl 1-trifluoromethanesulfonylindole-2,3-dicarboxylate



1d **2d** **3d**

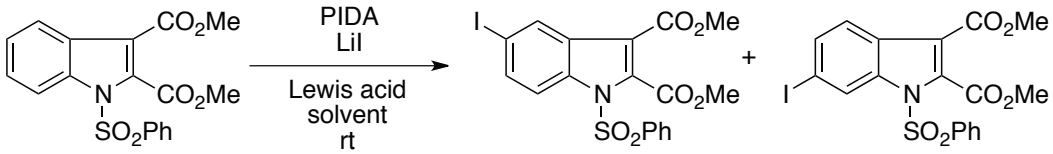
Entry	Lewis acid	Solvent	Yield (%)[a]	
			2d	**3d**
1	$ZnCl_2$	CF_3CH_2OH	8	20
2	$BF_3{\cdot}OEt_2$	CF_3CH_2OH	5	18
3	$BF_3{\cdot}OEt_2$	$(CH_2Cl)_2$	9	24
4	$BF_3{\cdot}OEt_2$	MeCN	32	37

a) The yields were determined by ^{1}H NMR.

In summary, the protective group on the indole nitrogen significantly affected the selectivity of bromination using PIDA and LiBr. Preferential bromination at the 6-position proceeded using an electron-withdrawing group, such as benzenesulfonyl and trifluoromethanesulfonyl groups, as the protective group for nitrogen. Protection of nitrogen with a benzenesulfonyl group gave the best result, and the 6-bromoindole derivative was obtained in 65% yield using a combination of PIDA and LiBr (Table 3, Entry 4).

We next applied this method to the iodination of dimethyl indole-2,3-dicarboxylates. The reaction of dimethyl 1-benzenesulfonylindole-2,3-dicarboxylate (**1c**) was conducted using 1.5 equivalents of PIDA, 1.5 equivalents of LiI instead of LiBr, and 2 equivalents of $ZnCl_2$, but no reaction occurred (Table 5, Entry 1). We then used $BF_3{\cdot}OEt_2$ instead of $ZnCl_2$ and increased the amounts of reagents to 5.0 equivalents. The reaction proceeded giving the 5-iodoindole derivative (**5c**) in 39% yield and 6-iodoindole derivative (**6c**) in 26% yield, and preferential iodination at the 6-position was not observed (Entry 2). The use of other solvents, MeCN and CH_2Cl_2, improved the yields of both **5c** and **6c** (Entries 3 and 4), and **6c** was obtained in 47% yield with CH_2Cl_2 (Entry 4) although **5c** was generated preferentially.

Table 5. Iodination of dimethyl 1-benzenesulfonylindole-2,3-dicarboxylate



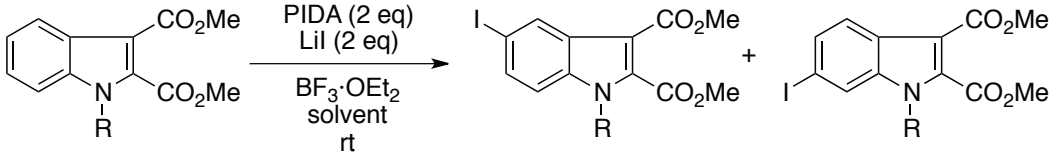
1c **5c** **6c**

Entry	PIDA (eq)	LiI (eq)	Lewis acid (eq)	Solvent	Time (h)	Yield (%)[a]	
						5c	**6c**
1	1.5	1.5	$ZnCl_2$ (2.0)	CF_3CH_2OH	24	-	-
2	2.0	2.0	$BF_3{\cdot}OEt_2$ (5.0)	CF_3CH_2OH	24	39	26
3	2.0	2.0	$BF_3{\cdot}OEt_2$ (5.0)	MeCN	24	56	38
4	2.0	2.0	$BF_3{\cdot}OEt_2$ (5.0)	CH_2Cl_2	4	52	47

a) The yields were determined by ^{1}H NMR.

From the results shown in Table 5 (Entry 1), the iodination seemed to be less reactive than the bromination. In fact, no reaction proceeded with dimethyl 1-trifluoromethanesulfonyl-indole-2,3-dicarboxylate (**1d**) using PIDA and LiI in the presence of $BF_3{\cdot}Et_2O$. We then examined the effect of using an electron-donating group as the protective group for nitrogen on the indole ring as well as a non-protective group on the nitrogen. The reaction of dimethyl 1-benzylindole-2,3-dicarboxylate (**1b**) proceeded to give 5-iodoindole derivative (**5b**) in 44% yield and 6-iodoindole derivative (**6b**) in 15% yield, with preferential generation of **5b** (Table 6, Entry 1). The use of other solvents, MeCN and CH_2Cl_2, gave iodination products but the results were similar to those with CF_3CH_2OH (Entries 2 and 3). We also conducted the reaction with non-protected dimethyl indole-2,3-dicarboxylate (**1a**). The reaction proceeded but the iodination occurred mainly at the 5-position, even with changing the solvent (Table 6, Entries 4–6).

Table 6. Iodination of dimethyl indole-2,3-dicarboxylate derivatives



1 **5** **6**

Entry	R	Solvent	Time (h)	Yield (%)[a]	
				5	**6**
1	Bn (**1b**)	CF_3CH_2OH	24	44 (**5b**)	15 (**6b**)
2	Bn (**1b**)	MeCN	15	69 (**5b**)	20 (**6b**)

3	Bn (**1b**)	CH_2Cl_2	41	46 (**5b**)	14 (**6b**)
4	H (**1a**)	CF_3CH_2OH	24	35 (**5a**)	1 (**6a**)
5	H (**1a**)	MeCN	1	51 (**5a**)	7 (**6a**)
6	H (**1a**)	CH_2Cl_2	2	38 (**5a**)	8 (**6a**)

a) The yields were determined by ^{1}H NMR.

Regarding the selectivity of halogenation, the introduction of electron-withdrawing protective group on the indole nitrogen is the most important. This is because the electron-withdrawing protective group caused the decrease of electron density on 5-position, and the electron density on 6-position appeared to increase relatively, which resulted in accelerating the halogenation at 6-position. The addition of Lewis acid enhanced the reactivity of PIDA promoting the halogenation. $BF_3{\cdot}OEt_2$ and $ZnCl_2$ were suitable Lewis acid for activation of PIDA in our previous study, then we chose these Lewis acids as an activator for these reactions. As for solvents, the use of THF, MeCN, CH_2Cl_2, $(CH_2Cl)_2$, and CF_3CH_2OH promoted the PIDA and LiX mediated decarboxylative halogenation reaction[15] and CF_3CH_2OH gave the best result in this bromination and CH_2Cl_2 was suitable solvent for this iodination although the details of solvent effect are unclear. In this study, we achieved the selective bromination at 6-position using PIDA-LiBr with $ZnCl_2$ compared with our previous report,[10] and we speculate the reason that the bromination ability of reagents may affect the selectivity, which could be supported by the comparison of the bromination and the iodination results. That is, the combination of PIDA and LiBr was found to be more reactive than that of PIDA and LiI, which might affect the selectivity, whereas the possibility of the generation of different active species from PIDA-LiBr and PIDA-LiI cannot be ruled out. Finally, the mechanism of the generation of **4c** could be via both **2c** and **3c** since **2c** and **3c** underwent further bromination to give **4c** by the treatment of Br_2 in our previous study.[10]

In conclusion, we investigated the halogenation of dimethyl indole-2,3-dicarboxylate derivatives using PIDA and alkali metal halide in the presence of Lewis acid. The position of halogenation on the indole ring depended on the nature of the protective group on the nitrogen of the indole ring, and use of an electron-withdrawing group was intended to facilitate halogenation at the 6-position. Selective bromination at the 6-position was achieved using a benzenesulfonyl group as a protective group on nitrogen of the indole ring, and the best result was obtained using 1.5 equivalents of PIDA and 1.5 equivalents of LiBr in the presence of 2.0 equivalents of $ZnCl_2$ in CF_3CH_2OH, affording 6-position brominated product (**3c**) in 65% yield (Table 3, Entry 4). Selective iodination at 6-position could not be achieved, but almost same amount of iodination products at 5- and 6-position were obtained by the reaction of dimethyl 1-benzenesulfonylindole-2,3-dicarboxylate with 2 equivalents of PIDA and 2

equivalents of LiI in the presence of 5 equivalents of $BF_3 \cdot Et_2O$ in a yield of 47% of **6c** concomitant with **5c** in 52% yield (Table 5, Entry 4).

EXPERIMENTAL

^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet), coupling constant (Hz) and integration. The high-resolution mass spectra (HRMS) was recorded on a double-focusing mass spectrometer using electrospray ionization (ESI). Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without further purification. Compounds **1a**-**1d**, **2a**-**2d**, **3b**-**3d**, and **4c** are known compounds.[10] Compounds **5a**–**5c** and **6a**–**6c** were identified as follows. The mixture of **5c** and **6c** obtained by reaction of **2c** was treated with 1 equivalent of tetra-*n*-butylammonium fluoride (TBAF) to deprotect the benzenesulfonyl group. The residue was purified by preparative TLC to give **5a** and **6a**, respectively. The **5a** and **6a** thus obtained were subjected to benzylation or benzenesulfonylation, respectively, to afford **5b** and **6b**, and **5c** and **6c**, as a single product.

Typical procedure for the bromination of dimethyl 1-benzenesulfonylindole-2,3-dicarboxylate (1c) using PIDA and LiBr.

To a solution of LiBr (13 mg, 0.15 mmol) in CF_3CH_2OH (1.0 ml) was added PIDA (48.0 mg, 0.15 mmol) and **1c** (37.0 mg, 0.1 mmol) successively. Then, $ZnCl_2$ (27.0 mg, 0.2 mmol) was added and the reaction mixture was stirred at room temperature for 0.5 h. Na_2SO_3 aqueous solution was added and the mixture was extracted with CH_2Cl_2. Combined organic layers were washed with water, then dried over Na_2SO_4. The organic layer was concentrated *in vacuo* and the residue was purified by column chromatography (residue was charged with CH_2Cl_2 on silica gel and eluted with *n*-hexane to *n*-hexane : EtOAc = 3 : 1) to give a mixture (45.7 mg) of **2c**, **3c**, and **4c**. The yields were determined by ^1H NMR.

Typical procedure for the iodination of dimethyl 1-benzenesulfonylindole-2,3-dicarboxylate (1c) using PIDA and LiI.

To a solution of LiI (724 mg, 5.4 mmol) in CH_2Cl_2 (27 mL) was added PIDA (1.74 g, 5.4 mmol) and **1c** (1.01 g, 2.7 mmol) successively. Then, $BF_3 \cdot OEt_2$ (1.73 mL, 13.5 mmol) was added and the reaction mixture was stirred at room temperature for 4 h. Na_2SO_3 aqueous solution was added and the mixture was extracted with CH_2Cl_2. Combined organic layers were washed with water, then dried over Na_2SO_4. The organic layer was concentrated *in vacuo* and the residue was purified by column chromatography (residue was charged with CH_2Cl_2 : *n*-hexane = 20 : 1 on silica gel and eluted with *n*-hexane to *n*-hexane : EtOAc = 4 :1) to give the mixture (1.34 g) of **5c** and **6c**. The yields were determined by ^1H NMR.

Dimethyl 1-benzenesulfonyl-5-iodoindole-2,3-dicarboxylate (5c)

A colorless crystal (*n*-hexane); mp 144 °C; ^{1}H NMR ($CDCl_3$) δ: 3.93 (3H, s), 4.11 (3H, s), 7.51 (2H, t, *J* = 8.0 Hz), 7.62 (1H, t, *J* = 7.6 Hz), 7.68 (1H, dd, *J* = 8.8, 1.6 Hz), 7.77 (1H, d, *J* = 8.8 Hz), 8.06 (2H, d, *J* = 7.6 Hz), 8.46 (1H, d, *J* = 1.6 Hz); ^{13}C NMR ($CDCl_3$) δ: 52.3, 53.9, 89.6, 111.3, 115.6, 127.7, 128.1, 129.6, 131.5, 133.5, 135.0, 135.1, 136.2, 136.8, 162.3, 162.7; HRMS (FAB) *m/z*: Calcd for $C_{18}H_{14}INO_6S$: 498.9587. Found: 498.9577.

Dimethyl 1-benzenesulfonyl-6-iodoindole-2,3-dicarboxylate (6c)

A yellow crystal (*n*-hexane); mp 188 °C; ^{1}H NMR ($CDCl_3$) δ: 3.91 (3H, s), 4.11 (3H, s), 7.54 (2H, t, *J* = 7.8 Hz), 7.62-7.66 (2H, m), 7.85 (1H, d, *J* = 8.8 Hz), 8.08 (2H, d, *J* = 8.0 Hz), 8.38 (1H, s); ^{13}C NMR ($CDCl_3$) δ: 52.2, 53.9, 91.0, 112.1, 122.7, 124.1, 125.6, 127.7, 129.7, 134.1, 135.0, 135.6, 136.1, 136.8, 162.3, 162.7; HRMS (FAB) *m/z*: Calcd for $C_{18}H_{14}INO_6S$: 498.9587. Found: 498.9581.

Dimethyl 5-iodoindole-2,3-dicarboxylate (5a)

A yellow crystal (*n*-hexane-CH_2Cl_2); mp 194 °C; ^{1}H NMR ($CDCl_3$) δ: 3.99 (3H, s), 4.00 (3H, s), 7.22 (1H, d, *J* = 8.4 Hz), 7.64 (1H, dd, *J* = 8.4, 1.6 Hz), 8.44 (1H, d, *J* = 1.6 Hz), 9.26 (1H, s); ^{13}C NMR ($CDCl_3$) δ: 52.0, 52.9, 86.7, 110.9, 113.7, 128.7, 129.0, 131.7, 133.6, 134.5, 160.9, 163.9; HRMS (FAB) *m/z*: Calcd for $C_{12}H_{10}INO_4$: 358.9655. Found: 358.9624.

Dimethyl 6-iodoindole-2,3-dicarboxylate (6a)

A colorless crystal (*n*-hexane-CH_2Cl_2); mp 216 °C; ^{1}H NMR ($CDCl_3$) δ: 3.98 (3H, s), 4.00 (3H, s), 7.55 (1H, dd, *J* = 8.4, 1.4 Hz), 7.81 (1H, d, *J* = 8.8 Hz), 7.82 (1H, s), 9.16 (1H, s); ^{13}C NMR ($CDCl_3$) δ: 52.0, 52.9, 90.7, 112.1, 120.9, 124.4, 126.2, 128.2, 131.6, 135.6, 160.9, 164.0; HRMS (FAB) *m/z*: Calcd for $C_{12}H_{10}INO_4$: 358.9655. Found: 358.9636.

Dimethyl 1-benzyl-5-iodoindole-2,3-dicarboxylate (5b)

A yellow oil; ^{1}H NMR ($CDCl_3$) δ: 3.91 (3H, s), 3.93 (3H, s), 5.41 (2H, s), 7.06-7.08 (3H, m), 7.26-7.28 (3H, m), 7.54 (1H, dd, *J* = 8.8, 1.4 Hz), 8.50 (1H, d, *J* = 1.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 48.8, 51.8, 53.2, 87.0, 107.6, 112.8, 126.6, 127.5, 128.1, 128.9, 131.3, 133.2, 135.4, 135.5, 135.6, 162.8, 164.0; HRMS (FAB) *m/z*: Calcd for $C_{19}H_{16}INO_4$: 449.0124. Found: 449.0141.

Dimethyl 1-benzyl-6-iodoindole-2,3-dicarboxylate (6b)

A colorless crystal (*n*-hexane); mp 141 °C; ^{1}H NMR ($CDCl_3$) δ: 3.88 (3H, s), 3.92 (3H, s), 5.40 (2H, s), 7.07 (2H, d, *J* = 6.4 Hz), 7.26-7.30 (3H, m), 7.55 (1H, dd, *J* = 8.4, 1.4 Hz), 7.68 (1H, s), 7.88 (1H, d, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 48.6, 51.7, 53.2, 89.0, 108.7, 119.8, 124.1, 124.7, 126.5, 128.1, 128.9, 131.7, 134.8, 135.5, 137.5, 162.8, 164.1; HRMS (FAB) *m/z*: Calcd for $C_{19}H_{16}INO_4$: 449.0124. Found: 449.0106.

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