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A regioselective double Stille coupling reaction of bicyclic stannolanes†

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A regioselective double Stille coupling reaction was explored using bicyclic stannolanes that were easily prepared from the radical cascade reaction of β-amino-α-methylene esters. Various 1-bromo-2-iodoarenes underwent the double coupling reaction to afford benzoisoindole derivatives in a regioselective manner, where the carbon attached to the iodine selectively coupled with the vinylic carbon, and then the carbon attached to bromine coupled with the alkyl carbon. The combination of intra- and intermolecular coupling reactions provided hexahydroindeno[1,2-*b*]pyrrole derivatives in good yields. The yields were further improved in the presence of excess amounts of CsF. An attempt to identify the reaction intermediate was made wherein the decomposition of the stannolanes with aqueous HCl and HBr afforded trigonal bipyramidal (TBP) pentacoordinated tin complexes, as confirmed by microanalyses and ^{119}Sn NMR. Using DCl for the decomposition selectively introduced a deuterium to the *E*-position of the exomethylene unit. The complexes smoothly underwent the intramolecular Stille coupling reaction in the presence of both a palladium catalyst and DABCO, affording hexahydroindeno[1,2-*b*]pyrroles in good yields. These results suggest that the double coupling reaction progresses through a TBP tin complex, promoting the second intramolecular coupling reaction between the aryl halide and Csp^3–tin bond.

Introduction

Palladium-catalysed coupling is a key reaction in organic synthesis.[1] Organotin compounds are frequently used as a coupling partner in the Migita–Kosugi–Stille coupling reaction.[2,3] Vinylic and aromatic groups on tin compounds are frequently employed as a coupling partner, whereas alkyl groups on tin compounds are usually inert and rarely used in the reaction unless an activating unit is present on the tin compound.[4] When two or more carbon–tin bonds exist in one organotin compound, these compounds may be used in a one-pot multi-coupling reaction, which is recognized as a useful domino method in organic synthesis.[5] For example, this is a useful strategy for preparing polycyclic aromatic hydrocarbons (PAHs), which are the compounds of interest in the development of organoelectronic devices.[6] However, this double coupling strategy is limited to the coupling between Csp^2–Csp^2 type species, and there are only rare reports on the double coupling between Csp^2–Csp^3 species.[7] Thus, the quantitative difference between the reactivities of the sp^2 carbon–tin bond and the ordinary sp^3 carbon–tin bond in this double coupling reaction remains unclear.

Recently, we developed a one-step synthesis of a bicyclic stannolane through a highly cumulated cascade radical reaction wherein a radical addition–cyclization–substitution occurred in one pot.[8] This process prompted us to sequentially develop a new type of double coupling reaction.[9] In this study, we report the details of a regioselective double coupling reaction of stannolanes. We also explored the substrate scope of aryl halides and pseudohalides. With our methodology, multicyclic benzoisoindoles[10] and hexahydroindeno[1,2-*b*]pyrroles[11] are readily prepared in a few steps from simple compounds. These structures are known to feature in biologically active compounds.[12,13] The identity of the intermediate in the double coupling reaction was explored through acidic hydrolysis of the stannolanes to afford pentacoordinated trigonal bipyramidal (TBP) tin complexes.

Results and discussion

Double Stille coupling reaction with various 1,2-substituted benzenes

We first examined various 1,2-disubstituted benzenes for the double coupling reaction with stannolane **1a**. The results are summarized in Table 1.

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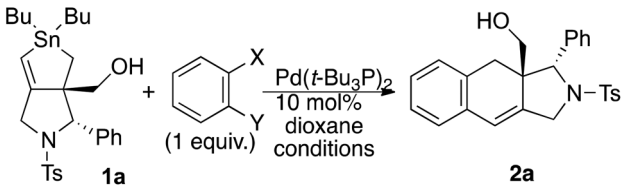
†Electronic supplementary information (ESI) available: NMR for compounds **2**, **4**, **5**, **6**, and **7**, and an ORTEP chart for **6e**. CCDC 845991. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6ob01018k

Table 1 Double coupling reaction of **1a** with various 1,2-disubstituted benzenes

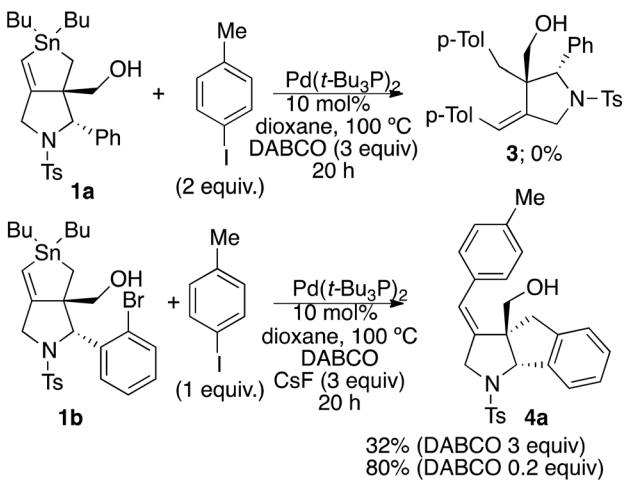


Entry	X	Y	Additives[a]	Time (h)	Temp. (°C)	**2a**; yield[b] (%)
1	Cl	Cl	DABCO (3)	20	100	0
2	OTf	OTf	DABCO (3), LiCl (2.3)	24	100	18
3	OTf	OTf	DABCO (3), CuI (2)	24	80	21
4	Br	Br	DABCO (3)	20	100	76
5	Br	I	DABCO (3), CsF (5)	24	100	44
6	I	I	DABCO (0.2), CsF (3)	24	100	79

[a] Equivalents in parentheses. [b] Isolated yield.

The use of dichlorobenzene did not give any double coupling product **2a** (entry 1).[14] Ditriflate underwent a slow and sluggish reaction to give **2a** in only 18% yield. The yield of **2a** was improved to 21% when CuI was used as an additive (entry 3).[15] Dibromobenzene gave the coupling product **2a** in 76% yield (entry 4) and iodobromobenzene also afforded **2a** in 44% yield (entry 5). Diiodobenzene underwent a smooth double coupling reaction to give **2a** in 79% yield (entry 6). The addition of CsF was necessary to obtain **2a** in good yield. Thus, iodoarenes and bromoarenes are the best candidates for the double coupling reaction.

To investigate the reactivity of the sp^2 and sp^3 carbon–tin bonds, we attempted to introduce two different aromatic groups to **1a** using two equivalents of iodobenzene (Scheme 1). However, we could not obtain **3** under these conditions. This is in contrast to the result that the double coupling product **4a** was obtained in 32% yield when **1b** was used as the coupling partner. These results clearly indicate that the sp^3 carbon–tin bond is less reactive and produces no coupling product with any intermolecular coupling partner. The yield of **4a** was improved to 80% when three equivalents of CsF were used in the reaction. With this improvement, the amount of DABCO might be reduced to 20 mol%. Thus, the presence of the fluoride anion is effective in promoting the intramolecular coupling reaction with the sp^2 carbon–tin bond as well as the sp^3 carbon–tin bond.[16]



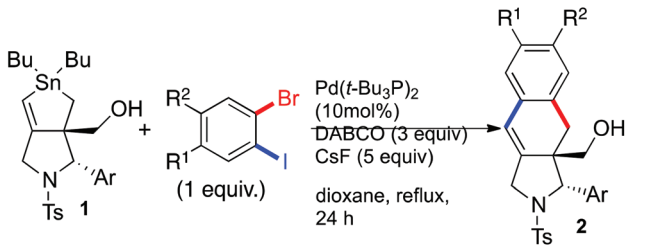
Scheme 1 Inter- and intramolecular double coupling reactions.

Intermolecular and inter- and intramolecular regioselective double coupling reactions

We next examined various iodobromobenzenes for the coupling reaction with stannolane **1**. The results are summarized in Table 2.

The double coupling reaction progressed smoothly and products **2** were isolated in moderate to good yields. For example, 1-bromo-4-chloro-2-iodobenzene underwent the double coupling reaction to give **2b** in 68% yield (entry 1), whereas the double coupling of **1a** with 2-bromo-4-chloro-1-iodobenzene afforded its regioisomer **2c** in 38% yield (entry 2). The regioselectivity was estimated by ^{1}H NMR integration to be 94/6 in the formation of **2b** and 95/5 in the formation of **2c**. Other double couplings with various substituted iodobromobenzenes provided the regioselective formation of benzoisoindole **2**. The selectivity ranged from 83/17 to 99/1 and nearly complete regioselective double coupling was achieved. The major and minor isomers formed in the reaction shown in entry 7, **2h** and **2g**, were inseparable by usual chromatographic methods. The regioselectivity was determined by the first coupling between haloarenes and the sp^2-carbon–tin bond site. We expected that the aryl carbon-iodine bond would react faster than the aryl carbon-bromine bond. When the substituent of the dihaloarene is located at the *m*-position to the aryl–iodine bond site, high regioselectivity (>95/5) was achieved (entries 1, 3, 4, 6, 8, and 10). Conversely, a substituent at the *p*-position to the aryl–iodine bond affected the selectivity very much. For example, the presence of an electron-withdrawing group such as a nitro or a trifluoromethyl group at the *para* position to the carbon–iodine bond caused the regioselectivity to slightly

Table 2 Regioselective double coupling reaction of **1** with iodobenzenes



Entry	1	Ar	R^1	R^2	2; yield[a] (%)	Regioisomeric ratio[b]
1	**1a**	Ph	Cl	H	**2b**; 68	94/6
2	**1a**	Ph	H	Cl	**2c**; 38	95/5
3	**1a**	Ph	Me	H	**2d**; 53	95/5
4	**1a**	Ph	MeO	H	**2e**; 44	>99/1
5	**1a**	Ph	H	OMe	**2f**; 51	>99/1
6	**1a**	Ph	NO_2	H	**2g**; 63	94/6
7	**1a**	Ph	H	NO_2	**2h**; 38	83/17
8	**1a**	Ph	CF_3	H	**2i**; 58	96/4
9	**1a**	Ph	H	CF_3	**2j**; 54	90/10
10	**1c**	2-MeC_6H_4	Me	H	**2k**; 50	95/5
11	**1d**	3-$MeOC_6H_4$	H	NO_2	**2l**; 55	84/16
12	**1c**	2-MeC_6H_4	H	CF_3	**2m**; 19	98/2
13	**1c**	2-MeC_6H_4	Cl	H	**2n**; 28	87/13
14	**1c**	2-MeC_6H_4	H	F	**2o**; 35	94/6
15	**1d**	3-$MeOC_6H_4$	H	Cl	**2p**; 26	80/20

[a] Isolated yield. [b] Determined by integration of ^{1}H NMR spectra.

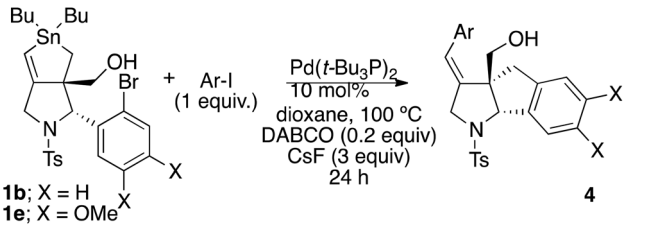
decrease to 90/10 or 83/17 (entries 7, 9 and 11), whereas an electron-donating substituent at this position maintained high regioselectivity (entry 5). Thus, the regioselectivity is partially affected by the electronic effect of the substituents on the dihaloarenes.

The number of synthetic methods to prepare the multi-substituted benzoisoindole **2** was limited because it is usually difficult to control the position of substituents during the synthesis of such heterocyclic compounds. However, in the present synthesis, the starting materials **1** were prepared in an optically pure form from simple Michael/Mannich reactions followed by a radical cascade reaction. Thus, this methodology provides a new convenient preparation of benzoisoindoles in a few steps in a highly regioselective manner.

The inter- and intramolecular double coupling reactions of **1b** and **1e** were examined using various iodobenzenes. The results are summarized in Table 3.

The inter- and intramolecular double coupling reactions progressed smoothly in the presence of iodobenzene and 10 mol% of $Pd(PtBu_3)_2$, affording hexahydroindeno[1,2-*b*]-pyrroles **4** in good yields. For example, 4-methoxyiodobenzene underwent the coupling reaction at the vinylic carbon–tin bond site, giving a double coupling product **4b** in 68% yield (entry 1). Various substituted iodobenzenes smoothly reacted to give compound **4**, except for 4-nitroiodobenzene, which gave a complex mixture (entry 4). Note that all aryl groups derived from iodobenzene were selectively introduced to the *E*-position of the alkylidene group. Thus, the intermolecular

Table 3 Inter- and intramolecular double coupling reactions of **1b** and **1e**



Entry	1	X	Ar	4; yield[a] (%)
1	**1b**	H	4-$MeOC_6H_4$	**4b**; 68
2	**1b**	H	3-$MeOC_6H_4$	**4c**; 83
3	**1b**	H	2-Me-4,5-$(MeO)_2C_6H_2$	**4d**; 74
4	**1b**	H	4-$O_2NC_6H_4$	**4e**; 0
5	**1e**	OMe	4-MeC_6H_4	**4f**; 56
6	**1e**	OMe	4-$MeOC_6H_4$	**4g**; 75
7	**1e**	OMe	3-$MeOC_6H_4$	**4h**; 74
8	**1e**	OMe	2-Me-4,5-$(MeO)_2C_6H_2$	**4i**; 74
9	**1e**	OMe	Ph	**4j**; 74

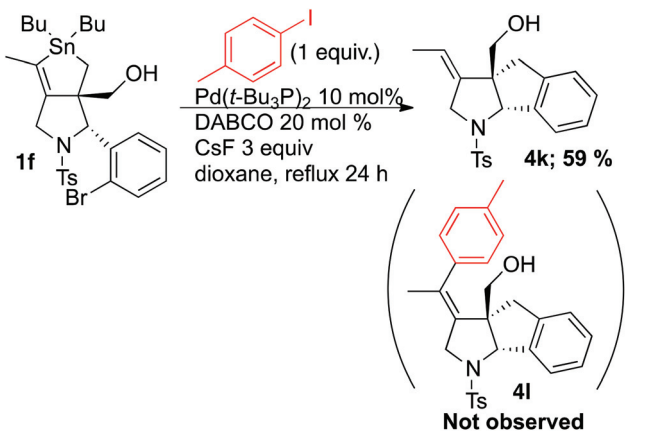
[a] Isolated yield.

coupling progressed selectively with the retention of the vinylic tin unit configuration. Dimethoxy-substituted stannolane **1e** also acted as a good double coupling donor to afford compound **4** in good yield (entries 5–9).

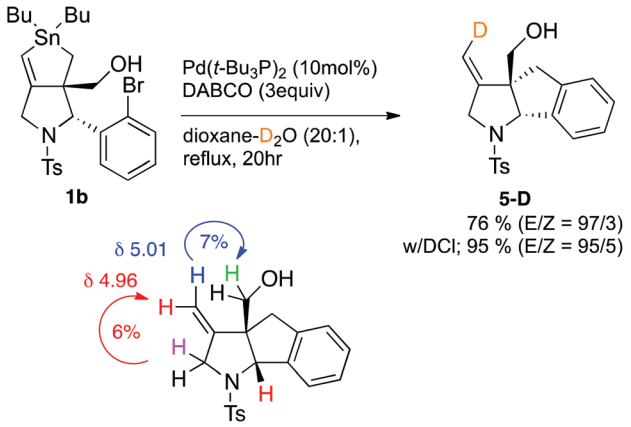
We explored this strategy for the synthesis of tetrasubstituted alkenes from **1f**; however, we only obtained compound **4k** in 59% yield, and not the desired compound **4l** that was expected. This is probably because of the steric hindrance caused by the methyl group at the vinylic position, which prevents the Stille coupling reaction with iodotoluene (Scheme 2).

Attempt to identify the reaction intermediate

We performed several experiments to identify the reaction intermediate. As we previously reported,[9] compound **1b** gave exomethylene hexahydroindeno[1,2-*b*]pyrrole **5** when treated in the absence of aryl halide (Scheme 3). Thus, the vinylic tin unit was replaced by hydrogen during the reaction. To identify the origin of the hydrogen, we performed the reaction with dry



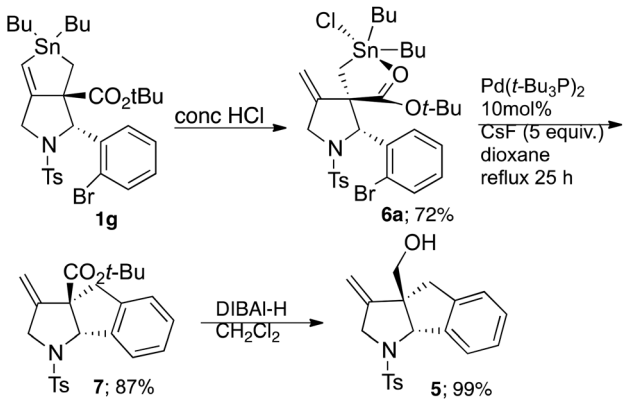
Scheme 2 Double coupling reaction of **1f**.



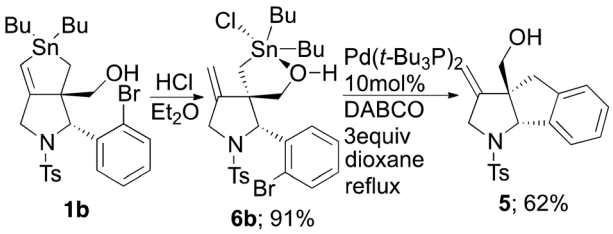
Scheme 3 Introduction of deuterium and elucidation of stereochemistry of **5**.

dioxane containing small amounts of D_2O (20 : 1). As expected, compound **5-D** instead of **5** was isolated in 76% yield. Note that the deuterium atom was selectively installed at the *E*-position of the exomethylene unit with 93/7 selectivity. The D position in the alkene unit of **5D** was determined by NOE experiments wherein 6% and 7% NOE enhancements were observed when the TsN-CH_2 protons at δ = 5.01 and CH_2OH protons at δ = 5.96 were irradiated, respectively. We concluded that the water in dioxane is the origin of the hydrogen atom introduced to the vinyl tin unit in the substitution reaction. Note that the yield of **5-D** was greatly improved to 95% without any change in the *E*/*Z* selectivity or D content when the reaction was performed in the presence of DCl.

We then attempted to identify the reaction intermediate of the double coupling reaction. The exposure of stannolane **1g** to concentrated HCl resulted in the formation of a penta-coordinated trigonal bipyramidal (TBP) tin complex **6a** in 72% yield (Scheme 4).[8a,17] We exposed the TBP complex **6a** to the standard coupling reaction conditions in the presence of five equivalents of CsF, affording the intermolecular coupling product **7** in 87% yield. To confirm the structure of **7**,



Scheme 4 Intramolecular coupling reaction through the TBP complex of **1g**.

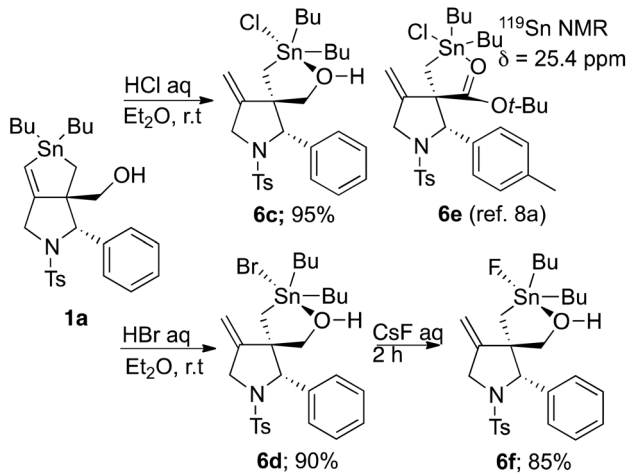


Scheme 5 Intramolecular coupling reaction through the TBP complex of **1b**.

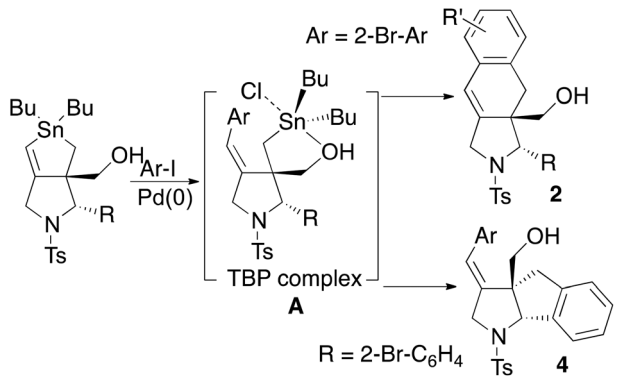
reduction was performed in the presence of DIBAL-H to give compound **5** in almost quantitative yield. Note that the intramolecular coupling progressed only when CsF was employed in the reaction.

The acidic treatment of **1b** also yielded the corresponding TBP complex **6b** in 91% yield (Scheme 5). This is supported by the fact that a signal for the OH proton in **6b** was observed in the ^{1}H NMR at δ 2.84 (dd, J = 7.9, 3.8 Hz). Microanalysis data indicated that a chlorine atom is contained in **6b**. Compound **6b** afforded the intramolecular coupling product **5** in 62% yield by treatment with the catalytic amounts of Pd(tBu$_3$P)$_3$ in the presence of DABCO. We believe that the coordination of an oxygen atom to the tin atom promoted the coupling reaction of the alkyl tin unit; however, some basic additive, such as CsF, is necessary to achieve an efficient reaction.[9]

To obtain further information on the TBP complex, we performed simple acidic decomposition of **1a** and analysed the products using NMR and microanalytical studies (Scheme 6). Treatment of **1a** with HCl and HBr gave the corresponding products **6c** and **6d**, respectively, in good yields. There are several observations that should be noted for these compounds. Again, the OH proton signal was observed in the ^{1}H NMR spectra for these compounds. Microanalyses of these compounds indicated that compounds **6c** and **6d** included a halogen atom. Furthermore, the ^{119}Sn NMR signals of **6c** and



Scheme 6 Conversion to TBP complexes of **1a**.



Scheme 7 Plausible reaction mechanism.

6d in $CDCl_3$ appeared at 33.3 and 28.8 ppm, respectively, which are highly up-field shifted compared with those of trialkylchlorotin compounds, such as Bu_3SnCl (152.8 ppm in $CDCl_3$),[18] but close to the chemical shift of TBP tin complex **6e**, which shows a ^{119}Sn NMR peak at 25.4 ppm.[8a] These results clearly suggested that the hydroxyl groups in compounds **6c** and **6d** coordinate to the tin atom to form a penta-coordinated tin complex, such as **6e**. Unfortunately we have not obtained any crystalline form of compounds **6b** to **6d** to date, and no further evidence for the complex is available. Note that the bromine atom in compound **6d** was replaced by a chlorine or a fluorine atom by treatment with aqueous NaCl or CsF solution. For example, compound **6f** was obtained in 85% yield by the simple stirring of a biphasic mixture of **6d** in ether and aqueous CsF. We examined the intermolecular Stille coupling reaction of compound **6f** with an excess of bromobenzene (10 equiv.). However, a complex mixture was obtained, and no expected products were observed.

Considering these results, we suggest that the reaction mechanism is as follows (Scheme 7): aryliodide reacts with the vinylic carbon–tin bond to afford arylalkene intermediate **A**, a TBP complex in which the hydroxy group coordinates to a tin atom.[16] The aryl group is selectively introduced at the *E*-position of the exomethylene unit. This intermediate is sufficiently reactive toward the intramolecular reaction by activation in the presence of CsF or DABCO to give the double coupling adduct **2** from bromoiodoarenes or **4** from *o*-bromoaryl-substituted precursor **1**. Conversely, in the intermolecular reaction, intermediate **A** is less reactive and does not give any intermolecular adduct.

Conclusions

We have successfully developed a regioselective double Stille coupling reaction with stannolanes. 1,2-Bromoiodoarene served as a good partner for the double coupling reaction. When a bromoarene was installed in a suitable position on the stannolanes, an inter- and intramolecular double coupling reaction smoothly occurred. Since the stannolanes are readily obtained in good yields from simple aza-1,6-enynes, this methodology provides a facile preparation of heterocyclic compounds such as benzoisoindoles and hexahydroindeno[1,2-*b*]pyrroles.

Experimental

General

All ^1H and ^{13}C NMR spectra were recorded on a JEOL lamda-500 or JNM-ECA 500 Delta2 (500 MHz for ^1H and 126 MHz for ^{13}C) spectrometer. Palladium complexes were purchased from Aldrich. Stannolanes **1** were prepared by using the previously reported method.[8a] All the reactions in this paper were performed under a nitrogen atmosphere unless otherwise mentioned. High resolution mass spectra (HRMS) were recorded on a JEOL JMS T-100LP LC-ESI mass spectrometer.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2a, Table 1, entry 4). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.015 g, 0.030 mmol), DABCO (0.096 g, 0.86 mmol) and 1,2-dibromobenzene (0.067 g, 0.28 mmol) were added to a solution of **1a** (0.168 g, 0.286 mmol) in 1,4-dioxane (2.0 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2a** in 76% yield as viscous oil (0.094 g, 0.22 mmol).

$[\alpha]_D$ +33.6 (*c* 1.83, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 8.3 Hz, 2H), 7.18 (d, J = 4.2 Hz, 3H), 7.14 (d, J = 8.1 Hz, 2H), 7.07 (t, J = 7.4 Hz, 1H), 7.11–6.98 (m, 2H), 7.01 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 6.4 Hz, 1H), 6.94 (d, J = 6.1 Hz, 1H), 6.43 (s, 1H), 5.29 (s, 1H), 4.42 (dd, J = 15.1, 2.3 Hz, 1H), 4.33 (dd, J = 15.1, 1.3 Hz, 1H), 3.4–3.6 (br, 1H), 3.26 (d, J = 10.7 Hz, 1H), 3.10 (d, J = 10.7 Hz, 1H), 2.58 (d, J = 16.1 Hz, 1H), 2.35 (s, 3H), 2.08 (d, J = 16.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 139.9, 139.3, 135.7, 133.2, 132.3, 129.5 (2C), 128.8, 128.5 (2C), 127.5, 127.4, 127.3 (2C), 126.8 (2C), 126.22, 126.21, 122.3, 69.1, 62.0, 53.0, 51.1, 31.8, 21.6; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{25}NNaO_3S$ 454.1453, found 454.1447.

Preparation of (3*S*,3a*R*)-7-chloro-3a-hydroxymethyl-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2b). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0114 g, 0.0223 mmol), DABCO (0.0750 g, 0.669 mmol), CsF (0.1018 g, 1.5 mmol), and 1-bromo-4-chloro-2-iodobenzene (0.0708 g, 0.223 mmol) were added to a solution of **1a** (0.1306 g, 0.222 mmol) in 1,4-dioxane (2.2 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2b** in 68% yield as pale yellow viscous oil (0.0708 g, 0.152 mmol).

$[\alpha]_D$ +47.2 (*c* 1.79, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 8.3 Hz, 2H), 7.22–7.17 (m, 3H), 7.15 (d, J = 7.9 Hz, 2H), 7.09–7.00 (m, 2H), 6.98 (dd, J = 8.0, 2.2 Hz, 1H), 6.94 (d, J = 2.1 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 6.37 (d, J = 2.0 Hz, 1H),

5.25 (s, 1H), 4.42 (dd, J = 15.3, 2.4 Hz, 1H), 4.33 (dd, J = 15.3, 1.7 Hz, 1H), 3.23 (dd, J = 10.6, 4.7 Hz, 1H), 3.08 (ddd, J = 10.6, 5.9, 1.5 Hz, 1H), 2.53 (d, J = 16.1 Hz, 1H), 2.36 (s, 3H), 1.99 (dd, J = 15.9, 1.5 Hz, 1H), 1.70–1.64 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 141.1, 139.6, 135.6, 133.9, 132.2, 131.5, 129.9, 129.5 (2C), 128.5 (2C), 128.1–127.4 (br, 2C), 127.6, 127.3 (2C), 127.2, 126.0, 121.3, 69.0, 61.9, 53.1, 50.9, 31.2, 21.6; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{24}ClNNaO_3S$ 488.1063, found 488.1055.

Preparation of (3*S*,3a*R*)-6-chloro-3a-hydroxymethyl-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2c). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0114 g, 0.0223 mmol), DABCO (0.0760 g, 0.678 mmol), CsF (0.1015 g, 0.668 mmol), and 2-bromo-4-chloro-1-iodobenzene (0.0716 g, 0.226 mmol) were added to a solution of **1a** (0.1319 g, 0.224 mmol) in 1,4-dioxane (2.2 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2c** in 38% yield as pale yellow viscous oil (0.0708 g, 0.085 mmol).

$[\alpha]_D$ +6.6 (c 1.12, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 8.2 Hz, 2H), 7.24–7.18 (m, 3H), 7.16 (d, J = 7.7 Hz, 2H), 7.11–6.98 (m, 2H), 7.05 (dd, J = 8.1, 2.1 Hz, 2H), 6.94 (s, 1H), 6.88 (d, J = 8.1 Hz, 1H), 6.41 (s, 1H), 5.25 (s, 1H), 4.41 (dd, J = 15.3, 2.4 Hz, 1H), 4.34 (dd, J = 15.0, 1.2 Hz, 1H), 3.23 (dd, J = 10.6, 4.4 Hz, 1H), 3.07 (dd, J = 11.0, 5.3 Hz, 1H), 2.53 (d, J = 16.2 Hz, 1H), 2.37 (s, 3H), 2.04 (d, J = 16.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 139.8, 139.6, 135.6, 135.1, 132.7, 130.8, 129.5 (2C), 128.9, 128.5 (2C), 128.0–127.4 (br, 2C), 127.6, 127.3 (2C), 127.2, 126.8, 121.4, 69.0, 61.9, 52.8, 50.9, 31.7, 21.6; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{25}ClNO_3S$ 466.1244, found 466.1253.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-7-methyl-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2d). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0182 g, 0.0356 mmol), DABCO (0.0056 g, 0.052 mmol), CsF (0.1289 g, 0.849 mmol), and 4-bromo-3-iodotoluene (0.0775 g, 0.261 mmol) were added to a solution of **1a** (0.1540 g, 0.261 mmol) in 1,4-dioxane (4 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2d** in 53% yield as viscous oil (0.0619 g, 0.140 mmol).

$[\alpha]_D$ +12.0 (c 0.53, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.45 (m, 2H), 7.23–7.17 (m, 3H), 7.17–7.13 (m, 2H), 7.10–6.97 (m, 2H), 6.84–6.81 (m, 2H), 6.77 (d, J = 1.5 Hz, 1H), 6.39 (t, J = 2.0 Hz, 1H), 5.24 (s, 1H), 4.40 (dd, J = 15.1, 2.4 Hz, 1H), 4.32 (dd, J = 15.2, 1.6 Hz, 1H), 3.26 (dd, J = 10.7, 4.6 Hz, 1H), 3.07 (dd, J = 9.4, 5.2 Hz, 1H), 2.48 (d, J = 16.0 Hz, 1H), 2.36 (s, 3H), 2.23 (s, 3H), 2.09–1.95 (m, 1H), 1.54 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 139.9, 139.2, 136.3, 135.7, 132.1, 130.0, 129.4 (2C), 128.6, 128.4 (2C), 128.1, 128.0–127.4 (br, 2C), 127.4, 127.3 (2C), 127.1, 122.4, 69.1, 62.1, 53.1, 50.9, 31.4, 21.6, 21.0; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{27}NNaO_3S$ 468.1609, found 468.1600.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-7-methoxy-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2e). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0169 g, 0.0330 mmol), DABCO (0.0074 g, 0.066 mmol), CsF (0.1544 g, 1.016 mmol), and 1-bromo-2-iodo-4-methoxybenzene (0.0983 g, 0.314 mmol) were added to a solution of **1a** (0.1849 g, 0.314 mmol) in 1,4-dioxane (5 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2e** in 44% yield as viscous oil (0.0638 g, 0.138 mmol).

$[\alpha]_D$ −55.5 (c 1.62, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.24–7.17 (m, 3H), 7.15 (d, J = 8.5 Hz, 2H), 7.12–7.01 (m, 2H), 6.85 (dd, J = 8.3, 1.0 Hz, 1H), 6.57 (dd, J = 8.2, 2.7 Hz, 1H), 6.53 (d, J = 2.7 Hz, 1H), 6.39 (t, J = 2.1 Hz, 1H), 5.24 (s, 1H), 4.40 (dd, J = 15.2, 2.4 Hz, 1H), 4.33 (dd, J = 15.1, 1.7 Hz, 1H), 3.72 (s, 3H), 3.26 (dd, J = 10.6, 4.4 Hz, 1H), 3.05 (dd, J = 11.0, 6.8 Hz, 1H), 2.46 (d, J = 15.9 Hz, 1H), 2.36 (s, 3H), 1.99 (dt, J = 15.7, 1.4 Hz, 1H), 1.54 (dd, J = 6.0, 4.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.5, 143.3, 140.1, 139.9, 135.7, 133.3, 129.5 (2C), 129.4, 128.4 (2C), 127.7, 127.5, 127.3 (2C), 125.0 (2C), 122.3, 112.3, 112.2, 69.1, 62.1, 55.4, 53.3, 50.9, 30.9, 21.6; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{27}NNaO_4S$ 484.1559, found 484.1562.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-6-methoxy-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2f). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0104 g, 0.02 mmol), DABCO (0.0050 g, 0.04 mmol), CsF (0.1519 g, 1.0 mmol), and 2-bromo-1-iodo-4-methoxybenzene (30 μL, 0.20 mmol) were added to a solution of **1a** (0.1195 g, 0.20 mmol) in 1,4-dioxane (4.5 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 10 : 1 then 3 : 1) to give **2f** in 63% yield as viscous oil (0.059 g, 0.13 mmol).

$[\alpha]_D$ −31.8 (c 0.02, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.19 (d, J = 5.5 Hz, 3H), 7.15 (d, J = 8.0 Hz, 2H), 7.11–6.95 (m, 2H), 6.88 (d, J = 8.3 Hz, 1H), 6.60 (dd, J = 8.3, 2.6 Hz, 1H), 6.53 (d, J = 2.5 Hz, 1H), 6.38 (t, J = 2.2 Hz, 1H), 5.26 (s, 1H), 4.39 (dd, J = 15.0, 2.4 Hz, 1H), 4.32 (dd, J = 15.0, 1.6 Hz, 1H), 3.69 (s, 3H), 3.26 (d, J = 10.6 Hz, 1H), 3.07 (d, J = 10.7 Hz, 1H), 2.53 (d, J = 16.1 Hz, 1H), 2.36 (s, 3H), 2.09–2.02 (m, 1H), 1.87 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 143.3, 140.0, 136.3, 135.7, 135.0, 129.4 (2C), 128.5 (2C), 128.0–127.6 (br, 2C), 127.4, 127.3 (2C), 127.2, 125.4, 121.8, 115.0, 111.5, 69.1, 62.0, 55.3, 52.8, 50.9, 32.3, 21.6; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{27}H_{28}NO_4S$ 462.1739, found 462.1728.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-7-nitro-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2g). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0115 g, 0.023 mmol), DABCO (0.0753 g, 0.671 mmol), CsF (0.1022 g, 0.673 mmol), and 1-bromo-2-iodo-4-nitrobenzene (0.0736 g, 0.224 mmol) were added to a solution of **1a** (0.1315 g, 0.223 mmol) in 1,4-

dioxane (2.2 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 1 : 1) to give **2g** in 51% yield as viscous oil (0.0545 g, 0.114 mmol).

$[\alpha]_D$ +56.4 (*c* 1.57, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (dt, *J* = 8.4, 2.3 Hz, 1H), 7.80 (dd, *J* = 2.4, 1.3 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.25–7.18 (m, 3H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.07–6.97 (m, 2H), 6.51 (t, *J* = 1.9 Hz, 1H), 5.30 (s, 1H), 4.47 (ddd, *J* = 15.9, 2.5, 1.0 Hz, 1H), 4.43–4.30 (m, 1H), 3.21 (d, *J* = 10.6 Hz, 1H), 3.17 (d, *J* = 10.6 Hz, 1H), 2.75 (d, *J* = 16.6 Hz, 1H), 2.36 (s, 3H), 2.09 (d, *J* = 17.7 Hz, 1H), 1.90–1.76 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 143.6, 142.7, 141.1, 139.2, 135.5, 133.6, 129.5 (2C), 129.4, 128.7 (2C), 127.8, 127.7–127.3 (br, 2C), 127.2 (2C), 122.3, 120.9, 120.6, 68.9, 62.1, 53.0, 50.8, 32.0, 21.6; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{26}H_{24}N_2NaO_5S$ 499.1304, found 499.1308.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-6-nitro-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2h). Under a nitrogen atmosphere, $Pd(t\text{-}Bu_3P)_2$ (0.0105 g, 0.021 mmol), DABCO (0.0682 g, 0.607 mmol), CsF (0.0921 g, 0.606 mmol), and 2-bromo-1-iodo-4-nitrobenzene (0.0668 g, 0.204 mmol) were added to a solution of **1a** (0.1198 g, 0.204 mmol) in 1,4-dioxane (2.0 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 1 : 1) to give **2h** in 38% yield as pale yellow viscous oil (0.0367 g, 0.077 mmol).

$[\alpha]_D$ −16.6 (*c* 1.16, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.83 (d, *J* = 2.2 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.24–7.19 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 1H), 7.05–6.93 (m, 2H), 6.60–6.47 (m, 1H), 5.31 (s, 1H), 4.47 (dd, *J* = 15.9, 2.5 Hz, 1H), 4.39 (dd, *J* = 16.0, 1.6 Hz, 1H), 3.21 (d, *J* = 10.8 Hz, 1H), 3.13 (d, *J* = 10.8 Hz, 1H), 2.72 (d, *J* = 16.2 Hz, 1H), 2.36 (s, 3H), 2.09 (d, *J* = 16.3 Hz, 1H), 1.77–1.68 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.6, 145.2, 143.6, 139.2, 138.5, 135.5, 134.8, 129.5 (2C), 128.7 (2C), 127.8 (2C), 127.3 (2C), 127.4–127.1, 126.4, 123.8, 122.6, 121.1, 76.9, 68.9, 62.0, 52.9, 51.1, 31.7, 21.6; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{26}H_{24}N_2NaO_5S$ 499.1304, found 499.1294.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-3-phenyl-2-tosyl-7-(trifluoromethyl)-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2i). Under a nitrogen atmosphere, $Pd(t\text{-}Bu_3P)_2$ (0.0107 g, 0.021 mmol), DABCO (0.0713 g, 0.636 mmol), CsF (0.0972 g, 0.640 mmol), and 1-bromo-2-iodo-4-(trifluoromethyl)benzene (0.0750 g, 0.214 mmol) were added to a solution of **1a** (0.1253 g, 0.213 mmol) in 1,4-dioxane (2.1 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 1 : 1) to give **2i** in 58% yield as pale yellow viscous oil (0.0622 g, 0.125 mmol).

$[\alpha]_D$ +38.2 (*c* 1.45, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.23–7.18 (br, 5H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 7.8 Hz, 2H), 6.47 (s, 1H), 5.29 (s, 1H), 4.46 (d, *J* = 15.4 Hz, 1H), 4.35 (d, *J* = 15.3 Hz, 1H), 3.23 (d, *J* = 10.6 Hz, 1H), 3.15 (d, *J* = 10.7 Hz, 1H), 2.67 (d, *J* = 16.3 Hz, 1H), 2.36 (s, 3H), 2.18–2.14 (br, 1H), 2.08 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 141.5, 139.5, 137.3, 135.6, 132.9, 129.5 (2C), 129.2 (d, *J* = 32.3 Hz), 129.0, 128.6 (2C), 127.7, 128.0–127.5 (br, 2C) 127.3 (2C), 124.1 (q, *J* = 272.0 Hz), 124.1 (q, *J* = 3.8 Hz), 122.7 (q, *J* = 3.8 Hz), 121.4, 68.9, 62.0, 52.9, 50.9, 31.7, 21.6; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{24}F_3NNaO_3S$ 522.132, found 522.1339.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-3-phenyl-2-tosyl-6-(trifluoromethyl)-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2j). Under a nitrogen atmosphere, $Pd(t\text{-}Bu_3P)_2$ (0.0112 g, 0.022 mmol), DABCO (0.0741 g, 0.661 mmol), CsF (0.0999 g, 0.658 mmol), and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.0769 g, 0.219 mmol) were added to a solution of **1a** (0.1289 g, 0.219 mmol) in 1,4-dioxane (2.2 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 1 : 1) to give **2j** in 54% yield as pale yellow viscous oil (0.0596 g, 0.119 mmol).

$[\alpha]_D$ +30.8 (*c* 1.93, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.3 Hz, 2H), 7.32 (ddd, *J* = 7.8, 1.9, 0.9 Hz, 1H), 7.24–7.17 (m, 5H), 7.16 (dd, *J* = 7.8, 0.9 Hz, 2H), 7.04 (d, *J* = 7.8 Hz, 2H), 6.48 (d, *J* = 1.9 Hz, 1H), 5.30 (s, 1H), 4.45 (d, *J* = 14.1 Hz, 1H), 4.37 (dd, *J* = 15.7, 1.9 Hz, 1H), 3.23 (dd, *J* = 10.7, 4.7 Hz, 1H), 3.11 (dd, *J* = 10.7, 5.5 Hz, 1H), 2.66 (d, *J* = 16.3 Hz, 1H), 2.36 (s, 3H), 2.26–2.11 (m, 1H), 2.07 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 142.5, 139.5, 135.5 (2C), 133.9, 129.5 (2C), 129.2 (q, *J* = 32.2 Hz), 128.6 (2C), 127.8–128.5 (br, 2C), 127.7, 127.3 (2C), 126.2, 125.5 (q, *J* = 3.6 Hz), 124.1 (q, *J* = 272.1 Hz), 123.9 (q, *J* = 4.2 Hz), 121.4, 68.9, 61.9, 53.0, 51.0, 31.7, 21.6; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{25}F_3NO_3S$ 500.1507, found 500.1513.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-7-methyl-3-(*o*-tolyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2k). Under a nitrogen atmosphere, $Pd(t\text{-}Bu_3P)_2$ (0.0106 g, 0.021 mmol), DABCO (0.1038 g, 0.925 mmol), CsF (0.2922 g, 1.92 mmol), and 4-bromo-3-iodotoluene (0.030 mL, 0.208 mmol) were added to a solution of **1c** (0.1254 g, 0.208 mmol) in 1,4-dioxane (10 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2k** in 50% yield as viscous oil (0.0478 g, 0.104 mmol).

$[\alpha]_D$ +63.2 (*c* 1.47, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.97 (t, *J* = 7.4 Hz, 1H), 6.83 (t, *J* = 7.5 Hz, 1H), 6.75 (s, 2H), 6.70 (d, *J* = 6.1 Hz, 3H), 6.32 (s, 1H), 5.55 (s, 1H), 4.35 (d, *J* = 15.0 Hz, 1H), 4.26 (d, *J* = 15.0 Hz, 1H), 3.20 (d, *J* = 10.5 Hz, 1H), 3.02 (d, *J* = 10.5 Hz, 1H), 2.50 (d, *J* = 15.9 Hz, 1H), 2.39 (s, 3H), 2.35–2.30 (m, 1H), 2.29 (s, 3H), 2.15 (s, 3H), 2.01 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 139.2, 138.4, 136.3, 135.9, 135.7, 132.1, 130.4, 130.0, 129.4 (2C), 128.6,

128.1, 127.7, 127.3 (2C), 127.1, 127.0, 126.2, 122.5, 64.8, 62.2, 53.6, 51.0, 30.2, 21.6, 21.0, 19.7; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{29}NNaO_3S$ 482.1766, found 482.1765.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-3-(3-methoxyphenyl)-6-nitro-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2l). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0105 g, 0.020 mmol), CsF (0.0978 g, 0.64 mmol), and 2-bromo-1-iodo-4-nitrobenzene (0.0706 g, 0.22 mmol) were added to a solution of **1d** (0.1268 g, 0.20 mmol) in 1,4-dioxane (5 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **2l** in 55% yield as viscous oil (0.0568 g, 0.112 mmol).

$[\alpha]_D$ −47.1 (*c* 0.28, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 1H), 7.83 (s, 1H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.14–7.09 (m, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 6.95–6.40 (br, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.50 (s, 1H), 5.27 (s, 1H), 4.46 (d, *J* = 16.3 Hz, 1H), 4.36 (d, *J* = 15.8 Hz, 1H), 3.84–3.50 (m, 4H), 3.20 (d, *J* = 10.7 Hz, 1H), 3.13 (d, *J* = 10.7 Hz, 1H), 2.75 (d, *J* = 16.3 Hz, 1H), 2.36 (s, 3H), 2.15–2.06 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7, 146.6, 145.2, 143.6, 140.7, 138.5, 135.4, 134.8, 133.2, 129.7, 129.5 (3C), 127.3 (2C), 126.4, 123.8, 122.5, 121.0, 112.8, 68.8, 61.9, 55.2, 53.0, 51.1, 31.5, 21.6; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{27}N_2O_6S$ 507.1590, found 507.1596.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-6-(trifluoromethyl)-3-(*o*-tolyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2m). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0109 g, 0.0213 mmol), DABCO (0.1112 g, 0.99 mmol), CsF (0.1893 g, 1.246 mmol), and 2-bromo-1-iodo-4-(trifluoromethyl)benzene (0.040 mL, 0.213 mmol) were added to a solution of **1c** (0.1286 g, 0.213 mmol) in 1,4-dioxane (8.5 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2m** in 19% yield as viscous oil (0.0205 g, 0.04 mmol).

$[\alpha]_D$ +60.7 (*c* 0.68, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.22–7.01 (m, 6H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.47 (s, 1H), 5.64 (s, 1H), 4.47 (dd, *J* = 15.4, 2.3 Hz, 1H), 4.36 (dd, *J* = 15.4, 1.3 Hz, 1H), 3.25 (d, *J* = 10.5 Hz, 1H), 3.16 (d, *J* = 10.4 Hz, 1H), 2.72 (d, *J* = 16.3 Hz, 1H), 2.46 (s, 3H), 2.36 (s, 3H), 2.13 (d, *J* = 16.2 Hz, 1H), 1.82 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 141.5, 138.0, 137.2, 135.8, 132.8, 130.6, 129.4 (2C), 129.4, 129.1, 129.0, 127.5, 127.3, 127.2 (2C), 126.3, 124.6 (q, *J* = 273.3 Hz), 124.1, 122.7, 121.5, 64.7, 62.1, 53.3, 51.0, 30.6, 21.6, 19.7; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{28}H_{27}F_3NO_3S$ 514.1658, found 514.1663.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-7-chloro-3-(*o*-tolyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2n). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0105 g, 0.0205 mmol), DABCO (0.0827 g, 0.737 mmol), CsF (0.2419 g, 1.592 mmol), and 1-bromo-2-iodo-4-chlorobenzene (0.030 mL, 0.205 mmol) were added to a solution of **1c** (0.1239 g, 0.205 mmol) in 1,4-dioxane (8.5 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **2n** in 28% yield as viscous oil (0.0205 g, 0.04 mmol).

$[\alpha]_D$ +62.1 (*c* 0.89, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.98 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.93 (d, *J* = 1.6 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 7.7 Hz, 1H), 6.38 (s, 1H), 5.62 (s, 1H), 4.44 (dd, *J* = 15.4, 2.1 Hz, 1H), 4.34 (d, *J* = 15.5 Hz, 1H), 3.25 (d, *J* = 10.5 Hz, 1H), 3.13 (d, *J* = 10.3 Hz, 1H), 2.61 (d, *J* = 16.0 Hz, 1H), 2.46 (s, 3H), 2.36 (s, 3H), 2.04 (d, *J* = 16.0 Hz, 1H), 1.78 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 141.2, 138.1, 135.8, 135.8, 133.8, 132.2, 131.4, 130.5, 129.9, 129.4 (2C), 127.5, 127.3, 127.2 (2C), 127.2, 126.3, 126.0, 121.5, 64.7, 62.0, 53.5, 51.0, 30.0, 21.6, 19.7; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{26}ClNNaO_3S$ 502.1220, found 502.1209.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-6-fluoro-3-(*o*-tolyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2o). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0106 g, 0.0208 mmol), DABCO (0.0803 g, 0.716 mmol), CsF (0.1740 g, 1.15 mmol), and 2-bromo-4-fluoro-1-iodobenzene (0.030 mL, 0.208 mmol) were added to a solution of **1c** (0.1256 g, 0.208 mmol) in 1,4-dioxane (12 mL) and the reaction mixture was heated to the refluxing temperature for 20 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 2 : 1) to give **2o** in 35% yield as pale yellow oil (0.0323 g, 0.073 mmol).

$[\alpha]_D$ +79.3 (*c* 1.13, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 77.51 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.06 (dd, *J* = 7.7, 6.9 Hz, 1H), 6.95–6.86 (m, 2H), 6.78–6.71 (m, 2H), 6.66 (d, *J* = 8.9 Hz, 1H), 6.41 (s, 1H), 5.61 (s, 1H), 4.42 (d, *J* = 15.0 Hz, 1H), 4.33 (d, *J* = 15.0 Hz, 1H), 3.26 (d, *J* = 10.5 Hz, 1H), 3.12 (d, *J* = 10.5 Hz, 1H), 2.61 (d, *J* = 16.1 Hz, 1H), 2.45 (s, 3H), 2.36 (s, 3H), 2.10 (d, *J* = 16.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 143.3, 139.7, 138.6, 138.2, 135.8, 135.7, 130.5, 129.4 (2C), 127.6, 127.4, 127.3 (2C), 126.2, 124.2, 121.5, 116.1, 116.0, 113.3 (d, *J* = 21.7 Hz), 64.7, 62.0, 53.1, 50.9, 30.8, 21.6, 19.7; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{26}FNNaO_3S$ 486.1515, found 486.1506.

Preparation of (3*S*,3a*R*)-3a-hydroxymethyl-6-chloro-3-(*m*-methoxyphenyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2p). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0151 g, 0.030 mmol), CsF (0.1285 g, 0.85 mmol), and 2-bromo-4-chloro-1-iodobenzene (0.040 mL, 0.30 mmol) were added to a solution of **1d** (0.1835 g, 0.30 mmol) in 1,4-dioxane (12 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **2p** in 26% yield as pale yellow oil (0.0386 g, 0.078 mmol).

$[\alpha]_D$ −5.81 (*c* 1.39, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.2 Hz, 2H), 7.34–7.24 (m, 1H), 7.21–7.11 (m, 1H),

7.16 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 7.8 Hz, 1H), 6.94 (s, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.72 (d, J = 7.5 Hz, 1H), 6.67–6.57 (m, 1H), 6.39 (s, 1H), 5.22 (d, J = 12.1 Hz, 1H), 4.41 (d, J = 15.8 Hz, 1H), 4.31 (d, J = 15.0 Hz, 1H), 3.80–3.58 (br, 3H), 3.23 (d, J = 10.5 Hz, 1H), 3.10 (d, J = 10.9 Hz, 1H), 2.55 (d, J = 16.2 Hz, 1H), 2.37 (s, 3H), 2.07 (d, J = 16.2 Hz, 1H), 1.73–1.66 (br, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 139.8, 135.7, 135.1, 132.8, 132.7, 130.8, 129.6, 129.4 (2C), 128.9, 127.3, 127.2 (2C), 126.8, 121.4, 120.4, 112.7, 101.5, 101.3, 68.9, 62.0, 55.1, 52.8, 51.0, 31.6, 21.6; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{26}ClNNaO_4S$ 518.1169, found 518.1181.

Preparation of (3a*R*,8b*S*,*E*)-3a-hydroxymethyl-3-(4-methylbenzylidene)-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4a). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.014 g, 0.027 mmol), DABCO (0.0065 g, 0.0579 mmol), CsF (0.1141 g, 0.75 mmol), and 4-iodotoluene (0.0420 g, 0.19 mmol) were added to a solution of **1b** (0.121 g, 0.18 mmol) in 1,4-dioxane (3 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 3 : 1) to give **4a** in 80% yield as viscous oil (0.0643 g, 0.14 mmol).

$[\alpha]_D$ −19.6 (c 0.66, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 7.3 Hz, 1H), 7.36 (d, J = 8.1 Hz, 2H), 7.25 (dd, J = 18.0, 6.5 Hz, 1H), 7.21 (t, J = 6.6 Hz, 1H), 7.11 (d, J = 7.9 Hz, 2H), 7.02 (d, J = 7.9 Hz, 3H), 6.45 (s, 1H), 5.46 (s, 1H), 4.30 (dd, J = 15.1, 1.9 Hz, 1H), 4.09 (dd, J = 15.2, 2.2 Hz, 1H), 3.48 (d, J = 11.4 Hz, 1H), 3.18 (d, J = 16.5 Hz, 1H), 3.08 (d, J = 11.2 Hz, 1H), 2.87 (d, J = 16.4 Hz, 1H), 2.46 (s, 3H), 2.34 (s, 3H), 1.34–1.24 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 141.7, 140.9, 140.6, 137.5, 135.9, 133.1, 129.9 (2C), 129.2 (2C), 128.7 (2C), 128.6, 128.0 (2C), 127.5, 126.6, 124.9, 124.5, 73.0, 64.4, 59.4, 56.0, 38.3, 21.7, 21.2. HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{27}H_{28}NO_3S$ 446.1790, found 446.1798.

Preparation of (3a*R*,8b*S*,*E*)-3a-hydroxymethyl-3-(4-methoxybenzylidene)-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4b). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0131 g, 0.026 mmol), DABCO (0.0059 g, 0.053 mmol), CsF (0.1093 g, 0.72 mmol), and 4-iodoanisole (0.0561 g, 0.24 mmol) were added to a solution of **1b** (0.1492 g, 0.22 mmol) in 1,4-dioxane (4 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 2 : 1) to give **4b** in 68% yield as viscous oil (0.0698 g, 0.15 mmol).

$[\alpha]_D$ −64.1 (c 0.46, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90–7.81 (m, 2H), 7.65 (d, J = 7.5 Hz, 1H), 7.35 (d, J = 8.6 Hz, 2H), 7.23 (d, J = 7.5 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.06 (d, J = 9.3 Hz, 2H), 7.01 (d, J = 6.8 Hz, 1H), 6.83 (d, J = 8.6 Hz, 2H), 6.42 (s, 1H), 5.44 (s, 1H), 4.28 (dd, J = 15.0, 2.0 Hz, 1H), 4.08 (dd, J = 15.1, 2.0 Hz, 1H), 3.80 (s, 3H), 3.48 (d, J = 11.3 Hz, 1H), 3.18 (d, J = 16.4 Hz, 1H), 3.08 (d, J = 11.3 Hz, 1H), 2.87 (d, J = 16.4 Hz, 1H), 2.45 (s, 3H), 1.71–1.56 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 143.9, 141.5, 140.8, 139.7, 135.7, 130.0 (2C), 129.8 (2C), 128.6, 128.2, 127.9 (2C), 127.4, 126.6, 124.6, 124.5, 113.8 (2C), 73.0, 64.4, 59.3, 56.1, 55.4, 38.1, 21.7; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{27}H_{28}NO_4S$ 462.1739, found 462.1736.

Preparation of (3a*R*,8b*S*,*E*)-3a-hydroxymethyl-3-(3-methoxybenzylidene)-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4c). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0144 g, 0.028 mmol), DABCO (0.0072 g, 0.064 mmol), CsF (0.1313 g, 0.86 mmol), and 3-iodoanisole (0.0655 g, 0.28 mmol) were added to a solution of **1b** (0.1839 g, 0.28 mmol) in 1,4-dioxane (4.2 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 2 : 1) to give **4c** in 83% yield as a white solid (0.1053 g, 0.23 mmol).

Mp 138.5–139.5 °C; $[\alpha]_D$ −37.7 (c 0.56, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 7.8 Hz, 2H), 7.65 (d, J = 7.4 Hz, 1H), 7.36 (d, J = 7.8 Hz, 2H), 7.28–7.19 (m, 3H), 7.01 (d, J = 7.2 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 6.71 (d, J = 7.6 Hz, 1H), 6.67 (s, 1H), 6.46 (s, 1H), 5.46 (s, 1H), 4.29 (d, J = 15.1 Hz, 1H), 4.08 (d, J = 15.2 Hz, 1H), 3.78 (s, 3H), 3.47 (d, J = 11.3 Hz, 1H), 3.15 (d, J = 16.3 Hz, 1H), 3.07 (d, J = 11.4 Hz, 1H), 2.87 (d, J = 16.3 Hz, 1H), 2.46 (s, 3H), 1.47–1.43 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 143.9, 141.5, 141.3, 140.8, 137.4, 135.7, 129.8 (2C), 129.5, 128.6, 127.9 (2C), 127.4, 126.5, 124.7, 124.4, 121.1, 114.5, 112.8, 72.9, 64.5, 59.5, 55.9, 55.3, 38.3, 21.7; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{27}H_{28}NO_4S$ 462.1739, found 462.1729.

Preparation of (3a*R*,8b*S*,*E*)-3-(4,5-dimethoxy-2-methylbenzylidene)-3a-hydroxymethyl-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4d). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0192 g, 0.038 mmol), DABCO (0.0077 g, 0.069 mmol), CsF (0.1225 g, 0.81 mmol), and 2-iodo-4,5-dimethoxytoluene (0.0695 g, 0.25 mmol) were added to a solution of **1b** (0.1609 g, 0.24 mmol) in 1,4-dioxane (4.0 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **4d** in 74% yield as viscous oil (0.0898 g, 0.18 mmol).

$[\alpha]_D$ −13.8 (c 2.99, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 2H), 7.65 (d, J = 6.3 Hz, 1H), 7.36 (d, J = 7.6 Hz, 2H), 7.25 (td, J = 7.2, 1.5 Hz, 1H), 7.21 (t, J = 7.3 Hz, 1H), 7.02 (dd, J = 7.5, 1.2 Hz, 1H), 6.65 (s, 1H), 6.57 (s, 1H), 6.38 (t, J = 1.7 Hz, 1H), 5.40 (s, 1H), 4.30 (dd, J = 15.0, 1.9 Hz, 1H), 4.11 (dd, J = 15.0, 2.0 Hz, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 3.33 (dd, J = 11.2, 4.3 Hz, 1H), 3.11 (d, J = 9.6 Hz, 1H), 3.03 (d, J = 16.4 Hz, 1H), 2.71 (d, J = 16.4 Hz, 1H), 2.45 (s, 3H), 1.92 (s, 3H), 1.61–1.55 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.4, 146.5, 143.8, 141.3, 141.0, 140.6, 135.9, 129.8 (2C), 128.7, 128.6, 128.0 (2C), 127.5, 127.2, 126.6, 124.3, 124.1, 113.0, 112.6, 72.7, 64.8, 59.4, 56.2, 55.9, 55.6, 38.6, 21.7, 19.5; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{29}H_{32}NO_5S$ 506.2001, found 506.1997.

Preparation of (3a*R*,8b*S*,*E*)-6,7-dimethoxy-3a-hydroxymethyl-3-(4-methylbenzylidene)-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno

[1,2-*b*]pyrrole (4f). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0107 g, 0.021 mmol), DABCO (0.0043 g, 0.038 mmol), CsF (0.0905 g, 0.60 mmol), and 4-iodotoluene (0.0441 g, 0.20 mmol) were added to a solution of **1e** (0.1353 g, 0.19 mmol) in 1,4-dioxane (3.0 mL) and the reaction mixture was heated to the refluxing temperature for 22.5 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 2 : 1) to give **4f** in 56% yield as viscous oil (0.0527 g, 0.10 mmol).

$[\alpha]_D$ −71.4 (*c* 1.76, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.11 (s, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 7.02 (d, *J* = 7.9 Hz, 2H), 6.51 (s, 1H), 6.44 (s, 1H), 5.41 (s, 1H), 4.31 (d, *J* = 15.2 Hz, 1H), 4.18–4.07 (m, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.47 (d, *J* = 11.2 Hz, 1H), 3.15 (d, *J* = 16.1 Hz, 1H), 3.04 (d, *J* = 11.2 Hz, 1H), 2.82 (d, *J* = 16.0 Hz, 1H), 2.45 (s, 3H), 2.33 (s, 3H), 1.74–1.61 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.0, 149.0, 143.8, 140.8, 137.4, 135.9, 133.2, 133.0, 132.2, 129.8 (2C), 129.1 (2C), 128.7 (2C), 127.9 (2C), 124.5, 108.4, 106.7, 73.6, 64.6, 60.5, 59.7, 56.1, 56.0, 38.6, 21.7, 21.2; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{29}H_{32}NO_5S$ 506.2001, found 506.2002.

Preparation of (3a*R*,8b*S*,*E*)-6,7-dimethoxy-3a-hydroxymethyl-3-(4-methoxybenzylidene)-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4g). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0107 g, 0.021 mmol), DABCO (0.0047 g, 0.042 mmol), CsF (0.1004 g, 0.66 mmol), and 4-iodoanisole (0.0500 g, 0.21 mmol) were added to a solution of **1e** (0.1385 g, 0.19 mmol) in 1,4-dioxane (3.0 mL) and the reaction mixture was heated to the refluxing temperature for 22.5 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 1 : 1) to give **4g** in 75% yield as pale yellow viscous oil (0.0748 g, 0.14 mmol).

$[\alpha]_D$ −52.1 (*c* 2.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.11 (s, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 2H), 6.51 (s, 1H), 6.41 (s, 1H), 5.40 (s, 1H), 4.30 (d, *J* = 15.1 Hz, 1H), 4.11 (d, *J* = 14.9 Hz, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.79 (s, 3H), 3.49 (d, *J* = 11.2 Hz, 1H), 3.16 (d, *J* = 16.0 Hz, 1H), 3.05 (d, *J* = 11.2 Hz, 1H), 2.83 (d, *J* = 16.0 Hz, 1H), 2.44 (s, 3H), 1.37–1.33 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 149.9, 149.0, 143.8, 140.0, 135.9, 133.2, 132.3, 130.1 (2C), 129.8 (2C), 128.3, 127.9 (2C), 124.2, 113.8 (2C), 108.3, 106.7, 73.6, 68.2, 64.6, 59.6, 56.0, 56.0, 55.3, 38.3, 21.7; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{31}NNaO_6S$ 544.1770, found 544.1761.

Preparation of (3a*R*,8b*S*,*E*)-6,7-dimethoxy-3a-hydroxymethyl-3-(3-methoxybenzylidene)-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4h). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0120 g, 0.023 mmol), DABCO (0.0077 g, 0.069 mmol), CsF (0.1120 g, 0.74 mmol), and 3-iodoanisole (0.0562 g, 0.24 mmol) were added to a solution of **1e** (0.1737 g, 0.24 mmol) in 1,4-dioxane (4.0 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 1 : 1) to give **4h** in 74% yield as pale yellow viscous oil (0.0924 g, 0.18 mmol).

$[\alpha]_D$ −51.4 (*c* 3.08, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 7.9 Hz, 1H), 7.09 (s, 1H), 6.79 (d, *J* = 9.2 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 6.67 (s, 1H), 6.51 (s, 1H), 6.44 (s, 1H), 5.41 (s, 1H), 4.30 (d, *J* = 15.3 Hz, 1H), 4.11 (d, *J* = 14.4 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.46 (d, *J* = 11.2 Hz, 1H), 3.12 (d, *J* = 16.0 Hz, 1H), 3.04 (d, *J* = 11.1 Hz, 1H), 2.81 (d, *J* = 16.1 Hz, 1H), 2.44 (s, 3H), 1.51–1.43 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 150.0, 149.0, 143.9, 141.7, 137.4, 135.9, 133.3, 132.3, 129.8 (2C), 129.4, 127.9 (2C), 124.4, 121.1, 114.5, 112.7, 108.4, 106.8, 73.5, 64.7, 60.5, 59.8, 56.0, 56.0, 55.3, 38.7, 21.7; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{31}NNaO_6S$ 544.1770, found 544.1774.

Preparation of (3a*R*,8b*S*,*E*)-3-(4,5-dimethoxy-2-methylbenzylidene)-6,7-dimethoxy-3a-hydroxymethyl-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4i). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0136 g, 0.027 mmol), DABCO (0.0057 g, 0.051 mmol), CsF (0.1060 g, 0.698 mmol), and 2-iodo-4,5-dimethoxytoluene (0.0696 g, 0.25 mmol) were added to a solution of **1e** (0.1677 g, 0.23 mmol) in 1,4-dioxane (3.5 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 3 : 1 then 1 : 1) to give **4i** in 74% yield as pale yellow viscous oil (0.0958 g, 0.170 mmol).

$[\alpha]_D$ −55.2 (*c* 3.19, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.86 (d, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 7.10 (s, 1H), 6.64 (s, 1H), 6.57 (s, 1H), 6.51 (s, 1H), 6.34 (s, 1H), 5.35 (s, 1H), 4.29 (d, *J* = 15.1 Hz, 1H), 4.13 (d, *J* = 14.4 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 3.29 (d, *J* = 11.1 Hz, 1H), 3.06 (d, *J* = 11.8 Hz, 1H), 3.01 (d, *J* = 17.2 Hz, 1H), 2.68 (d, *J* = 16.0 Hz, 1H), 2.42 (s, 3H), 1.93 (s, 3H), 1.82–1.69 (m, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 150.0, 149.1, 148.4, 146.5, 143.7, 141.0, 136.0, 133.1, 132.5, 129.8 (2C), 128.7, 127.9 (2C), 127.3, 123.5, 113.1, 112.6, 108.5, 106.7, 73.3, 64.8, 60.5, 59.7, 56.2, 56.1, 56.0, 55.9, 55.6, 39.2, 21.6; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{31}H_{35}NNaO_7S$ 588.2032, found 588.2022.

Preparation of (3a*R*,8b*S*,*E*)-3-benzylidene-6,7-dimethoxy-3a-hydroxymethyl-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]-pyrrole (4j). Under a nitrogen atmosphere, Pd(*t*-$Bu_3P)_2$ (0.0128 g, 0.025 mmol), DABCO (0.0076 g, 0.068 mmol), CsF (0.1171 g, 0.77 mmol), and iodobenzene (0.0469 g, 0.23 mmol) were added to a solution of **1e** (0.1693 g, 0.23 mmol) in 1,4-dioxane (4,0 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **4j** in 74% yield as pale yellow viscous oil (0.0846 g, 0.17 mmol).

$[\alpha]_D$ −85.7 (*c* 2.82, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.25 (d, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.09 (s, 1H), 6.49 (s, 1H), 6.47 (s, 1H), 5.41 (s, 1H), 4.29 (d, *J* =

14.6 Hz, 3H), 4.12 (d, J = 15.2 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.46 (d, J = 11.2 Hz, 1H), 3.11 (d, J = 16.1 Hz, 1H), 3.01 (d, J = 11.4 Hz, 1H), 2.80 (d, J = 16.1 Hz, 1H), 2.44 (s, 3H), 1.35 (s, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 150.0, 149.0, 143.9, 141.5, 136.0, 135.9, 133.2, 132.2, 129.8 (2C), 128.7 (2C), 128.4 (2C), 127.9 (2C), 127.5, 124.6, 108.3, 106.7, 77.4, 73.5, 64.7, 59.8, 56.1, 56.0, 38.6, 21.7; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{28}H_{29}NNaO_5S$ 514.1664, found 514.1659.

(3a*R*,8b*S*,*Z*)-3-Ethylidene-1-tosyl-3a-hydroxymethyl-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole (4k). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0112 g, 0.018 mmol), DABCO (0.0036 g, 0.035 mmol), CsF (0.0892 g, 0.528 mmol), and 4-iodotoluene (0.0407 g, 0.176 mmol) were added to a solution of **1f** (0.1198 g, 0.176 mmol) in 1,4-dioxane (2.0 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **4k** in 59% yield as colourless viscous oil (0.0386 g, 0.104 mmol).

$[\alpha]_D$ −23.2 (c 0.92, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 6.5 Hz, 1H), 7.35 (d, J = 7.7 Hz, 2H), 7.27–7.20 (m, 2H), 7.10 (d, J = 6.8 Hz, 1H), 5.45 (qt, J = 6.8, 2.6 Hz, 1H), 5.24 (s, 1H), 4.07 (ddq, J = 15.1, 3.2, 1.7 Hz, 1H), 4.01 (ddd, J = 15.1, 2.5, 1.4 Hz, 1H), 3.07 (d, J = 16.0 Hz, 1H), 3.03 (d, J = 11.0 Hz, 1H), 2.96 (d, J = 16.0 Hz, 1H), 2.93 (d, J = 11.4 Hz, 1H), 2.45 (s, 3H), 1.54 (dt, J = 6.9, 1.6 Hz, 3H), 1.35–1.20 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 141.4, 140.9, 140.5, 135.9, 129.9, 128.5, 127.5, 127.4, 126.4, 124.7, 118.8, 70.7, 65.7, 59.7, 50.4, 39.2, 21.7, 14.8; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{23}NNaO_3S$ 392.1296, found 392.1294.

Preparation of (3a*R*,8b*S*)-3a-hydroxymethyl-3-(*E*-deuterio) methylene-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno-[1,2-*b*]pyrrole (5-D). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0185 g, 0.036 mmol) and DABCO (0.1261 g, 1.12 mmol) were added to a solution of **1b** (0.2421 g, 0.36 mmol) in dry 1,4-dioxane (15 mL) with D_2O (0.75 mL) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **5-D** in 76% yield as colourless viscous oil (0.0984 g, 0.27 mmol).

$[\alpha]_D$ +16.4 (c 3.28, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.81 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 7.6 Hz, 2H), 7.29–7.14 (m, 2H), 7.10 (d, J = 8.8 Hz, 1H), 5.27 (s, 1H), 5.01 (t, J = 2.0 Hz, 1H), 4.13 (dd, J = 15.1, 2.3 Hz, 1H), 3.95 (dd, J = 15.1, 1.9 Hz, 1H), 3.11 (d, J = 15.7 Hz, 1H), 3.08 (d, J = 10.8 Hz, 1H), 2.99 (d, J = 16.5 Hz, 1H), 2.96 (d, J = 12.1 Hz, 1H), 2.43 (s, 3H), 1.75–1.68 (m, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 149.2, 144.0, 141.3, 140.8, 135.5, 129.9 (2C), 128.6, 127.6 (2C), 127.5, 126.4, 124.7, 108.3 (t, J = 23.7 Hz), 70.8, 65.2, 59.8, 52.9, 39.0, 21.7; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{20}DNNaO_3S$ 379.1203, found 379.1196.

Preparation of 5-D in the presence of DCl. Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.01664 g, 0.033 mmol) and DABCO (0.1280 g, 1.14 mmol) were added to a solution of **1b** (0.2173 g, 0.33 mmol) in dry 1,4-dioxane (15 mL) with D_2O (0.75 mL) and conc. aq. DCl (4 drops) and the reaction mixture was heated to the refluxing temperature for 24 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **5-D** in 95% yield as pale colourless viscous oil (0.1104 g, 0.31 mmol).

Preparation of TBP complex 6a. A solution of **1g** (0.6488 g, 0.88 mmol) in ether (88 mL) was added to 12 M HCl (4.4 mL) and the reaction mixture was stirred at room temperature for 1.5 h. The organic phase was separated and washed with brine (2 × 20 mL). After being dried over Na_2SO_4, the organic phase was filtered and concentrated *in vacuo*. The obtained crude product was purified through flash chromatography (silica gel/hexane–EtOAc 5 : 1 then 2 : 1) to give **6a** in 72% yield (0.4903 g, 0.63 mmol) as colourless viscous oil.

$[\alpha]_D$ +10.6 (c 3.13, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.47 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.06–6.99 (m, 3H), 6.87 (t, J = 7.1 Hz, 1H), 6.56 (d, J = 6.8 Hz, 1H), 5.88 (s, 1H), 5.35 (s, 1H), 5.13 (s, 1H), 4.53 (d, J = 12.9 Hz, 1H), 4.11 (d, J = 12.9 Hz, 1H), 2.31 (s, 3H), 1.57 (s, 9H), 1.41–1.14 (m, 13H), 0.93–0.80 (m, 6H), 0.50 (d, J = 13.8 Hz, J^{119}Sn–^{1}H = 54.1 Hz, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 178.8, 147.1, 143.1, 137.7, 137.1, 132.7, 129.4, 129.1 (2C), 127.5, 126.9 (2C), 124.4, 112.6, 87.4, 69.2, 60.3, 52.9, 28.1, 28.0, 27.9 (3C), 27.8, 26.8, 26.7, 22.1, 21.7, 21.5, 19.3, 13.8, 13.7; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{32}H_{45}BrClNNaO_4SSn$ 798.0840, found 798.0853.

Preparation of TBP complex 6b. A solution of **1b** (0.2208 g, 0.33 mmol) in ether (25 mL) was added to 12 M HCl (2.0 mL) and the reaction mixture was stirred at room temperature for 17 h. The organic phase was separated and washed with brine (3 × 10 mL). After being dried over Na_2SO_4, the organic phase was filtered and concentrated *in vacuo*. The obtained crude product was purified through flash chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **6b** in 91% yield (0.2108 g, 0.30 mmol) as colourless viscous oil.

$[\alpha]_D$ +21.7 (c 0.16, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.53–7.45 (m, 3H), 7.15 (d, J = 7.9 Hz, 2H), 7.11–7.00 (m, 2H), 6.86–6.79 (m, 1H), 5.37 (s, 1H), 5.12 (s, 1H), 5.03 (s, 1H), 4.28 (dt, J = 13.6, 2.4 Hz, 1H), 4.16 (d, J = 13.7 Hz, 1H), 3.42 (dt, J = 10.5, 3.0 Hz, 1H), 3.31 (dd, J = 10.9, 7.6 Hz, 1H), 2.84 (dd, J = 7.9, 3.8 Hz, 1H), 2.37 (s, 3H), 1.72–1.46 (m, 4H), 1.46–1.03 (m, 9H), 0.91 (t, J = 7.3 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H), 0.54 (dd, J = 13.9, 2.5 Hz, J^{119}Sn–^{1}H = 56.7 Hz, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 147.2, 144.0, 138.8, 138.0, 132.9, 129.7 (2C), 129.4, 128.7, 127.8, 127.5 (2C), 124.3, 112.7, 77.2, 68.0, 67.2, 55.7, 51.7, 28.2, 28.2, 26.9, 26.8, 22.2, 21.6, 19.2, 19.1, 13.8, 13.6; HRMS (ESI-TOF) m/z $[M - HCl + Na]^+$ calcd for $C_{28}H_{38}BrNNaO_3SSn$ 690.0675, found 690.0655.

Preparation of TBP complex 6c. A solution of **1a** (0.2697 g, 0.46 mmol) in ether (25 mL) was added to 12 M HCl (2.5 mL) and the reaction mixture was stirred at room temperature for 3 h. The organic phase was separated and washed with brine (2 × 10 mL). After being dried over Na_2SO_4, the organic phase was filtered and concentrated *in vacuo*. The obtained crude product was purified through flash chromatography (silica gel/

hexane–EtOAc 5 : 1 then 1 : 1) to give **6c** in 95% yield (0.2471 g, 0.44 mmol) as colourless viscous oil.

$[\alpha]_D$ −77.1 (*c* 3.18, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.16–7.09 (m, 4H), 6.99 (d, J = 8.1 Hz, 2H), 6.92 (d, J = 7.3 Hz, 2H), 5.26 (s, 1H), 5.15 (s, 1H), 4.80 (s, 1H), 4.55 (d, J = 3.3 Hz, 1H), 4.36 (d, J = 13.8 Hz, 1H), 3.97 (d, J = 13.8 Hz, 1H), 3.68 (dd, J = 9.9, 4.5 Hz, 1H), 3.37 (dd, J = 9.9, 2.8 Hz, 1H), 2.31 (s, 3H), 1.67–1.46 (m, 4H), 1.39–1.17 (m, 8H), 1.08 (d, J = 13.7 Hz, J^{119}Sn–^{1}H = 48.5 Hz, 1H), 0.92 (t, J = 8.0 Hz, 3H), 0.81 (t, J = 7.4 Hz, 3H), 0.73 (d, J = 13.6 Hz, J^{119}Sn–^{1}H = 70.2 Hz, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 148.0, 143.3, 137.3, 135.1, 129.2 (2C), 128.5 (2C), 128.2, 128.1 (2C), 126.9 (2C), 110.7, 69.6, 68.0, 55.4, 51.0, 28.1, 28.1, 26.9, 26.8, 21.5, 20.7, 20.4, 19.4, 13.7, 13.6; ^{119}Sn NMR (186 MHz, $CDCl_3$) δ 33.3; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{28}H_{41}ClNO_3SSn$ 626.15176, found 626.15087; Anal. Calcd for $C_{28}H_{40}ClNO_3SSn$: C, 53.82; H, 6.45; N, 2.24. Found: C, 53.76; H, 6.56; N, 2.22.

Preparation of TBP complex 6d. A solution of **1a** (0.2239 g, 0.38 mmol) in ether (21 mL) was added to 12 M HCl (2.1 mL) and the reaction mixture was stirred at room temperature for 1.5 h. The organic phase was separated and washed with aqueous NaBr solution (2 × 20 mL). After being dried over Na_2SO_4, the organic phase was filtered and concentrated *in vacuo* to give **6d** in 90% yield (0.2295 g, 0.34 mmol) as colourless viscous oil.

$[\alpha]_D$ −83.6 (*c* 0.87, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.21 (t, J = 7.3 Hz, 1H), 7.15–7.11 (m, 4H), 6.99 (d, J = 7.9 Hz, 2H), 6.91 (d, J = 7.1 Hz, 2H), 5.27 (s, 1H), 5.16 (s, 1H), 4.81 (s, 1H), 4.68 (s, 1H), 4.37 (d, J = 13.8 Hz, 1H), 3.97 (d, J = 13.9 Hz, 1H), 3.73 (t, J = 8.6, 3.8 Hz, 1H), 3.37 (d, J = 9.8 Hz, 1H), 2.31 (s, 3H), 1.67–1.47 (m, 4H), 1.40–1.22 (m, 8H), 1.19 (d, J = 14.4 Hz, J^{119}Sn–^{1}H = 73.6 Hz, 1H), 0.92 (t, J = 7.3 Hz, 3H), 0.81 (t, J = 7.7 Hz, 3H), 0.78 (d, J = 14.4 Hz, J^{119}Sn–^{1}H = 50.2 Hz, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 147.9, 143.4, 137.3, 135.0, 129.2 (2C), 128.5 (2C), 128.2 (2C), 128.1, 126.9 (2C), 110.7, 69.5, 68.1, 55.8, 51.0, 28.5 (d, J^{13}C −^{119}Sn = 28.0 Hz), 28.4 (d, J^{13}C–^{119}Sn = 28.0 Hz), 26.8 (d, J^{13}C–^{119}Sn = 82.9 Hz, J^{13}C–^{117}Sn = 80.5 Hz), 26.7 (d, J^{13}C–^{119}Sn = 84.6 Hz, J^{13}C–^{117}Sn = 78.8 Hz), 21.5, 21.0 (d, J^{13}C–^{119}Sn = 435.6 Hz, J^{13}C–^{117}Sn = 416.4 Hz), 20.9 (d, J^{13}C–^{119}Sn = 428.2 Hz, J^{13}C–^{117}Sn = 410.8 Hz), 20.3 (d, J^{13}C–^{119}Sn = 400.0 Hz, J^{13}C–^{117}Sn = 381.4 Hz), 13.7, 13.6; ^{119}Sn NMR (186 MHz, $CDCl_3$) δ 28.8; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{28}H_{40}BrNNaO_3SSn$ 692.08319, found 692.08200; Anal. Calcd for $C_{28}H_{40}BrNO_3SSn$: C, 50.25; H, 6.02; N, 2.09. Found: C, 50.45; H, 6.13; N, 1.96.

Preparation of TBP complex 6f. A solution of **6d** (0.125 g, 0.18 mmol) in ether (20 mL) was added to aqueous CsF solution (5 g in 20 mL) and the biphasic mixture was stirred at room temperature for 2 h. The organic phase was separated and dried over Na_2SO_4. After filtration, the organic phase was concentrated *in vacuo* to give **6f** in 85% yield (0.0926 g, 0.152 mmol) as colourless oil.

$[\alpha]_D$ −82.5 (*c* 0.08, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.19 (t, J = 7.4 Hz, 1H), 7.16–7.08 (m, 4H), 6.97 (d, J = 7.9 Hz, 2H), 6.91 (d, J = 7.7 Hz, 2H), 5.22 (s, 1H), 5.12 (s, 1H), 4.70 (s, 1H), 4.32 (d, J = 13.9 Hz, 1H), 3.95 (d, J = 14.0 Hz, 1H), 3.52 (d, J = 10.3 Hz, 1H), 3.23 (d, J = 10.4 Hz, 1H), 2.30 (s, 3H), 1.91 (s, 1H), 1.67–0.97 (m, 13H), 0.91 (t, J = 7.1 Hz, 3H), 0.85 (t, J = 7.7 Hz, 3H), 0.57 (d, J = 13.7 Hz, J^{119}Sn–^{1}H = 73.2 Hz, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 148.7, 143.1, 138.0, 135.8, 129.3 (2C), 128.5 (2C), 128.4 (2C), 128.2, 127.1 (2C), 110.4, 69.9, 67.9, 55.3, 51.3, 27.9 (2C), 27.1 (2C), 21.6, 19.0, 18.8, 16.6, 13.9 (2C); ^{119}Sn NMR (186 MHz, $CDCl_3$) δ 15.56 (d, J = 2081.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −183.8 (d, J = 2052.9 Hz); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{28}H_{40}FNNaO_3SSn$ 632.1633, found 632.1626.

Preparation of (3a*R*,8b*S*)-*tert*-butyl-3-methylene-1-tosyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrole-3a-carboxylate (7). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.0172 g, 0.034 mmol) and CsF (0.2548 g, 1.70 mmol) were added to a solution of **6a** (0.2451 g, 0.32 mmol) in 1,4-dioxane (3.2 mL) and the reaction mixture was heated to the refluxing temperature for 25 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 15 : 1 then 8 : 1) to give **7** in 87% yield as pale yellow viscous oil (0.1172 g, 0.280 mmol).

$[\alpha]_D$ +21.3 (*c* 0.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.83 (d, J = 7.5 Hz, 2H), 7.75–7.67 (m, 1H), 7.31 (d, J = 9.1 Hz, 2H), 7.28–7.23 (m, 2H), 7.12 (d, J = 6.1 Hz, 1H), 5.80 (s, 1H), 5.29 (s, 1H), 5.09 (s, 1H), 4.17 (dt, J = 14.2, 2.5 Hz, 1H), 3.90 (dt, J = 14.2, 1.8 Hz, 1H), 3.49 (d, J = 16.9 Hz, 1H), 3.22 (d, J = 16.4 Hz, 1H), 2.41 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 160.8, 147.4, 143.5, 140.9, 139.7, 136.1, 129.7 (2C), 128.7, 127.9 (2C), 127.8, 126.5, 124.4, 109.8, 81.9, 72.7, 63.5, 53.0, 41.2, 27.7 (3C), 21.6; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{27}NNaO_4S$ 448.1559, found 448.1560.

Conversion of compound 7 to 5. DIBAL (1.5 M in CH_2Cl_2, 2 mL, 3 mmol) was added to a solution of **7** (1.8 mg, 0.0042 mmol) in CH_2Cl_2 (5 mL) at −50 °C and the reaction mixture was stirred for 11 h. The reaction mixture was allowed to heat to room temperature and aqueous Rochell's salt solution (15 mL) was added. The resulting biphasic mixture was extracted with EtOAc (2 × 20 mL). The organic phase was combined and dried over Na_2SO_4. After filtration, the solution was concentrated *in vacuo* to give the crude product that was purified by using recycled GPC to give **5** in 99% yield (1.5 mg, 0.0042 mmol) as a white solid.

Mp 165.0–166.0 °C; $[\alpha]_D$ +15.8 (*c* 1.02, $CHCl_3$); ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.68–7.62 (m, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.28–7.20 (m, 2H), 7.11 (d, J = 6.6 Hz, 1H), 5.27 (s, 1H), 5.08 (t, J = 2.2 Hz, 1H), 5.04 (s, 1H), 4.15 (ddd, J = 15.1, 3.2, 1.5 Hz, 1H), 4.00–3.93 (m, 1H), 3.14–3.06 (m, 2H), 3.00 (t, J = 10.4 Hz, 2H), 2.44 (s, 3H), 1.71–1.61 (m, 1H); ^{13}C NMR (126 MHz, $CHCl_3$) δ 149.4, 144.0, 141.3, 140.7, 135.6, 129.9 (2C), 128.6, 127.7 (2C), 127.5, 126.4, 124.7, 108.4, 70.8, 65.3, 59.9, 52.9, 39.1, 21.7; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{21}NNaO_3S$ 378.1140, found 378.1129.

Coupling reaction of 6b to give 5 (Scheme 5). Under a nitrogen atmosphere, Pd(t-Bu_3P)$_2$ (0.01615 g, 0.0316 mmol) and DABCO (0.1130 g, 0.948 mmol) were added to a solution of **6b** (0.2108 g, 0.299 mmol) in dry 1,4-dioxane (13 mL) and the reaction mixture was heated to the refluxing temperature for

25 h. The solution was filtered, and concentrated *in vacuo*. The residue was subjected to flash column chromatography (silica gel/hexane–EtOAc 5 : 1 then 1 : 1) to give **5** in 62% yield as colourless viscous oil (0.0656 g, 0.185 mmol).

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Notes and references

1 Review: C. C. C. J. Seechurn, M. O. Kitching, T. J. Colacot and V. Snieckus, *Angew. Chem., Int. Ed.*, 2012, **51**, 5062.

2 (*a*) M. Kosugi, K. Sasazawa, Y. Shimizu and T. Migita, *Chem. Lett.*, 1977, 301; (*b*) D. Milstein and J. K. Stille, *J. Am. Chem. Soc.*, 1978, **100**, 3636.

3 (*a*) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508; (*b*) T. N. Mitchell, *Synthesis*, 1992, 803; (*c*) V. Farina, V. Krishnamurthy and W. K. Scott, *Org. React.*, 1997, **50**, 1; (*d*) M. A. J. Duncton and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1235; (*e*) T. N. Mitchell, in *Metal-Catalysed Cross-Coupling Reactions*, ed. A. de Meijere and F. Diederich, Wiley-VCH Verlag GmbH & Co., Weinheim, 2nd edn, 2004, ch. 3, vol. 1.

4 (*a*) D. Milstein and J. K. Stille, *J. Am. Chem. Soc.*, 1979, **101**, 4992; (*b*) J. W. Labadie and J. K. Stille, *J. Am. Chem. Soc.*, 1983, **105**, 6129; (*c*) R. J. Linderman, D. M. Graves, W. R. Kwochka, A. F. Ghannam and T. V. Anklekar, *J. Am. Chem. Soc.*, 1990, **112**, 7438; (*d*) R. K. Bhatt, D. S. Shin, J. R. Falck and C. Mioskowski, *Tetrahedron Lett.*, 1992, **33**, 4885; (*e*) E. Vedejs, A. R. Haight and W. O. Moss, *J. Am. Chem. Soc.*, 1992, **114**, 6556; (*f*) J. Ye, R. K. Bhatt and J. R. Falck, *J. Am. Chem. Soc.*, 1994, **116**, 1; (*g*) Y. Y. Belosludtsev, R. K. Bhatt and J. R. Falck, *Tetrahedron Lett.*, 1995, **36**, 5881; (*h*) S. Jarosz, *Tetrahedron Lett.*, 1996, **37**, 3063; (*i*) J. R. Falck, R. K. Bhatt, K. M. Reddy and J. Ye, *Synlett*, 1997, 481; (*j*) E. Fouquet, M. Pereyre and A. L. Rodriguez, *J. Org. Chem.*, 1997, **62**, 5242; (*k*) M. S. Jensen, C. Yang, Y. Hsiao, N. Rivera, K. M. Wells, J. Y. L. Chung, N. Yasuda, D. L. Hughes and P. J. Reider, *Org. Lett.*, 2000, **2**, 1081; (*l*) K. W. Kells and J. M. Chong, *J. Am. Chem. Soc.*, 2004, **126**, 15666; (*m*) M. Goli, A. He and J. R. Falck, *Org. Lett.*, 2011, **13**, 344; (*n*) L. Li, C. Y. Wang, R. Huang and M. R. Biscoe, *Nat. Chem.*, 2013, **5**, 607.

5 (*a*) N. B. Carter, R. Mabon, R. Walmsley, A. M. E. Richecœur and J. B. Sweeney, *Synlett*, 2006, 1747; (*b*) M. Shimizu and T. Hiyama, *Eur. J. Org. Chem.*, 2013, 8069; (*c*) M. Shimizu, I. Nagao, S.-i. Kiyomoto and T. Hiyama, *Aust. J. Chem.*, 2012, **65**, 1277; (*d*) I. Nagao, M. Shimizu and T. Hiyama, *Angew. Chem., Int. Ed.*, 2009, **48**, 7573.

6 (*a*) J. Wu, W. Pisula and K. Müllen, *Chem. Rev.*, 2007, **107**, 718; (*b*) A. R. Murphy and J. M. J. Fréchet, *Chem. Rev.*, 2007, **107**, 1066.

7 M. Shimizu, Y. Tomioka, I. Nagao and T. Hiyama, *Synlett*, 2009, 3147.

8 (*a*) A. Kamimura, S. Ishikawa, F. Noguchi, T. Moriyama, M. So, T. Murafuji and H. Uno, *Chem. Commun.*, 2012, **42**, 6592; (*b*) A. Kamimura, T. Yoshinaga, F. Noguchi, K. Miyazaki and H. Uno, *Org. Chem. Front.*, 2015, **2**, 713; (*c*) A. Kamimura, K. Miyazaki, T. Kawamoto and H. Uno, *Tetrahedron*, 2016, **72**, DOI: 10.1016/j.tet.2016.04.0782.

9 A. Kamimura, M. So, S. Ishikawa and H. Uno, *Org. Lett.*, 2013, **15**, 1402.

10 R. Pedrosa, C. Andrés and J. Nieto, *J. Org. Chem.*, 2002, **67**, 782.

11 (*a*) A. Alizadeh, R. Ghanbaripour, M. Feizabadi, L.-G. Zhu and M. Dusek, *RSC Adv.*, 2015, **5**, 80518; (*b*) P. Zhou, W.-J. Hao, J.-P. Zhang, B. Jiang, G. Licd and S.-J. Tu, *Chem. Commun.*, 2015, **51**, 13012; (*c*) K. Pradhan, S. Paul and A. R. Das, *RSC Adv.*, 2015, **5**, 12062; (*d*) Y. Luo and J. Wu, *Org. Lett.*, 2012, **14**, 1592; (*e*) F. Behler, F. Habecker, W. Saak, T. Klüner and J. Christoffers, *Eur. J. Org. Chem.*, 2011, 4231; (*f*) J. D. Harling and B. S. Orlek, *Tetrahedron*, 1998, **54**, 14905.

12 For bioactive compounds of benzoisoindoles: (*a*) D. Middlemiss, *Ger. Pat*, 2259498; *Chem. Abstr.*, 1973, **79**, 66171u; (*b*) R. Achini and W. Oppolzer, *Ger. Pat*, 2348593; *Chem. Abstr.*, 1974, **81**, 13386c; (*c*) A. Achini, W. Oppolzer and E. Pfenninger, *Swiss Pat*, 611886, 1979; *Chem. Abstr.*, 1979, **91**, 140720p; (*d*) A. Achini, W. Oppolzer and E. Pfenninger, *Swiss Pat*, 611884, 1979; *Chem. Abstr.*, 1980, **92**, 41756u; (*e*) J. F. Debernardis, M. D. Meyer and K. B. Sippy, *U.S. Pat*, WO9006927, 1990; *Chem. Abstr.*, 1991, **114**, 815704; (*f*) R. M. Bowman and H. W. Gschwend, *U.S. Pat*, 4014899, 1977; *Chem. Abstr.*, 1977, **87**, 53077h.

13 For bioactive compounds of indenopyrroles: (*a*) B. R. Huck, L. Llamas, M. J. Robarge, T. C. Dent, J. Song, W. F. Hodnick, C. Crumrine, A. Stricker-Krongrad, J. Harrington, K. R. Brunden and Y. L. Bennani, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 4130; (*b*) L. Qiao, L.-Y. Zhao, S.-B. Rong, X.-W. Wu, S. Wang, T. Fujii, M. G. Kazanietz, L. Rauser, J. Savage, B. L. Roth, J. Flippen-Anderson and A. P. Kozikowski, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 955; (*c*) F. Behler, F. Habecker, W. Saak, T. Klüner and J. Christoffers, *Eur. J. Org. Chem.*, 2011, 4231; (*d*) W. Zhou, G. An, G. Zhang, J. Han and Y. Pan, *Org. Biomol. Chem.*, 2011, **9**, 583.

14 A. F. Littke, L. Schwarz and G. C. Fu, *J. Am. Chem. Soc.*, 2002, **124**, 6343.

15 (*a*) V. Farina, S. B. Kapadia, C. Wang and I. Liebeskind, *J. Org. Chem.*, 1994, **59**, 5905; (*b*) X. Han, B. M. Stoltz and E. J. Corey, *J. Am. Chem. Soc.*, 1999, **121**, 7600; (*c*) S. P. H. Mee, V. Lee and J. E. Baldwin, *Chem. – Eur. J.*, 2005, **11**, 3294.

16 (*a*) A. García-Martínez, J. Osío Barcina, A. de Fresno Cerezo and L. R. Subramanian, *Synlett*, 1994, 1047; (*b*) E. Fouquet, M. Pereyre and A. L. Rodriguez, *J. Org. Chem.*, 1997, **62**, 5242; (*c*) K. Fugami, S.-y. Ohnuma, M. Kameyama, T. Saotome and M. Kosugi, *Synlett*, 1999, 63; (*d*) T. Okitsu, K. Iwastuka and A. Wada, *Chem. Commun.*, 2008, **41**, 6330.

17 Crystallographic data (excluding structure factors) for the structure **6e** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 845991.

18 M. Nádvorník, J. Holeček, K. Handlíř and A. Lyčka, *J. Organomet. Chem.*, 1984, **275**, 43.