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Supporting Information

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Palladium(0)-Catalyzed Alkynyl and Allenyl Iminium Ion Cyclizations Leading to 1,4-Disubstituted 1,2,3,6-Tetrahydropyridines

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Supplementary Material

General Techniques

Reactions were carried out in clean, dry glassware under argon atmosphere using high quality solvents. Anhydrous solutions of reaction mixtures were transferred *via* an oven-dried cannula. Anhydrous dichloromethane (CH_2Cl_2) and methanol (MeOH) were obtained by distillation from phosphorus (V) oxide and magnesium, respectively. Anhydrous *N*,*N*-dimethylformamide (DMF) and acetonitrile (ACN) were obtained by distillation from calcium hydride. Anhydrous toluene and 1,4-dioxane (DOX) were obtained by distillation from sodium benzophenone ketyl. Yields refer to chromatographically and spectroscopically homogenous materials. Reagents were purchased at the highest commercial quality and used without further purification. Reactions were monitored by thin layer chromatography separations carried out on 0.2 mm E. Merck silica gel plates (60 F254) using UV light as a visualizing agent and phosphomolybdic acid, *p*-anisaldehyde, or potassium permanganate solutions and heat as developing agents. Flash chromatographies were performed with Kanto silica gel 60 N (spherical, neutral, 63-210 μm grade). Isolations of 1,2,3,6-tetrahydropyridines were performed on 0.75 mm Wakogel® B-5F PLC plates or gel permeation chromatography (GPC) on a Japan Analytical Industry Model LC-918 (recycling preparative HPLC) using UV detector 3702 and refractive index detector RI-50. Melting points were obtained on a Yazawa apparatus with micro cover glass and are uncorrected. Infrared (IR) data were recorded on SensIR technologies' TravelIR™. Absorbance frequencies are reported in reciprocal centimeters (cm^{-1}). ^{1}H and ^{13}C nuclear magnetic resonance (NMR) were recorded on JEOL AL 400 (400 and 100 MHz respectively). Chemical shifts are reported in delta (δ) units, in parts per million ppm) relative to the singlet at 7.25 ppm for chloroform-*d*. Splitting pattern are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad. Coupling constants (*J*) are reported in

Hertz (Hz). Low and high resolution mass spectral (LRMS and HRMS) were obtained from Mass Spectrometry Resource, Graduate School of Pharmaceutical Sciences, Tohoku University, on a JEOL JMS-DX303 and JMS-700 spectrometer respectively.

Preparation of Substrates

Substrates **9a**[1a] and **9g**[2a] were prepared according to the literature procedure.

Substrate **9b** was prepared by mesylation (MsCl, Et_3N, CH_2Cl_2, 0 °C - rt) of 1-phenyl-3-butyn-1-ol,[3] substitution with azide (NaN_3, DMF, rt), reduction of azide ($LiAlH_4$, THF, 0 °C - rt), and reductive amination of *p*-anisaldehyde ($NaBH(OAc)_3$, $ClCH_2CH_2Cl$, rt).[4]

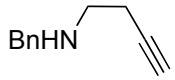
Substrates **9c-d** were prepared by mesylation (MsCl, Et_3N, CH_2Cl_2, rt) of 1-phenyl-3-butyn-1-ol[3] and substitution with primary amines (*i*$PrNH_2$ or *t*$BuNH_2$), CH_3CN, 80 °C).

Substrates **9e** was prepared by reductive amination of benzaldehyde with methyl 2-amino-4-pentynoate[5] ($NaBH(OAc)_3$, $ClCH_2CH_2Cl$, rt).[4]

Substrate **9f** was prepared by Mitsunobu reaction[6a] of cis-2-ethynylcyclohexanol[7] ($(PhO)_2PON_3$, PPh_3, DIAD, THF, 0 °C - rt), reduction ($LiAlH_4$, THF, 0 °C - rt), and reductive amination of benzaldehyde ($NaBH(OAc)_3$, $ClCH_2CH_2Cl$, rt).[4]

N-Benzyl-3-butynylamine (**9a**)[1]

Colorless oil. IR (neat): 3294, 2914, 2823, 2117, 1603, 1495, 1453, 1360, 1175, 1119, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.34-7.25 (m, 5H), 3.82 (s, 2H), 2.81 (t, *J*=6.6 Hz, 2H), 2.42 (dt, *J*=2.7, 6.6 Hz, 2H), 1.99 (t, *J*=2.7 Hz, 1H), 1.60 (br-s, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 140.1, 128.4, 128.1, 127.0, 82.5, 69.5, 53.4, 47.3, 19.6. LRMS (EI) *m/z* (relative intensity) 159 $[M]^+$ (2), 128 (3), 120 (76), 91 (100), 65 (9), 39 (4). HRMS (EI, $[M]^+$): calcd for $C_{11}H_{13}N$, 159.1048; found, 159.1026.

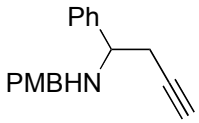


9a

N-(4-Methoxyphenyl)methyl-1-phenyl-3-butynylamine (**9b**)

Pale yellow oil. IR (neat): 3290, 2908, 2834, 2117, 1611, 1511, 1492, 1453, 1243, 1173, 1034 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.40-7.26 (m, 5H), 7.20 (d, *J*=8.6 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 3.85 (t, *J*=8.6 Hz, 1H), 3.80 (s, 3H), 3.64 (d, *J*=13.1 Hz, 1H), 3.51 (d, *J*=13.1 Hz, 1H), 2.54-2.52 (m, 2H), 2.01 (t, *J*=2.7 Hz, 1H), 1.95 (br-s, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 158.3, 142.3, 132.3, 129.1, 128.3, 127.4, 127.0, 113.6, 81.6, 70.5, 60.6, 55.3, 50.8, 28.3. LRMS (EI) *m/z* (relative intensity) 265 $[M]^+$ (1), 226 (50),

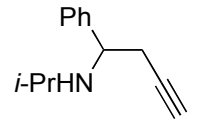
121 (100), 77 (6), 51 (2). HRMS (EI, $[M]^+$): calcd for $C_{18}H_{19}NO$, 265.1467; found, 265.1478.



9b

N-Isopropyl-1-phenyl-3-butynylamine (**9c**)

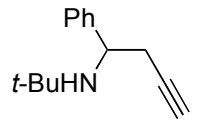
Yellow oil. IR (neat): 3294, 2960, 2865, 2117, 1602, 1493, 1474, 1453, 1380, 1366, 1167, 1125, 1071 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.36-7.23 (m, 5H), 3.94 (dd, *J*=5.9, 7.1 Hz, 1H), 2.64 (qq, *J*=6.1, 6.5 Hz, 1H), 2.55 (ddd, *J*=5.9, 16.6, 2.7 Hz, 1H), 2.48 (ddd, *J*=7.1, 16.6, 2.7 Hz, 1H), 2.01 (dd, *J*=2.7, 2.4 Hz, 1H), 1.56 (br-s, 1H), 1.04 (d, *J*=6.1 Hz, 1H), 1.01 (d, *J*=6.5 Hz, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 143.0, 128.2, 127.2, 126.9, 81.6, 70.4, 58.6, 45.8, 28.6, 24.2, 22.2. LRMS (EI) *m/z* (relative intensity) 187 $[M]^+$ (1), 148 (100), 128 (16), 106 (56), 77 (8), 51 (3). HRMS (EI, $[M]^+$): calcd for $C_{13}H_{17}N$, 187.1361; found, 187.1352.



9c

N-(*tert*-Butyl)-1-phenyl-3-butynylamine (**9d**)

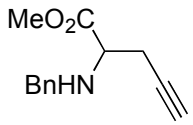
Yellow oil. IR (neat): 3307, 2960, 2865, 2117, 1602, 1492, 1474, 1453, 1389, 1364, 1229, 1214, 1071 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.40 (d, *J*=7.1 Hz, 2H), 7.32-7.19 (m, 3H), 3.98 (dd, *J*=5.9, 8.1 Hz, 1H), 2.48 (ddd, *J*=5.9, 16.9, 2.7 Hz, 1H), 2.41 (ddd, *J*=8.1, 16.9, 2.7 Hz, 1H), 1.99 (dd, *J*=2.7, 2.7 Hz, 1H), 1.51 (br-s, 1H), 1.01 (s, 9H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 146.0, 128.1, 126.8, 126.7, 82.1, 70.0, 56.5, 51.3, 30.2, 30.1. LRMS (EI) *m/z* (relative intensity) 201 $[M]^+$ (1), 186 (6), 162 (87), 128 (24), 106 (100), 79 (13), 58 (15). HRMS (EI, $[M]^+$): calcd for $C_{14}H_{19}N$, 201.1517; found, 201.1521.



9d

Methyl *N*-benzyl-2-amino-4-pentynoate (**9e**)

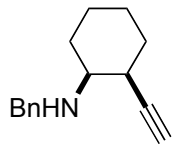
Colorless oil. IR (neat): 3290, 2952, 2848, 2119, 1735, 1603, 1495, 1453, 1436, 1198, 1173, 1136 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.36-7.24 (m, 5H), 3.88 (d, *J*=13.2 Hz, 1H), 3.76 (s, 3H), 3.73 (d, *J*=13.2 Hz, 1H), 3.47 (t, *J*=5.9 Hz, 1H), 2.63 (dd, *J*=5.9, 2.6 Hz, 2H), 2.05 (t, *J*=2.6 Hz, 1H), 2.12-1.86 (br-s, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 173.3, 139.2, 128.3, 128.1, 127.0, 79.4, 71.1, 58.7, 52.1, 51.8, 23.4. LRMS (EI) *m/z* (relative intensity) 217 $[M]^+$ (0.7), 178 (46), 158 (49), 106 (9), 91 (100), 65 (8). HRMS (EI, $[M]^+$): calcd for $C_{13}H_{15}NO_2$, 217.1103; found, 217.1104.



9e

Cis-*N*-Benzyl-2-ethynyl-cyclohexylamine (**9f**)[8]

Pale yellow oil. IR (neat): 3301, 2931, 2854, 2109, 1603, 1495, 1447, 1362, 1129, 1027 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.37-7.22 (m, 5H), 3.90 (d, *J*=13.1 Hz, 1H), 3.76 (d, *J*=13.1 Hz, 1H), 3.09 (m, 1H), 2.57-2.52 (m, 1H), 2.12 (d, *J*=2.4 Hz, 1H), 1.93-1.89 (m, 1H), 1.75-1.37 (m, 7H), 1.26-1.16 (m, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 140.5, 128.2, 128.0, 126.7, 84.4, 71.6, 56.5, 50.1, 32.5, 30.1, 29.4, 25.0, 21.9. LRMS (EI) *m/z* (relative intensity) 213 $[M]^+$ (19), 170 (38), 146 (47), 122 (34), 91 (100), 65 (13). HRMS (EI, $[M]^+$): calcd for $C_{15}H_{19}N$, 213.1517; found, 213.1490.

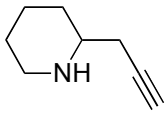


9f

2-(2-Propynyl)-piperidine (**9g**)[2a]

Colorless oil. IR (neat): 3307, 2929, 2856, 2117, 1711, 1453, 1441, 1331, 1121, 1054 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 3.11-3.07 (m, 1H), 2.69-2.62 (m, 2H), 2.29 (ddd, *J*=5.1, 16.6, 2.7 Hz, 1H), 2.20 (ddd, *J*=7.6, 16.6, 2.7 Hz, 1H), 2.02 (dd, *J*=2.7, 2.7 Hz, 1H), 1.82-1.58 (m, 4H), 1.46-1.29 (m, 2H), 1.22-1.11 (m, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 81.8, 70.0, 55.5, 47.1, 32.4, 26.8, 26.2, 24.7. FAB-MS (EI) *m/z* (relative intensity) 124 $[M+H]^+$. FAB-HRMS (EI, $[M+H]^+$): calcd for $C_8H_{14}N$, 124.1121; found,

124.1116.



9g

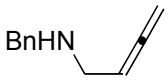
Substrate **10a**[9] was prepared according to the literature procedure.

Substrates **10b-c** were prepared by Cu-catalyzed substitution of RMgBr (R=Bu or Ph) on bis-trimethylsilyl protected 4-methoxy-2-butynylamine,[10a] hydrolysis of bis-trimethylsilylamine (MeOH, reflux),[10b] and reductive amination of benzaldehyde or *p*-anisaldehdye ($NaBH(OAc)_3$, $ClCH_2CH_2Cl$, rt).[4]

Substrate **10d** was prepared by Boc-protection of 1-phenyl-2-propynylamine[11a] (Boc_2O, CH_2Cl_2, rt), Crabbe reaction (paraformaldehyde, iPr_2NH, cat. CuBr, 1,4-dioxane, reflux),[11b] Boc-deprotection (TMSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C),[11c] and reductive amination of *p*-anisaldehdye ($NaBH(OAc)_3$, $ClCH_2CH_2Cl$, rt).[4]

N-Benzyl-2,3-butadienylamine (**10a**)[9]

Yellow oil. IR (neat): 3330, 3027, 2833, 1955, 1603, 1495, 1453, 1358, 1102, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.35-7.22 (m, 5H), 5.24 (tt, *J*=6.4, 6.4 Hz, 1H), 4.78 (dt, *J*=6.4, 3.2 Hz, 2H), 3.82 (s, 2H), 3.28 (dt, *J*=6.4, 3.2 Hz, 2H), 1.51 (br-s, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 208.0, 139.9, 128.2, 128.1, 126.8, 89.2, 76.1, 53.1, 47.2. LRMS (EI) *m/z* (relative intensity) 159 $[M]^+$ (6), 144 (2), 130 (1), 120 (68), 91 (100), 77 (3), 65 (11). HRMS (EI, $[M]^+$): calcd for $C_{11}H_{13}N$, 159.1048; found, 159.1019.

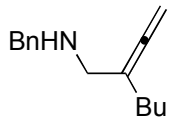


10a

N-Benzyl-2-butyl-2,3-butadienylamine (**10h**)

Colorless oil. IR (neat): 3342, 2927, 2858, 1955, 1603, 1495, 1453, 1358, 1106, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.33-7.23 (m, 5H), 4.80 (tt, *J*=3.2, 3.2 Hz, 2H), 3.80 (s, 2H), 3.19 (t, *J*=3.2 Hz, 2H), 1.97 (tt, *J*=3.2, 3.7 Hz, 2H), 1.54 (br-s, 1H), 1.46-1.31 (m, 4H), 0.90 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 204.7, 140.2, 128.2, 128.1, 126.7, 102.5, 76.7, 53.1, 50.4, 30.1, 29.8, 22.6, 14.1. LRMS (EI) *m/z* (relative intensity) 215 $[M]^+$ (4), 200 (4), 172 (8), 120 (95), 91 (100), 65 (9). HRMS (EI,

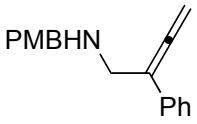
[M]$^+$): calcd for $C_{15}H_{21}N$, 215.3339; found, 215.1674.



10h

N-Benzyl-2-phenyl-2,3-butadienylamine (**10i**)

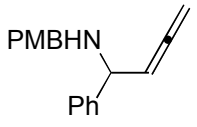
Pale pink oil. IR (neat): 3334, 2931, 2833, 1939, 1611, 1584, 1511, 1493, 1451, 1301, 1243, 1173, 1104, 1034 cm^{-1}. ^{1}H NMR (400 M Hz, $CDCl_3$): δ 7.39 (d, *J*=7.6 Hz, 2H), 7.32 (dd, *J*=7.6, 7.8 Hz, 2H), 7.26-7.19 (m, 3H), 5.18 (t, *J*=2.9 Hz, 2H), 3.801 (s, 2H), 3.797 (s, 3H), 1.68 (br-s, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 207.5, 158.2, 134.6, 131.9, 129.1, 128.2, 126.6, 125.8, 113.4, 103.7, 79.1, 55.1, 52.3, 48.0. LRMS (EI) *m*/*z* (relative intensity) 265 [M]$^+$ (27), 150 (13), 121 (100), 91 (3), 77 (4). HRMS (EI, [M]$^+$): calcd for $C_{18}H_{19}NO$, 265.1467; found, 265.1450.



10i

N-Benzyl-1-phenyl-2,3-butadienylamine (**10j**)

Pale orange oil. IR (neat): 3323, 2933, 2833, 1953, 1611, 1584, 1511, 1492, 1453, 1301, 1243, 1173, 1034 cm^{-1}. ^{1}H NMR (400 M Hz, $CDCl_3$): δ 7.39-7.32 (m, 4H), 7.28-7.21 (m, 3H), 6.85 (d, *J*=8.8 Hz, 2H), 5.31 (ddd, *J*=6.8, 6.8, 7.0 Hz, 1H), 4.88-4.79 (m, 2H), 4.28 (ddd, *J*=7.0, 2.2, 2.0 Hz, 1H), 3.80 (s, 3H), 3.72 (d, *J*=13.2 Hz, 1H), 3.68 (d, *J*=13.2 Hz, 1H), 1.75 (br-s, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 207.3, 158.3, 142.9, 132.2, 129.2, 128.3, 127.2, 127.1, 113.6, 94.5, 77.0, 60.9, 55.3, 50.8. LRMS (EI) *m*/*z* (relative intensity) 265 [M]$^+$ (4), 226 (49), 121 (100), 77 (6). HRMS (EI, [M]$^+$): calcd for $C_{18}H_{19}NO$, 265.1467; found, 265.1455.



10j

Procedure for the Three-Component Coupling Reactions

General procedure for the *p*-methoxyphenylative cyclization of **9a** (Table 1, Entries 1-6):

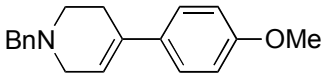
To a test tube containing **9a** (0.15 mmol, see Table 1S-1), *p*-methoxyphenylboronic acid (**8A**) (0.18 mmol), and $Pd(PPh_3)_4$ (3.0 μmol) were added anhydrous solvent (toluene, $ClCH_2CH_2Cl$, CH_3CN, MeOH, DMF, or THF, 0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for the time described in Table 1S-1. The mixture was cooled down to room temperature, and then *N*,*N*-diethanolaminomethyl polystyrene[12] (PS-DEAM™, 1.63 mmol/g, 0.36 mmol) and THF (2 mL) were added to remove an excess of **8A**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times to afford **1aA** in the yield described in Table 1.

Table 1S-1

Solvent	**9a** (mg)	**8A** (mg)	$Pd(PPh_3)_4$ (mg)	Time (h)	**1aA** (mg, mmol, %)
toluene	23.4	27.1	3.5	3	20.0, 0.0716, 49
$ClCH_2CH_2Cl$	24.3	27.1	3.6	2	4.2, 0.0150, 10
CH_3CN	24.2	27.5	3.7	3	3.1, 0.0111, 7
MeOHl	23.7	26.8	3.8	8	27.3, 0.0977, 66
DMF	24.9	27.7	3.7	4	14.4, 0.0515, 33
THF	23.7	27.2	3.7	1	32.9, 0.118 , 79

1,2,3,6-Tetrahydro-4-(4-methoxyphenyl)-1-(phenylmethyl)-pyridine (**1aA**)[13a]

White solid. Mp: 112-116 °C. IR (neat): 2912, 2798, 1603, 1513, 1492, 1366, 1239, 1185, 1129, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.38-7.24 (m, 7H), 6.83 (d, *J*=8.8 Hz, 2H), 5.96 (m, 1H), 3.79 (s, 3H), 3.63 (s, 2H), 3.15 (m, 2H), 2.70 (t, *J*=5.6 Hz, 2H), 2.52 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 158.5, 138.2, 134.2, 133.5, 129.1, 128.2, 127.0, 125.9, 120.2, 113.5, 62.8, 55.3, 53.4, 50.0, 28.2. LRMS (EI) *m/z* (relative intensity) 279 $[M]^+$ (100), 248 (5), 188 (15), 161 (13), 121 (8), 91 (38), 65 (3). HRMS (EI, $[M]^+$): calcd for $C_{19}H_{21}NO$, 279.1623; found, 279.1612.



1aA

General procedure for the arylative cyclization of **9a** (Table 1, Entries 7-12 and Table 2, Entry 1):

To a test tube containing **9a** (0.15 mmol, see Table 1S-2), arylboronic acid **8B-H** (0.18 mmol), and $Pd(PPh_3)_4$ (3.0 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for the time described in Table 1S-1. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.36 mmol) and THF (2 mL) were added to remove an excess of **8B-H**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC to afford **1aB-aH** in the yield described in Table 1 and 2.

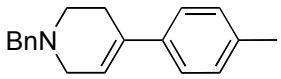
Table 1S-2

9a (mg)	**8** (mg)	$Pd(PPh_3)_4$ (mg)	Time (h)	**1** (mg, mmol, %)
24.6	**8B**; 25.3	3.9	1	**1aB**; 29.3, 0.111, 72
24.2	**8C**; 24.7	3.5	1	**1aC**; 35.1, 0.133, 88
23.6	**8D**; 24.3	3.5	2	**1aD**; 27.0, 0.103, 69
24.2	**8E**; 22.4	3.8	2	**1aE**; 27.0, 0.108, 72
24.5	**8F**; 24.3	3.7	1	**1aF**; 34.2, 0.134, 87
23.5	**8G**; 22.9	3.6	1	**1aG**; 31.1, 0.122, 83
24.5	**8H**; 30.3	3.7	4	**1aH**; 13.0, 0.0446, 29

1,2,3,6-Tetrahydro-4-(4-methylphenyl)-1-(phenylmethyl)-pyridine (**1aB**)[13a] was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2).

Colorless oil. IR (neat): 2917, 2796, 1515, 1493, 1453, 1362, 1125, 1046, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.39-7.25 (m, 7H), 7.11 (d, *J*=8.1 Hz, 2H), 6.03-6.01 (m, 1H), 3.63 (s, 2H), 3.17-3.15 (m, 2H), 2.70 (t, *J*=5.7 Hz, 2H), 2.56-2.54 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 138.1, 137.9, 136.4, 134.6, 129.1, 128.8, 128.1, 126.9, 124.6, 120.9, 62.8, 53.4, 50.0, 28.2, 21.2. LRMS (EI) *m/z* (relative intensity) 263 $[M]^+$ (100), 172 (28), 129 (19), 105 (10), 91 (60), 65 (7). HRMS (EI, $[M]^+$): calcd for

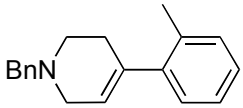
$C_{19}H_{21}N$, 263.1674; found, 263.1672.



1aB

1,2,3,6-Tetrahydro-4-(2-methylphenyl)-1-(phenylmethyl)-pyridine (**1aC**)[13a, b] was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2).

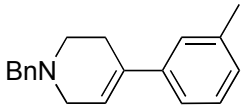
Colorless oil. IR (neat): 2917, 2796, 1493, 1453, 1368, 1160, 1127, 1042, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.40-7.10 (m, 9H), 5.53 (m, 1H), 3.67 (s, 2H), 3.16-3.15 (m, 2H), 2.69 (t, *J*=5.5 Hz, 2H), 2.38-2.33 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 142.7, 138.0, 136.9, 134.9, 129.9, 129.1, 128.1, 126.9, 126.6, 125.4, 123.5, 62.7, 52.9, 49.9, 30.9, 20.1. LRMS (EI) *m/z* (relative intensity) 263 $[M]^+$ (100), 186 (12), 172 (41), 129 (28), 91 (57), 65 (5). HRMS (EI, $[M]^+$): calcd for $C_{19}H_{21}N$, 263.1674; found, 263.1671.



1aC

1,2,3,6-Tetrahydro-4-(3-methylphenyl)-1-(phenylmethyl)-pyridine (**1aD**) was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2).

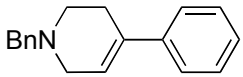
Pale yellow oil. IR (neat): 2916, 2796, 1602, 1493, 1453, 1366, 1160, 1129, 1046, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.39-7.18 (m, 8H), 7.04 (d, *J*=6.1 Hz, 1H), 6.04 (m, 1H), 3.64 (s, 2H), 3.17-3.16 (m, 2H), 2.71 (t, *J*=5.6 Hz, 2H), 2.55 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 140.7, 138.1, 137.5, 134.9, 129.1, 128.1, 128.0, 127.5, 126.9, 125.6, 121.9, 121.6, 62.7, 53.4, 50.0, 28.2, 21.7. LRMS (EI) *m/z* (relative intensity) 263 $[M]^+$ (100), 172 (27), 145 (13), 129 (16), 105 (6), 91 (42). HRMS (EI, $[M]^+$): calcd for $C_{19}H_{21}N$, 263.1674; found, 263.1680.



1aD

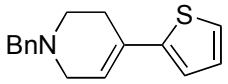
1,2,3,6-Tetrahydro-4-phenyl-1-(phenylmethyl)-pyridine (**1aE**)[13a] was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times.

Pale yellow oil. IR (neat): 2912, 2796, 1600, 1493, 1453, 1362, 1198, 1160, 1129, 1046, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.39-7.20 (m, 10H), 6.06 (m, 1H), 3.64 (s, 2H), 3.18-3.17 (m, 2H), 2.72 (t, *J*=5.7 Hz, 2H), 2.56 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 140.7, 138.0, 134.8, 129.1, 128.1, 128.1, 126.9, 126.8, 124.7, 121.8, 62.8, 53.4, 50.0, 28.1. LRMS (EI) *m/z* (relative intensity) 249 $[M]^+$ (100), 172 (21), 158 (14), 131 (14), 91 (54). HRMS (EI, $[M]^+$): calcd for $C_{18}H_{19}N$, 249.1517; found, 249.1512.



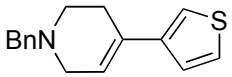
1aE

1,2,3,6-Tetrahydro-1-(phenylmethyl)-4-(2-thienyl)-pyridine (**1aF**)[13a] was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times.
Yellow oil. IR (neat): 2914, 2798, 1493, 1453, 1362, 1210, 1156, 1127, 1065, 1036 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.38-7.25 (m, 5H), 7.11 (dd, *J*=1.3, 4.5 Hz, 1H), 6.96-6.94 (m, 2H), 6.08 (m, 1H), 3.63 (s, 2H), 3.16-3.13 (m, 2H), 2.70 (t, *J*=5.7 Hz, 2H), 2.56 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 145.2, 138.0, 129.5, 129.0, 128.1, 127.0, 127.0, 123.1, 121.6, 120.9, 62.6, 53.0, 49.7, 28.4. LRMS (EI) *m/z* (relative intensity) 255 $[M]^+$ (100), 164 (24), 137 (31), 91 (64), 65 (10). HRMS (EI, $[M]^+$): calcd for $C_{16}H_{17}NS$, 255.1082; found, 255.1080.



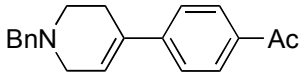
1aF

1,2,3,6-Tetrahydro-1-(phenylmethyl)-4-(3-thienyl)-pyridine (**1aG**)[13a] was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times.
Yellow oil. IR (neat): 2912, 2796, 1493, 1453, 1364, 1196, 1158, 1127, 1044 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.38-7.08 (m, 7H), 7.09 (d, *J*=1.7 Hz, 1H), 6.06 (t, *J*=3.4 Hz, 1H), 3.63 (s, 2H), 3.16-3.14 (m, 2H), 2.70 (t, *J*=5.7 Hz, 2H), 2.54-2.53 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 142.4, 138.1, 130.3, 129.1, 128.2, 126.9, 125.2, 124.5, 120.9, 118.5, 62.7, 53.5, 49.8, 28.2. LRMS (EI) *m/z* (relative intensity) 255 $[M]^+$ (100), 164 (16), 135 (20), 91 (53), 65 (6). HRMS (EI, $[M]^+$): calcd for $C_{16}H_{17}NS$, 255.1082; found, 255.1078.



1aG

4-(4-Acetylphenyl)-1,2,3,6-tetrahydro-1-(phenylmethyl)-pyridine (**1aH**)[13a] was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (66:33:2) repeated two times.
White solid. Mp: 100-101 °C. IR (neat): 2917, 2804, 1673, 1600, 1557, 1495, 1453, 1358, 1272, 1250, 1233, 1196, 1162, 1119 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.90 (d, *J*=8.6 Hz, 2H), 7.46 (d, *J*=8.6 Hz, 2H), 7.39-7.27 (m, 5H), 6.23-6.21 (m, 1H), 3.65 (s, 2H), 3.21-3.19 (m, 2H), 2.73 (t, *J*=5.6 Hz, 2H), 2.59 (m, 5H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 197.3, 145.2, 137.9, 135.4, 134.0, 129.0, 128.3, 128.2, 127.0, 124.7, 124.4, 62.7, 53.4, 49.9, 28.0, 26.7. LRMS (EI) *m/z* (relative intensity) 291 $[M]^+$ (100), 200 (11), 172 (14), 129 (10), 91 (45), 65 (3). HRMS (EI, $[M]^+$): calcd for $C_{20}H_{21}NO$, 291.1623; found, 291.1606.



1aH

General procedure for the *p*-acetylphenylative cyclization of **9a** (Table 2, Entries 2-4):
To a test tube containing **9a** (0.15 mmol, see Table 2S-1), *p*-acetylphenylboronic acid (**8H**) (0.18 mmol), PdCp(η^3-allyl) (4.5 μmol), and phosphine ligand (PCy_3, PPh_2Cy, or $PPhCy_2$, 18 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for the time described in Table 1S-1. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.36 mmol) and THF (2 mL) were added to remove an excess of **8H**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (66:33:2) repeated two times to afford **1aH** in the yield described in Table 2.

Table 2S-1

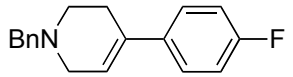
9a (mg)	**8H** (mg)	[Pd] (mg)	PR_3 (mg)	Time (h)	**1aH** (mg, mmol, %)
24.1	30.1	1.0	PCy_3; 5.5	4	8.6, 0.0295, 19
23.7	30.9	1.2	PPh_2Cy; 5.4	2	19.5, 0.0669, 45
24.3	29.9	1.0	$PPhCy_2$; 5.1	2	29.4, 0.101, 66

General procedure for the arylative cyclization of **9a** (Table 2, Entries 5-10):
To a test tube containing **9a** (0.15 mmol, see Table 2S-2), arylboronic acid **8E·H-L** (0.18 mmol), K_2CO_3 (0.18 mmol), PdCp(η^3-allyl) (4.5 μmol), and $PPhCy_2$ (18 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 1 h except for Entry 9 (4 h). The mixture was cooled down to room temperature, diluted with EtOAc, washed with saturated aqueous Na_2CO_3 and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC to afford **1aE·aH-aL** in the yield described in Table 2.

Table 2S-2

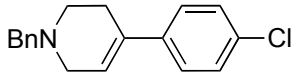
9a (mg)	**8** (mg)	K_2CO_3 (mg)	[Pd] (mg)	$PPhCy_2$ (mg)	**1** (mg, mmol, %)
23.3	**8H**; 29.5	25.0	1.2	5.1	**1aH**; 34.1, 0.117, 80
23.4	**8E**; 22.0	25.8	1.1	5.1	**1aE**; 29.1, 0.117, 79
24.4	**8I**; 25.7	25.7	1.0	5.3	**1aI**; 35.0, 0.131, 85
23.3	**8J**; 27.8	25.2	1.0	5.3	**1aJ**; 35.1, 0.124, 85
23.7	**8K**; 24.3	25.2	1.1	5.3	**1aK**; 29.8, 0.107, 72
23.8	**8L**; 30.7	25.1	1.0	5.2	**1aL**; 30.3, 0.103, 69

4-(4-Fluorophenyl)-1,2,3,6-tetrahydro-1-(phenylmethyl)-pyridine (**1aI**)[13a, c, d] was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2).
Pale yellow oil. IR (neat): 2916, 2798, 1602, 1509, 1493, 1453, 1362, 1229, 1160, 1129 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.39-7.27 (m, 7H), 6.98 (t, *J*=8.7 Hz, 2H), 6.00 (m, 1H), 3.64 (s, 2H), 3.16-3.15 (m, 2H), 2.71 (t, *J*=5.6 Hz, 2H), 2.53-2.52 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 161.6 (d, *J*=244 Hz), 138.0, 136.8 (d, *J*=3.3 Hz), 133.9, 129.1, 128.1, 127.0, 126.2 (d, *J*=7.4 Hz), 121.7, 114.9 (d, *J*=21 Hz), 62.8, 53.3, 49.9, 28.3. LRMS (EI) *m/z* (relative intensity) 267 $[M]^+$ (100), 176 (14), 149 (17), 109 (9), 91 (49), 65 (4). HRMS (EI, $[M]^+$): calcd for $C_{18}H_{18}FN$, 267.1423; found, 267.1408.



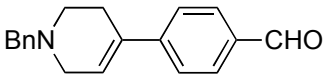
1aI

4-(4-Chlorophenyl)-1,2,3,6-tetrahydro-1-(phenylmethyl)-pyridine (**1aJ**) was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times.
White solid. Mp: 61-63 °C. IR (neat): 2908, 2806, 1648, 1492, 1455, 1362, 1339, 1320, 1160, 1125, 1094 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.38-7.25 (m, 9H), 6.06-6.04 (m, 1H), 3.63 (s, 2H), 3.17-3.15 (m, 2H), 2.71 (t, *J*=5.7 Hz, 2H), 2.53-2.51 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 139.1, 138.0, 133.8, 132.4, 129.0, 128.2, 128.1, 127.0, 126.0, 122.4, 62.7, 53.3, 49.9, 28.1. LRMS (EI) *m/z* (relative intensity) 283 $[M]^+$ (100), 285 (37), 192 (16), 172 (15), 165 (14), 129 (25), 91 (60), 65 (6). HRMS (EI, $[M]^+$): calcd for $C_{18}H_{18}ClN$, 283.1128; found, 283.1113.



1aJ

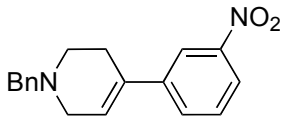
4-(4-Formylphenyl)-1,2,3,6-tetrahydro-1-(phenylmethyl)-pyridine (**1aK**) was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (66:33:2) repeated two times.
Pale yellow oil. IR (neat): 2914, 2798, 2748, 1696, 1600, 1563, 1493, 1453, 1364, 1214, 1171, 1127 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 9.98 (s, 1H), 7.82 (d, *J*=8.5 Hz, 2H), 7.53 (d, *J*=8.2 Hz, 2H), 7.39-7.26 (m, 5H), 6.25 (m, 1H), 3.66 (s, 2H), 3.22-3.21 (m, 2H), 2.74 (t, *J*=5.7 Hz, 2H), 2.59 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 191.8, 146.8, 138.0, 134.9, 134.2, 129.9, 129.2, 128.3, 127.2, 125.3, 125.3, 62.6, 53.3, 49.7, 27.8. LRMS (EI) *m/z* (relative intensity) 277 $[M]^+$ (100), 248 (3), 186 (12), 172 (13), 131 (9), 91 (66), 65 (5). HRMS (EI, $[M]^+$): calcd for $C_{19}H_{19}NO$, 277.1467; found, 277.1458.



1aK

1,2,3,6-Tetrahydro-4-(3-nitrophenyl)-1-(phenylmethyl)-pyridine (**1aL**) was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times.
Yellow oil. IR (neat): 2914, 2800, 1522, 1493, 1453, 1354, 1160, 1129, 1046, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 8.23 (s, 1H), 8.08 (d, *J*=8.1 Hz, 1H), 7.69 (d, *J*=7.6 Hz,

1H), 7.47 (dd, *J*=8.1, 8.0 Hz, 1H), 7.39-7.26 (m, 5H), 6.23 (m, 1H), 3.66 (s, 2H), 3.21 (m, 2H), 2.75 (t, *J*=5.6 Hz, 2H), 2.59 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 148.2, 142.3, 137.8, 133.0, 130.6, 129.0, 128.2, 127.1, 124.7, 121.5, 119.6, 62.6, 53.2, 49.7, 28.1. LRMS (EI) *m/z* (relative intensity) 294 $[M]^+$ (100), 203 (16), 172 (15), 130 (7), 91 (75), 65 (4). HRMS (EI, $[M]^+$): calcd for $C_{18}H_{18}N_2O_2$, 294.1368; found, 294.1363.



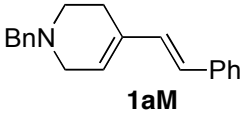
1aL

Procedure for the styrylative cyclization of **9a** (Table 2, Entry 11):

To a test tube containing **9a** (24.1 mg, 0.151 mmol), **8M** (27.9 mg, 0.189 mmol), PdCp(η^3-allyl) (1.1 mg, 5.2 μmol), and $PPhCy_2$ (5.1 mg, 19 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 1 h. The mixture was cooled down to room temperature, and then PS-DEAM^{TM} (1.63 mmol/g, 0.22 g, 36 mmol) and THF (2 mL) were added to remove an excess of **8M**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times to yield 35.5 mg (0.129 mmol, 85%) of **1aM**.

1,2,3,6-Tetrahydro-4-[(1*E*)-2-phenylethenyl]-1-(phenylmethyl)-pyridine (**1aM**)[14]

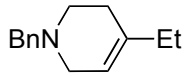
White solid. Mp: 96-100 °C. IR (neat): 2916, 2807, 1492, 1449, 1364, 1237, 1154, 1115, 959 cm^{-1}. ^{1}H NMR (400 M Hz, $CDCl_3$): δ 7.40-7.17 (m, 10H), 6.79 (d, *J*=16.1 Hz, 1H), 6.44 (d, *J*=16.1 Hz, 1H), 5.81 (m, 1H), 3.62 (s, 2H), 3.13 (d, *J*=2.5 Hz, 2H), 2.67 (t, *J*=5.7 Hz, 2H), 2.42 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 138.1, 137.5, 134.1, 130.7, 129.0, 128.4, 128.1, 127.1, 127.0, 126.9, 126.1, 125.7, 62.7, 53.4, 49.7, 25.6. LRMS (EI) *m/z* (relative intensity) 275 $[M]^+$ (100), 198 (7), 184 (13), 129 (11), 115 (7), 91 (47), 65 (4). HRMS (EI, $[M]^+$): calcd for $C_{20}H_{21}N$, 275.1674; found, 275.1669.



1aM

Procedure for the ethylative cyclization of **9a** (Table 2, Entry 12):
To a test tube containing **9a** (24.5 mg, 0.154 mmol), PdCp(η^3-allyl) (1.1 mg, 5.2 μmol), and $PPhCy_2$ (5.2 mg, 19 μmol) were added anhydrous THF (0.4 mL), 1.0 M solution of triethylborane (**8N**) in THF (0.23 mL, 0.23 mmol), and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 65 °C for 6 h. The mixture was cooled down to room temperature, diluted with EtOAc, washed with saturated aqueous Na_2CO_3 and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) to yield 24.3 mg (0.121 mmol, 78%) of **1aN**.

4-Ethyl-1,2,3,6-tetrahydro-1-(phenylmethyl)-pyridine (**1aN**)
Colorless oil. IR (neat): 2962, 2898, 2796, 1600, 1495, 1453, 1362, 1337, 1121, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.36-7.23 (m, 5H), 5.36-5.34 (m, 1H), 3.57 (s, 2H), 2.96 (d, *J*=2.9 Hz, 2H), 2.54 (t, *J*=5.9 Hz, 2H), 2.08 (m, 2H), 1.98 (q, *J*=7.4 Hz, 2H), 1.00 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 138.3, 137.9, 129.1, 128.0, 126.8, 117.3, 62.9, 53.1, 50.0, 29.6, 29.4, 12.0. LRMS (EI) *m/z* (relative intensity) 201 $[M]^+$ (45), 172 (100), 110 (11), 91 (99), 65 (8). HRMS (EI, $[M]^+$): calcd for $C_{14}H_{19}N$, 201.1517; found, 205.1505.

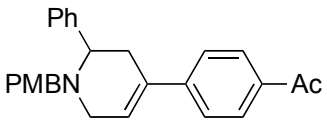


1aN

Procedure for the arylative cyclization of **9b** with **8H** (Table 3, Entry 1):
To a test tube containing **9b** (40.5 mg, 0.153 mmol), **8H** (29.9 mg, 0.182 mmol), K_2CO_3 (25.2 mg, 0.182 mmol), PdCp(η^3-allyl) (1.2 mg, 5.6 μmol), and $PPhCy_2$ (5.6 mg, 20 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 1 h. The mixture was cooled down to room temperature, diluted with EtOAc, washed with saturated aqueous Na_2CO_3 and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated three times to yield 43.9 mg (0.110 mmol, 72%) of **1bH**.

4-(4-Acetylphenyl)-1,2,3,6-tetrahydro-1-[(4-methoxyphenyl)methyl]-2-phenyl-pyridine (**1bH**)

Pale orange amorphous mass. IR (neat): 3344, 2912, 2833, 1677, 1600, 1509, 1356, 1245, 1171, 1032 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.89 (d, *J*=8.7 Hz, 2H), 7.50 (d, *J*=8.0 Hz, 2H), 7.46 (d, *J*=8.7 Hz, 2H), 7.40 (dd, *J*=8.0, 7.2 Hz, 2H), 7.31 (t, *J*=7.2 Hz, 1H), 7.22 (d, *J*=8.5 Hz, 2H), 6.84 (d, *J*=8.5 Hz, 2H), 6.26-6.24 (m, 1H), 3.80 (d, *J*=12.9 Hz, 1H), 3.79 (s, 3H), 3.68 (dd, *J*=4.6, 8.8 Hz, 1H), 3.50-3.44 (m, 1H), 3.03-2.96 (m, 1H), 2.95 (d, *J*=12.9 Hz, 1H), 2.86-2.73 (m, 2H), 2.58 (s, 3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 197.1, 158.2, 144.4, 142.9, 135.2, 133.2, 130.5, 129.6, 128.4, 128.2, 127.5, 127.1, 124.5, 123.9, 113.3, 64.0, 58.4, 55.1, 52.3, 36.8, 26.5. LRMS (EI) *m/z* (relative intensity) 397 $[M]^+$ (57), 273 (54), 258 (79), 121 (100), 105 (8), 77 (12). HRMS (EI, $[M]^+$): calcd for $C_{27}H_{27}NO_2$, 397.2042; found, 397.2023.



1bH

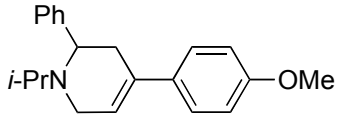
Procedure for the arylative cyclization of **9c** with **8A** (Table 3, Entry 2):

To a test tube containing **9c** (27.0 mg, 0.144 mmol), **8A** (27.6 mg, 0.182 mmol), and $Pd(PPh_3)_4$ (4.0 mg, 3.5 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 8 h. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.22 g, 0.36 mmol) and THF (2 mL) were added to remove an excess of **8A**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (90:10:2) repeated three times to yield 34.5 mg (0.112 mmol, 78%) of **1cA**.

1,2,3,6-Tetrahydro-1-isopropyl-4-(4-methoxyphenyl)-2-phenyl-pyridine (**1cA**)

Yellow oil. IR (neat): 2966, 2931, 1607, 1511, 1248, 1173, 1038 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.42-7.26 (m, 7H), 6.82 (d, *J*=9.8 Hz, 2H), 6.12 (dd, *J*=2.2, 4.6 Hz, 1H), 3.78 (s, 3H), 3.75 (dd, *J*=4.3, 9.4 Hz, 1H), 3.54-3.48 (m, 1H), 3.37-3.30 (m, 1H), 3.02 (qq, *J*=6.8, 6.4 Hz, 1H), 2.77-2.60 (m, 2H), 1.10 (d, *J*=6.8 Hz, 3H), 0.83 (d, *J*=6.4 Hz,

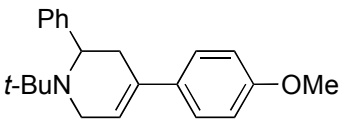
3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 158.4, 143.3, 133.6, 133.0, 128.3, 128.0, 127.0, 125.8, 120.2, 113.5, 61.8, 55.3, 48.1, 43.5, 38.7, 21.5, 12.6. LRMS (EI) *m/z* (relative intensity) 307 $[M]^+$ (100), 292 (56), 160 (30), 132 (35), 91 (11). HRMS (EI, $[M]^+$): calcd for $C_{21}H_{25}NO$, 307.1936; found, 307.1924.



1cA

Procedure for the arylative cyclization of **9d** with **8A** (Table 3, Entry 3):
To a test tube containing **9d** (29.3 mg, 0.146 mmol), **8A** (27.1 mg, 0.178 mmol), and $Pd(PPh_3)_4$ (3.9 mg, 3.4 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 8 h. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.22 g, 0.36 mmol) and THF (2 mL) were added to remove an excess of **8A**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with toluene-EtOAc-Et_3N (98:2:2) repeated two times to yield 35.6 mg (0.111 mmol, 76%) of **1dA**.

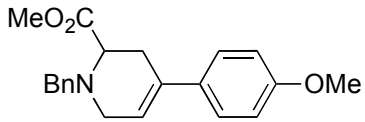
1-*tert*-Butyl-1,2,3,6-tetrahydro-4-(4-methoxyphenyl)-2-phenyl-pyridine (**1dA**)
Yellow solid. Mp: 81-84 °C. IR (neat): 2968, 2925, 1605, 1511, 1287, 1241, 1183, 1028 cm^{-1}. ^{1}H NMR (400 M Hz, $CDCl_3$): δ 7.38 (d, *J*=7.1 Hz, 2H), 7.32 (d, *J*=8.8 Hz, 2H), 7.26-7.15 (m, 3H), 6.85 (d, *J*=8.8 Hz, 2H), 6.18-6.16 (m, 1H), 4.58 (d, *J*=6.1 Hz, 1H), 3.79 (s, 3H), 3.64-3.60 (m, 1H), 3.46 (dd, *J*=2.9, 18.6 Hz, 1H), 2.99-2.95 (m, 1H), 2.61 (d, *J*=16.9 Hz, 1H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 158.4, 145.6, 133.8, 133.1, 127.9, 127.9, 126.2, 125.9, 122.6, 113.5, 55.3, 54.7, 54.2, 41.4, 33.5, 28.3. LRMS (EI) *m/z* (relative intensity) 321 $[M]^+$ (100), 306 (59), 264 (35), 237 (28), 160 (46), 146 (79). HRMS (EI, $[M]^+$): calcd for $C_{22}H_{27}NO$, 321.2093; found, 321.2079.



1dA

Procedure for the arylative cyclization of **9e** with **8A** (Table 3, Entry 4):
To a test tube containing **9e** (32.9 mg, 0.151 mmol), **8A** (27.6 mg, 0.182 mmol), and $Pd(PPh_3)_4$ (9.1 mg, 7.9 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 65 °C for 12 h. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.22 g, 0.36 mmol) and THF (2 mL) were added to remove an excess of **8A**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated three times to yield 34.0 mg (0.101 mmol, 67%) of **1eA**.

1,2,3,6-Tetrahydro-4-(4-methoxyphenyl)-1-(phenylmethyl)-2-pyridinecarboxylic acid methyl ester (**1eA**)
Pale yellow oil. IR (neat): 2950, 2834, 1733, 1607, 1511, 1453, 1366, 1243, 1177, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.39-7.24 (m, 7H), 6.85 (d, *J*=9.0 Hz, 2H), 5.95 (dd, *J*=2.9, 3.9 Hz, 1H), 3.94 (d, *J*=13.2 Hz, 1H), 3.87 (d, *J*=13.2 Hz, 1H), 3.80 (s, 3H), 3.73 (t, *J*=4.9 Hz, 1H), 3.63-3.56 (m, 1H), 3.38-3.31 (m, 1H), 2.84-2.83 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 173.0, 158.5, 138.4, 133.1, 131.8, 128.8, 128.2, 127.0, 125.9, 120.4, 113.6, 59.1, 58.6, 55.3, 51.4, 49.2, 30.7. LRMS (EI) *m/z* (relative intensity) 337 $[M]^+$ (7), 278 (100), 246 (81), 186 (18), 91 (66). HRMS (EI, $[M]^+$): calcd for $C_{21}H_{23}NO_3$, 337.1678; found, 337.1670.



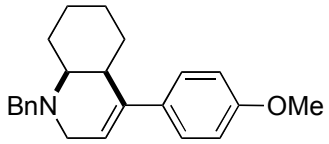
1eA

Procedure for the arylative cyclization of **9f** with **8A** (Table 3, Entry 5):
To a test tube containing **9f** (28.0 mg, 0.131 mmol), **8A** (24.0 mg, 0.158 mmol), and $Pd(PPh_3)_4$ (7.7 mg, 6.7 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (15 μL, 0.20 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 65 °C for 12 h. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.22 g, 0.36 mmol) and THF (2 mL)

were added to remove an excess of **8A**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (90:10:2) repeated three times to yield 27.8 mg (0.0834 mmol, 64%) of **1fA**.

Cis-1,2,4a,5,6,7,8,8a-octahydro-4-(4-methoxyphenyl)-1-(phenylmethyl)-quinoline (**1fA**)

Colorless oil. IR (neat): 2927, 2852, 1607, 1509, 1451, 1277, 1245, 1173, 1036 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.39-7.21 (m, 7H), 6.83 (d, *J*=8.0 Hz, 2H), 5.67-5.66 (m, 1H), 4.10 (d, *J*=12.8 Hz, 1H), 3.78 (s, 3H), 3.25-3.21 (m, 2H), 2.88 (d, *J*=17.6 Hz, 1H), 2.80-2.78 (m, 2H), 2.08-2.07 (m, 1H), 1.88-1.28 (m, 7H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 158.6, 140.1, 139.9, 133.5, 128.8, 128.2, 127.1, 126.7, 121.4, 113.7, 57.8, 57.4, 55.3, 52.3, 40.1, 28.5, 26.1, 25.2, 21.9. LRMS (EI) *m/z* (relative intensity) 333 $[M]^+$ (100), 290 (23), 276 (14), 250 (16), 242 (14), 121 (8), 91 (58). HRMS (EI, $[M]^+$): calcd for $C_{23}H_{27}NO$, 333.2093; found, 333.2096.



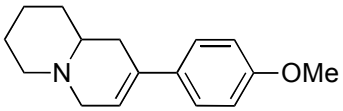
1fA

Procedure for the arylative cyclization of **9g** with **8A** (Table 3, Entry 6):

To a test tube containing **9g** (18.0 mg, 0.146 mmol), **8A** (27.0 mg, 0.178 mmol), PdCp(η^3-allyl) (1.0 mg, 4.7 μmol), and $PPhCy_2$ (5.1 mg, 19 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 24 h. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.22 g, 36 mmol) and THF (2 mL) were added to remove an excess of **8A**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC eluting with EtOAc-MeOH (15:1) repeated three times to yield 22.9 mg (0.0941 mmol, 64%) of **1gA**.

1,3,4,6,9,9a-Hexahydro-8-(4-methoxyphenyl)-2H-quinolizine (**1gA**)

White solid. Mp: 83-87 °C. IR (neat): 2927, 2734, 1603, 1511, 1457, 1293, 1252, 1237, 1181, 1129, 1027 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.31 (d, *J*=9.1 Hz, 2H), 6.84 (d, *J*=9.1 Hz, 2H), 5.95-5.93 (m, 1H), 3.79 (s, 3H), 3.46-3.41 (m, 1H), 3.03-3.00 (m, 1H), 2.90-2.84 (m, 1H), 2.46-2.03 (m, 4H), 1.85-1.65 (m, 4H), 1.40-1.26 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 158.4, 133.6, 133.3, 125.8, 119.3, 113.5, 57.6, 55.8, 55.4, 55.3, 35.7, 33.8, 26.1, 24.5. LRMS (EI) *m/z* (relative intensity) 243 $[M]^+$ (100), 160 (59), 145 (21), 129 (13), 109 (8). HRMS (EI, $[M]^+$): calcd for $C_{16}H_{21}NO$, 243.1623; found, 243.1605.



1gA

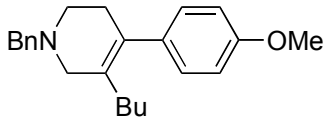
General procedure for the arylative cyclization of **10a·h-i** (Table 4, Entries 1, 3, 7, 8):
To a test tube containing **10a·h-j** (0.15 mmol, see Table 4S-1), **8A·M** (0.18 mmol), and $Pd(PPh_3)_4$ (3.0 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 1 h. The mixture was cooled down to room temperature, and then PS-DEAM™ (1.63 mmol/g, 0.36 mmol) and THF (2 mL) were added to remove an excess of **8A·M**. The mixture was agitated at room temperature for 2 h. The mixture was filtered and thoroughly washed with $CHCl_3$. The filtrate was concentrated *in vacuo* and the residue was purified by preparative TLC to afford arylative cyclization product **1aA·aM·hA·iA** in the yield described in Table 4.

Table 4S-1

10 (mg)	**8** (mg)	$Pd(PPh_3)_4$ (mg)	**1** (mg, mmol, %)
10a; 23.0	**8A**; 27.0	3.6	**1aA**; 34.1, 0.122, 84
10a; 24.0	**8M**; 27.2	3.9	**1aM**; 34.3, 0.125, 83
10h; 32.4	**8A**; 26.9	3.9	**1hA**; 44.2, 0.132, 88
10i; 39.6	**8A**; 27.1	3.8	**1iA**; 29.4, 0.0763, 51

5-Butyl-1,2,3,6-tetrahydro-4-(4-methoxyphenyl)-1-(phenylmethyl)-pyridine (**1hA**) was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times.

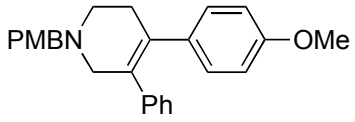
Colorless oil. IR (neat): 2923, 2833, 1607, 1509, 1453, 1241, 1173, 1038 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.40-7.25 (m, 5H), 7.08 (d, *J*=8.7 Hz, 2H), 6.84 (d, *J*=8.7 Hz, 2H), 3.80 (s, 3H), 3.64 (s, 2H), 3.04 (s, 2H), 2.61 (t, *J*=5.7 Hz, 2H), 2.36 (br-s, 2H), 1.91 (t, *J*=7.8 Hz, 2H), 1.33-1.13 (m, 4H), 0.78 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 157.7, 138.0, 135.1, 131.3, 130.3, 129.2, 128.1, 126.9, 113.3, 113.3, 63.0, 56.3, 55.2, 50.3, 32.8, 32.0, 30.9, 22.8, 14.1. LRMS (EI) *m/z* (relative intensity) 335 $[M]^+$ (4), 278 (100), 214 (28), 199 (21), 171 (13), 149 (10), 105 (4), 91 (40). HRMS (EI, $[M]^+$): calcd for $C_{23}H_{29}NO$, 335.2249; found, 335.2224.



1hA

1,2,3,6-Tetrahydro-4-(4-methoxyphenyl)-1-[(4-methoxypheny)methyl]-5-phenyl-pyridi ne (**1iA**) was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated three times.

Pale yellow oil. IR (neat): 2908, 2833, 1607, 1509, 1463, 1291, 1243, 1175, 1034 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.31 (d, *J*=8.7 Hz, 2H), 7.15-7.08 (m, 3H), 7.01 (d, *J*=8.3 Hz, 2H), 6.92 (d, *J*=8.8 Hz, 2H), 6.87 (d, *J*=8.7 Hz, 2H), 6.63 (d, *J*=8.8 Hz, 2H), 3.81 (s, 3H), 3.71 (s, 3H), 3.64 (s, 2H), 3.33 (s, 2H), 2.74 (t, *J*=5.6 Hz, 2H), 2.58 (br-s, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 158.5, 157.5, 141.0, 134.1, 132.3, 132.1, 130.4, 129.8, 129.7, 129.1, 127.7, 126.0, 113.5, 112.9, 62.1, 58.1, 55.3, 55.1, 49.9, 32.1. LRMS (EI) *m/z* (relative intensity) 385 $[M]^+$ (67), 308 (15), 264 (11), 205 (7), 121 (100), 91 (7). HRMS (EI, $[M]^+$): calcd for $C_{26}H_{27}NO_2$, 385.2042; found, 385.2026.



1iA

General procedure for the arylative cyclization of **10a·j** (Table 4, Entries 2, 9):

To a test tube containing **10a·j** (0.15 mmol, see Table 4S-2), **8H** (0.18 mmol), K_2CO_3 (0.18 mmol), and $Pd(PPh_3)_4$ (3.0 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 1 h. The mixture was cooled down to

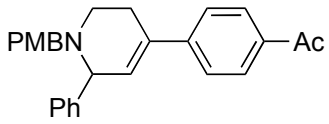
room temperature, diluted with EtOAc, washed with saturated aqueous Na_2CO_3 and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC to afford arylative cyclization product **1aH·jH** in the yield described in Table 4.

Table 4S-2

10 (mg)	**8H** (mg)	K_2CO_3 (mg)	$Pd(PPh_3)_4$ (mg)	**1** (mg, mmol, %)
10a; 23.4	29.8	25.1	3.6	**1aH**; 32.7, 0.112, 76
10j; 40.2	30.4	25.5	3.7	**1jH**; 48.9, 0.123, 81

4-(4-Acetylphenyl)-1,2,3,6-tetrahydro-1-[(4-methoxyphenyl)methyl]-6-phenyl-pyridine (**1jH**) was isolated by preparative TLC eluting with hexane-EtOAc-Et_3N (66:33:2) repeated three times.

Pale yellow amorphous mass. IR (neat): 2931, 2794, 1677, 1600, 1509, 1356, 1266, 1243, 1179, 1032 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.88 (d, *J*=8.3 Hz, 2H), 7.49 (d, *J*=7.3 Hz, 2H), 7.45 (d, *J*=8.3 Hz, 2H), 7.36 (dd, *J*=7.3, 7.3 Hz, 2H), 7.27 (t, *J*=7.3 Hz, 1H), 7.20 (d, *J*=8.5 Hz, 2H), 6.84 (d, *J*=8.5 Hz, 2H), 6.09 (m, 1H), 4.11 (d, *J*=2.2 Hz, 1H), 3.79 (s, 3H), 3.79-3.76 (m, 1H), 3.13-3.10 (m, 2H), 2.75-2.71 (m, 1H), 2.57 (s, 3H), 2.49-2.41 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 197.3, 158.3, 145.0, 142.9, 135.4, 133.0, 130.9, 129.7, 129.2, 128.4, 128.4, 128.3, 127.3, 124.8, 113.4, 66.8, 58.0, 55.3, 47.5, 27.9, 26.7. LRMS (EI) *m/z* (relative intensity) 397 $[M]^+$ (42), 320 (11), 258 (50), 230 (15), 202 (7), 173 (9), 149 (12), 121 (100), 105 (16), 77 (14). HRMS (EI, $[M]^+$): calcd for $C_{27}H_{27}NO_2$, 397.2042; found, 397.2023.



1jH

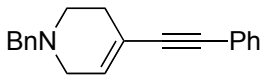
Procedure for the ethylative cyclization of **10a** (Table 4, Entry 4):

To a test tube containing **10a** (23.5 mg, 0.148 mmol) and $Pd(PPh_3)_4$ (3.9 mg, 3.4 μmol) were added anhydrous THF (0.4 mL), 1.0 M solution of triethylborane (**8N**) in THF (0.23 mL, 0.23 mmol), and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 2 h. The mixture was cooled down to room temperature, diluted with EtOAc, washed with

saturated aqueous Na_2CO_3 and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) to yield 19.5 mg (0.0969 mmol, 66%) of **1aN**.

Procedure for the phenylethynylative cyclization of **10a** (Table 4, Entry 5):
To a test tube containing **10a** (24.1 mg, 0.151 mmol), CuI (1.1 mg, 5.8 μmol), and $Pd(PPh_3)_4$ (3.7 mg, 3.2 μmol) were added anhydrous THF (0.6 mL), phenylacetylene (**8O**) (25 μL, 0.23 mmol), and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 1 h. The mixture was cooled down to room temperature and concentrated *in vacuo*. The residue was purified by preparative TLC eluting with hexane-EtOAc-Et_3N (80:20:2) repeated two times to yield 35.2 mg (0.129 mmol, 85%) of **1aO**.

1,2,3,6-Tetrahydro-4-(phenylethynyl)-1-(phenylmethyl)-pyridine (**1aO**)
Yellow oil. IR (neat): 2917, 2798, 1596, 1490, 1453, 1441, 1362, 1160, 1136, 1104, 1028 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.42-7.25 (m, 10H), 6.11 (t, *J*=1.6 Hz, 1H), 3.61 (s, 2H), 3.10-3.08 (m, 2H), 2.62 (t, *J*=5.6 Hz, 2H), 2.38-2.37 (m, 2H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 138.0, 132.0, 131.3, 128.9, 128.1, 128.1, 127.8, 127.0, 123.3, 119.1, 89.8, 87.9, 62.6, 53.0, 49.4, 30.2. LRMS (EI) *m/z* (relative intensity) 273 $[M]^+$ (100), 182 (19), 155 (22), 127 (13), 91 (55). HRMS (EI, $[M]^+$): calcd for $C_{20}H_{19}N$, 273.1517; found, 273.1519.



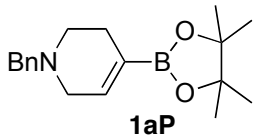
1aO

Procedure for the borative cyclization of **10a** (Table 4, Entry 6):
To a test tube containing **10a** (23.3 mg, 0.146 mmol), bis(pinacolato)diboron (**8P**) (77.0 mg, 0.303 mmol), and $Pd(PPh_3)_4$ (3.6 mg, 3.1 μmol) were added anhydrous THF (0.6 mL) and 37% aqueous formaldehyde (17 μL, 0.23 mmol) under argon. The resulting mixture was sealed with a screw cap and agitated at 50 °C for 1 h. The mixture was cooled down to room temperature and concentrated *in vacuo*. The residue was purified by GPC to yield 25.3 mg (0.0925 mmol, 63%) of **1aP**.

1,2,3,6-Tetrahydro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(phenylmethyl)-p

yridine (**1aP**)

Colorless oil. IR (neat): 2977, 2916, 2798, 1640, 1602, 1453, 1397, 1331, 1314, 1293, 1144, 1075, 1011 cm^{-1}. ^1H NMR (400 M Hz, $CDCl_3$): δ 7.35-7.22 (m, 5H), 6.49 (m, 1H), 3.57 (s, 2H), 3.04-3.03 (m, 2H), 2.54 (t, *J*=5.6 Hz, 2H), 2.28-2.27 (m, 2H), 1.25 (s, 12H). ^{13}C NMR (100 M Hz, $CDCl_3$): δ 140.1, 138.2, 129.0, 128.0, 126.8, 83.2, 63.0, 53.9, 49.8, 27.3, 24.9. LRMS (EI) *m/z* (relative intensity) 299 $[M]^+$ (79), 208 (20), 189 (12), 160 (39), 129 (100), 102 (27), 91 (65), 75 (12). HRMS (EI, $[M]^+$): calcd for $C_{18}H_{26}BNO_2$, 299.2057; found, 299.2035.



1aP

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