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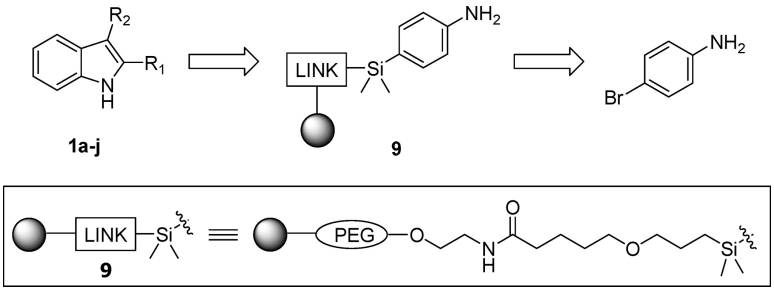

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Synthesis of 2,3-Disubstituted Indole on Solid Phase by the Fischer Indole Synthesis

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2,3-Disubstituted indoles were synthesized by solid-phase reaction using the Fischer indole synthesis. A "traceless" silicon linker was employed with the silicon−carbon bonding being cleaved with TFA. An oxygen atom was placed into the middle of the spacer/linker so as to enhance solid-phase synthesis by better solvation.

Introduction

There are many indole compounds extracted from natural substances. Since the indole moiety is well-known for its good physiological activities, various indole derivatives can be utilized for many purposes. Indole derivatives can be synthesized on solid phase. Their synthesis with ease helps in the construction of indole libraries for pharmacological activity screening. Many synthetic chemistries have been developed for solid-phase indole synthesis;[1] for example, the Waldmann group[2] and the Takahashi group[3] recently reported traceless Fisher indole synthesis on solid phase, utilizing externally supplied hydrazine compounds as a nitrogen source. In contrast with them, our method involved the hydrazines as precursors for Fisher indole synthesis, which were formed from amines during solid-phase reaction, and an α-methylene ketone building block library was needed rather than a hydrazine building block. In particularly, we focused on the Fisher indole synthesis using a silicon traceless linker. Each functional group on a drug could affect the outcome of medicinal activity dramatically.[4] The silicon traceless linker was reported by the Ellman group.[5] Here, we modified the Ellman silicon linker to enhance solvation potency by the insertion of an oxygen moiety in the middle of the linker.

The Fischer indole method was employed to synthesize 16 2,3-disubstituted indole derivatives, **1a**−**p**, using **9**. Group **1a**−**p** was obtained by cleaving the silicon−carbon bond with TFA, a hydrogen atom taking the place of a silicon atom when the silicon−carbon bond was broken. The traceless linker was prepared from 4-bromoaniline by substituting silicon for bromine.

Results and Discussion

Solution-Phase Synthesis of Linker 7. The amine group of 4-bromoaniline was protected using di-*tert*-butyl dicarbonate ($(Boc)_2O$) to give **2**,[6] which was silylated using allylchlorodimethylsilane,[7] to give **3** in 35% yield. To introduce the hydroxyl group to the terminal double bond of **3**, hydroboration−oxidation was employed using 9-BBN and hydrogen peroxide to give alcohol **4**. Alcohol **4** was reacted with 6-bromohexene by Williamson ether synthesis to give a 50% yield of **5**. Ozonolysis in the dichloromethane followed by quenching of H_2O_2/HCOOH was carried out; however, the yield was low, and the result was unsatisfactory. Ozonolysis in the dichloromethane/NaOH/MeOH gave a 60% yield of the methyl ester **6**, which was hydrolyzed to give a 90% yield of carboxylic acid **7**. (Scheme 2)

Solid-Phase Synthesis of Indole 1a−p. Resin **8** was prepared by coupling **7** with TentaGel S NH_2 resin swollen in DMF.[8] Resin **8** was swollen in dichloromethane/TFA (1:1), and the solution was shaken for 10 min at room temperature to give **9**, which was swollen in 2 N HCl, 5% sodium nitrite was added, and the solution was shaken for 2.5 h at 0 °C. Resin **9** was washed in cold water, and the resin was swollen in HCl before being shaken with tin(II) chloride at room temperature for 2 h and then at 60 °C for 2.5 h.[9] The reaction was monitored by the ninhydrin test for the recognition of amine existence. Hydrazine resin **10** was washed in cold water and then in acetic acid. After the addition of ketone to resin **10**, the solution was shaken for 23 h at 70 °C to give the 2,3-disubstitued indole resin **11a**−**p**.[10] Finally, the 2,3-disubstituted indoles **1a**−**p** were obtained by silicon−carbon cleavage by shaking in a solution of TFA/CH_2Cl_2 (1:1) for 23 h[11] (Scheme 3).

Conclusion

Sixteen 2,3-disubstituted indoles were synthesized by solid-phase reaction using the Fischer indole synthesis, as shown in Table 1. All of the reaction products were quite pure, more than 95% by HPLC. This scheme will be expanded for the construction of a larger indole library from the α-methylene ketone building block and investigated for biological activity extensively. A "traceless" silicon linker was employed with the silicon−carbon bonding being cleaved with TFA. This cleavage reaction worked very well in all cases. An oxygen atom was placed into the middle of the spacer/linker so as to enhance solid-phase synthesis by better solvation. On first trial, the linker, which does not have

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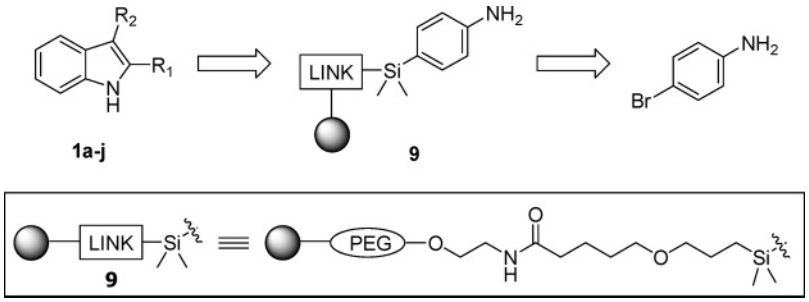
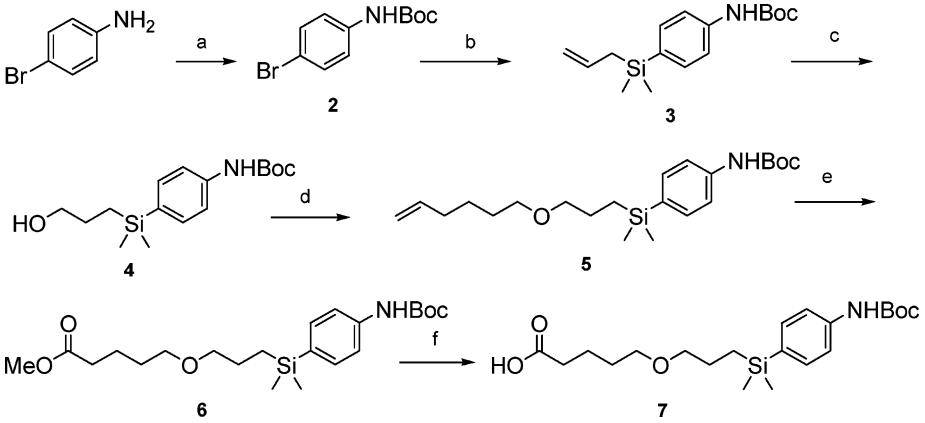
Scheme 1. Construction of an Indole Library by the Fischer Indole Method

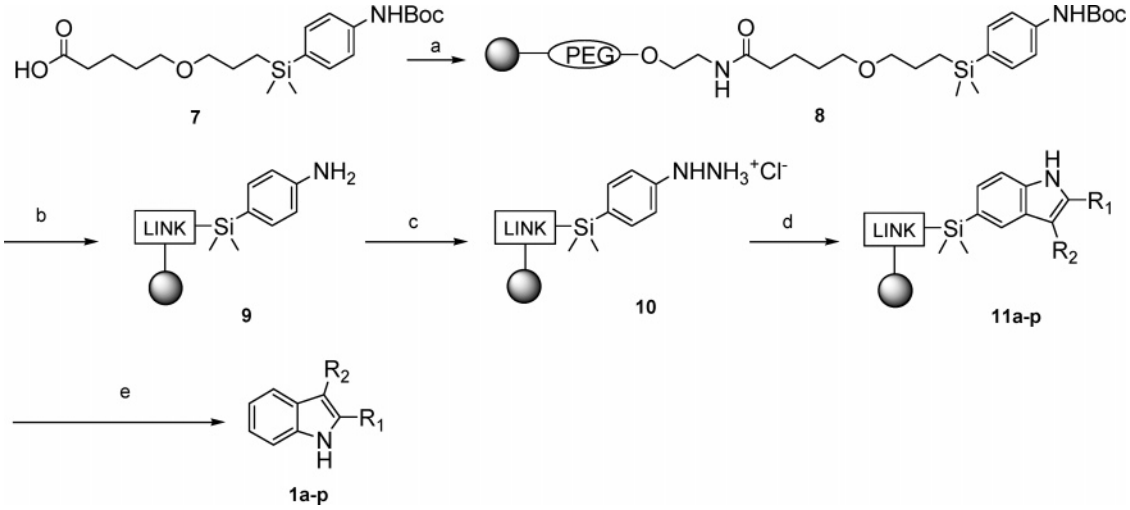


Scheme 2. Synthesis of Linker **7**



(a) $(Boc)_2O$, Et_3N, DMAP, CH_2Cl_2, 0 °C, 99%. (b) KH, 0 °C, THF, then *tert*-BuLi, LiCl, allylchlorodimethylsilane, −78 °C, 35%. (c) 9-BBN (0.5 M in THF), H_2O_2, KOH, room temperature, 67%. (d) NaH, 6-bromohexene, Bu_4NI, THF, 0 °C, 50%. (e) O_3, 2.5 M NaOH in MeOH, CH_2Cl_2, −78 °C, 60%. (f) *tert*-BuOK, H_2O, diethyl ether, room temperature, 90%.

Scheme 3. Synthesis of the Indole Library on Solid Phase



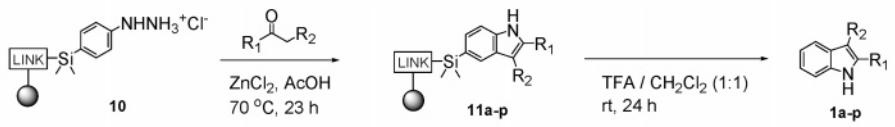
(a) TentaGel S NH_2, EDC, HOBT, TEA, DMF, room temperature, 24 h. (b) 50% TFA in CH_2Cl_2, room temperature, 10 min. (c) (i) 5% $NaNO_2$ aq, 2 N HCl, 0 °C, 2.5 h; (ii) $SnCl_2$, HCl, 60 °C, 2.5 h. (d) R_1, R_2-ketone, $ZnCl_2$, AcOH, 70 °C, 23 h. (e) 50% TFA in CH_2Cl_2, room temperature, 23 h.

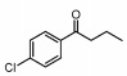
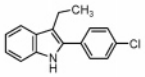
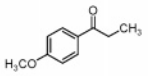
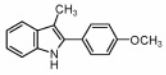
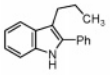
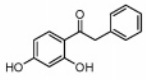
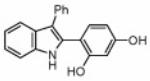
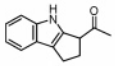
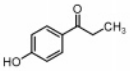
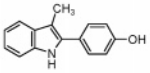
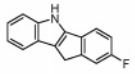
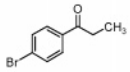
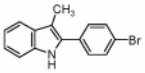
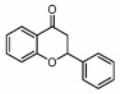
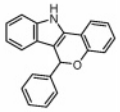
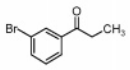
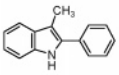
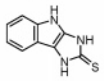
oxygen in the middle, was applied to the solid-phase reaction. It turned out that the formation of diazonium salt failed due to a deficiency of solvation, possibly. Linker **9** was straightforwardly prepared from the *p*-bromoaniline, and the modification of linker **9** could be successful from other amines.

Experimental Section

General Method. Reagents were purchased from Aldrich, Fluka, and TCI and were used without purification. When purification was necessary, the traditional purification method[12] was used. Reactions were monitored by TLC on a Merck 60 F_{254} (0.25 mm) plate and were viewed by UV inspection, staining (5−10% of phosphomolybdic acid in ethanol) or both. Merck silica gel (silica gel 60, 230−400 mesh ASTM) was used for column chromatographic separation. The resin was TentaGel S NH_2 130 mesh with a loading amount of 0.27 mmol/g. THF and diethyl ether were purified by reflux distillation from sodium metal and benzophenone under an argon atmosphere, respectively. Dichloromethane, acetonitrile, and triethylamine were dried using calcium hydride. ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra in $CDCl_3$ were obtained on a Gemini Varian-200 spectrometer

Table 1. Synthesis of Indoles



Entry	Ketones	Indoles	Yield (%)	Column Cond. (*n*-Hex. : EtOAc)	Entry	Ketones	Indoles	Yield (%)	Column Cond. (*n*-Hex. : EtOAc)
1a			53	7 : 1	1i			81	20 : 1
1b			35	20 : 1	1j			58	10 : 1
1c			30	20 : 1	1k			60	10 : 1
1d			22	20 : 1	1l			55	10 : 1
1e			40	2 : 1	1m			40	10 : 1
1f			55	3 : 1	1n			87	10 : 1
1g			28	20 : 1	1o			30	10 : 1
1h			14	10 : 1	1p			28	1 : 1

using TMS as the internal standard. FT-IR spectra were recorded on a JASCO FT-IR 430 spectrometer. The solid sample was pressed into a pellet mixed with potassium bromide (KBr). A VG70-VSEQ mass spectrometer (VG Analitical, U.K.) was used to measure HRMS(FAB), and a glycerol matrix was employed. The FAB source was ionized by a 35 KeM Cs^+ ion beam and accelerated to 8 KV in resolution 1000.

Compound 2. 4-Bromoaniline (5.00 g, 29.06 mmol) was dissolved in anhydrous dichloromethane (CH_2Cl_2, 150 mL), and the solution was stirred at 0 °C for 1 h under nitrogen gas, followed by the addition of triethylamine (Et_3N, 2.94 g, 29.06 mmol), di-*tert*-butyl dicarbonate (6.34 g, 29.06 mmol), and *N*,*N*-(dimethylamino)pyridine (DMAP, 3.55 g, 29.06 mmol). When the reaction was complete, the dichloromethane was removed under vacuum. The residue was dissolved in *n*-hexane/EtOAc (10:1), followed by filtration. The precipitate was filtered from the solution through filter paper, and the filtrate was washed twice in water (150 mL), followed by brine (100 mL) to give a clear oil that was dried over anhydrous $MgSO_4$, followed by drying under high vacuum to give 7.83 g (99% yield) of product. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.33 (dd, J = 66.2, 8.8 Hz, 4H,), 1.42 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.5, 137.7, 131.9, 129.6, 121.6, 83.7, 27.8; MS (FAB) *m*/*z* 272.19 [M + H]$^+$.

Compound 3. Compound **2** (1.00 g, 3.76 mmol) was dissolved in anhydrous THF (20 mL) under nitrogen gas at 0 °C. KH (35%, 540 mg, 4.40 mmol) was added. The solution was stirred for 5 min. Allylchlorodimethylsilane (2.47 g, 17.81 mmol) and lithium chloride (37 mg, 0.1 mmol) were added to the solution and kept at −70 °C. *tert*-Butyllithium (*tert*-BuLi, 1.7 M, 6.48 mL) was added dropwise into the solution. The solution was stirred for 3 h, and the temperature was slowly raised to room temperature from −78 °C. When the reaction was complete, a small amount of water was added, followed by ethyl acetate (50 mL) before washing twice with water (50 mL), twice with 1 M sodium bisulfate (50 mL), and once with brine (50 mL). The organic layer was dried over anhydrous $MgSO_4$ and purified by chromatography by elution with *n*-hexane/EtOAc (20:1) to afford 384 mg (35% yield) of product **3**. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.43 (m, 4H,), 6.59 (s, 1H), 5.80 (m, 1H), 4.90 (d, J = 5.2 Hz, 1H), 4.82 (s, 1H), 1.74 (d, J = 8.0 Hz, 2H), 1.54 (s, 9H), 0.26 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 152.6, 139.0, 134.6, 134.4, 117.7, 113.2, 80.5, 60.3, 28.2, 23.7, −3.4; MS (FAB) *m*/*z* 292.28 [M + H]$^+$.

Compound 4. To a dried flask under nitrogen was added Boc-protected **3** (1.36 g, 4.67 mmol) and 9-BBN (14 mL, 0.5 M in THF). The reaction mixture was stirred 24 h at room temperature. The flask was cooled to 0 °C, and 2.0 M aqueous KOH (11.6 mL, 23.2 mmol) was added, followed

by 30% aqueous H_2O_2 (11.6 mL). After 5 min, the mixture was taken up in EtOAc (100 mL), washed with water (100 mL × 3) and brine (100 mL), dried over anhydrous $MgSO_4$, and concentrated. Column chromatography (eluting with 20:1 *n*-hexane/EtOAc) gave 960 mg (67% yield) of product **4**. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.20 (m, 4H), 6.62 (bs, 1H), 3.39 (t, J = 6.6 Hz, 2H), 1.89 (bs, 1H), 1.35 (s, 10H), 0.56 (m, 3H), 0.08 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 152.7, 139.0, 134.2, 132.6, 117.8, 80.4, 65.4, 28.2, 26.9, 11.3, −3.1; MS (FAB) *m*/*z* 332.31 $[M + Na]^+$.

Compound 5. Compound **4** (389 mg, 1.25 mmol) was dissolved in dry THF 20 mL. Sodium hydride (150 mg, 3.75 mmol) was added to the solution and stirred for ∼5 min at 0 °C. After the addition of 6-bromo-1-hexene (410 mg, 2.50 mmol) and Bu_4NI (46 mg, 0.124 mmol), the solution was stirred for 6 h at 0 °C, followed by stirring for 48 h at room temperature. When the reaction was completed, a small amount of NH_4Cl was added. After the addition of diethyl ether (180 mL), the solution was washed with 180 mL of NH_4Cl, followed by 180 mL of brine. The organic compound was separated and dried over $MgSO_4$. The residue was purified on a column of silica gel and eluted with *n*-hexane/EtOAc (3:1) to give 245 mg (50% yield) of **5**. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.48 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 5.76 (m, 1H), 4.95 (m, 2H), 3.60 (t, J = 8.0 Hz, 4H), 2.04 (q, J = 14.2, 7.0 Hz, 2H), 1.52 (m, 8H), 1.44 (s, 9H), 0.729 (m, 2H), 0.27 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.6, 143.1, 138.5, 136.2, 133.9, 126.0, 114.5, 80.0, 65.6, 49.7, 33.3, 28.3, 28.0, 27.0, 25.9, 11.3, −3.1; MS (FAB) *m*/*z* 392.30 $[M + H]^+$.

Compound 6. Compound **5** (130 mg, 0.33 mmol) was dissolved with dry dichloromethane. After NaOH (2.5 M in MeOH, 1 mL) was added to the solution, the solution was kept at −78 °C. Ozone gas was bubbled through the solution for ∼20 min. The color of the compound changed into dark yellow at −78 °C during the period of ozonolysis and changed back to clear at room temperature. When the temperature was raised to room temperature, ethyl ether (10 mL) and water (5 mL) were added for workup. The ether layer was separated and dried over anhydrous $MgSO_4$. The residue was loaded onto a column of silica gel and eluted with *n*-hexane/EtOAc (3:1) to give 81 mg (60% yield) of pure product **6**. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.44 (d, J = 7.6 Hz, 2H), 7.15 (d, J = 7.6 Hz, 2H), 3.65 (s, 3H), 3.56 (t, J = 7.0 Hz, 4H), 2.32 (t, J = 6.6 Hz, 2H), 1.60−1.22 (m, 6H), 1.44 (s, 9H), 0.73 (m, 2H), 0.27 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 173.8, 154.6, 142.8, 136.4, 133.9, 126.0, 80.1, 65.4, 51.4, 49.3, 33.5, 28.2, 27.8, 26.9, 21.9, 11.3, −3.1; HRMS (FAB) calcd for $C_{22}H_{37}NNaO_5Si$, 446.2339; found, 446.2346 $[M + Na]^+$.

Compound 7. Potassium *tert*-butoxide (97 mg, 0.821 mmol) was added to dry ethyl ether (2 mL). Into this reaction mixture, 3.74 μL (0.206 mmol) of water was added in one portion, followed by stirring for 5 min at 0 °C under nitrogen gas. After methyl ester **6** (40 mg, 0.0944 mmol) in ethyl ether (2 mL) was added, the solution was stirred for 1 h at room temperature. Then the solution was acidified with ethyl ether (10 mL) and 10% acetic acid (10 mL). The ether layer was separated and dried over anhydrous $MgSO_4$ to give 32 mg (90% yield) of pure product **7**. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.45 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 3.66 (m, 2H), 3.55 (t, J = 6.6 Hz, 2H), 2.31 (m, 2H), 1.59−1.25 (m, 6H), 1.43 (s, 9H), 0.70 (m, 2H), 0.27 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 178.3, 154.6, 142.7, 136.3, 134.0, 126.1, 80.3, 65.4, 49.0, 33.4, 28.2, 27.7, 26.8, 21.7, 11.4, −3.2; MS (FAB) *m*/*z* 432.30 $[M + Na]^+$.

Compound 8. TentaGel S NH_2 resin (203 mg, 0.055 mmol, 0.27 mmol/g, 130 μm) was swelled in anhydrous DMF (6 mL). Compound **7** (27 mg, 0.066 mmol), EDC (15.8 mg, 0.0825 mmol), HOBt (11.1 mg, 0.0825 mmol), and Et_3N (11.5 μL, 0.0825 mmol) were added in order. After the solution was shaken for 24 h in N_2, the resin was washed three times in DMF (10 mL), three times in DMF/H_2O (1:1, 10 mL), three times in H_2O (10 mL), three times in MeOH (10 mL), and three times in CH_2Cl_2 (10 mL). The organic layer was separated and dried under high vacuum. The ninhydrin test confirmed that resin **8** shows no color change, and two carbonyl peaks at 1697 and 1669 cm^{-1} were observed on the measured IR spectrum. IR (KBr) 3509.81, 2871.49, 1958.36, 1697.05, 1669.09, 1599.66, 1540.85, 1453.10, 1345.11, 1107.90, 948.81, 841.78, 760.78, 700.03 cm^{-1}.

Preparation of Ninhydrin Test Solution. The following solutions were prepared: (1) 5 g of ninhydrin dissolved in 100 mL of ethanol, (2) 80 g of liquefied phenol dissolved in 20 mL of ethanol, and (3) 2 mL of a 0.001 M aqueous solution of potassium cyanide added to 98 mL of pyridine. Sample a few resin beads and wash several times with ethanol. Transfer to a small glass tube and add 2 drops of each of the solutions above. Mix well and heat to 120 °C for 4−6 min. A positive test is indicated by blue resin beads.

Compound 9. Resin **8** (120 mg, 0.0324 mmol) was swelled in TFA/CH_2Cl_2 (1:1) 4 mL, and the solution was shaken for 10 min at room temperature. Then the resin was washed five times in dichloromethane (10 mL). Resin **9** was obtained by drying the resin without the Boc protecting group under high vacuum. IR (KBr) 3458.71, 2914.88, 1975.71, 1784.80, 1622.80, 1455.03, 1354.75, 1169.69, 952.66, 809.96, 700.03 cm^{-1}.

Compound 10. Resin **9** (100 mg, 0027 mmol) was swelled in 2 N HCI (4 mL). Then the solution was stirred for 2.5 h at 0 °C in addition of 5% sodium nitrite (1.5 mL). After the solvent was removed, the resin was swelled at high density in addition of HCl (2 mL). After addition of tin chloride(II) (100 mg, 0.53 mmol), the solution was stirred for 2 h at room temperature, and then for 2.5 h at 60 °C. Resin **10** was washed five times in cold water (10 mL) and three times in acetic acid (10 mL) and then used in the next step. IR (KBr) 3564.77, 2870.52, 1640.80, 1454.06, 1350.89, 1106.94, 951.70, 701.00 cm^{-1}.

Compounds 11a−p. Resin **10** (100 mg, 0.027 mmol) was swelled in acetic acid (4 mL). R_1, R_2-ketone (0.27 mmol, 10 equiv), and zinc chloride (0.27 mmol, 10 equiv) were added. Then the solution was stirred for 23 h at 70 °C. The resin was washed five times each in acetic acid (5 mL), in THF/CH_2Cl_2, (1:1, 5 mL), in DMF (5 mL), in CH_2Cl_2 (5 mL), and in MeOH (5 mL) to give resin **11a−p** (Table 1).

Compounds 1a−p. Resins **11a−p** (100 mg, 0.027 mmol) was swelled in TFA/CH_2Cl_2 (1:1, 2 mL), and the solution was shaken for 23 h. The resin was filtered out after addition of dichloromethane (10 mL) to the solution. The solvent was removed by the rotary evaporator to give products **1a−p** (Table 1).

Analytical Data for Compound 1a.[13] ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.93 (m, 2H), 7.66 (d, J = 7.0 Hz, 2H), 7.42 (t, J = 7.2 Hz, 2H), 7.25 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 136.5, 135.4, 128.7, 127.3, 125.9, 125.5, 122.2, 121.8, 120.2, 119.7, 118.0, 111.4; MS (FAB) 193 (M^+); HRMS (FAB) calcd for $C_{14}H_{11}N$, 193.0891; found, 193.0893.

Compound 1b.[14] ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.85 (bs, 1H), 7.59−7.10 (m, 9H), 2.41 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 135.7, 133.9, 133.2, 129.9, 128.7, 127.6, 127.2, 122.2, 119.4, 118.9, 110.6, 9.6; MS (FAB) 273 (M^+); HRMS (FAB) calcd for $C_{16}H_{15}NO$, 273.1154; found, 273.1157.

Compound 1c.[15] ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.93 (bs, 1H), 7.67−7.10 (m, 9H), 2.93 (q, J = 15, 7.2 Hz, 2H), 1.34 (t, J = 7.8 Hz, 3H);^{13}C NMR (50 MHz, $CDCl_3$) δ: 133.9, 133.3, 128.9, 128.8, 127.8, 127.4, 122.1, 119.4, 115.3, 110.7, 17.7, 15.6; MS (FAB) 207 (M^+); HRMS (FAB) calcd for $C_{15}H_{13}N$, 207.1048; found, 207.1028.

Compound 1d.[16] ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.00 (bs, 1H), 7.66−7.12 (m, 9H), 2.86 (t, J = 7.6 Hz, 2H), 1.74 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H); MS (FAB) 221 (M^+); HRMS (FAB) calcd for $C_{16}H_{15}N$, 221.1204; found, 221.1222.

Compound 1e. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.40 (bs, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.48−7.18 (m, 8H), 6.44 (m, 3H); MS (FAB) 235 (M^+); HRMS (FAB) calcd for $C_{17}H_{17}N$, 235.1361; found, 235.1370.

Compound 1f.[17] ^{1}H NMR (200 MHz, CD_3OD) δ: 8.25 (dd, J = 266.0, 9.2 Hz, 4H), 7.47−7.23 (m, 4H), 1.60 (s, 3H); MS (FAB) 301 (M^+); HRMS (FAB) calcd for $C_{20}H_{15}NO_2$, 301.1103; found, 301.1102.

Compound 1g. (CAS No.: 102547-50-2) ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.00 (bs, 1H), 7.62−7.18 (m, 8H), 2.45 (s, 3H); MS (FAB) 223 (M^+); HRMS (FAB) calcd for $C_{15}H_{13}NO$, 223.0997; found, 223.0992.

Compound 1h. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.02 (bs, 1H), 7.72−7.15 (m, 8H), 2.46 (s, 3H); MS (FAB) 285 (M^+); HRMS (FAB) calcd for $C_{15}H_{12}BrN$, 285.0153; found, 285.0140.

Compound 1i. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.24−7.10 (m, 8H), 2.90 (q, J = 15.0, 7.6 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H); MS (FAB) 285 (M^+); HRMS (FAB) calcd for $C_{15}H_{12}BrN$, 285.0153; found, 285.0155.

Compound 1j.[18] ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.93 (bs, 1H), 7.64−7.04 (m, 4H), 7.51 (dd, J = 95.2, 8.8 Hz, 4H), 3.85 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 158.8, 135.5, 133.9, 129.9, 128.9, 125.7, 121.8, 119.3, 118.6, 114.1, 110.5, 107.5, 55.2, 9.5; MS (FAB) 255 (M^+); HRMS (FAB) calcd for $C_{16}H_{14}ClN$, 255.0815; found, 255.0801.

Compound 1k. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.26 (bs, 1H), 7.89−7.06 (m, 8H), 3.73 (s, 2H); MS (FAB) 204 (M − H); HRMS (EI) calcd for $C_{15}H_{10}N$, 204.0813; found, 204.0823.

Compound 1l. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.80 (bs, 1H), 7.45−7.01 (m, 4H), 2.82 (m, 4H), 2.53 (m, 2H).

Compound 1m. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.60 (d, J = 9.6 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.21 (m, 1H), 2.96 (m, 2H), 2.60 (m, 3H), 2.26 (s, 3H).

Compound 1n. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.35 (bs, 1H), 7.64−7.04 (m, 7H), 3.73 (s, 2H); MS (FAB) 223 (M^+); HRMS (EI) calcd for $C_{15}H_{10}FN$, 223.0797; found, 223.0780.

Compound 1o. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.37−6.94 (m, 13H), 1.57 (s, 1H).

Compound 1p. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.28−7.20 (m, 2H), 6.96−6.82 (m, 2H), 6.15 (bs, 1H), 5.81 (bs, 1H).

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Supporting Information Available. ^{1}H NMR and ^{13}C NMR spectra for synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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