Synthesis of 3-Aryl- and 3-Heteroaryl-7-azaindoles

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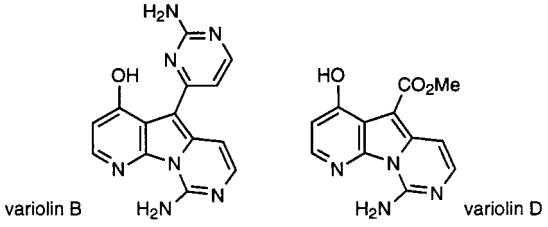
Abstract: The synthesis of 1-protected 3-trimethylstannyl-7-azaindoles and their coupling with aryl and heteroaryl halides is described.

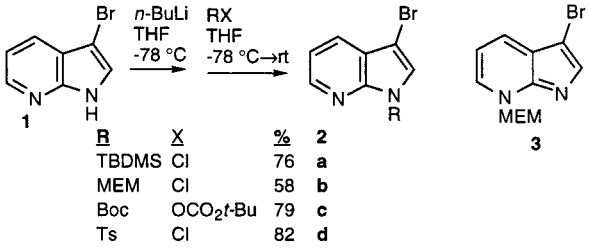
Key words: variolins, marine alkaloids, 3-trimethylstannyl-7-azaindole, palladium catalysis, coupling reactions

The variolins, which occur in the Antarctic sponge *Kirkpatrickia varialosa*, are a small group of marine heterocyclic substances[1,2] of which variolins B and D are typical. These substances were isolated after the examination of extracts which were shown to be active against P388 murine leukemia cells. Subsequent in vitro testing showed variolin B to be the most active in tests which included antiviral activity (*Herpes simplex* Type I, *polio* Type I). Each of these variolins is based on a fused pyrimidino-7-azaindole, strictly a pyrido[3',2':4,5]pyrrolo[1,2-*c*]pyrimidine. There is only one report on the synthesis of this tricyclic heterocyclic ring system.[3]



The retrosynthetic analysis of the structures of these molecules necessitate the conversion of a 3-halo-7-azaindole into a 3-aryl(heteroaryl)-7-azaindole. Consequently we describe here an investigation into the synthesis of 3-aryl-7-azaindoles via the palladium(0)-catalyzed coupling of 3-stannyl-7-azaindoles. We have selected organotin reagents rather than other possibilities such as boronic acids or organozinc reagents for coupling reactions because of its easier manipulation and purification. Although the coupling reactions of 1-protected 2-tributylstannylindoles,[4–7] 1-tosyl-3-trimethylstannylindole[8] and 2-trimethylstannyl-1-phenylsulfonyl-7-azaindole[9] have been described no reports on the synthetic utility of 3-stannyl-7-azaindoles are known.

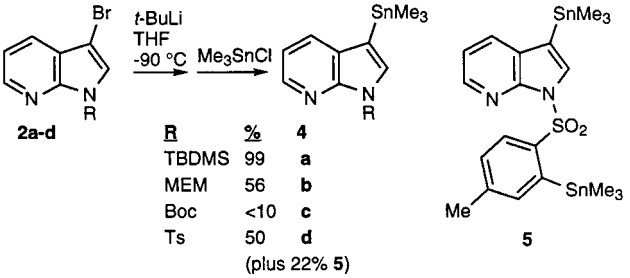
7-Azaindole[10] was converted into the known 3-bromo-7-azaindole **(1)**[11] and protected at the pyrrole nitrogen using butyllithium in THF to deprotonate producing an anion which was then trapped at low temperature giving **2a–d** (Scheme 1). Although the anion from **1** is ambident, in only one case (trapping with MEM chloride) a product **3** from the alkylation at the six-membered ring nitrogen was obtained (**2b**:**3**; 3.5:1). Differentiation between the two derivatives was based on the observation of a NOE between H-2 or H-6 and the methylene (N-CH_2-O) for **2b** and **3**, respectively. The difference in the coupling constant between the protons 5 and 6 of **2b** ($J_{5,6}$ = 4.8 Hz) and **3** ($J_{5,6}$ = 6.2 Hz) confirms by analogy the introduction of R at *N*-1 for **2a** ($J_{5,6}$ = 4.4 Hz), **2c** ($J_{5,6}$ = 4.9 Hz) and **2d** ($J_{5,6}$ = 4.8 Hz).



R	X	%	2
TBDMS	Cl	76	a
MEM	Cl	58	b
Boc	OCO_2t-Bu	79	c
Ts	Cl	82	d

Scheme 1

Each of the 1-protected 3-bromo-7-azaindoles **2** was converted into the corresponding 3-trimethylstannyl derivative **4** by treatment with *tert*-butyllithium at low temperature followed by chlorotrimethylstannane (Scheme 2). There was considerable variation in the efficiency of these transformations, conversion to the *tert*-butyldimethylsilyl protected 7-azaindole **4a** being the most efficient while the yield from **2c** was insufficient to allow



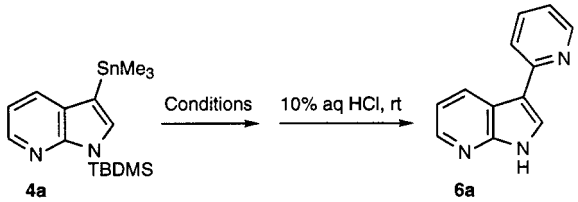
R	%	4
TBDMS	99	a
MEM	56	b
Boc	<10	c
Ts	50	d

(plus 22% **5**)

Scheme 2

proper characterization. In the case of the 1-(*p*-toluenesulfonyl)-protected azaindole **2d**, lithiation on the arylsulfonyl ring[12] also occurred, and with excess *tert*-butyllithium it was possible to produce the doubly stannylated **5** in 85% yield.

1-*tert*-Butyldimethylsilyl-3-trimethylstannyl-7-azaindole **(4a)** was chosen for further study to seek optimum coupling conditions with 2-bromopyridine. This protected azaindole has the further advantage that simple extraction into dilute acid, following the coupling procedure, was sufficient to remove the *N*-protection. Scheme 3 shows the results of this study: the best condition, tetrakis(triphenylphosphine)palladium(0) with lithium chloride in refluxing tetrahydrofuran, was used subsequently in the couplings summarized in Schemes 4 and 5.

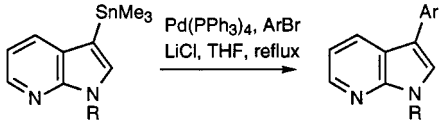


4a **6a**

Conditions	%
$Pd(OAc)_2$, PPh_3, LiCl, reflux	10
$Pd(PPh_3)_2Cl_2$, PPh_3, LiCl, THF, reflux	23
$Pd_2(dba)_3.CHCl_3$, PPh_3, LiCl, THF, reflux	37
$Pd(PPh_3)_4$, LiCl, THF, reflux	45
$Pd(PPh_3)_4$, DMF, 50 °C	27
$Pd(PPh_3)_4$, LiCl, DMF, 50 °C	37
$Pd(PPh_3)_4$, dioxane, reflux	38
$Pd(PPh_3)_4$, LiCl, dioxane, reflux	44

Scheme 3

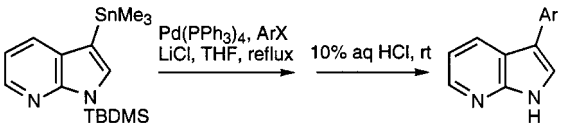
The influence of the different protecting groups on the coupling process was assessed using both 2-bromopyridine and 5-bromopyrimidine and these experiments are summarized in Scheme 4. There was not much difference in the reactivities of TBDMS, MEM and Ts protected 7-azaindoles. The pyrimidine couplings were consistently somewhat more efficient than those with 2-bromopyridine.



4a,b,d	Ar	R	%	6	
	pyridin-2-yl	TBDMS	45	a	R = H
	pyridin-2-yl	MEM	45	b	
	pyridin-2-yl	Ts	42	c	
	pyrimidin-5-yl	TBDMS	74	d	R = H
	pyrimidin-5-yl	MEM	50	e	
	pyrimidin-5-yl	Ts	60	f	

Scheme 4

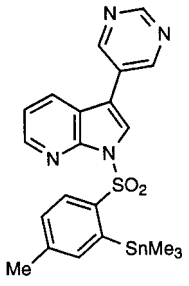
Settling for the efficiency and simple *N*-protecting group removal during workup, we examined the coupling of stannane **4a** with a wide range of aryl and heteroaryl halides, and the results are given in Scheme 5.



4a	Ar	X	%	6
	4-methoxyphenyl	Br	38	g
	4-nitrophenyl	Br	50	h
	thien-3-yl	Br	57	i
	2-methylthiopyrimidin-4-yl	Cl	60	j
	2-methylthiopyrimidin-5-yl	Br	53	k

Scheme 5

The coupling of the bis(trimethylstannyl)indole **5** with 5-bromopyrimidine produced **6l** in a yield of 62%. Taking into account a yield of 63% for the hydrolytic removal of the *N*-protecting group to give **6d**, this also represents an efficient method for the synthesis of 3-aryl-7-azaindoles.



6l

Melting points were determined in a capillary tube and are uncorrected. TLC was carried out on silica gel 60 F_{254} (Merck 0.063–0.200 mm) and spots were located with UV light. Column chromatography was carried out on silica gel 60 SDS (0.060–0.2 mm). Flash chromatography was carried out on silica gel (60 A CC, Merck). Organic extracts were dried over anhyd Na_2SO_4, and solutions were evaporated under reduced pressure with a rotatory evaporator. IR spectra were recorded on a Nicolet 205 FT-IR spectrophotometer. NMR spectra were measured with Varian Gemini-200 (200 MHz), Varian Gemini-300 (300 MHz) and Varian VXR-500 (500 MHz) spectrometers; data are given in δ referenced to TMS. Mass spectra were recorded in the electron impact (EI) mode with a Hewlett-Packard model 5989A. High resolution mass spectra were performed on a Autospec/VG by Departament de Química Orgànica Biològica (C.S.I.C.) Barcelona. Elemental analyses were performed on a C. E. Instrument EA-1108 in the Serveis Científico-Tècnics de la Universitat de Barcelona.

3-Bromo-7-azaindole (1)

This compound was prepared as described[11] in 80% yield; mp 186–187 °C (CH_2Cl_2) (Lit[11] mp 188 °C).

IR (KBr): ν = 3077 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.19 (dd, *J* = 8.0, 4.8 Hz, 1 H, H-5), 7.41 (s, 1 H, H-2), 7.93 (dd, *J* = 8.0, 1.4 Hz, 1H, H-4), 8.37 (dd, *J* = 4.8, 1.4, 1 H, H-6), 11.4 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 89.0 (s, C-3), 116.4 (d, C-5), 119.9 (s, C-3a), 124.3 (d, C-2), 127.9 (d, C-4), 143.5 (d, C-6), 147.4 (s, C-7a).

MS (EI): *m*/*z* (%) = 198 (^{81}BrM$^+$, 97), 197 (11), 196 (^{79}BrM$^+$, 100), 117 (M – Br, 54), 90 (100).

N-Protection of 3-Bromo-7-azaindole (1); General Procedure

To a solution of **1** (1 equiv) in THF, cooled at –78 °C, was added slowly BuLi (1.6 M in hexane, 1.1 equiv). After stirring for 15 min, the alkylating agent (in THF for solids, 1.1 equiv) was added. When the addition was complete, the cooling bath was removed and the mixture was allowed to rise to r.t. Et_2O was added and the organic layer was washed with brine, dried and evaporated. The crude product was purified by flash column chromatography using mixtures of hexane and CH_2Cl_2.

3-Bromo-1-tert-butyldimethylsilyl-7-azaindole (2a)

From **1** (2.7 g, 13.71 mmol) and TBDMS-Cl (2.3 g, 15.07 mmol). Reaction time 3 h. After purification, **2a** (3.2 g, 76%) was obtained as a white solid; mp 80 °C (hexane/CH_2Cl_2).

IR (KBr): ν = 2950, 1397, 793 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.64 (s, 6 H, 2 CH_3), 0.95 (s, 9 H, *t*-C_4H_9), 7.11 (dd, *J* = 8.0, 4.4 Hz, 1 H, H-5), 7.26 (s, 1 H, H-2), 7.83 (dd, *J* = 8.0, 1.4 Hz, 1 H, H-4), 8.32 (dd, *J* = 4.4, 1.4 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = –4.3 (q, 2 CH_3), 18.9 [s, C(*C*$H_3)_3$], 26.4 [q, *C*$(CH_3)_3$], 91.2 (s, C-3), 116.5 (d, C-5), 121.6 (s, C-3a), 126.6 (d, C-2), 129.4 (d, C-4), 143.5 (d, C-6), 152.5 (s, C-7a).

MS (EI): *m*/*z* (%) = 312 (^{81}BrM$^+$, 30), 310 (^{79}BrM$^+$, 29), 256 (44), 255 (100), 254 (44), 253 (^{79}BrM – *t*-Bu, 90), 240 (47), 238 (^{79}BrM – *t*-Bu – Me, 51).

HRMS: *m*/*z* calcd for $C_{13}H_{19}{}^{79}BrN_2Si$: 310.0501, found: 310.0503.

3-Bromo-1-methoxyethoxymethyl-7-azaindole (2b)

From **1** (500 mg, 3.38 mmol) and MEM-Cl (315 mL, 3.72 mmol). Reaction time 4 h**.** A mixture of **2b** and **3** was obtained. Separation by column chromatography eluting with CH_2Cl_2/MeOH (9:1) produced **2b** (418 mg, 58%) as a colourless oil and **3** (120 mg, 17%) as a yellow oil.

IR (film): ν = 1560, 1420, 1310, 1150, 1087 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.34 (s, 3 H, OCH_3), 3.50–3.60 (m, 4 H, CH_2), 5.73 (s, 2 H, CH_2), 7.17 (dd, *J* = 7.6, 4.8 Hz, 1 H, H-5), 7.41 (s, 1 H, H-2), 7.86 (d, *J* = 7.6 Hz, 1 H, H-4), 8.36 (d, *J* = 4.8 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 58.9 (q, OCH_3), 68.0 (t, CH_2), 71.4 (t, CH_2), 73.5 (t, CH_2), 90.2 (s, C-3), 116.9 (d, C-5), 119.9 (s, C-3a), 126.7 (d, C-2), 127.6 (d, C-4), 144.3 (d, C-6), 146.9 (s, C-7a).

MS (EI): *m*/*z* (%) = 286 (^{81}BrM$^+$, 2), 284 (^{79}BrM$^+$, 2), 211 (14), 209 (^{79}BrM – OC_2H_4OMe, 15), 198 (18), 196 (^{79}BrM – MEM, 18).

HRMS: *m*/*z* calcd for $C_{11}H_{13}{}^{79}BrN_2O_2$: 284.0160, found: 284.0161.

3-Bromo-7-methoxyethoxymethyl-7-azaindole (3)

IR (film): ν = 3019, 1216, 1108, 1017, 770 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.33 (s, 3 H, OCH_3), 3.42–3.60 (m, 2 H, CH_2), 3.65–3.82 (m, 2 H, CH_2), 6.17 (s, 2 H, CH_2), 7.06 (dd, *J* = 7.2, 6.2 Hz, 1 H, H-5), 7.79 (s, 1 H, H-2), 8.98 (d, *J* = 6.2 Hz, 1 H, H-6), 8.12 (d, *J* = 7.2 Hz, 1 H, H-4).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 58.8 (q, OCH_3), 69.8 (t, CH_2), 71.1 (t, CH_2), 80.0 (t, CH_2), 87.7 (s, C-3), 109.6 (d, C-5), 119.9 (s, C-3a), 128.5 (d, C-2), 130.9 (d, C-4), 142.7 (d, C-6), 147.0 (s, C-7a).

MS (EI): *m*/*z* (%) = 286 (^{81}BrM$^+$, 2), 284 (^{79}BrM$^+$, 2), 227 (2), 225 (^{79}BrM – $MeOC_2H_4$, 2), 198 (18), 196 (^{79}BrM – MEM, 22), 149 (25).

HRMS: *m*/*z* calcd for $C_{11}H_{13}{}^{79}BrN_2O_2$: 284.0160, experimental: 284.0155.

3-Bromo-1-*tert*-butoxycarbonyl-7-azaindole (2c)

From **1** (500 mg, 3.53 mmol) and Boc_2O (554 mg, 3.53 mmol). Reaction time 2 h; yield: 594 mg (79%); red oil.

IR (film): ν = 1736, 1410, 1314, 1251, 1155 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.67 (s, 9 H, *t*-C_4H_9), 7.29 (dd, *J* = 7.9, 4.9 Hz, 1 H, H-5), 7.71 (s, 1 H, H-2), 7.86 (dd, *J* = 7.9, 1.6 Hz, 1 H, H-4), 8.55 (dd, *J* = 4.9, 1.6 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 28.0 [q, C(*C*$H_3)_3$], 84.7 [s, *C*$(CH_3)_3$], 94.9 (s, C-3), 119.0 (d, C-5), 122.4 (s, C-3a), 125.4 (d, C-2), 128.0 (d, C-4), 146.3 (d, C-6), 147.1 (s, C-7a).

MS (EI): *m*/*z* (%) = 298 (^{81}BrM$^+$, 0.3), 296 (^{79}BrM$^+$, 0.4), 198 (^{79}BrM – Boc, 17), 196 (17), 116 (7).

HRMS: *m*/*z* calcd for $C_{12}H_{13}{}^{79}BrN_2O_2$: 296.0160, found: 296.0163.

3-Bromo-1-(4-methylphenylsulfonyl)-7-azaindole (2d)

From **1** (2 g, 10.15 mmol) and TsCl (2.32 g, 11.16 mmol). Reaction time 2 h; yield: 2.93 g (82%); white solid; mp 133–134 °C (CH_2Cl_2).

IR (KBr): ν = 1375, 1175 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.36 (s, 3 H, CH_3), 7.20–7.30 (m, 3 H, H-5, H-3', 5'), 7.78 (s, 1 H, H-2), 7.79 (dd, *J* = 7.6, 1.2 Hz, 1 H, H-4), 8.07 (d, *J* = 8.0 Hz, 2 H, H-2', 6'), 8.47 (dd, *J* = 4.8, 1.2 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.6 (q, CH_3), 95.3 (s, C-3), 119.3 (d, C-5), 122.3 (s, C-3a), 124.8 (d, C-2), 128.0 (d, C-3', 5'), 128.4 (d, C-4), 129.5 (s, C-4'), 129.7 (d, C-2', 6'), 134.8 (s, C-1'), 145.5 (s, C-7a), 145.9 (d, C-6).

MS (EI): *m*/*z* (%) = 352 (^{81}BrM$^+$, 2), 350 (^{79}BrM$^+$, 2), 288 (13), 286 (13), 197 (2), 195 (^{79}BrM – Ts, 2), 116 (12).

HRMS: *m*/*z* calcd for $C_{14}H_{11}{}^{79}BrN_2O_2S$: 349.9725, found: 349.9734.

Anal. calcd for $C_{14}H_{11}BrN_2O_2S$ (350.0): C, 47.88; H, 3.16; N, 7.98; S, 9.13. Found C, 47.98; H, 3.24; N, 7.78; S, 9.23

3-Trimethylstannyl-7-azaindoles 4; General Procedure

To a solution of **2** (1 equiv) in THF cooled at –90 °C was added quickly *t*-BuLi (1.7 M in pentane, 2 equiv) and the mixture was stirred for 5 min at the same temperature. After this time, Me_3SnCl (1 M in THF) was added and the mixture was stirred for 1 h at –90 °C and then for 1 h at r.t. The mixture was diluted with Et_2O and the organic layer washed with brine, dried and evaporated.

1-*tert*-Butyldimethylsilyl-3-trimethylstannyl-7-azaindole (4a)

From **2a** (1g, 3.21 mmol) and Me_3SnCl (4.82 mmol); yield: 1.26 g (99%); white solid; mp 87–88 °C (Et_2O).

IR (film): ν = 2950, 1484, 1398, 1166 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.35 (s, 9 H, 3 CH_3), 0.63 (s, 6 H, 2 CH_3), 0.94 (s, 9 H, *t*-C_4H_9), 7.01 (dd, *J* = 7.7, 4.7 Hz, 1 H, H-5), 7.13 (s, 1 H, H-2), 7.81 (dd, *J* = 7.7, 1.5 Hz, 1 H, H-4), 8.26 (dd, *J* = 4.7, 1.5 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = –9.2 (q, CH_3), –4.3 (q, CH_3), 19.5 [s, C(*C*$H_3)_3$], 26.5 [q, *C*$(CH_3)_3$], 109.7 (s, C-3), 115.6 (d, C-5), 128.6 (s, C-3a), 129.7 (d, C-2), 136.9 (d, C-4), 142.2 (d, C-6).

MS (EI): *m*/*z* (%) = 396 (^{120}SnM$^+$, 21), 395 (5), 394 (^{118}SnM$^+$, 17), 392 (^{116}SnM$^+$, 6), 385 (M, 12), 383 (13), 382 (18), 381 (M – Me, 100), 380 (42), 379 (81), 232 (M – $SnMe_3$, 2).

HRMS: *m*/*z* calcd for $C_{16}H_{28}N_2Si{}^{120}Sn$: 396.1044, found: 396.1039.

1-Methoxyethoxymethyl-3-trimethylstannyl-7-azaindole (4b)
From **2b** (700 mg, 2.45 mmol) and Me_3SnCl (3.68 mmol) following the general procedure was obtained an oil (900 mg) which was characterized as a mixture of **4b** and 1-MEM-7-azaindole. Microdistillation (120 °C/0.5 Torr) permitted the separation of byproduct and isolation of **4b** (510 mg, 56%) as a colourless oil.

IR (film): ν = 2926, 1497, 1420, 1130, 1090, 770 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 0.36 (s, 9 H, 3 CH_3), 3.34 (s, 3 H, OCH_3), 3.42–3.52 (m, 2 H, CH_2), 3.60–3.68 (m, 2 H, CH_2), 5.74 (s, 2 H, CH_2), 7.08 (dd, *J* = 7.7, 4.7 Hz, 1 H, H-5), 7.29 (s, 1 H, H-2), 7.85 (dd, *J* = 7.7, 1.5 Hz, 1 H, H-4), 8.32 (dd, *J* = 4.7, 1.5 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = –8.8 (q, CH_3), 59.0 (q, OCH_3), 67.9 (t, CH_2), 71.4 (t, CH_2), 73.4 (t, CH_2), 108.3 (s, C-3), 116.1 (d, C-5), 126.5 (s, C-3a), 129.7 (d, C-2), 134.1 (d, C-4), 142.8 (d, C-6), 150.0 (s, C-7a).

MS (EI): *m*/*z* (%) = 370 ($^{120}SnM^+$, 7), 368 ($^{118}SnM^+$, 4), 366 ($^{116}SnM^+$, 2), 355 (^{120}SnM-Me, 46), 353 (34), 351 (19), 131 (52).

HRMS: *m*/*z* calcd for $C_{14}H_{22}N_2O_2{}^{120}Sn$: 370,0703, found: 370, 0693.

1-(4-Methylphenylsulfonyl)-3-trimethylstannyl-7-azaindole (4d)
From **2d** (500 mg, 1.80 mmol) and Me_3SnCl (1.99 mmol); yield: 307 mg (50%); colourless oil.

IR (film): ν = 1389, 1375, 1175, 1152 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 0.38 (s, 9 H, 3 CH_3), 2.36 (s, 3 H, CH_3), 7.14 (dd, *J* = 7.8, 4.8 Hz, 1 H, H-5), 7.27 (d, *J* = 8.0 Hz, 2 H, H-3', 5'), 7.58 (s, 1 H, H-2), 7.77 (dd, *J* = 7.8, 1.4 Hz, 1 H, H-4), 8.10 (d, *J* = 8.0 Hz, 2 H, H-2', 6'), 8.41 (dd, *J* = 4.8, 1.4 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = –9.1 (q, CH_3), 21.5 (q, CH_3), 114.1 (s, C-3), 119.2 (d, C-5), 119.5 (s, C-3a), 128.6 (d, C-3', 5'), 129.2 (s, C-4'), 130.2 (d, C-2', 6'), 140.0 (d, C-2), 132.0 (d, C-4), 136.2 (s, C-1'), 145.0 (d, C-6), 145.6 (s, C-7a).

MS (EI): *m*/*z* (%) = 436 ($^{120}SnM^+$, 8), 435 (2), 434 ($^{118}SnM^+$, 6), 432 ($^{116}SnM^+$, 3), 421 (^{120}SnM – Me, 100), 420 (39), 419 (74), 391 (^{120}SnM – 3Me, 32), 390 (12), 389 (24).

HRMS: *m*/*z* calcd for $C_{17}H_{20}N_2O_2Si^{120}Sn$: 436.0267, found: 436.0279.

1-(4-Methyl-2-trimethylstannylphenylsulfonyl)-3-trimethylstannyl-7-azaindole (5)
From **2d** (100 mg, 0.36 mmol) and Me_3SnCl (0.76 mmol) following the general procedure **5** (147 mg, 85%) was obtained as a colourless oil.

IR (film): ν = 1380, 1360, 1175, 1152 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 0.38 (s, 9 H, 3 CH_3), 0.46 (s, 9 H, 3 CH_3), 2.36 (s, 3 H, CH_3), 7.10–7.30 (m, 2 H, H-5, 5'), 7.48 (s, 1 H, H-3'), 7.55 (s, 1 H, H-2), 7.76 (dd, *J* = 7.6, 1.4 Hz, 1 H, H-4), 8.30–8.44 (m, 2 H, H-6, 6').

^{13}C NMR ($CDCl_3$, 50 MHz): δ = –9.2 (q, CH_3), –5.9 (q, CH_3), 21.5 (q, CH_3), 118.5 (d, C-5), 128.9 (s, C-3a), 129.8 (d, C-6'), 129.7 (d, C-5'), 130.8 (d, C-2), 132.3 (d, C-4), 137.6 (d, C-3'), 141.6 (s, C-2'), 143.1 (s, C-4'), 143.4 (s, C-7a), 144.7 (d, C-6), 148.6 (s, C-1').

MS (EI): *m*/*z* (%) = 585 (^{120}SnM – Me, 22), 584 (15), 583 (28), 582 (19), 581 (25), 165 (100), 105 (54).

Anal. calcd for $C_{20}H_{28}N_2O_2SSn_2$ (597.8): C, 40.17; H, 4.72; N, 4.69; S, 5.36. Found C, 40.41; H, 4.87; N, 4.62; S, 5.09.

Coupling Reactions of Aryl Bromides with *N*-Protected 3-Trimethylstannyl-7-azaindoles 4; General Procedure
A solution of **4** (1 equiv), the appropriate aryl bromide (2 or 5 equiv), LiCl (3 equiv), and $(Ph_3P)_4Pd$ (0.2 equiv) in THF was refluxed for 48 h under argon. The mixture was diluted with Et_2O and the organic layer washed with brine. The organic layer was dried and evaporated to give the crude product which was purified by flash column chromatography on silica gel using mixtures of CH_2Cl_2 and MeOH as eluents. When the azaindole was protected with TBDMS, the reaction mixture was extracted with aq HCl (10%), the aqueous extract was basified with NaOH (50%) and extracted with CH_2Cl_2. The organic solution was dried and evaporated to give the crude product which was purified by column chromatography on silica gel.

3-(Pyridin-2-yl)-7-azaindole (6a)
From **4a** (100 mg, 0.25 mmol) and 2-bromopyridine (50 μL, 0.5 mmol). Reaction time 24 h; yield: 22 mg (45%); white solid; mp 180–181°C (CH_2Cl_2/MeOH).

IR (KBr): ν = 1592, 1583, 1534, 1459, 1416, 1278 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 7.14 (ddd, *J* = 6.6, 5.0, 1.4 Hz, 1 H, H-5'), 7.21 (dd, *J* = 7.8, 4.8, 1 H, H-5), 7.69–7.72 (m, 2 H, H-3', 4'), 7.95 (s, 1 H, H-2), 8.39 (dd, *J* = 4.8, 1.0 Hz, 1 H, H-4), 8.67 (d, *J* = 5.0 Hz, 1 H, H-6'), 8.75 (dd, *J* = 7.8, 1.0 Hz, 1 H, H-6), 11.8 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 115.6 (s, C-3), 116.0 (d, C-5), 118.6 (s, C-3a), 119.7 (d, C-5'), 120.4 (d, C-3'), 124.6 (d, C-2), 130.4 (d, C-4), 136.3 (d, C-4'), 142.8 (d, C-6), 148.6 (s, C-7a), 149.5 (d, C-6'), 154.5 (s, C-2').

MS (EI): *m*/*z* (%) = 195 (M^+, 100), 194 (M – H, 50), 167 (15).

HRMS: *m*/*z* calcd for $C_{12}H_9N_3$: 195.0780, found: 195.0806.

Anal. calcd for $C_{12}H_9N_3$ (195.2): C, 73.83; H, 4.65; N,21.53. Found C, 73.74; H, 4.52; N, 21.58.

1-Methoxyethoxymethyl-3-(pyridin-2-yl)-7-azaindole (6b)
From **4b** (200 mg, 0.54 mmol) and 2-bromopyridine (103 μL, 1.08 mmol). Reaction time 24 h; yield: 64 mg (45%); yellow oil.

IR (film): ν = 1591, 1543, 1438, 1429, 1092 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 3.34 (s, 3 H, OCH_3), 3.46–3.55 (m, 2 H, CH_2), 3.60–3.70 (m, 2 H, CH_2), 5.82 (s, 2 H, CH_2), 7.12 (ddd, *J* = 7.0, 5.0, 1.8 Hz, 1 H, H-5'), 7.21 (dd, *J* = 8.0, 4.8 Hz, 1 H, H-5), 7.65 (m, 2 H, H-3', 4'), 7.93 (s, 1 H, H-2), 8.38 (dd, *J* = 4.8, 1.6 Hz, 1 H, H-6), 8.65 (d, *J* = 5.0 Hz, 1 H, H-6'), 8.72 (dd, *J* = 8.0, 1.6 Hz, 1 H, H-4).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 59.7 (q, OCH_3), 68.8 (t, CH_2), 72.2 (t, CH_2), 74.5 (t, CH_2), 116.7 (s, C-3), 118.2 (d, C-5), 119.5 (s, C-3a), 120.6 (d, C-5'), 121.4 (d, C-3'), 127.6 (d, C-2), 131.0 (d, C-4), 137.0 (d, C-4'), 144.5 (d, C-6), 149.5 (s, C-7a), 150.3 (d, C-6'), 154.8 (s, C-2').

MS (EI): *m*/*z* (%) = 284 (M+1, 4), 283 (M^+, 21), 209 (40), 208 (M – OC_2H_4OMe, 68), 195 (M – MEM, 100).

HRMS: *m*/*z* calcd for $C_{16}H_{17}N_3O_2$: 283.1321, found: 283.1326.

1-(4-Methylphenylsulfonyl)-3-(pyridin-2-yl)-7-azaindole (6c)
From **4d** (100 mg, 0.23 mmol) and 2-bromopyridine (44 μL, 0.46 mmol). Reaction time 28 h; yield: 33 mg (42%); yellow solid; mp 117–118 °C (CH_2Cl_2).

IR (KBr): ν = 1605, 1395, 1360, 1175 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 2.36 (s, 3 H, CH_3), 7.20 (ddd, *J* = 7.5, 4.5, 1.5 Hz, 1 H, H-5'), 7.26 (dd, *J* = 8.0, 4.5 Hz, 1 H, H-5), 7.27 (d, *J* = 8.0 Hz, 2 H, H-3", 5"), 7.67 (dt, *J* = 7.5, 1.5 Hz, 1 H, H-3'), 7.74 (td, *J* = 7.5, 1.5 Hz, 1 H, H-4'), 8.11 (d, *J* = 8.0 Hz, 2 H, H-2", 6"), 8.22 (s, 1 H, H-2), 8.47 (dd, *J* = 4.5, 1.5 Hz, 1 H, H-6), 8.67 (dt, *J* = 4.5, 1.5 Hz, 1 H, H-6'), 8.72 (dd, *J* = 8.0, 1.5 Hz, 1 H, H-4).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.6 (q, CH_3), 119.3 (s, C-3a), 119.5 (d, C-5), 120.6 (d, C-3'), 121.2 (s, C-3), 121.9 (d, C-5'), 124.4 (d, C-2), 128.1 (d, C-3", 5"), 129.6 (d, C-2", 6"), 131.4 (d, C-4),

135.1 (s, C-4"), 136.6 (d, C-4'), 145.3 (d, C-6), 147.7 (s, C-7a), 149.6 (d, C-6'), 152.6 (s, C-2').

MS (EI): *m/z* (%) = 350 (M+1, 10), 349 (M^+, 40), 286 (29), 285 (100), 195 (25), 194 (M – Ts, 58), 167 (48).

HRMS: *m/z* calcd for $C_{19}H_{15}N_3O_2S$: 349.0885, found: 349.0874.

3-(Pyrimidin-5-yl)-7-azaindole (6d)
Method A: From **4a** (100 mg, 0.25 mmol) and 5-bromopyrimidine (200 mg, 1.25 mmol). Reaction time 48 h; yield: 36 mg (74%); white solid; mp 247–248 °C (CH_2Cl_2/MeOH).

IR (KBr): ν = 3036, 1581, 1428, 1296, 1277 cm^{-1}.

^1H NMR ($CDCl_3$+CD_3OD, 200 MHz): δ = 7.21 (dd, *J* = 7.6, 4.8 Hz, 1H, H-5), 7.65 (s, 1 H, H-2), 8.19 (d, *J* = 7.6 Hz, 1 H, H-4), 8.32 (d, *J* = 4.8 Hz, 1 H, H-6), 9.00 (s, 2 H, H-4', 6'), 9.08 (s, 1 H, H-2').

^{13}C NMR ($CDCl_3$+CD_3OD, 50 MHz): δ = 108.9 (s, C-3), 117.4 (d, C-5), 119.0 (s, C-3a), 124.9 (d, C-2), 129.2 (d, C-4), 130.1 (s, C-5'), 143.5 (d, C-6), 148.5 (s, C-7a), 154.9 (d, C-4', 6'), 156.3 (d, C-2').

MS (EI): *m/z* (%) = 197 (M+1, 14), 196 (M^+, 100), 195 (M – H, 18), 142 (M – $C_2H_2N_2$, 40).

HRMS: *m/z* calcd for $C_{11}H_8N_4$: 196.0749, found: 196.0744.

Anal. calcd for $C_{11}H_8N_4$•1/8H_2O (198.5): C, 66.57; H, 4.19; N, 28.23. Found C, 66.61; H, 4.13; N, 28.14.

Method B: A solution of **6l** in 10% methanolic NaOH (10 mL) was stirred at r.t. for 2 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 and washed with brine. The organic solution was dried and evaporated to give a crude product which was purified by column chromatography on silica gel. Elution with CH_2Cl_2/MeOH 95:5 gave **6d** (20 mg, 63%).

1-Methoxyethoxymethyl-3-(pyrimidin-5-yl)-7-azaindole (6e)
From **4b** (100 mg, 0.27 mmol) and 5-bromopyrimidine (87 mg, 0.54 mmol). Reaction time 20 h. Compound **6e** (37 mg, 50%) was obtained as a yellow gum.

IR (KBr): ν = 1530, 1425, 1099, 1072 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 3.36 (s, 3 H, OCH_3), 3.42–3.55 (m, 2 H, CH_2), 3.62–3.75 (m, 2 H, CH_2), 5.84 (s, 2 H, CH_2), 7.24 (dd, *J* = 8.0, 4.8 Hz, 1 H, H-5), 7.71 (s, 1 H, H-2), 8.16 (dd, *J* = 8.0, 1.4 Hz, 1 H, H-4), 8.44 (dd, *J* = 4.8, 1.4 Hz, 1 H, H-6), 9.03 (s, 2 H, H-4', 6'), 9.16 (s, 1 H, H-2').

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 59.0 (q, OCH_3), 68.4 (t, CH_2), 71.5 (t, CH_2), 73.9 (t, CH_2), 109.8 (s, C-3), 117.6 (d, C-5), 118.1 (s, C-3a), 125.8 (d, C-2), 127.7 (d, C-4), 128.9 (s, C-5'), 144.5 (d, C-6), 148.6 (s, C-7a), 154.4 (d, C-4', 6'), 156.5 (d, C-2').

MS (EI): *m/z* (%) = 285 (M+1, 5), 284 (M^+, 26), 210 (37), 209 (M – OC_2H_4OMe, 72), 197 (13), 196 (M – MEM, 100).

HRMS: *m/z* calcd for $C_{15}H_{16}N_4O_2$: 284.1273, found: 284.1273.

1-(4-Methylphenylsulfonyl)-3-(5-pyrimidin-5-yl)-7-azaindole (6f)
From **4d** (100 mg, 0.23 mmol) and 5-bromopyrimidine (73 mg, 0.46 mmol). Reaction time 29 h; yield: 48 mg (60%); white solid mp 185–186 °C (CH_2Cl_2).

IR (KBr): ν = 1377, 1189, 1006 cm^{-1}.

^1H NMR ($CDCl_3$,200 MHz): δ = 2.39 (s, 3 H, CH_3), 7.20–7.38 (m, 3 H, H-5, 3", 5"), 8.02 (s, 1 H, H-2), 8.04 (dd, *J* = 7.8, 1.2 Hz, 1 H, H-4), 8.15 (d, *J* = 8.4 Hz, 2 H, H-2", 6"), 8.53 (dd, *J* = 4.8, 1.2 Hz, 1 H, H-6), 9.99 (s, 2 H, H-4', 6'), 9.22 (s, 1 H, H-2').

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.4 (q, CH_3), 113.6 (s, C-3), 120.2 (d, C-5), 121.1 (s, C-3a), 124.4 (d, C-2), 128.0 (s, C-5'), 128.9 (d, C-4), 129.0 (d, C-3", 5"), 130.5 (d, C-2", 6"), 135.1 (s, C-4"), 146.4 (s, C-1"), 146.6 (d, C-6), 148.0 (s, C-7a), 155.6 (d, C-4', 6'), 158.2 (d, C-2').

MS (EI): *m/z* (%) = 351 (M+1, 1), 350 (M^+, 8), 287 (6), 286 (33), 196 (10), 195 (M – Ts, 11), 142 (10), 141 (24), 91 (100).

HRMS: *m/z* calcd for $C_{18}H_{14}N_4O_2S$: 350.0837, found: 350.0832.

Anal. calcd for $C_{18}H_{14}N_4O_2S$ (350.3): C, 61.69; H, 4.03; N, 15.99. Found C, 61.58; H, 3.98; N, 15.67.

3-(4-Methoxyphenyl)-7-azaindole (6g)
From **4a** (200 mg, 0.50 mmol) and 4-bromoanisole (126 μL, 1.01 mmol). Reaction time 32 h; yield: 42 mg (38%); white solid; mp 215–217 °C (CH_2Cl_2/MeOH).

IR (KBr): ν = 3128, 1537, 1242 cm^{-1}.

^1H NMR ($CDCl_3$+CD_3OD, 300 MHz): δ = 3.87 (s, 3 H, OCH_3), 7.01 (d, *J* = 8.8 Hz, 2 H, H-3', 5'), 7.18 (dd, *J* = 7.9, 4.9 Hz, 1 H, H-5), 7.48 (s, 1 H, H-2), 7.56 (d, *J* = 8.8 Hz, 2 H, H-2', 6'), 8.22–8.32 (m, 2 H, H-4, 6).

^{13}C NMR (DMSO-d_6, 75 MHz): δ = 55.3 (q, OCH_3), 114.5 (s, C-3), 114.6 (d, C-3', 5'), 116.0 (d, C-5), 117.9 (s, C-3a), 123.2 (d, C-2), 127.6 (s, C-1'), 127.7 (d, C-2', 6'), 128.1 (d, C-4), 142.4 (d, C-6), 148.5 (s, C-7a), 157.8 (s, C-4').

MS (EI): *m/z* (%) = 225 (M+1, 14), 224(M^+, 88), 209 (M – Me, 100), 181 (44).

HRMS: *m/z* calcd for $C_{14}H_{22}N_2O$: 224.0949, found: 224.0949

3-(4-Nitrophenyl)-7-azaindole (6h)
From **4a** (100 mg, 0.25 mmol) and 4-bromonitrobenzene (102 mg, 0.50 mmol). Reaction time 24 h; yield: 30 mg (50%); yellow solid; mp 258–259 °C (CH_2Cl_2/MeOH).

IR (KBr): ν = 3500, 1591, 1508, 1332, 1284 cm^{-1}.

^1H NMR (DMSO-d_6, 200 MHz): δ = 7.23 (dd, *J* = 7.8, 4.8, 1 H, H-5), 7.56 (s, 1 H, H-2), 8.04 (d, *J* = 8.6 Hz, 2 H, H-2', 6'), 8.26 (d, *J* = 8.6 Hz, 2 H, H-3', 5'), 8.32 (d, *J* = 4.8 Hz, 1 H, H-6), 8.42 (d, *J* = 7.8 Hz, 1 H, H-4), 12.35 (br s, 1 H, NH).

^{13}C NMR (DMSO-d_6, 50 MHz): δ = 112.5 (s, C-3), 115.7 (s, C-3a), 117.0 (d, C-5), 124,6 (d, C-2', 6'), 126.4 (d, C-3', 5'), 127.2 (d, C-2), 128.1 (d, C-4), 142.7 (s, C-7a), 143.8 (d, C-6), 144.8 (s, C-1'), 149.6 (s, C-4').

MS (EI): *m/z* (%) = 240 (M+1, 16), 239 (M^+, 100), 209 (M – NO, 51), 193 (M – NO_2, 38), 166 (M – NO_2 – CH_2N, 40).

HRMS: *m/z* calcd for $C_{13}H_9N_3O_2$: 239.0695, found: 239.0693.

Anal. Calcd for $C_{13}H_9N_3O_2$.1/3 H_2O(245.7): C, 63.67, H, 3.97; N, 17.13. Found C, 63.64; H, 3.72; N, 17.20.

3-(Thien-3-yl)-7-azaindole (6i)
From **4a** (200 mg, 0.50 mmol) and 3-bromothiophene (240 μL, 2.57 mmol). Reaction time 48 h; yield: 57 mg (57%); white solid; mp 165 °C (CH_2Cl_2).

IR (KBr): ν = 3142, 1562, 1409, 1288 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 7.23 (dd, *J* = 7.8, 4.8 Hz, 1 H, H-5), 7.56 (d, *J* = 1.2 Hz, 1 H, H-2'), 7.59 (d, *J* = 2.7 Hz, 1 H, H-5'), 7.73 (dd, *J* = 2.7, 1.2 Hz, 1 H, H-4'), 7.87 (br s, 1 H, H-2), 8.25 (dd, *J* = 4.8, 1.4 Hz, 1 H, H-6), 8.32 (d, *J* = 7.8, 1.4 Hz, 1 H, H-4), 11.80 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$+CD_3OD, 75MHz): δ = 110.6 (s, C-3), 116.3 (d, C-5), 117.6 (s, C-3a), 118.1 (d, C-4'), 124.1 (d, C-2), 126.5 (d, C-5'), 127.0 (d, C-2'), 128.1 (d, C-4), 135.9 (s, C-3'), 143.3 (d, C-6), 149.2 (s, C-7a).

MS (EI): *m/z* (%) = 201 (M+1, 14), 200 (M^+, 100), 173 (15), 155 (16).

Anal. Calcd for $C_{11}H_8N_2S$ (200.2): C, 65.97; H, 4.03; N, 13.99; S, 16.01. Found C, 65.70; H, 4.00; N, 13.91 S, 15.90.

3-(2-Methylthiopyrimidin-4-yl)-7-azaindole (6j)
From **4a** (100 mg, 0.25 mmol) and 4-chloro-2-methylthiopyrimidine[13] (203 mg, 1.26 mmol). Reaction time 48 h; yield: 37 mg (60%); mp: 217–218 °C (CH_2Cl_2/MeOH).

IR (KBr): ν = 1570, 1406, 1339 cm^{-1}.

^1H NMR (DMSO-d_6, 300 MHz): δ = 2.60 (s, 3 H, SCH_3), 7.24 (dd, *J* = 8.0, 4.4, 1 H, H-5), 7.63 (d, *J* = 5.2, 1 H, H-5'), 8.32 (d, *J* = 4.4, 1 H, H-6), 8.46 (d, *J* = 5.2, 1 H, H-6'), 8.56 (s, 1 H, H-2), 8.75 (d, *J* = 8.0, 1 H, H-4), 12.2 (br s, 1 H, NH).

^{13}C NMR (DMSO-d_6, 75 MHz): δ = 13.7 (q, SCH_3), 111.2 (d, C-5), 111.5 (s, C-3), 117.3 (d, C-2), 117.5 (s, C-3a), 130.1 (d, C-5'), 130.2 (d, C-4), 143.8 (d, C-6), 149.3 (s, C-7a), 156.5 (d, C-6'), 161.6 (s, C-4'), 171.2 (s, C-2').

MS (EI): *m*/*z* (%) = 243 (6), 242 (M^+, 84), 196 (26), 195 (M – MeS, 67).

HRMS: *m*/*z* calcd for $C_{12}H_{10}N_4S$: 242.0626, found: 242.0631.

3-(2-Methylthiopyrimidin-5-yl)-7-azaindole (6k)
From **4a** (50 mg, 0.12 mmol) and 5-bromo-2-methylthiopyrimidine[14] (52 mg, 0.24 mmol). Reaction time 32 h; yield: 16 mg (53%); white solid; mp 212–213 °C (CH_2Cl_2/MeOH).

IR (KBr): ν = 3120, 1530, 1460, 1424, 1408, 1299 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 2.64 (s, 3 H, SCH_3), 7.13 (dd, *J* = 7.8, 4.6 Hz, 1 H, H-5), 7.51 (s, 1 H, H-2), 8.06 (d, *J* = 7.8 Hz, 1 H, H-4), 8.21 (d, *J* = 4.6 Hz, 1 H, H-6), 8.71 (s, 2 H, H-4', 6'), 10.8 (br, 1 H, NH).

^{13}C NMR ($CDCl_3$+CD_3OD, 50 MHz): 13.8 (q, SCH_3), 108.3 (s, C-3), 116.5 (d, C-5), 118.1 (s, C-3a), 123.2 (d, C-2), 124.2 (s, C-5'), 127.9 (d, C-4), 143.0 (d, C-6), 148.0 (s, C-7a), 154.6 (d, C-4', 6'), 170.0 (s, C-2').

MS (EI): *m*/*z* (%) = 243 (M+1, 16), 242 (M^+, 100), 241 (M – H, 10), 209 (72), 195 (M – MeS, 20), 170 (27), 142 (41), 115 (34).

HRMS: *m*/*z* calcd for $C_{12}H_{10}N_4S$: 242.0626, found 242.0626.

3-(5-Pyrimidin-5-yl)-1-(2-trimethylstannyl-4-methylphenylsulfonyl)-7-azaindole (6l)
From **5** (270 mg, 0.45 mmol) and 5-bromopyrimidine (287 mg, 1.80 mmol). Reaction time 24 h; yield: 145 mg (62%); white solid; mp 141–142 °C (CH_2Cl_2).

IR (KBr): ν = 1414, 1399, 1187, 1006 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): 0.49 (s, 9 H, 3 CH_3), 2.39 (s, 3 H, CH_3), 7.25 (br d, *J* = 8.5 Hz, 1 H, H-5"), 7.30 (dd, *J* = 8.0, 4.5 Hz, 1 H, H-5), 7. 52 (br s, 1 H, H-3"), 7.99 (s, 1 H, H-2), 8.06 (dd, *J* = 8.0, 1.5 Hz, 1 H, H-4), 8.34 (d, *J* = 8.5 Hz, 1 H, H-6"), 8.50 (dd, *J* = 4.5, 1.5 Hz, 1 H, H-6), 9.02 (s, 2 H, H-4', 6'), 9.24 (s, 1 H, H-2').

^{13}C NMR ($CDCl_3$, 50 MHz): δ = –5.98 (q, CH_3), 21.6 (q, CH_3), 112.3 (s, C-3), 119.4 (d, C-5), 120.3 (s, C-3a), 123.9 (d, C-2), 127.3 (s, C-5'), 128.0 (d, C-4), 129.4 (d, C-6"), 129.8 (d, C-5"), 137.7 (d, C-3"), 140.7 (s, C-4"), 143.7 (s, C-2"), 144.1 (s, C-7a), 145.6 (d, C-6), 147.3 (s, C-1"), 154.8 (d, C-4', 6'), 157.4 (d, C-2').

MS (EI): *m*/*z* (%) = 499 (^{120}SnM – Me, 44), 498 (19), 497 (33), 435 (9), 434 (3), 433 (7), 405 (26), 404 (11), 403 (21), 196 (M – Ts, 35), 141 (79), 105 (100).

HRMS: *m*/*z* calc. for $C_{20}H_{19}N_4O_2Si^{120}Sn$ (M^+ – Me): 499.0251, found: 499.0241.

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