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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 aford 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 performed wherein the decomposition of the stannolanes with aqueous HCl and HBr afforded trigonal bipyramidal (TBP) pentacoordinated tin complexes, as confirmed by microanalyses and ¹¹⁹Sn 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 Csp³-tin bond.

Introduction

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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 onepot multicoupling 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 Csp²-Csp² type species, and there are only rare reports on the double coupling between Csp²-Csp³ species.⁷ Thus, the quantitative difference between the reactivities of the sp² carbon-tin bond and the ordinary sp³ carbon-tin bond in this double coupling reaction remains unclear.

Recently, we developed a one-step synthesis of a bicyclic

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 substrate scope for aryl halides and pseudohalides. With our methodology, multicyclic benzoisoindoles¹⁰ and hexahydroindeno[1,2-*b*]pyrroles¹¹ 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.

stannolane through a highly cumulated cascade radical

reaction wherein a radical addition-cyclization-substitution

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.

The use of dichlorobenzene did not give any double coupling products **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 Cul was used as an additive (entry 3).¹⁵ Dibromobenzene gave the coupling product **2a** in 76%

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⁺ Electronic Supplementary Information (ESI) available: NMR for compounds 2, 4,

^{5, 6,} and 7, and ORTEP chart for 6e. See DOI: 10.1039/x0xx00000x

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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.

Table 1. Double coupling reaction of 1a with various 1,2-disubstituted benzene									
Bu Sn N Ts	Bu OH ''Ph 1a	+ (1 ec	X Pd(<i>t</i> -Bu ₃ P) ₂ 10 mol% Y dioxane quiv.) conditions	H	10 2a	Ph N−Ts			
Entry	х	Y	Additives ^a	Time	Tem	2a;			
				(h)	р	Yield			
					(°C)	(%) ^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), Cul (2)	24	80	21			
4	Br	Br	DABCO (3)	20	100	76			
5	Br	I	DABCO (3), CsF (5)	24	100	44			
6	Ι	I	DABCO (0.2), CsF (3)	24	100	79			

a. equivalents in parentheses. b. isolated yield.

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 sp³ carbon-tin bond is less reactive and produces no coupling product with any intermolecular coupling partner. The yield of ${\bf 4a}$ 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 20mol%. Thus, the presence of the fluoride anion is effective in promoting the intramolecular coupling reaction with the sp²-tin bond as well as the sp³-tin bond.16



Scheme 1 Inter- and intramolecular double coupling reaction

Intermolecular and inter- and intramolecular regioselective double coupling reaction

Table 2. Regioselective double coupling reaction of 1 with iodobenzenes

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



a. Isolated yield. b. Determined by integration of 1H NMR spectra

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

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double coupling reaction to give **2b** in 68% yield (entry 1), whereas the double coupling of 1a with 2-bromo-4-chloro-1iodobenzene afforded its regioisomer 2c in 38% yield (entry 2). The regioselectivity was estimated by ¹H 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 sp²carbon-tin bond site. We expected that the aryl-iodine bond reacted faster than the aryl-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 trifluoromethyl group at the para position to the carbon-iodine bond caused the regioselectivity to slight 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 multisubstituted 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 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 reaction of **1b** and **1e** was examined using various iodobenzenes. The results are summarized in Table 3.



Entry	1	Х	Ar	View Article (%)
1	1b	Н	4-MeOC₆H₄ DOI: 10.	1039/C6 4BB68 018K
2	1b	н	3-MeOC ₆ H ₄	4c ; 83
3	1b	Н	2-Me-4,5-(MeO) ₂ C ₆ H ₂	4d ; 74
4	1b	Н	$4-O_2NC_6H_4$	4e ; 0
5	1e	OMe	4-MeC ₆ H ₄	4f ; 56
6	1e	OMe	4-MeOC ₆ H ₄	4g ; 75
7	1e	OMe	3-MeOC ₆ H ₄	4h ; 74
8	1e	OMe	2-Me-4,5-(MeO) ₂ C ₆ H ₂	4i ; 74
9	1e	OMe	Ph	4j ; 74

a. Isolated yield.

The inter- and intramolecular double coupling reaction progressed smoothly in the presence of iodobenzene and 10 mol% of Pd(PtBu₃)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 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 Eposition of the alkylidene group. Thus, the intermolecular coupling progressed selectively with the retention of the tin unit configuration. Dimethoxy-substituted vinylic 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

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unit was replaced by hydrogen during the reaction. To identify the origin of the hydrogen, we performed the reaction with dry dioxane containing small amounts of D₂O (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-CH₂ protons at $\delta = 5.01$ and CH₂OH protons at $\delta = 5.96$ were irradiated, respectively. We concluded that the water in dioxane is the origin of the hydrogen atom introduced in the substitution reaction to the vinyl tin unit. 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 DCI.



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



Scheme 4 Intramolecular coupling reaction through TBP complex of 1g

The acidic treatment of **1b** also yielded the corresponding TBP complex **6b** in 91% yield (Scheme 5). This is supported by the fact that the signal for the OH proton in **6b** was observed in the ¹H 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 intramolecular coupling product **5** in 62% yield by treatment with the catalytic amounts of Pd(tBu₃P)₃ in the presence of DABCO. We believe that the coordination of an oxygen atom to the tin atom to promoted the coupling reaction of the alkyl tin unit; however, some basic additive, such as CsF, is necessary to achieve an efficient reaction.⁹



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

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 an OH proton signal was observed in the ¹H NMR spectra for these compounds. Microanalyses of these compounds indicated that compounds 6c and 6d included a halogen atom. Furthermore, the ¹¹⁹Sn NMR signals of 6c and 6d in CDCl₃ appeared at 33.3 and 28.8 ppm, respectively, which are highly up-field shifted compared with those of trialkychlorotin compounds, such as Bu₃SnCl (152.8 ppm in CDCl₃),¹⁸ but close to the chemical shift of TBP tin complex 6e, which shows a ¹¹⁹Sn 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 pentacoordinated 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); The 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 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 ¹³C NMR spectra were recorded on JEOL lamda-500 or JNM-ECA 500 Delta2 (500 MHz for ¹H and 126 MHz for ¹³C) spectrometer. Palladium complexes were purchased from Aldrich. Stannolanes **1** were prepared by the previous reported method.^{8a} All the reactions in this paper were performed under nitrogen atmosphere unless otherwise mentioned. High resolution mass spectra (HRMS) were measured by JEOL JMS T-100LP LC-ESI mass spectrometer.

Preparation of ((3S,3aR)-3a-hydroxymethyl-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1H-benzo[f]isoindole (2a, Table 1, entry 4): Under 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 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 viscose oil (0.094 g, 0.22 mmol).

[α]_D +33.6 (c 1.83, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.52 (d, J = 8.3 Hz, 2 H), 7.18 (d, J = 4.2 Hz, 3 H), 7.14 (d, J = 8.1 Hz, 2 H), 7.07 (t, J = 7.4 Hz, 1 H), 7.11 – 6.98 (m, 2 H), 7.01 (t, J = 7.5 Hz, 1 H), 6.95 (d, J = 6.4 Hz, 1 H), 6.94 (d, J = 6.1 Hz, 1 H), 6.43 (s, 1 H), 5.29 (s, 1 H), 4.42 (dd, J = 15.1, 2.3 Hz, 1 H), 4.33 (dd, J = 15.1, 1.3 Hz, 1 H), 3.4 – 3.6 (br, 1H), 3.26 (d, J = 10.7 Hz, 1 H), 3.10 (d, J = 10.7 Hz, 1 H), 2.58 (d, J = 16.1 Hz, 1 H), 2.35 (s, 3 H), 2.08 (d, J = 16.0 Hz, 1 H); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₆H₂₅NNaO₃S 454.1453, found 454.1447.

Preparation of (3S,3aR)-7-chloro-3a-hydroxymethyl-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1H-benzo[f]isoindole (2b): Under nitrogen atmosphere, Pd(*t*-Bu₃P)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 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)

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to give **2b** in 68% yield as pale yellow viscose oil (0.0708 g, 0.152 mmol).

 $[\alpha]_{D}$ +47.2 (c 1.79, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₆H₂₄ClNNaO₃S 488.1063, found 488.1055. Preparation of (3S,3aR)-6-chloro-3a-hydroxymethyl-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1H-benzo[f]isoindole (2c): Under nitrogen atmosphere, Pd(t-Bu₃P)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 1,4dioxane (2.2 mL) and the reaction mixture was heated to 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 viscose oil (0.0708 g, 0.085 mmol).

[α]_D +6.6 (c 1.12, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₆H₂₅CINO₃S 466.1244, found 466.1253.

Preparation of (3S,3aR)-3a-hydroxymethyl-7-methyl-3phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2d): Under nitrogen atmosphere, Pd(*t*-Bu₃P)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 1,4dioxane (4 mL) and the reaction mixture was heated to 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 viscose oil (0.0619 g, 0.140 mmol).

[α]_D +12.0 (c 0.53, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) δ 143.3, 139.9, 139.2, 136.3, 135.7, 132.1, Journal Name

130.0, 129.4 (2C), 128.6, 128.4 (2C), 128.1, 128.0-127, 4 (p_{10} , 2C), 127.4, 127.3 (2C), 127.1, 122.4, 69.1, 62,1,153,19/50,9,031.4, 21.6, 21.0; HRMS (ESI-TOF) m/z [M + Na]⁺ calcd for C₂₇H₂₇NNaO₃S 468.1609, found 468.1600.

Preparation of (35,3aR)-3a-hydroxymethyl-7-methoxy-3phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2e): Under nitrogen atmosphere, Pd(*t*-Bu₃P)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 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 viscose oil (0.0638 g, 0.138 mmol).

[α]_D -55.5 (c 1.62, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₇NNaO₄S 484.1559, found 484.1562.

Preparation of (35,3aR)-3a-hydroxymethyl-6-methoxy-3phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2*f*): Under nitrogen atmosphere, Pd(*t*-Bu₃P)₂ (0.0104 g, 0.02 mmol), DABCO (0.0050 g, 0.04 mmol), CsF (0.1519 g, 1.0 mmol), and 2bromo-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 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 viscose oil (0.059 g, 0.13 mmol).

[α]_D-31.8 (c 0.02, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₈NO₄S 462.1739, found 462.1728.

Preparation of (35,3aR)-3a-hydroxymethyl-7-nitro-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2g): Under 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)

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were added to a solution of **1a** (0.1315 g, 0.223 mmol) in 1,4dioxane (2.2 mL) and the reaction mixture was heated to 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 viscose oil (0.0545 g, 0.114 mmol).

[α]_D +56.4 (c 1.57, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 (3S,3aR)-3a-hydroxymethyl-6-nitro-3-phenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2h): Under nitrogen atmosphere, Pd(*t*-Bu₃P)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 1,4dioxane (2.0 mL) and the reaction mixture was heated to 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 viscose oil (0.0367 g, 0.077 mmol).

[α]_D –16.6 (c 1.16, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₆H₂₄N₂NaO₅S 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 nitrogen atmosphere, Pd(*t*-Bu₃P)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 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 viscose oil (0.0622 g, 0.125 mmol).

 $[\alpha]_D$ +38.2 (c 1.45, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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 = 45.3 Hz, 1H), 3.23 (d, J = 10.6 Hz, 1H), 3.15 (d, J = 10.7 Hz, 1H), 2.678 (d) J^{E} 16.3 Hz, 1H), 2.36 (s, 3H), 2.18 – 2.14 (br, 1H), 2.08 (d, J = 16.3Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) 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 = 272.0Hz), 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 C₂₇H₂₄F₃NNaO₃S 522.132, found 522.1339.

Preparation of (3*S*,3*aR*)-3a-hydroxymethyl-3-phenyl-2-tosyl-6-(trifluoromethyl)-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2j): Under nitrogen atmosphere, $Pd(t-Bu_3P)_2$ (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 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 viscose oil (0.0596 g, 0.119 mmol).

[α]_D +30.8 (c 1.93, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₅F₃NO₃S 500.1507, found 500.1513.

Preparation of (3S,3aR)-3a-hydroxymethyl-7-methyl-3-(o-tolyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2k): Under nitrogen atmosphere, Pd(t-Bu₃P)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 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 viscose oil (0.0478 g, 0.104 mmol).

[α]_D +63.2 (c 1.47, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₈H₂₉NNaO₃S 482.1766, found 482.1765.

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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 (2I): Under 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 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 **2I** in 55% yield as viscose oil (0.0568 g, 0.112 mmol).

 $\begin{bmatrix} \alpha \end{bmatrix}_{D} -47.1 (c 0.28, CHCl_{3}); {}^{1}H NMR (500 MHz, CDCl_{3}) \delta 7.93 (d, J = 8.2 Hz, 1H), 7.83 (s, 1H), 7.53 (d, J = 8.1 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.14 - 7.09 (m, 1H), 7.07 (d, J = 8.3 Hz, 1H), 6.95-6.40 (br, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.50 (s, 1H), 5.27 (s, 1H), 4.46 (d, J = 16.3 Hz, 1H), 4.36 (d, J = 15.8 Hz, 1H), 3.84 - 3.50 (m, 4H), 3.20 (d, J = 10.7 Hz, 1H), 3.13 (d, J = 10.7 Hz, 1H), 2.75 (d, J = 16.3 Hz, 1H), 2.36 (s, 3H), 2.15 - 2.06 (m, 1H); {}^{13}C NMR (126 MHz, CDCl_{3}) \delta 159.7, 146.6, 145.2, 143.6, 140.7, 138.5, 135.4, 134.8, 133.2, 129.7, 129.5 (3C), 127.3 (2C), 126.4, 123.8, 122.5, 121.0, 112.8, 68.8, 61.9, 55.2, 53.0, 51.1, 31.5, 21.6; HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₇H₂₇N₂O₆S 507.1590, found 507.1596.$

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 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 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 viscose oil (0.0205 g, 0.04 mmol).

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

Preparation of (3S,3aR)-3a-hydroxymethyl-7-chloro-3-(o-tolyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (2n): Under nitrogen atmosphere, Pd(t-Bu₃P)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 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 viscose oil (0.0205 g, 0.04/mm8)):^{1018K} [α]_D +62.1 (c 0.89, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₆CINNaO₃S 502.1220, found 502.1209.

Preparation of (35,3aR)-3a-hydroxymethyl-6-fluoro-3-(o-tolyl)-2-tosyl-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindole (20): Under nitrogen atmosphere, Pd(t-Bu₃P)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 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).

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

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 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 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, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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),

Preparation

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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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₆CINNaO₄S 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 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 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 viscose oil (0.0643 g, 0.14 mmol).

[α]_D –19.6 (c 0.66, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₈NO₃S 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 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 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 viscose oil (0.0698 g, 0.15 mmol).

[α]_D –64.1 (c 0.46, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₈NO₄S 462.1739, found 462.1736. of (3a*R*,8b*S*,*E*)-3a-hydroxymethyl-3_n(3_e

methoxybenzylidene)-1-tosyl-1,2,3,3a,4,8% 10.1039/C6OB01018K**hexahydroindeno[1,2-***b***]pyrrole (4c): Under nitrogen atmosphere, Pd(***t***-Bu₃P)₂ (0.0144 g, 0.028 mmol), DABCO (0.0072 g, 0.064 mmol), CsF (0.1313 g, 0.86 mmol), and 3iodoanisole (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 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 white solid (0.1053 g, 0.23 mmol).

Mp 138.5-139.5 °C; $[\alpha]_D$ –37.7 (c 0.56, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₇H₂₈NO₄S 462.1739, found 462. 1729.

Preparation of (3aR,8bS,E)-3-(4,5-dimethoxy-2methylbenzylidene)-3a-hydroxymethyl-1-tosyl-1,2,3,3a,4,8bhexahydroindeno[1,2-b]pyrrole (4d): Under nitrogen atmosphere, Pd(t-Bu₃P)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 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 viscose oil (0.0898 g, 0.18 mmol).

[α]_D –13.8 (c 2.99, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₉H₃₂NO₅S 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 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

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reaction mixture was heated to 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 viscose oil (0.0527 g, 0.10 mmol).

[α]_D –71.4 (c 1.76, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.86 (d, J = 7.9 Hz, 2H), 7.35 (d, J = 7.9 Hz, 2H), 7.11 (s, 1 H), 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₉H₃₂NO₅S 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 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 4iodoanisole (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 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 viscose oil (0.0748 g, 0.14 mmol).

[α]_D –52.1 (c 2.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₉H₃₁NNaO₆S 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 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 3iodoanisole (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 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 viscose oil (0.0924 g, 0.18 mmol).

 $[\alpha]_D$ –51.4 (c 3.08, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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, $J^{12.3}$) (c, $G^{12.1}$), 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₉H₃₁NNaO₆S 544.1770, found 544.1774.

Preparationof(3aR,8bS,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 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 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 viscose oil (0.0958 g, 0.170 mmol).

[α]_D –55.2 (c 3.19, CHCl₃); ¹H NMR (500 MHz, CHCl₃) 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); ¹³C NMR (126 MHz, CHCl₃) 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 C₃₁H₃₅NNaO₇S 588.2032, found 588.2022.

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

b]pyrrole (4j): Under 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 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 viscose oil (0.0846 g, 0.17 mmol).

[α]_D –85.7 (c 2.82, CHCl₃); ¹H NMR (500 MHz, CHCl₃) 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); ¹³C NMR (126 MHz, CHCl₃) 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,

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38.6, 21.7; HRMS (ESI-TOF) m/z $[M + Na]^{+}$ calcd for $C_{28}H_{29}NNaO_5S$ 514.1664, found 514.1659.

((3aR,8bS,Z)-3-ethylidene-1-tosyl-3a-hydroxymethyl-1-tosyl-

1,2,3,3a,4,8b-hexahydroindeno[1,2-*b***]pyrrole (4k):** Under 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 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 viscose oil (0.0386 g, 0.104 mmol).

[α]_D –23.2 (c 0.92, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₁H₂₃NNaO₃S 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 nitrogen atmosphere, $Pd(t-Bu_3P)_2$ (0.0185 g, 0.036 mmol) and DABCO (0.1261 g, 1.12 mmol) and 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 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 viscose oil (0.0984 g, 0.27 mmol).

 $\begin{bmatrix} \alpha \end{bmatrix}_{D} +16.4 \text{ (c } 3.28, \text{ CHCl}_3 \end{bmatrix}; {}^{1}\text{H} \text{NMR} (500 \text{ MHz}, \text{CHCl}_3) \delta 7.81 \text{ (d,} \\ J = 8.0 \text{ Hz}, 2\text{H}), 7.65 \text{ (d,} J = 8.3 \text{ Hz}, 1\text{H}), 7.33 \text{ (d,} J = 7.6 \text{ Hz}, 2\text{H}), \\ 7.29 - 7.14 \text{ (m, 2H)}, 7.10 \text{ (d,} J = 8.8 \text{ Hz}, 1\text{H}), 5.27 \text{ (s, 1H)}, 5.01 \text{ (t,} \\ J = 2.0 \text{ Hz}, 1\text{H}), 4.13 \text{ (dd,} J = 15.1, 2.3 \text{ Hz}, 1\text{H}), 3.95 \text{ (dd,} J = 15.1, \\ 1.9 \text{ Hz}, 1\text{H}), 3.11 \text{ (d,} J = 15.7 \text{ Hz}, 1\text{H}), 3.08 \text{ (d,} J = 10.8 \text{ Hz}, 1\text{H}), \\ 2.99 \text{ (d,} J = 16.5 \text{ Hz}, 1\text{H}), 2.96 \text{ (d,} J = 12.1 \text{ Hz}, 1\text{H}), 2.43 \text{ (s, 3H)}, \\ 1.75 - 1.68 \text{ (m, 1H)}; {}^{13}\text{C} \text{NMR} (126 \text{ MHz}, \text{CHCl}_3) \delta 149.2, 144.0, \\ 141.3, 140.8, 135.5, 129.9 \text{ (2C)}, 128.6, 127.6 \text{ (2C)}, 127.5, 126.4, \\ 124.7, 108.3 \text{ (t,} J = 23.7 \text{ Hz}), 70.8, 65.2, 59.8, 52.9, 39.0, 21.7; \\ \text{HRMS} \text{ (ESI-TOF) m/z } [\text{M} + \text{Na}]^{+} \text{ calcd for } \text{C}_{20}\text{H}_{20}\text{DNNaO}_3\text{S} \\ 379.1203, \text{ found } 379.1196. \end{bmatrix}$

Preparation of (5-D) by the presence of DCI: Under nitrogen atmosphere, $Pd(t-Bu_3P)_2$ (0.01664 g, 0.033 mmol) and DABCO (0.1280 g, 1.14 mmol) and 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. DCI aq (4 drops) and the reaction mixture was heated to 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 viscose oil (0.1104 g, 0.31 mmol).

Preparation of TBP complex 6a: A solution of $1g_{w}(Q_{0.6488,H}g_{*}, 0.88 \text{ mmol})$ in ether (88 mL) was added to $12M^{3}H^{2}(P^{2}(4.441))$ 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 dried over Na₂SO₄, the organic phase was filtered and concentrated in vacuo. 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 viscose oil.

[α]_D +10.6 (c 3.13, CHCl₃); ¹H NMR (500 MHz, CHCl₃) 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⁻¹H = 54.1 Hz, 1H); ¹³C NMR (126 MHz, CHCl₃) 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 C₃₂H₄₅BrClNNaO₄SSn 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 12M 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 dried over Na₂SO₄, the organic phase was filtered and concentrated in vacuo. 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 viscose oil.

[α]_D +21.7 (c 0.16, CHCl₃); ¹H NMR (500 MHz, CHCl₃) 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⁻¹H = 56.7 Hz, 1H); ¹³C NMR (126 MHz, CHCl₃) 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 C₂₈H₃₈BrNNaO₃SSn 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 12M 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 dried over Na₂SO₄, the organic phase was filtered and concentrated in vacuo. 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 viscose oil.

 $[\alpha]_{\rm D} -77.1 (c 3.18, CHCl_3); {}^{1}\text{H NMR} (500 \text{ MHz}, CHCl_3) \delta 7.16 - 7.09 (m, 4H), 6.99 (d,$ *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* $= 13.7 Hz, <math>J^{119}\text{Sn}$ -

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¹H = 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⁻¹H = 70.2 Hz, 1H); ¹³C NMR (126 MHz, CHCl₃) 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; ¹¹⁹Sn NMR (186 MHz, CDCl₃) δ 33.3; HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₈H₄₁CINO₃SSn 626.15176, found 626.15087; Anal. Calcd. for C₂₈H₄₀CINO₃SSn: 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 12M 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 dried over Na₂SO₄, the organic phase was filtered and concentrated in vacuo to give **6d** in 90% yield (0.2295 g, 0.34 mmol) as colourless viscose oil.

[α]_D –83.6 (c 0.87, CHCl₃); ¹H NMR (500 MHz, CHCl₃) 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, $J^{119}\text{Sn}^{-1}\text{H}$ = 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, CHCl₃) 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, $J^{13}C - {}^{119}Sn = 28.0 \text{ Hz}$), 28.4 (d, $J^{13}C - {}^{119}Sn = 28.0 \text{ Hz}$), 26.8 (d, $J^{13}C - {}^{119}Sn = 82.9 \text{ Hz}, J^{13}C - {}^{117}Sn = 80.5 \text{ Hz}), 26.7 \text{ (d, } J^{13}C - {}^{119}Sn$ = 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, $J^{13}C - {}^{117}Sn = 410.8 \text{ Hz}$, 20.3 (d, $J^{13}C - {}^{119}Sn = 400.0 \text{ Hz}$, $J^{13}C - {}^{119}Sn = 400.0 \text{ Hz}$, $J^{13}C - {}^{119}Sn = 400.0 \text{ Hz}$, $J^{13}C - {}^{119}Sn = {}^{110}Sn = {}^{110}Sn$ 117 Sn = 381.4 Hz), 13.7, 13.6; 119 Sn NMR (186 MHz, CDCl₃) δ 28.8; HRMS (ESI-TOF) m/z [M + Na]⁺ calcd for C₂₈H₄₀BrNNaO₃SSn 692.08319, found 692.08200; Anal. Calcd. for C₂₈H₄₀BrNO₃SSn: 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 (5g 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.

[α]_D –82.5 (c 0.08, CHCl₃); ¹H NMR (500 MHz, CHCl₃) 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–¹H = 73.2 Hz, 1H); ¹³C NMR (126 MHz, CHCl₃) 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); ¹¹⁹Sn NMR (186 MHz, CDCl₃) δ 15.56 (d, *J* = 2081.5 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ –183.8 (d, *J* = 2052.9 Hz); HRMS (ESI-TOF) m/z [M + Na]⁺ calcd for C₂₈H₄₀FNNaO₃SSn 632.1633, found 632.1626. Journal Name

Preparation of (3aR,8bS)-tert-butyl 3-methylenent to sple 1,2,3,3a,4,8b-hexahydroindeno[1,2-b]pyrole 3a-carboxylate (7): Under nitrogen atmosphere, Pd(t-Bu₃P)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 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 viscose oil (0.1172 g, 0.280 mmol). [α]_D +21.3 (c 0.45, CHCl₃); ¹H NMR (500 MHz, CHCl₃) δ 7.83 (d,

 $J = 7.5 Hz, 2H), 7.75 - 7.67 (m, 1H), 7.31 (d, J = 9.1 Hz, 2H), 7.28 - 7.23 (m, 2H), 7.12 (d, J = 6.1 Hz, 1H), 5.80 (s, 1H), 5.29 (s, 1H), 5.09 (s, 1H), 4.17 (dt, J = 14.2, 2.5 Hz, 1H), 3.90 (dt, J = 14.2, 1.8 Hz, 1H), 3.49 (d, J = 16.9 Hz, 1H), 3.22 (d, J = 16.4 Hz, 1H), 2.41 (s, 3H), 1.30 (s, 9H); ¹³C NMR (126 MHz, CHCl₃) <math>\delta$ 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 C₂₄H₂₇NNaO₄S 448.1559, found 448.1560.

Conversion of compound 7 to 5: DIBAL (1.5 M in CH₂Cl₂, 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 Na₂SO₄. After filtration, the solution was concentrated in vacuo to give crude product that was purified by recycled GPC top 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, CHCl₃); ¹H NMR (500 MHz, CHCl₃) 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); ¹³C NMR (126 MHz, CHCl₃) 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 $[M + Na]^{\dagger}$ calcd for C₂₀H₂₁NNaO₃S 378.1140, found 378.1129.

Coupling reaction of 6b to give 5 (Scheme 5): Under nitrogen atmosphere, $Pd(t-Bu_3P)_2$ (0.01615 g, 0.0316 mmol) and DABCO (0.1130 g, 0.948 mmol) and 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 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 viscose oil (0.0656 g, 0.185 mmol).

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Notes and references

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