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AgNTf$_2$-MEDIATED ARYLATION OF BROMOPYRROLOINDOLINES

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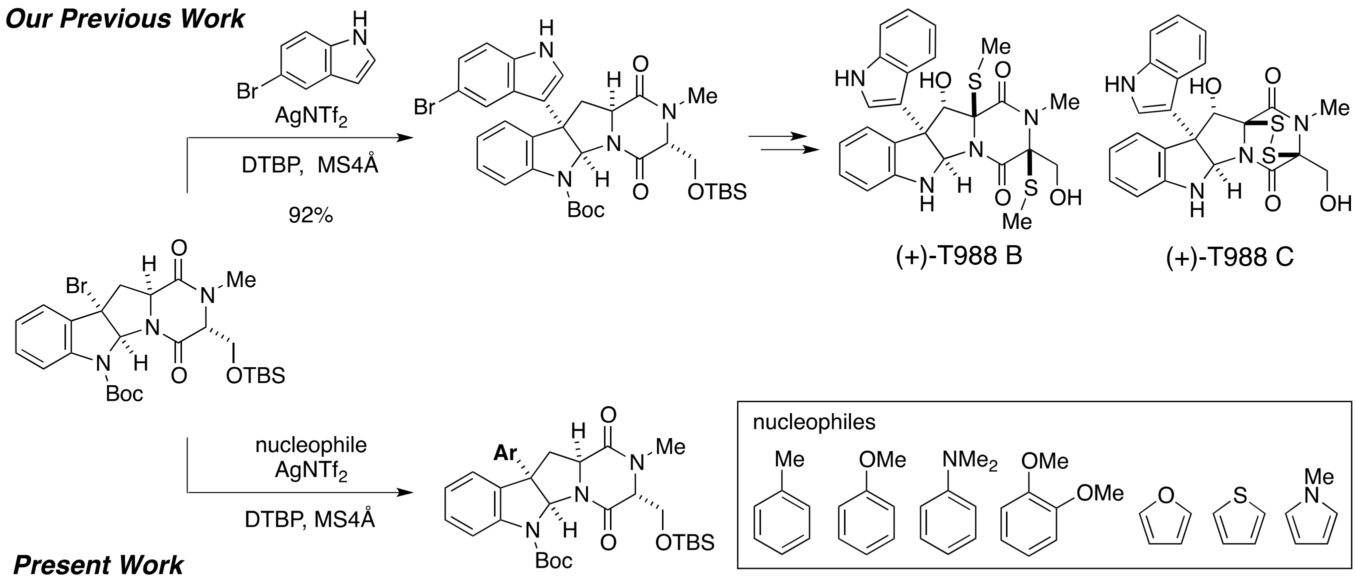
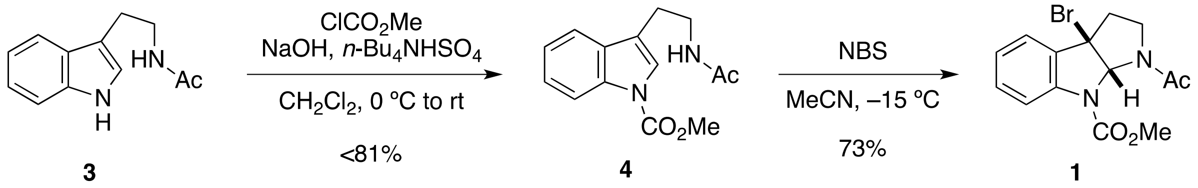
Abstract – The silver(I)-mediated arylation of bromopyrroloindolines was developed. The selection of silver salts was crucial to obtain arylated compounds in high yields. Among the various tested silver(I) salts, AgNTf$_2$ was the most effective agent for arylation. Reactions using various electron-rich aromatic compounds revealed that the developed conditions are suitable for the arylation of a broad range of aromatic compounds, including benzene derivatives, furan, thiophene, and pyrrole.

Hexahydropyrroloindole alkaloids have attracted considerable attention as promising lead compounds for antitumor agents because of their potent biological activity and broad structural diversity.[1] Recently, extensive synthetic studies[2] and the structure-activity relationship (SAR) of natural and unnatural derivatives of this family have thoroughly been investigated.[3] These studies indicated that substitution of an aryl group at the 3*a* position of the pyrroloindole skeleton is an indispensable structural motif to render significant bioactivities. To construct pyrroloindolines with aryl groups on the 3*a* position, several synthetic methodologies have been established.[4-8] Among these strategies, the arylation[4] of bromopyrroloindolines with electron-rich aromatic compounds is advantageous because of its synthetic convergence and versatility for synthesizing various congeners. In this regard, Movassaghi[4a,4c-f] and Qin[4b] have independently reported pioneering studies on the arylation of bromopyrroloindolines using silver(I) as the activating agent. Recently, during the project on the synthesis of a dimeric indole alkaloid, (+)-haplophytine, our group has found that AgNTf$_2$ is a suitable silver(I) salt to facilitate the arylation of iodoindolenine derivatives. The utility of the AgNTf$_2$-mediated reaction conditions developed by our group was demonstrated by the efficient total syntheses of (+)-T988 B and (+)-T988 C (Scheme 1).[4g] Herein, the AgNTf$_2$-mediated arylation of bromopyrroloindolines with a broad range of aromatic compounds was systematically examined.



Scheme 1. The key reaction in our total syntheses of T988 B and C and this study

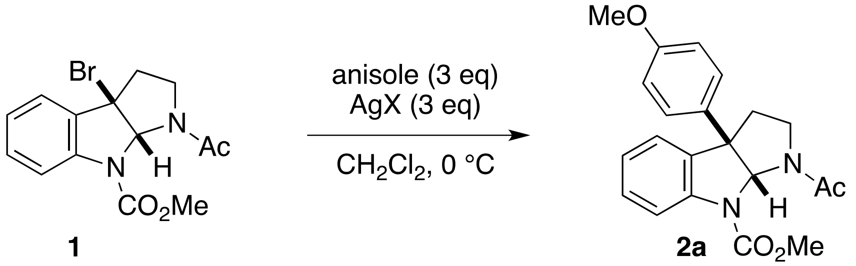
At the outset of our research, a simple bromopyrroloindoline **1** was selected as a model substrate, and arylation with anisole was examined using various silver salts. Bromopyrroloindoline **1** was prepared from *N*-acetyltryptamine (**3**) via the protection of the indole nitrogen and subsequent bromocyclization with *N*-bromosuccinimide (NBS).



Scheme 2. Preparation of bromopyrroloindoline (**1**)

Initially, **1**[9] was treated with three equivalents of anisole in dichloromethane at 0 °C in the presence of $AgBF_4$ according to the conditions reported by Movassaghi (entry 1).[4c] The desired coupling product **2a** was obtained, although in a low yield of 46%. Next, we examined a series of silver(I) salts, including AgOTf, $AgSbF_6$, and $AgNTf_2$, as the activating agents. The yield of **2a** was slightly improved with the use of AgOTf and $AgSbF_6$ (entries 2 and 3, respectively). As we expected, $AgNTf_2$ afforded the desired product in a high yield of 72% (entry 4);[4g] this yield was slightly improved with the increase in the amount of anisole up to five equivalents (entry 5).

Table 1. Ag-Mediated coupling of bromopyrroloindoline **1** with anisole

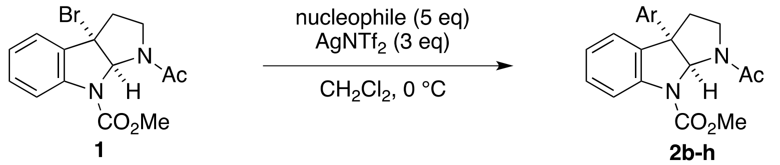


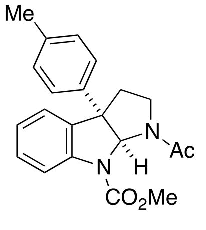
entry	AgX	yield (%)
1	$AgBF_4$	46
2	AgOTf	51
3	$AgSbF_6$	60
4	$AgNTf_2$	72
5[a]	$AgNTf_2$	74

[a] Five equivalents of anisole was used.

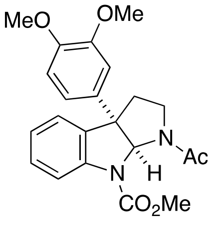
Having proved the efficiency of AgNTf$_2$, the scope of electron-rich aromatic compounds for arylation was investigated (Table 2). Toluene, veratrole, and furan were incorporated into the pyrroloindoline skeleton to afford **2b**, **2c**, and **2d** in 74%, 83%, and 67% yields, respectively. In these cases, other isomers were not detected. On the contrary, reaction with thiophene afforded a 9.1:1 mixture of regioisomers **2e** and **2f** in an excellent combined yield. Finally, bicyclic arene, naphthalene, also served as a good nucleophile to give a mixture of adducts **2g** and **2h** in moderate yields.

Table 2. AgNTf$_2$-Mediated arylation of bromopyrroloindoline **1** derived from tryptamine derivative

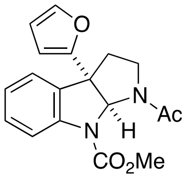




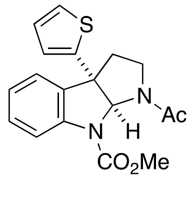
2b, 74%



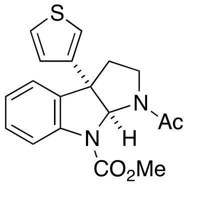
2c, 83%



2d, 67%

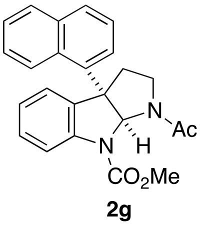


2e

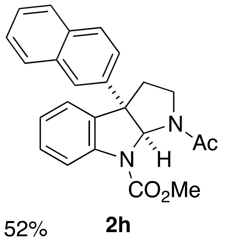


2f

90%
2e:**2f** = 9.1:1



2g

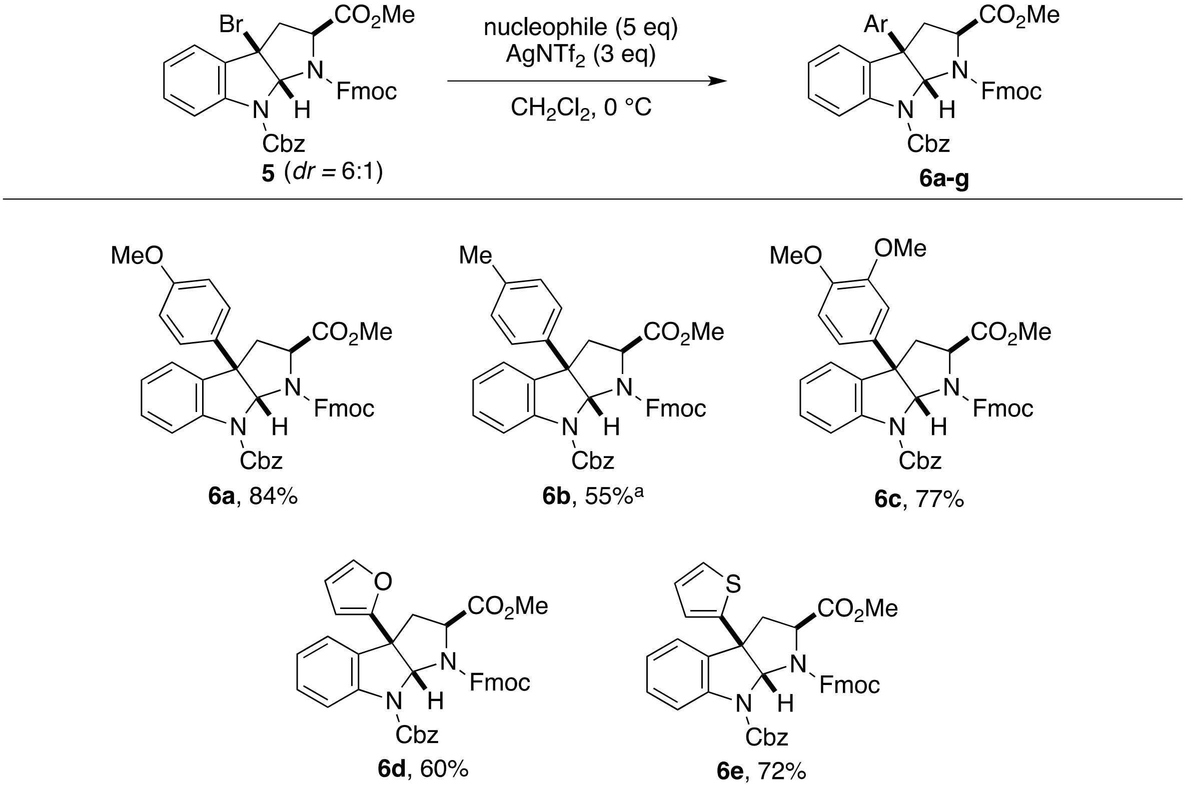


2h

52%
2g:**2h** = 1.4:1

Then, the scope of arylation to bromopyrroloindoline **5** derived from L-tryptophan methyl ester was investigated (Table 3).[10] As expected, anisole, toluene, veratrole, furan, and thiophene were successfully coupled with **5**, affording products **6a**–**e**, respectively. In all cases, the other regioisomer was not detected.

Table 3. AgNTf$_2$-Mediated arylation of bromopyrroloindoline **5** derived from L-tryptophane derivative



5 (*dr* = 6:1)

6a-g

6a, 84%

6b, 55%[a]

6c, 77%

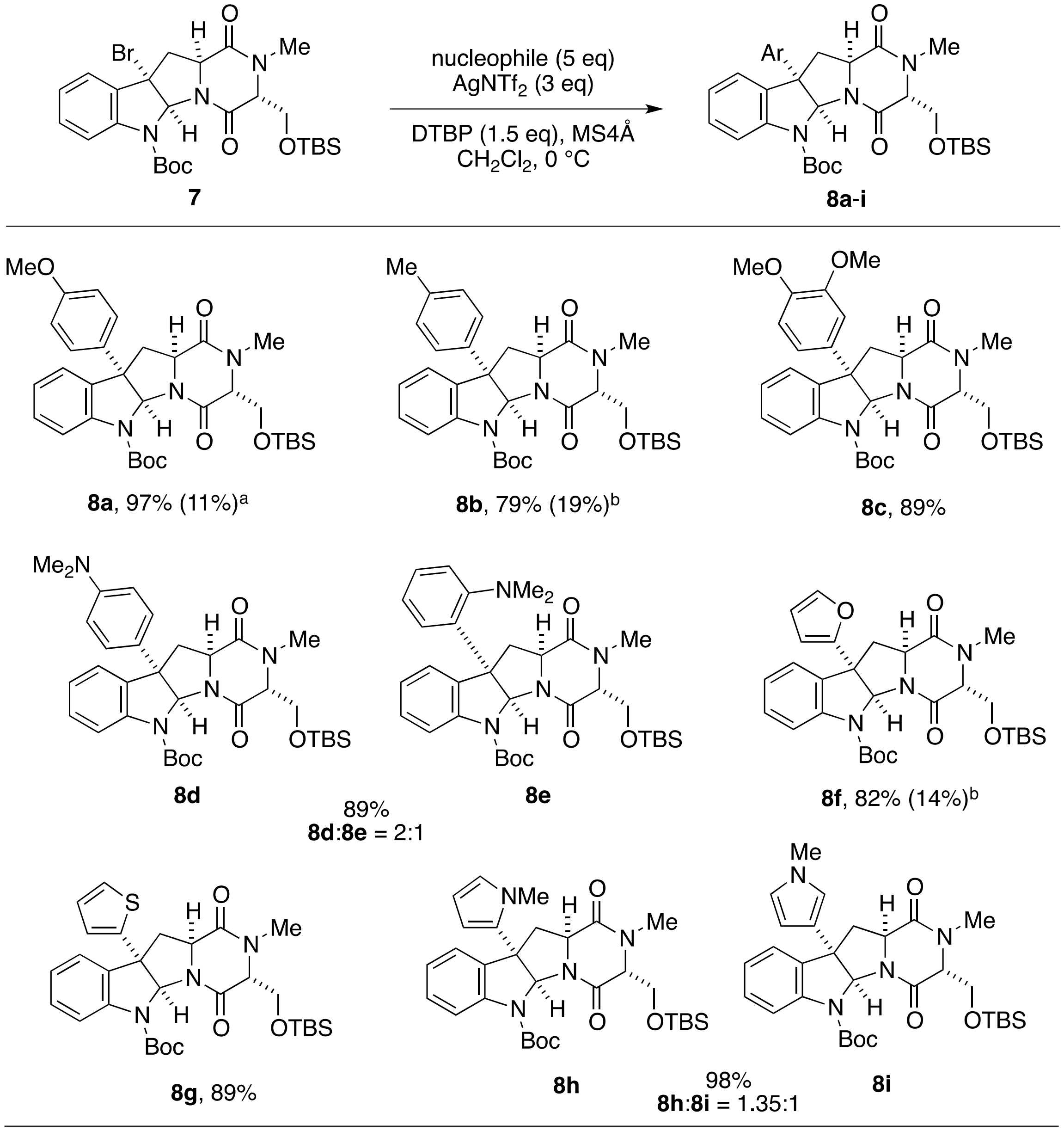
6d, 60%

6e, 72%

[a] Ten equivalents of toluene was used.

Considering applications to examine the SAR of T988 analogs, the arylation of highly functionalized bromopyrroloindoline **7** bearing a diketopiperadine unit, the intermediate in the total synthesis of T988s was examined.[4g] However, the established standard conditions, i.e., treatment with three equivalents of AgNTf$_2$ and five equivalents of anisole, afforded the desired product **8a** in merely 11% yield because of the cleavage of Boc and/or TBS groups (Table 4, data in parentheses). These side reactions were suppressed by the addition of 2,6-di-*tert*-butylpyridine and 4Å molecular sieves according to our previous study.[4g] Under these modified reaction conditions, various substituted benzenes, including anisole, toluene, veratrole, and *N,N*-dimethylaniline, were treated with **7** to furnish the corresponding coupling products **8a**–**e** in high-to-excellent yields. For *N*,*N*-dimethylaniline, a mixture of *ortho* and *para* products was obtained in a 2:1 ratio in a high combined yield. Furthermore, this methodology was applied to heteroaromatic compounds such as furan, thiophene, and *N*-methylpyrrole. The corresponding coupling products **8f**–**i** were obtained in high yield. For *N*-methylpyrrole, a mixture of products was obtained because of the coupling at 2- and 3-positions of the pyrrole ring. The established conditions using $AgNTf_2$ were superior to the conventional conditions. Thus, the arylation of **7** with a relatively less reactive toluene or acid-labile furan under the conditions[4c] reported by Movassaghi ($AgBF_4$, DTBMP, $EtNO_2$, 0 °C) led to low product yields (**8b**: 19%, **8f**: 14%).

Table 4. $AgNTf_2$-Mediated arylation of diketopiperazine-fused bromopyrroloindoline **7**



[a] The yield in the parenthesis resulted from the reaction under the condition optimized in Table 1.
[b] The yields in the parentheses resulted from the reaction under the Movassaghi's condition[4c]; $AgBF_4$ (3 eq), nucleophile (4 eq), and 2,6-di-*tert*-butyl-4-methylpyridine (1.2 eq) were used in nitroethane at 0 °C.

In conclusion, the $AgNTf_2$-mediated arylation of bromopyrroloindolines with various aromatic compounds was developed. The feasibility of the reaction conditions was demonstrated using several bromopyrroloindolines, including highly functionalized synthetic intermediate of alkaloid T988s.

EXPERIMENTAL

Materials were obtained from commercial suppliers and used without further purification unless otherwise mentioned. All reactions were carried out in oven-dried glassware under a slight positive pressure of argon unless otherwise noted. Anhydrous CH_2Cl_2 was purchased from Kanto Chemical Co. Inc. Anhydrous DMF was purchased from Wako Pure Chemical Industries. Flash column chromatography was performed on Silica Gel 60N (Kanto, spherical neutral, 40–50 μm) using the indicated eluent. Preparative TLC was performed on Merck 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel. Analytical TLC was performed on Merck 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel. All melting points were determined on a Yanaco micro melting point apparatus and uncorrected. IR spectra were measured on a JASCO FT/IR-4100 spectorometer. NMR spectra were recorded on a JNM-AL400 or a JEOL ECA600 spectrometer with tetramethylsilane (0 ppm) and chloroform (7.26 ppm) as an internal standard. Chemical shifts were expressed in δ (ppm) values, and coupling constants were expressed in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, and br = broad. Mass spectra were recorded on a Brucker micrOTOF II (ESI). Optical rotations were measured on a Horiba SEPA-300 high sensitive polarimeter.

Methyl carbamate 4

To a stirred solution of acetyltryptamine **3** (10.8 g, 53.4 mmol), *n*-Bu_4NHSO_4 (1.81 g, 5.34 mmol), and NaOH (10.8 g, 267 mmol) in CH_2Cl_2 (178 mL) was added $ClCO_2Me$ (12.4 mL, 160 mmol) at 0 °C. After stirring for 5 min, the resulting mixture was allowed to warm up to room temperature and stirring for 4 h. The reaction was quenched with 1 M aqueous HCl at 0 °C. The mixture was extracted with CH_2Cl_2 three times. The extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by recrystallization from EtOAc/hexanes to afford amide **4** including inseparable impurities (<11.2 g, <43.2 mmol, <81%) as a white powder; mp 137 °C; IR (neat, cm^{-1}) 3287, 3080, 2955, 2934, 1735, 1653, 1457, 1443, 1382, 1256, 1093, 747; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (1H, d, *J* = 7.6 Hz), 7.54 (1H, d, *J* = 8.0 Hz), 7.42 (1H, s), 7.34 (1H, dd, *J* = 8.0, 7.2 Hz), 7.26 (1H, dd, *J* = 7.6, 7.2 Hz), 5.77 (1H, brs), 4.01 (3H, s), 3.58 (1H, t, *J* = 6.8 Hz), 3.57 (1H, t, *J* = 6.8 Hz), 2.91 (2H, t, *J* = 6.8 Hz), 1.96 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 151.2, 135.5, 130.2, 124.7, 122.8, 122.5, 118.8, 118.6, 115.1, 53.6, 38.9, 25.0, 23.1; HRMS (ESI) calcd. for $C_{14}H_{17}N_2O_3$ $[M+H]^+$, 261.1234; found 261.1234.

Bromopyrroloindoline 1

To a stirred solution of amide **4** (1.81 g, 6.95 mmol) in MeCN (70 mL) was added NBS (1.87 g, 10.4 mmol) at –15 °C. After stirring for 1 h, the resulting mixture was gradually allowed to warm up to room temperature and stirring for 3 h. The reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was extracted with EtOAc three times. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: hexanes/toluene/acetone = 1/2/1) to afford bromopyrroloindoline **1** (1.71 g, 5.04 mmol, 73%) as a pale brown foam; IR (neat, cm^{-1}) 3001, 2954, 2884, 1717, 1668, 1656, 1481, 1443, 1399, 1325, 753; ^1H NMR (400 MHz, $CDCl_3$, 55 °C, a mixture of rotamers) δ 7.62 (1H, brs), 7.39 (1H, d, J = 8.0 Hz), 7.32 (1H, dd, J = 8.0, 7.2 Hz), 7.15 (1H, dd, J = 7.2, 7.2 Hz), 6.44 (1H, brs), 4.09 (1H, brs), 3.92 (3H, s), 2.82–2.70 (3H, brs), 2.28 (3H, brs); ^{13}C NMR (100 MHz, $CDCl_3$, 55 °C, a mixture of rotamers) δ 171.2, 170.0, 153.8, 141.1, 132.4, 130.6, 130.4, 128.7, 124.8, 123.9, 123.5, 117.2, 85.3, 68.1, 62.4, 54.4, 53.1, 45.1, 41.7, 38.8, 30.4, 28.8, 24.3, 23.8, 22.8, 21.8, 13.8, 10.8; HRMS (ESI) calcd. for $C_{14}H_{15}BrN_2NaO_3$ $[M+Na]^+$, 361.0158; found 361.0155.

General Procedure for Ag-Mediated Coupling of Bromopyrroloindoline 1

Anisole adduct 2a

Bromopyrroloindoline **1** (19.8 mg, 58.4 μmol) was dried azeotropically (concentration of a benzene solution) under reduced pressure and placed under an argon atmosphere. After addition of anhydrous CH_2Cl_2 (0.29 mL) and anisole (32.0 μL, 294 μmol), the solution was cooled to 0 °C and poured into a stirred suspension of $AgNTf_2$ (67.7 mg, 174 μmol) in CH_2Cl_2 (0.29 mL) via cannula at 0 °C. After stirring at the same temperature for 20 min, the reaction was quenched with saturated aqueous $NaHCO_3$ and vigorously stirred for 30 min at room temperature. The reaction mixture was extracted three times with CH_2Cl_2. The combined organic extracts were filtered through a pad of Celite and the filter cake was washed with CH_2Cl_2. The resulting solution was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 1/4) to afford an anisole adduct **2a** (15.3 mg, 41.8 μmol, 72%) as a white foam; IR (neat, cm^{-1}) 2952, 2918, 2848, 1713, 1654, 1483, 1442, 1404, 1253, 1033, 753; ^1H NMR (400 MHz, $CDCl_3$, 55 °C) δ 7.80–7.58 (1H, m), 7.29–7.22 (1H, m), 7.14–7.04 (4H, m), 6.82 (1H, d, J = 8.8 Hz), 6.20 (1H, br s), 4.47–4.26 (1H, m), 3.86 (3H, s), 3.75 (3H, s), 2.98–2.77 (1H, m), 2.58–2.00 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$, 55 °C) δ 170.4, 158.9, 154.0, 141.7, 135.3, 134.7, 128.6, 127.0, 124.1, 116.8, 114.3, 114.0, 84.7, 61.0, 55.2, 52.9, 44.6, 37.5, 21.9; HRMS (ESI) calcd. for $C_{21}H_{22}N_2NaO_4$ $[M+Na]^+$, 389.1472; found 389.1465.

Toluene adduct 2b

According to the general procedure described for **2a**, the toluene adduct **2b** was obtained from **1** with toluene in 59.8 μmol scale (15.5 mg, 44.2 μmol, 74%); a white foam; IR (neat, cm^{-1}) 2952, 2880, 1713, 1659, 1483, 1442, 1403, 1319, 816, 565; ^1H NMR (400 MHz, DMSO-d_6, 120 °C) δ 7.61 (1H, d, J = 8.0 Hz), 7.27 (1H, dd, J = 8.0, 7.4 Hz), 7.25 (1H, d, J = 8.0 Hz), 7.15–7.12 (4H, m), 7.09 (1H, dd, J = 8.0, 7.4

Hz), 6.29 (1H, s), 4.05 (1H, dd, *J* = 10.4, 6.8 Hz), 3.79 (3H, s), 2.88–2.78 (1H, m), 2.56–2.46 (2H, m), 2.26 (3H, s), 2.10 (3H, s); ^{13}C NMR (100 MHz, DMSO-*d*$_6$, 120 °C) δ 168.4, 152.9, 140.8, 139.2, 135.7, 135.0, 128.7, 127.7, 125.0, 123.6, 123.4, 115.6, 82.4, 59.6, 52.1, 45.0, 35.8, 21.3, 19.7; HRMS (ESI) calcd. for $C_{21}H_{22}N_2NaO_3$ [M+Na]$^+$, 373.1523; found 373.1526.

Veratrole adduct 2c

According to the general procedure described for **2a**, the veratrole adduct **2c** was obtained from **1** with veratrole in 60.7 μmol scale (19.9 mg, 50.2 μmol, 83%); a white foam; IR (neat, cm^{-1}) 3001, 2953, 2835, 1714, 1654, 1519, 1442, 1406, 1254, 1025, 743; ^{1}H NMR (400 MHz, CD_3CN, 75 °C) δ 7.64 (1H, d, *J* = 8.0 Hz), 7.27 (1H, dd, *J* = 8.0, 7.4 Hz), 7.23 (1H, d, *J* = 8.0 Hz), 7.09 (1H, dd, *J* = 8.0, 7.4 Hz), 6.84 (1H, d, *J* = 8.4 Hz), 6.81 (1H, d, *J* = 2.0 Hz), 6.75 (1H, dd, *J* = 8.4, 2.0 Hz), 6.29 (1H, s), 4.11–3.96 (1H, m), 3.79 (3H, s), 3.75 (3H, s), 3.73 (3H, s), 2.96–2.78 (1H, m), 2.58–2.45 (2H, m), 2.10 (3H, br s); ^{13}C NMR (100 MHz, CD_3CN, 75 °C) δ 170.9, 155.4, 151.1, 150.2, 143.2, 137.4, 137.1, 131.2, 129.8, 125.5, 125.4, 119.7, 114.1, 112.1, 84.9, 57.10, 57.05, 57.0, 53.8, 46.8, 37.5, 22.9; HRMS (ESI) calcd. for $C_{22}H_{24}N_2NaO_5$ [M+Na]$^+$, 419.1577; found 419.1567.

Furan adduct 2d

According to the general procedure described for **2a**, the furan adduct **2d** was obtained from **1** with furan in 59.0 μmol scale (12.8 mg, 39.2 μmol, 67%); a white foam; IR (neat, cm^{-1}) 2953, 2881, 1716, 1655, 1485, 1443, 1404, 1266, 1015, 739; ^{1}H NMR (400 MHz, DMSO-*d*$_6$, 120 °C) δ 7.62 (1H, d, *J* = 8.0 Hz), 7.53 (1H, d, *J* = 1.6 Hz), 7.30 (1H, d, *J* = 7.4 Hz), 7.30 (1H, dd, *J* = 8.0, 7.4 Hz), 7.11 (1H, dd, *J* = 7.4, 7.4 Hz), 6.37 (1H, dd, *J* = 3.6, 1.6 Hz), 6.32 (1H, s), 6.16 (1H, d, *J* = 3.6 Hz), 4.07 (1H, dd, *J* = 10.8, 8.0 Hz), 3.79 (3H, s), 2.98–2.86 (1H, m), 2.52–2.45 (1H, m), 2.39 (1H, dd, *J* = 12.8, 5.6 Hz), 2.12 (3H, s); ^{13}C NMR (150 MHz, CD_3CN, 75 °C) δ 170.9, 156.4, 155.3, 144.1, 143.5, 134.3, 130.2, 125.41, 125.38, 117.7, 111.7, 107.5, 82.6, 58.2, 53.7, 45.5, 37.0, 22.7; HRMS (ESI) calcd. for $C_{18}H_{18}N_2NaO_4$ [M+Na]$^+$, 349.1159; found 349.1159.

Thiophene adducts 2e and 2f

According to the general procedure described for **2a**, the thiophene adducts **2e** and **2f** were obtained from **1** with thiophene in 59.0 μmol scale (18.1 mg, 52.9 μmol, 90%, **2e**:**2f** = 9.1:1).

2'-Adduct **2e**; a white foam; IR (neat, cm^{-1}) 3071, 2952, 2881, 1714, 1660, 1482, 1442, 1403, 1269, 1051, 704; ^{1}H NMR (600 MHz, CD_3CN, 75 °C) δ 7.67 (1H, d, *J* = 7.2 Hz), 7.33 (1H, dd, *J* = 8.1, 7.2 Hz), 7.31 (1H, d, *J* = 7.5 Hz), 7.28 (1H, d, *J* = 4.5 Hz), 7.14 (1H, dd, *J* = 8.1, 7.5 Hz), 6.96 (1H, dd, *J* = 4.5, 4.2 Hz), 6.89–6.85 (1H, m), 6.22 (1H, s), 4.26–3.94 (1H, m), 3.81 (3H, s), 3.02–2.75 (1H, m), 2.66–2.55 (2H, m), 2.12 (3H, br s); ^{13}C NMR (150 MHz, CD_3CN, 75 °C) δ 170.9, 155.4, 148.4, 143.1, 136.6, 130.3, 128.5, 126.3, 125.6, 125.5, 125.3, 125.2, 85.8, 59.8, 53.8, 46.6, 38.8, 22.9; HRMS (ESI) calcd. for $C_{18}H_{18}N_2NaO_3S$ $[M+Na]^+$, 365.0930; found 365.0931.

3'-Adduct **2f**; a colorless oil; IR (neat, cm^{-1}) 2952, 2920, 2888, 2850, 1713, 1656, 1483, 1442, 1405, 1320, 1137, 1050, 789; ^1H NMR (400 MHz, DMSO-d_6, 120 °C) δ 7.61 (1H, d, J = 8.0 Hz), 7.49–7.45 (1H, m), 7.31 (1H, d, J = 7.6 Hz), 7.28 (1H, dd, J = 8.0, 7.6 Hz), 7.20–7.16 (1H, m), 7.11 (1H, dd, J = 7.6, 7.6 Hz), 6.98 (1H, dd, J = 4.8, 1.2 Hz), 6.25 (1H, s), 4.02 (1H, dd, J = 10.8, 7.2 Hz), 3.79 (3H, s), 2.90–2.77 (1H, m), 2.58–2.43 (2H, m), 2.10 (3H, s); ^{13}C NMR (100 MHz, DMSO-d_6, 120 °C) δ 168.5, 153.0, 143.1, 140.7, 134.7, 127.8, 126.6, 125.4, 123.5, 123.3, 120.2, 115.7, 82.1, 57.3, 52.1, 44.8, 36.1, 21.3; HRMS (ESI) calcd. for $C_{18}H_{18}N_2NaO_3S$ $[M+Na]^+$, 365.0930; found 365.0927.

Naphthalene adducts 2g and 2h

According to the general procedure described for **2a**, the naphthalene adducts **2g** and **2h** were obtained from **1** with naphthalene in 0.269 mmol scale (54.4 mg, 0.141 mmol, 52%, **2g**:**2h** = 1.4:1).

1'-Adduct **2g**; a white foam; IR (neat, cm^{-1}) 2953, 2917, 2849, 1714, 1659, 1484, 1442, 1401, 777, 752; ^1H NMR (400 MHz, $CDCl_3$, 55 °C, a mixture of two rotamers) δ 7.89 (1H, m), 7.78–7.77 (3H, m), 7.48–7.46 (2H, m), 7.35–7.31 (3H, m), 7.22 (1H, d, J = 7.6 Hz), 7.14 (1H, dd, J = 7.6, 7.2 Hz), 6.67 (1H, s), 4.59 (1H, brs), 3.80 (3H, s), 3.10 (1H, m), 2.96 (1H, m), 2.33 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$, 55 °C, a mixture of two rotamers) δ 154.0, 141.6, 136.8, 135.2, 135.1, 131.0, 130.0, 129.2, 128.9, 126.6, 126.4, 125.5, 124.8, 124.2, 123.9, 116.9, 83.5, 52.9, 44.5, 39.2, 38.9; HRMS (ESI) calcd. for $C_{24}H_{22}N_2N_aO_3$ $[M+Na]^+$, 409.1523; found 409.1505.

2'-Adduct **2h**; an orange oil; IR (neat, cm^{-1}) 3009, 2953, 2928, 1714, 1657, 1483, 1442, 1405, 751; ^1H NMR (400 MHz, $CDCl_3$, 55 °C, a mixture of two rotamers) δ 7.80–7.73 (4H, m), 7.64 (1H, s), 7.46–7.43 (2H, m), 7.30–7.28 (2H, m), 7.17 (1H, d, J = 7.2 Hz), 7.09 (1H, dd, J = 8.0, 7.2 Hz), 6.35 (1H, s), 4.46 (1H, m), 3.87 (3H, s), 2.95 (1H, m), 2.70 (1H, m), 2.53 (1H, m), 2.30 (3H, brs); ^{13}C NMR (100 MHz, $CDCl_3$, 55 °C, a mixture of two rotamers) δ154.1, 139.8, 135.0, 133.3, 132.6, 129.1, 128.9, 128.1, 127.5, 126.6, 126.5, 126.4, 126.3, 124.9, 124.4, 124.1, 116.9, 84.6, 53.0, 44.5, 37.7, 29.7; HRMS (ESI) calcd. for $C_{24}H_{22}N_2NaO_3$ $[M+Na]^+$, 409.1523; found 409.1509.

Preparation of Bromopyrroloindoline 5

To the stirred solution of L-tryptophane methyl ester hydrochloride (9.93 g, 39.0 mmol) and K_2CO_3 (5.57 g, 40.3 mmol) in H_2O (100 mL) was added Boc_2O (9.23 g, 40.5 mmol) in acetone (100 mL) at 0 °C. After stirring at the same temperature for 1 h, the reaction mixture was concentrated under reduced pressure. The residue was extracted three times with EtOAc. The extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was used in the next reaction without further purification.

To the stirred solution of the above crude Boc protected L-tryptophane derivative, NaOH (3.86 g, 96.6 mmol) and *n*-Bu_4NHSO_4 (1.33 g, 3.92 mmol) in CH_2Cl_2 (150 mL) was added CbzCl (11.0 mL, 78.0 mmol) at room temperature. After stirring at the same temperature for 30 min, the reaction was quenched with 1 M aqueous HCl. The mixture was extracted three times with CH_2Cl_2. The extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was used in the next reaction without further purification.

To the crude Boc and Cbz protected L-tryptophane derivative was added TFA (39 mL, 510 mmol) at 0 °C. After stirring for 2 h, the resulting mixture was allowed to warm up to room temperature and stirring for 2 h. The reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was extracted three times with CH_2Cl_2. The extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was used in the next reaction without further purification.

To the stirred solution of crude Cbz protected L-tryptophane derivative, in 1,4-dioxane (40 mL) and 10% aqueous $NaHCO_3$ (73 mL) was added FmocCl (11.2 g, 43.3 mmol) in 1,4-dioxane (80 mL) at 0 °C. After stirring at the same temperature for 40 min, the reaction was quenched with H_2O. The mixture was extracted three times with EtOAc. The extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by recrystallization from $CHCl_3$ to afford L-tryptophane derivative including inseparable impurities (<8.79 g, <15.3 mmol, <39%) as a white solid and the product was used in the next reaction without further purification.

To a stirred solution of the above tryptophan (7.70 g, 13.5 mmol) in CH_2Cl_2 (270 mL) was added NBS (2.41 g, 13.5 mmol) and PPTS (3.40 g, 13.5 mmol) at 0 °C. After the resulting mixture was stirred for 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2 three times. The extract was washed with H_2O, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: EtOAc/hexanes = 1/9 to 1/4) to afford bromopyrroloindoline **5** as a colorless foam (7.77 g, 11.8 mmol, 88%, dr = 6:1); IR (neat, cm^{-1}) 3032, 2952, 1723, 1715, 1479, 1415, 1320, 1248, 1208, 1168, 754, 698; ^1H NMR (400 MHz, $CDCl_3$, 50 °C, a mixture of two rotamer) δ 7.74–7.71 (3H, m), 7.52–7.10 (14H, m), 6.56 (1H, s), 5.28 (1H, m), 5.13 (1H, d, *J* = 12 Hz), 4.22 (1H, m), 4.13 (1H, m), 4.01 (1H, m), 3.67 (1H, s), 3.31 (1H, dd, *J* = 13.2, 6.8 Hz), 2.89 (1H, dd, *J* = 13.2, 10.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 50 °C, a mixture of two rotamer) δ□171.0, 153.2, 143.9, 143.7, 141.3, 140.9, 135.7, 132.8, 131.0, 128.5, 128.4, 128.2, 128.0, 127.7, 127.2, 127.0, 125.1, 125.0, 123.4, 123.3, 119.9, 118.3, 118.1, 84.3, 68.2, 59.8, 59.6, 59.5, 52.6, 52.5, 46.9, 41.9; HRMS (ESI) calcd. for $C_{35}H_{29}BrN_2NaO_6$ $[M+Na]^+$, 675.1107; found 675.1100.

Ag-Mediated Coupling of Bromopyrroloindoline 5

Anisole adduct 6a

According to the general procedure described for **2a**, the anisole adduct **6a** was obtained from **5** with anisole in 32.0 μmol scale (18.2 mg, 26.7 μmol, 84%); a white foam; IR (neat, cm^{-1}) 3064, 3034, 3006, 2952, 2897, 2836, 1749, 1716, 1480, 1415, 1254, 1031, 740; ^{1}H NMR (400 MHz, CDCl$_3$, 55 °C) δ 7.73–7.70 (3H, m), 7.55 (1H, d, *J* = 7.2 Hz), 7.47 (1H, d, *J* = 6.8 Hz), 7.38–7.11 (12H, m), 7.06 (2H, d, *J* = 8.0 Hz), 6.76 (2H, d, *J* = 8.4 Hz), 6.51 (1H, s), 5.26–5.05 (2H, m), 4.25–4.10 (4H, m), 3.73 (3H, s), 3.67 (3H, s), 3.01 (1H, dd, *J* = 12.4, 7.2 Hz), 2.70 (1H, m); ^{13}C NMR (100 MHz, CDCl$_3$, 55 °C) δ□172.3, 159.0, 153.3, 144.0, 141.29, 141.26, 141.17, 136.1, 135.3, 132.8, 129.1, 128.4, 128.0, 127.6, 127.1, 127.0, 126.94, 126.89, 125.2, 125.1, 123.6, 119.8, 114.4, 83.3, 67.7, 59.9, 55.2, 52.3, 47.0, 39.3, 19.3, 14.1; HRMS (ESI) calcd. for $C_{42}H_{36}N_2NaO_7$ [M+Na]$^+$, 703.2420; found 703.2391.

Toluene adduct 6b

According to the general procedure described for **2a**, the toluene adduct **6b** was obtained from **5** with toluene (32.6 μL, 306 μmol) in 0.310 mmol scale (11.4 mg, 171 μmol, 55%); a white foam; IR (neat, cm^{-1}) 3423, 3030, 2951, 1715, 1480, 1450, 1415, 1331, 1265, 1212, 1173, 1157, 753, 742; ^{1}H NMR (400 MHz, CD$_3$CN, 75 °C) δ 7.77 (1H, dd, *J* = 6.8, 5.6 Hz), 7.68 (1H, d, *J* = 8.4 Hz), 7.56–7.18 (17H, m), 7.09–7.03 (2H, m), 6.41 (1H, s), 5.26 (1H, d, *J* = 12.0 Hz), 5.10 (1H, d, *J* = 12.0 Hz), 4.32 (1H, dd, *J* = 10.4, 7.2 Hz), 4.22 (1H, dd, *J* = 9.2, 7.2 Hz), 4.13 (1H, dd, *J* = 7.2, 7.2 Hz), 4.00 (1H, dd, *J* = 9.2, 7.2 Hz), 3.60 (3H, s), 3.11 (1H, dd, *J* = 13.2, 7.2 Hz), 2.60 (1H, dd, *J* = 13.2, 10.4 Hz), 2.25 (3H, s); ^{13}C NMR (100 MHz, CD$_3$CN, 75 °C, a mixture of two diastereomers) δ□173.4, 154.9, 154.4, 145.4, 145.1, 142.5, 142.2, 139.5, 138.8, 138.7, 137.8, 137.1, 130.9, 130.8, 130.3, 129.8, 129.7, 129.4, 129.3, 129.2, 129.0, 128.5, 128.4, 126.9, 126.8, 126.4, 126.3, 125.9, 121.3, 121.2, 119.0, 84.5, 68.8, 68.6, 61.2, 61.1, 60.4, 53.2, 48.3, 39.8, 21.4, 21.2; HRMS (FAB) calcd. for $C_{42}H_{37}N_2O_6$ [M+H]$^+$, 665.2652; found 665.2676.

Veratrole adduct 6c

According to the general procedure described for **2a**, the veratrole adduct **6c** was obtained from **5** with veratrole in 520 μmol scale (284 mg, 399 μmol, 77%); a white foam; IR (neat, cm^{-1}) 3019, 2952, 1747, 1714, 1519, 1480, 1413, 1335, 1261, 1210, 1149, 1027, 754; ^{1}H NMR (400 MHz, CD$_3$CN, 75 °C) δ 7.81–7.78 (2H, m), 7.69 (1H, d, *J* = 8.4 Hz), 7.56 (1H, d, *J* = 8.0 Hz), 7.48 (1H, d, *J* = 7.2 Hz), 7.41–7.19 (12H, m), 6.82–6.77 (2H, m), 6.68 (1H, dd, *J* = 7.6, 1.6 Hz), 6.44 (1H, s), 5.28 (1H, d, *J* = 12.4 Hz), 5.13 (1H, d, *J* = 12.4 Hz), 4.34 (1H, dd, *J* = 6.8, 6.8 Hz), 4.24 (1H, dd, *J* = 12.8, 6.8 Hz), 4.15 (1H, dd, *J* = 12.8, 6.8 Hz), 4.01 (1H, dd, *J* = 9.6, 7.2 Hz), 3.75 (3H, s), 3.66 (3H, s), 3.63 (3H, s), 3.15 (1H, dd, *J* = 13.2, 7.2 Hz), 2.62 (1H, dd, *J* = 13.2, 9.6 Hz); ^{13}C NMR (100 MHz, CD$_3$CN, 75 °C, a mixture of two diastereomers) δ 173.6, 171.9, 155.0, 154.6, 151.2, 150.4, 145.5, 145.2, 142.6, 142.2, 137.9, 137.4, 135.3, 130.4, 130.3, 129.9, 129.8, 129.5, 129.3, 129.1, 128.6, 128.5, 126.5, 126.4, 126.0, 125.5, 121.4, 121.3, 119.6, 119.5, 119.1, 114.0, 111.7, 84.5, 68.9, 68.8, 61.3, 61.2, 60.5, 57.1, 53.4, 48.4, 39.9, 21.5, 15.0; HRMS (FAB) calcd. for $C_{43}H_{39}N_2O_8$ $[M+H]^+$, 711.2706; found 711.2715.

Furan adduct 6d

According to the general procedure described for **2a**, the furan adduct **6d** was obtained from **5** with furan in 577 μmol scale (222 mg, 346 μmol, 60%); a pale yellow foam; IR (neat, cm^{-1}) 3418, 2917, 2848, 1715, 1481, 1451, 1331, 1202, 1176, 741; ^{1}H NMR (400 MHz, CD_3CN, 75 °C) δ 7.77 (2H, dd, *J* = 7.2, 5.2 Hz), 7.68 (1H, d, *J* = 8.8 Hz), 7.53 (1H, d, *J* = 7.6 Hz), 7.46 (1H, d, *J* = 7.6 Hz), 7.37–7.18 (13H, m), 6.37 (1H, s), 6.27 (1H, dd, *J* = 3.2, 2.0 Hz), 5.90 (1H, d, *J* = 3.2 Hz), 5.24 (1H, d, *J* = 12.4 Hz), 5.10 (1H, d, *J* = 12.4 Hz), 4.34–4.29 (1H, m), 4.22 (1H, dd, *J* = 12.0, 6.8 Hz), 4.12 (1H, dd, *J* = 6.8, 6.8 Hz), 4.03 (1H, dd, *J* = 9.2, 7.6 Hz), 3.60 (3H, s), 2.97 (1H, dd, *J* = 13.2, 7.6 Hz), 2.69 (1H, dd, *J* = 13.2, 9.2 Hz); ^{13}C NMR (100 MHz, CD_3CN, 75 °C, a mixture of two diastereomers) δ 173.4, 154.7, 154.4, 145.5, 145.3, 144.6, 142.9, 142.6, 137.9, 134, 6, 130.8, 130.1, 129.9, 129.8, 129.6, 129.5, 129.4, 129.2, 129.1, 128.6, 128.5, 126.5, 126.4, 126.0, 125.5, 121.4, 121.3, 119.2, 112.0, 111.9, 108.5, 82.7, 68.9, 68.8, 60.8, 57.1, 53.4, 48.4, 37.8; HRMS (FAB) calcd. for $C_{39}H_{33}N_2O_7$ $[M+H]^+$, 641.2288; found 641.2279.

Thiophene adducts 6e

According to the general procedure described for **2a**, the thiophene adduct **6e** was obtained from **5** with thiophene in 31.1 μmol scale (14.7 mg, 22.4 μmol, 72%); a white foam; IR (neat, cm^{-1}) 3065, 3035, 2951, 1748, 1715, 1480, 1415, 1327, 1208, 740; ^{1}H NMR (400 MHz, CD_3CN, 75 °C) δ 7.74 (2H, dd, *J* = 7.2, 6.4 Hz), 7.68 (1H, d, *J* = 8.8 Hz), 7.49 (1H, d, *J* = 7.6 Hz), 7.43 (1H, d, *J* = 7.2 Hz), 7.36-7.14 (13H, m), 6.86 (1H, dd, *J* = 5.2, 3.6 Hz), 6.76 (1H, dd, *J* = 3.2, 0.8 Hz), 6.30 (1H, s), 5.22 (1H, d, *J* = 12.4 Hz), 5.09 (1H, d, *J* = 12.0 Hz), 4.22–4.00 (4H, m), 3.58 (3H, s), 3.12 (1H, dd, *J* = 13.2, 7.2 Hz), 2.67 (1H, dd, *J* = 13.2, 7.2 Hz); ^{13}C NMR (100 MHz, CD_3CN, 75 °C) δ□173.6, 154.9, 146.5, 145.8, 143.0, 142.6, 138.2, 137.2, 131.2, 130.1, 129.7, 129.6, 129.4, 129.0, 128.9, 128.8, 127.1, 126.8, 126.7, 126.4, 126.2, 125.7, 121.7, 85.5, 69.3, 61.4, 53.7, 49.1, 30.6, 21.8, 15.3; HRMS (ESI) calcd. for $C_{39}H_{32}N_2NaO_6S$ $[M+Na]^+$, 679.1873; found 679.1844.

General Procedure for Ag-Mediated Coupling of Bromopyrroloindoline 7

Anisole adduct 8a

A mixture of bromopyrroloindoline **3** (20.0 mg, 34.4 μmol) was dried azeotropically (concentration of a benzene solution) under reduced pressure and placed under an argon atmosphere. Anhydrous CH_2Cl_2 (0.34 mL) was poured, and the solution was cooled at 0 °C. To the stirred solution were added anisole (19 μL, 172 μmol), MS4Å powder (140 mg), and DTBP (11.6 μL, 51.7 μmol). After stirring at the same temperature for 45 min, $AgNTf_2$ (40.1 mg, 103 μmol) was added to the stirred suspension. After stirring at 0 °C for 10 min, the resulting suspension was filtered through a pad of Celite and the filter cake was washed with CH_2Cl_2. The filtrate was poured into saturated aqueous $NaHCO_3$, diluted with CH_2Cl_2, and vigorously stirred for 30 min at room temperature. The resulting mixture was extracted with CH_2Cl_2 three times. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 3/2) to afford the anisole adduct **8a** (20.3 mg, 33.4 μmol, 97%) as a white foam; $[\alpha]_D^{32}$ –48.2 (*c* 0.301, $CHCl_3$); IR (neat, cm^{-1}) 2954, 2930, 2857, 1717, 1698, 1684, 1674, 1654, 1253, 836, 756, 668; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (1H, d, *J* = 7.6 Hz), 7.25–7.19 (2H, m), 7.08–7.02 (3H, m), 6.85–6.79 (2H, m), 6.10 (1H, s), 4.66 (1H, dd, *J* = 9.6, 7.6 Hz), 4.13 (1H, dd, *J* = 10.8, 2.8 Hz), 3.91 (1H, dd, *J* = 10.8, 2.8 Hz), 3.77 (3H, s), 3.73 (1H, dd, *J* = 2.8, 2.8 Hz), 3.14 (1H, dd, *J* = 14.0, 7.6 Hz), 3.00 (1H, dd, *J* = 14.0, 9.6 Hz), 2.85 (3H, s), 1.59 (9H, s), 0.88 (9H, s), 0.07 (6H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 165.4, 158.6, 152.0, 140.3, 137.0, 135.0, 128.4, 127.0, 124.7, 123.9, 116.7, 114.3, 83.6, 82.0, 67.1, 62.8, 56.7, 56.5, 55.3, 39.0, 32.0, 28.3, 25.8, 18.2, –5.47, –5.54; HRMS (ESI) calcd. for $C_{33}H_{45}N_3NaO_6Si$ $[M+Na]^+$, 630.2970; found 630.2953.

Toluene adduct 8b

According to the general procedure described for **8a**, the toluene adduct **8b** was obtained from **7** with toluene in 33.9 μmol scale (15.9 mg, 26.9 μmol, 79%); a white foam; $[\alpha]_D^{32}$ –36.8 (*c* 0.741, $CHCl_3$); IR (neat, cm^{-1}) 2954, 2929, 2857, 1717, 1698, 1684, 1671, 1654, 1154, 838, 755, 668; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (1H, d, *J* = 8.0 Hz), 7.25–7.18 (2H, m), 7.10 (2H, d, *J* = 8.4 Hz), 7.07–7.02 (3H, m), 6.14 (1H, s), 4.65 (1H, dd, *J* = 10.0, 7.6 Hz), 4.13 (1H, dd, *J* = 10.8, 2.8 Hz), 3.91 (1H, dd, *J* = 10.8, 2.8 Hz), 3.73 (1H, dd, *J* = 2.8, 2.8 Hz), 3.14 (1H, dd, *J* = 14.2, 10.0 Hz), 3.01 (1H, dd, *J* = 14.2, 7.6 Hz), 2.85 (3H, s), 2.30 (3H, s), 1.59 (9H, s), 0.88 (9H, s), 0.06 (6H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 165.3, 152.0, 140.3, 140.0, 137.0, 129.6, 128.3, 125.6, 124.7, 123.9, 116.7, 83.4, 81.9, 67.2, 62.8, 57.0, 56.5, 39.0, 32.0, 28.3, 25.8, 20.9, 18.2, –5.5, –5.6 (one signal is missing due to overlap); HRMS (ESI) calcd. for $C_{33}H_{45}N_3NaO_5Si$ $[M+Na]^+$, 614.3021; found 614.3001.

Veratrole adduct 8c

According to the general procedure described for **8a**, the veratrole adduct **8c** was obtained from **7** with veratrole in 33.9 μmol scale (19.3 mg, 30.3 μmol, 89%); a white foam; $[\alpha]_D^{32}$ –22.4 (*c* 0.737, $CHCl_3$); IR (neat, cm^{-1}) 2954, 2930, 2857, 1716, 1699, 1684, 1671, 1654, 1520, 1152, 838, 756, 668; ^1H NMR (600 MHz, $CDCl_3$) δ 7.64 (1H, d, *J* = 8.4 Hz), 7.23–7.19 (2H, m), 7.04 (1H, dd, *J* = 7.8, 7.8 Hz), 6.77 (1H, d, *J* = 8.4 Hz), 6.70 (1H, dd, *J* = 8.4, 2.4 Hz), 6.67 (1H, d, *J* = 2.4 Hz), 6.18 (1H, s), 4.64 (1H, dd, *J* = 9.6, 7.2

Hz), 4.13 (1H, dd, *J* = 10.8, 2.7 Hz), 3.91 (1H, dd, *J* = 10.8, 2.7 Hz), 3.83 (3H, s), 3.79 (3H, s), 3.73 (1H, dd, *J* = 2.7, 2.7 Hz), 3.17 (1H, dd, *J* = 14.4, 7.2 Hz), 3.01 (1H, dd, *J* = 14.4, 9.6 Hz), 2.85 (3H, s), 1.59 (9H, s), 0.88 (9H, s), 0.059 (3H, s), 0.056 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 165.4, 152.0, 149.1, 148.1, 140.1, 137.1, 135.6, 128.4, 124.5, 123.9, 117.9, 116.7, 111.3, 83.2, 82.0, 67.1, 62.8, 56.9, 56.4, 55.9, 55.7, 38.5, 32.0, 28.3, 25.8, 18.2, –5.5, –5.6; HRMS (ESI) calcd. for $C_{34}H_{47}N_3NaO_7Si$ $[M+Na]^+$, 660.3075; found 660.3063.

_N,N_-Dimethylaniline adducts 8d and 8e

According to the general procedure described for **4a**, the *N*,*N*-dimethylaniline adducts **8d** and **8e** were obtained from **7** with *N*,*N*-dimethylaniline in 34.4 μmol scale (18.9 mg, 30.4 μmol, 89%, **8d**:**8e** = 2:1).

p-Adduct **8d**; a colorless oil; $[\alpha]_D^{32}$ –35.2 (*c* 0.420, $CHCl_3$); IR (neat, cm^{-1}) 2954, 2929, 2857, 1716, 1698, 1684, 1671, 1654, 1521, 838, 755, 668; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (1H, d, *J* = 8.4 Hz), 7.23–7.18 (2H, m), 7.06–6.98 (3H, m), 6.64 (2H, d, *J* = 7.2 Hz), 6.10 (1H, s), 4.64 (1H, dd, *J* = 9.6, 8.4 Hz), 4.13 (1H, dd, *J* = 10.8, 3.0 Hz), 3.91 (1H, dd, *J* = 10.8, 3.0 Hz), 3.72 (1H, dd, *J* = 3.0, 3.0 Hz), 3.11 (1H, dd, *J* = 14.4, 8.4 Hz), 3.01 (1H, dd, *J* = 14.4, 9.6 Hz), 2.91 (6H, s), 2.85 (3H, s), 1.59 (9H, s), 0.88 (9H, s), 0.064 (3H, s), 0.062 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 165.3, 152.1, 140.3, 137.5, 128.1, 126.6, 124.7, 123.8, 116.6, 112.7, 83.5, 81.8, 67.2, 62.8, 56.6, 56.5, 40.5, 38.9, 32.0, 28.3, 25.8, 18.2, –5.46, –5.54 (two signals are missing due to overlap); HRMS (ESI) calcd. for $C_{34}H_{49}N_4O_5Si$ $[M+H]^+$, 621.3467; found 621.3454.

o-Adduct **8e**; a colorless oil; $[\alpha]_D^{32}$ –135.4 (*c* 0.325, $CHCl_3$); IR (neat, cm^{-1}) 3011, 2930, 2857, 1716, 1699, 1684, 1671, 1653, 1457, 837, 755, 668; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (1H, d, *J* = 8.4 Hz), 7.44 (1H, d, *J* = 7.2 Hz), 7.32–7.25 (3H, m), 7.12 (1H, dd, *J* = 7.8, 7.2 Hz), 6.99 (1H, dd, *J* = 8.4, 7.2 Hz), 6.78 (1H, d, *J* = 8.4 Hz), 6.40 (1H, s), 4.77 (1H, dd, *J* = 10.2, 9.0 Hz), 4.15 (1H, dd, *J* = 10.8, 3.0 Hz), 3.91 (1H, dd, *J* = 10.8, 3.0 Hz), 3.72 (1H, dd, *J* = 3.0, 3.0 Hz), 3.00 (1H, dd, *J* = 13.8, 10.2 Hz), 2.92 (1H, dd, *J* = 13.8, 9.0 Hz), 2.85 (3H, s), 2.69 (3H, br s), 2.62 (3H, br s), 1.54 (9H, s), 0.90 (9H, s), 0.09 (6H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.6, 164.8, 154.0, 152.1, 141.0, 139.0, 137.1, 129.3, 128.9, 128.3, 126.7, 125.9, 125.4, 123.3, 116.7, 83.1, 81.5, 66.7, 62.4, 57.1, 56.6, 47.4, 46.7, 40.9, 31.7, 28.3, 25.9, 18.3, –5.37, –5.43; HRMS (ESI) calcd. for $C_{34}H_{48}N_4NaO_5Si$ $[M+Na]^+$, 643.3286; found 643.3265.

Furan adduct 8f

According to the general procedure described for **8a**, the furan adduct **8f** was obtained from **7** with furan in 33.9 μmol scale (15.8 mg, 27.8 μmol, 82%); a white foam; $[\alpha]_D^{32}$ –80.7 (*c* 0.640, $CHCl_3$); IR (neat, cm^{-1}) 2954, 2929, 2884, 2857, 1733, 1717, 1699, 1684, 1670, 1654, 1156, 837; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (1H, d, *J* = 8.4 Hz), 7.39–7.36 (1H, m), 7.29–7.24 (2H, m), 7.07 (1H, dd, *J* = 7.8, 7.2 Hz), 6.25–6.22 (1H, m), 6.12 (1H, s), 5.84 (1H, d, *J* = 3.6 Hz), 4.65 (1H, dd, *J* = 9.0, 9.0 Hz), 4.15–4.11 (1H, m), 3.93–3.89 (1H, m), 3.75–3.73 (1H, m), 3.07 (1H, dd, *J* = 13.8, 9.0 Hz), 2.86 (3H, s), 2.81 (1H, dd, *J* = 13.8, 9.0 Hz), 1.59 (9H, s), 0.89 (9H, s), 0.08 (3H, s), 0.07 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.6, 165.4, 154.2, 152.2, 142.9, 141.0, 134.3, 128.9, 124.5, 123.8, 116.8, 110.2, 107.1, 82.1, 81.0, 67.1, 62.8, 56.2, 53.5, 37.5, 31.9, 28.2, 25.8, 18.2, –5.5, –5.6; HRMS (ESI) calcd. for $C_{30}H_{41}N_3NaO_6Si$ $[M+Na]^+$, 590.2657; found 590.2647.

Thiophene adduct 8g

According to the general procedure described for **8a**, the thiophene adduct **8g** was obtained from **7** with thiophene in 33.8 μmol scale (17.5 mg, 30.0 μmol, 89%); $[\alpha]_D^{32}$ –33.7 (*c* 0.720, $CHCl_3$); IR (neat, cm^{-1}) 3007, 2954, 2928, 2857, 1733, 1717, 1699, 1684, 1653, 1457, 837, 668; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (1H, d, *J* = 8.4 Hz), 7.27–7.22 (2H, m), 7.20 (1H, d, *J* = 5.1 Hz), 7.06 (1H, dd, *J* = 7.8, 7.2 Hz), 6.89 (1H, dd, *J* = 5.1, 3.3 Hz), 6.69 (1H, d, *J* = 3.3 Hz), 6.09 (1H, s), 4.67 (1H, dd, *J* = 9.6, 8.4 Hz), 4.13 (1H, dd, *J* = 10.8, 3.0 Hz), 3.91 (1H, dd, *J* = 10.8, 2.4 Hz), 3.73 (1H, dd, *J* = 3.0, 2.4 Hz), 3.14 (1H, dd, *J* = 13.8, 8.4 Hz), 3.06 (1H, dd, *J* = 13.8, 9.6 Hz), 2.85 (3H, s), 1.59 (9H, s), 0.88 (9H, s), 0.07 (3H, s), 0.06 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.5, 165.3, 152.0, 146.8, 140.2, 136.5, 128.8, 127.0, 125.0, 124.4, 124.2, 123.9, 116.8, 83.8, 82.1, 67.1, 62.8, 56.1, 54.9, 39.5, 32.0, 28.3, 25.8, 18.2, –5.5, –5.6; HRMS (ESI) calcd. for $C_{30}H_{41}N_3NaO_5SSi$ $[M+Na]^+$, 606.2428; found 606.2411.

***N*-Methylpyrrole adducts 8h and 8i**

According to the general procedure described for **8a**, the *N*-methylpyrrole adducts **8h** and **8i** were obtained from **7** with *N*-methylpyrrole in 33.8 μmol scale (19.9 mg, 33.1 μmol, 98%, **8h**:**8i** = 1.35:1).

2'-*N*-Methylpyrrolyl compound **8h**; a colorless oil; $[\alpha]_D^{32}$ –61.9 (*c* 0.307, $CHCl_3$); IR (neat, cm^{-1}) 2954, 2929, 2857, 1716, 1698, 1684, 1671, 1653, 1507, 838, 668; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (1H, d, *J* = 8.4 Hz), 7.23–7.17 (2H, m), 7.02 (1H, dd, *J* = 7.8, 7.2 Hz), 6.52 (1H, dd, *J* = 3.0, 1.8 Hz), 6.14 (1H, dd, *J* = 1.8, 1.8 Hz), 5.98 (1H, s), 5.95 (1H, dd, *J* = 3.0, 1.8 Hz), 4.60 (1H, dd, *J* = 9.6, 7.8 Hz), 4.12 (1H, dd, *J* = 10.2, 3.0 Hz), 3.90 (1H, dd, *J* = 10.2, 3.0 Hz), 3.71 (1H, dd, *J* = 3.0, 3.0 Hz), 3.53 (3H, s), 3.02 (1H, dd, *J* = 13.8, 7.8 Hz), 2.91 (1H, dd, *J* = 13.8, 9.6 Hz), 2.84 (3H, s), 1.60 (9H, s), 0.88 (9H, s), 0.060 (3H, s), 0.057 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 165.2, 152.4, 140.2, 137.9, 127.9, 126.4, 124.2, 123.6, 122.8, 118.8, 116.5, 105.8, 83.5, 81.7, 67.1, 62.8, 56.3, 52.8, 38.7, 36.1, 32.0, 28.3, 25.8, 18.2, –5.5, –5.6; HRMS (ESI) calcd. for $C_{31}H_{44}N_4NaO_5Si$ $[M+Na]^+$, 603.2973; found 603.2954

3'-*N*-Methylpyrrolyl compound **8i**; a colorless oil; $[\alpha]_D^{32}$ –5.5 (*c* 0.332, $CHCl_3$); IR (neat, cm^{-1}) 2954, 2929, 2857, 1733, 1717, 1698, 1684, 1671, 1653, 1153, 838, 668; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (1H, d, *J* = 7.2 Hz), 7.24 (1H, dd, *J* = 7.2, 7.2 Hz), 7.12 (1H, d, *J* = 7.2 Hz), 7.04 (1H, dd, *J* = 7.2, 7.2 Hz), 6.55

(1H, dd, J = 2.4, 2.1 Hz), 6.18 (1H, s), 6.07 (1H, dd, J = 3.3, 2.1 Hz), 6.02 (1H, dd, J = 3.3, 2.4 Hz), 4.61 (1H, dd, J = 10.2, 8.4 Hz), 4.12 (1H, dd, J = 10.2, 2.4 Hz), 3.91 (1H, dd, J = 10.2, 2.4 Hz), 3.78 (1H, dd, J = 2.4, 2.4 Hz), 3.25 (3H, s), 3.24 (1H, dd, J = 13.8, 8.4 Hz), 2.89 (3H, s), 2.59 (1H, dd, J = 13.8, 10.2 Hz), 1.60 (9H, s), 0.84 (9H, s), 0.04 (3H, s), 0.01 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 165.6, 152.6, 140.8, 136.3, 131.4, 128.5, 125.3, 124.0, 123.9, 116.7, 108.2, 106.5, 82.3, 81.4, 67.1, 62.8, 56.7, 53.0, 40.4, 34.9, 31.9, 28.2, 25.8, 18.2, –5.5, –5.6; HRMS (ESI) calcd. for $C_{31}H_{44}N_4NaO_5Si$ $[M+Na]^+$, 603.2973; found 603.2961.

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9. See: Experimental information.
10. Due to the difficulty of separation of the isomers, **5** was used as a mixture of diastereomers (*dr* = 6:1). See: Experimental information.