Electronic Supplementary Material (ESI) for Dalton Transactions.

SUPPORTING INFORMATION

NIXANTPHOS: A Highly Active Ligand for Palladium Catalyzed Buchwald-Hartwig Amination of Unactivated Aryl Chlorides

Jianyou Mao,[a,*] Jiadi Zhang,[b] Shuguang Zhang,[b] and Patrick J. Walsh[a,b,*]

[a] Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Jiangsu National Synergetic Innovation Center for Advanced Materials, Nanjing Tech University, 30 South Puzhu Road, Nanjing 211816, People's Republic of China E-mail: ias_jymao@njtech.edu.cn

[b] Roy and Diana Vagelos Laboratories, Penn/Merck Laboratory for High-Throughput Experimentation, Department of Chemistry, University of Pennsylvania, 231 South, 34th Street, Philadelphia, Pennsylvania 19104-6323, United States E-mail: pwalsh@sas.upenn.edu

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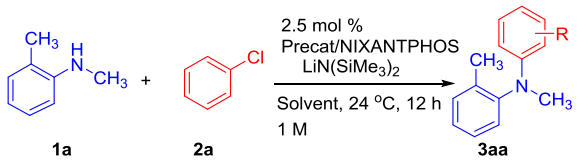
1. General Information

All reactions were carried out under an atmosphere of dry nitrogen. Anhydrous THF, DME and dioxane were purchased from Sigma-Aldrich and used without further purification . Unless otherwise stated, reagents were commercially available and used as purchased. Chemicals were obtained from Sigma-Aldrich, Acros, or Matrix Scientific and solvents were purchased from Fisher Scientific. The progress of the reactions was monitored by thin-layer chromatography using Whatman Partisil K6F 250 μm precoated 60 Å silica gel plates and visualized by short-wave ultraviolet light as well as by treatment with iodine. Flash chromatography was performed with silica gel (230–400 mesh). The NMR spectra were obtained using a Brüker 300, 360, 400 and 500 MHz Fourier-transform NMR spectrometer. The infrared spectra were obtained with KBr plates using a Perkin-Elmer Spectrum 1600 Series spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) using electrospray ionization (ESI) in positive or negative mode. Melting points were determined on a Unimelt Thomas-Hoover melting point apparatus and are uncorrected.

2. Procedure and characterization for Pd(NIXANTPHOS)catalyzed amination reactions

General Procedure A : To an oven-dried microwave vial equipped with a stir bar was added NIXANTPHOS precatalyst 4, *N*-methyl *o*-toluidine (**1a**) (74.9 µL, 0.60 mmol, 1.2 equiv), and aryl chloride (0.50 mmol, 1 equiv) under nitrogen atmosphere in a glove box. DME (0.5 mL) was added to the vial by syringe followed by $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol, 1.2 equiv). The microwave vial was sealed and removed from the glove box. The reaction mixture was stirred at room temperature for 12 h. Upon completion, the sealed vial was opened to air. The reaction mixture was quenched with five drops H_2O and passed through a short pad of silica gel and eluted with ethyl acetate (5.0 mL). The combined organics were concentrated in vacuo. The crude residue was purified by flash column chromatography to yield the corresponding product.

Optimization of the solvent



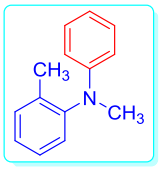
1a 2a 3aa

Entry	Solvent	NMR Yield(%)
1	THF	96
2	DME	99
3	Dioxane	54

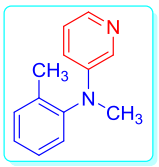
General Procedure B : To an oven-dried microwave vial equipped with a stir bar was added NIXANTPHOS precatalyst **4**, primary aniline derivatives (0.60 mmol, 1.2 equiv), and aryl chloride (0.50 mmol, 1 equiv) under nitrogen atmosphere in a glove box. DME (0.5 mL) was added to the vial by syringe followed by $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol, 1.2 equiv). The microwave vial was sealed and removed from the glove box. The reaction mixture was stirred at specified temperature for 48 h. Upon completion, the sealed vial was cooled to room temperature and opened to air. The reaction mixture was quenched with five drops H_2O and passed through a short pad of silica gel and eluted with ethyl acetate (5.0 mL). The combined organics were concentrated in vacuo. The crude residue was purified by flash column chromatography to yield

the corresponding product.

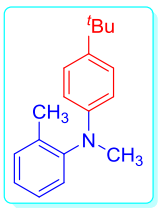
General Procedure C : To an oven-dried microwave vial equipped with a stir bar was added NIXANTPHOS precatalyst **4**, morpholine (87.1 µL, 1.2 mmol, 1.2 equiv), aryl chlorides (1.0 mmol, 1 equiv) under a nitrogen atmosphere in a glove box. DME (1.0 mL) was added to the vial by syringe followed by NaO*t*-Bu (115.3 mg, 1.2 mmol, 1.2 equiv). The microwave vial was sealed and removed from the glove box. The reaction mixture was stirred at 110 ^{o}C for 24 h. Upon completion, the sealed vial was cooled to room temperature and opened to air. The reaction mixture was quenched with five drops H_2O and passed through a short pad of silica gel and eluted with ethyl acetate (5.0 mL). The combined organics were concentrated in vacuo. The crude residue was purified by flash column chromatography to yield the corresponding product.



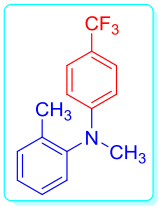
***N*-methyl-*N*-phenyl-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (11.5 mg, 0.0125 mmol), **1a** (75.0 µL, 0.60 mmol), LiN(SiMe$_3$)$_2$ (100.4 mg, 0.60 mmol) and chlorobenzene (**2a**) (50.8 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 50:1) to give the product (92.7 mg, 94% yield) as a colorless oil. R_f = 0.69 (hexanes:EtOAc = 50:1). The spectroscopic data for this product matched the literature data.[1]



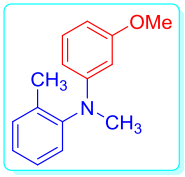
***N*-methyl-*N*-(3-pyridyl)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **1a** (75.0 µL, 0.60 mmol), LiN(SiMe$_3$)$_2$ (100.4 mg, 0.60 mmol) and 3-chloropyridine (**2b**) (47.5 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 50:1) to give the product (83.3 mg, 84% yield) as a colorless oil. R_f = 0.56 (hexanes:EtOAc = 50:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.98 – 7.96 (m, 2H), 7.31 – 7.22 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.06 – 7.03 (m, 1H), 6.76 – 6.73 (m, 1H), 3.24 (s, 3H), 2.14 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 145.7, 145.1, 138.5, 136.8, 135.5, 131.8, 128.4, 128.0, 127.3, 123.5, 119.1, 39.0, 17.9. IR (neat): 1577, 1565, 1492, 1426, 1351, 1339, 1247, 1109, 794, 770, 729, 708. HRMS: calcd for $C_{13}H_{15}N_2$ $[M+H]^+$ 199.1235, found 199.1231.



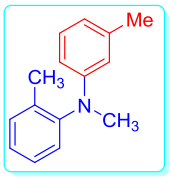
***N*-methyl-*N*-(4-*tert*-butylphenyl)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (11.5 mg, 0.0125 mmol), **1a** (75.0 µL, 0.60 mmol), LiN(SiMe$_3$)$_2$ (100.4 mg, 0.60 mmol) and 4-*tert*-butyl-chlorobenzene (**2d**) (83.5 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 100:1) to give the product (102.6 mg, 81% yield) as a colorless oil. R_f = 0.33 (hexanes:EtOAc = 100:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.27 (d, *J* = 7.4 Hz, 1H), 7.23 – 7.12 (m, 5H), 6.501 – 6.48 (m, 2H), 3.20 (s, 3H), 2.16 (s, 3H), 1.27 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 147.4, 147.1, 139.6, 137.0, 131.5, 128.3, 127.6, 126.4, 125.9, 112.9, 39.3, 34.0, 31.8, 18.2. IR (neat): 1618, 1575, 1523, 1493, 1358, 1328, 1193, 1162, 1114, 1063, 825, 773, 728. HRMS: calcd for $C_{13}H_{14}N$ $[M]^+$ 253.1830, found 253.1830.



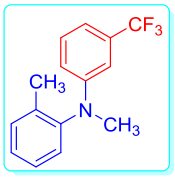
***N*-methyl-*N*-(trifluoromethylphenyl)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (2.3 mg, 0.0025 mmol), **1a** (75.0 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-chlorobenzotrifluoride (**2e**) (66.8 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 100:1) to give the product (130.0 mg, 98% yield) as a colorless oil. R_f = 0.43 (hexanes:EtOAc = 100:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38 (t, *J* = 8.5 Hz, 2H), 7.32 – 7.30 (m, 1H), 7.27 – 7.24 (m, 2H), 7.13 – 7.11 (m, 1H), 6.50 (d, *J* = 9.0 Hz, 2H), 3.25 (s, 3H), 2.12 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 151.5, 145.7, 136.9, 131.8, 128.6, 128.0, 127.5, 126.5 (*J* = 3.8 Hz), 125.3 (*J* = 268.6 Hz), 118.3 (*J* = 32.4 Hz), 111.9, 39.17, 17.87. IR (neat): 2961, 1615, 1599, 1516, 1492, 1363, 1339, 1269, 1256, 1201, 1126, 1106, 821, 769, 728. HRMS: calcd for $C_{15}H_{14}F_3N$ $[M]^+$ 265.1078, found 265.1083.



***N*-methyl-*N*-(3-methoxyphenyl)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (11.5 mg, 0.0125 mmol), **1a** (75.0 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 3-chloroanisole (**2f**) (61.2 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (109.1 mg, 96% yield) as a colorless oil. R_f = 0.54 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.28 – 7.12 (m, 4H), 7.08 – 7.05 (m, 1H), 6.28 (d, *J* = 7.5 Hz, 1H), 6.13 – 6.09 (m, 2H), 3.73 (s, 3H), 3.20 (s, 3H), 2.14 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 160.9, 150.76, 146.78, 137.1, 131.6, 129.8, 128.65, 127.69, 126.8, 106.3, 101.7, 99.5, 55.3, 39.3, 18.0. IR (neat): 2937, 1614, 1594, 1577, 1493, 1456, 1348, 1323, 1269, 1217, 1170, 1137, 1113, 1052, 826, 756, 729. HRMS: calcd for $C_{15}H_{17}NO$ $[M]^+$ 227.1310, found 227.1311.

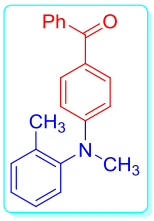


***N*-methyl-*N*-(3-methylphenyl)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (11.5 mg, 0.0125 mmol), **1a** (75.0 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 3-chlorotoluene (**2g**) (59.0 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 100:1) to give the product (100.4 mg, 95% yield) as a colorless oil. R_f = 0.40 (hexanes:EtOAc = 100:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.28 (d, *J* = 7.4 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.20-7.16 (m, 1H), 7.14 -7.12 (m, 1H), 7.07 - 7.03 (m, 1H), 6.53 (d, *J* = 7.4 Hz, 1H), 6.36 (s, 1H), 6.34 – 6.32 (m, 1H), 3.20 (s, 3H), 2.25 (s, 3H), 2.14 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 149.4, 147.1, 138.9, 137.0, 131.5, 129.0, 128.5, 127.7, 126.5, 118.0, 113.7, 110.4, 39.3, 22.0, 18.1. IR (neat): 2919, 1606, 1597, 1579, 1492, 1457, 1344, 1324, 1259, 1115, 768, 728, 692. HRMS: calcd for $C_{15}H_{18}N$ $[M+H]^+$ 212.1439, found 212.1437.

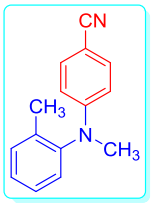


***N*-methyl-*N*-(3-trifluoromethylphenyl)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (2.3 mg, 0.0025 mmol), **1a** (75.0 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 3-chlorobenzotrifluoride (**2h**) (67.6 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 100:1) to give the product (127.3 mg, 96% yield) as a colorless oil. R_f = 0.40 (hexanes:EtOAc = 100:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.32 – 7.30 (m, 1H), 7.28 – 7.20 (m, 3H), 7.12 (d, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.75 (s, 1H), 6.60 – 6.58 (m, 1H), 3.25 (s, 3H), 2.12 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz,

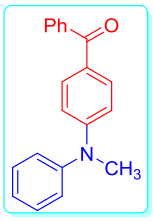
$CDCl_3$) δ: 149.4, 146.0, 136.9, 131.8, 131.6 (q, *J* = 31.3 Hz), 129.5, 128.5, 128.0, 127.3, 124.7 (q, *J* = 270.9 Hz), 116.0, 113.3 (q, *J* = 3.9 Hz), 108.6 (q, *J* = 4.0 Hz), 39.3, 17.9. IR (neat): 1614, 1587, 1494, 1455, 1359,1322, 1251, 1165, 1122, 1070, 991, 913, 779, 729, 698, 656. HRMS: calcd for $C_{15}H_{14}NF_3$ $[M]^+$ 265.1078, found 265.1081.



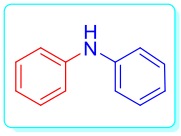
***N*-methyl-*N*-(4-benzophenone)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (11.5 mg, 0.0125 mmol), **1a** (75.0 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-chlorobenzophenone (**2i**) (108.3 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 100:1) to give the product (141.7 mg, 94% yield) as a colorless oil. R_f = 0.46 (hexanes:EtOAc = 50:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.74 – 7.71 (m, 4H), 7.51 – 7.49 (m, *J* = 7.3 Hz, 1H), 7.44 – 7.41 (m, 2H), 7.33 – 7.25 (m, 3H), 7.16 – 7.13 (m, 1H), 6.50 (d, *J* = 8.3 Hz, 2H), 3.30 (s, 3H), 2.14 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 195.3, 152.6, 145.3, 139.4, 136.7, 132.86, 131.84, 131.4, 129.64, 128.55, 128.2, 128.0, 127.7, 125.8, 111.4, 39.3, 17.9. IR (neat): 1463, 1591, 1576, 1550, 1515, 1491, 1358, 1318, 1283, 1257, 1192, 1176, 1142, 1114, 937, 920, 835, 771, 744, 729, 701, 675, 622. HRMS: calcd for $C_{21}H_{19}NO$ $[M+H]^+$ 301.1467, found 301.1468.



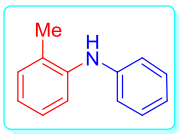
***N*-methyl-*N*-(4-cyanophenyl)-2-toluidine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **1a** (75.0 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-chlorobenzonitrile (**2j**) (68.8 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (102.3 mg, 92% yield) as a colorless oil. R_f = 0.37 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40 (d, *J* = 9.0 Hz, 2H), 7.33 – 7.31 (m, 1H), 7.29 – 7.26 (m, 2H), 7.12 – 7.10 (m, 1H), 6.46 (d, *J* = 8.5 Hz, 2H), 3.27 (s, 3H), 2.11 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 151.9, 144.9, 136.6, 133.6, 132.0, 128.5, 128.2, 127.9, 120.8, 112.2, 98.5, 39.1, 17.8. IR (neat): 2214, 1610, 1598, 1579, 1514, 1492, 1460, 1359, 1256, 1176, 1144, 1115, 1071, 823, 773, 729, 544. HRMS: calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1235, found 223.1225.



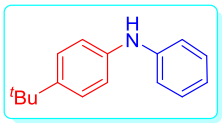
***N*-methyl-*N*-4-benzophenonephenylamine** The reaction was performed following the General Procedure A with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **1b** (65.0 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-chlorobenzophenone (**2i**) (108.3 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (122.1 mg, 85% yield) as a yellow solid. R_f = 0.41 (hexanes:EtOAc = 50:1). The spectroscopic data for this product matched the literature data.[2]



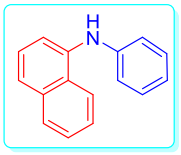
Diphenylamine The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and chlorobenzene (**2a**) (50.8 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (76.2 mg, 90 % yield) as a brown solid. R_f = 0.57 (hexanes:EtOAc = 10:1). The spectroscopic data for this product matched the literature data.[3]



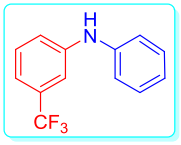
2-Methyl-*N*-phenylaniline The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (1.15 mg, 0.00125 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 2-chlorotoluene (**2k**) (58.4 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (87.0 mg, 95% yield) as a brown oil. R_f = 0.64 (hexanes:EtOAc = 10:1). ^{1}H NMR (360 MHz, $CDCl_3$) δ: 7.26-7.18 (m, 4H), 7.15-7.10 (m, 1H), 6.96-6.87 (m, 4H), 5.36 (brs, 1H), 2.25 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ: 144.2, 141.4, 131.2, 129.5, 128.5, 127.0, 122.2, 120.7, 119.0, 117.7, 18.1. IR (neat): 3393, 3047, 1596, 1583, 1497, 1482, 1465, 1419, 1311, 1295, 1251, 1176, 1112, 1028, 879, 746, 694. HRMS: calcd for $C_{13}H_{14}N$ $[M+H]^+$ 184.1126, found 184.1128.



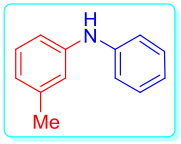
4-(*tert*-Butyl)-*N*-phenylaniline The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-*tert*-butyl-chlorobenzene (**2d**) (83.5 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (109.3 mg, 97% yield) as a light yellow solid. R_f = 0.41 (hexanes:EtOAc = 10:1). The spectroscopic data for this product matched the literature data.[4]



***N*-phenyl-1-naphthylamine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.23 mg, 0.00025 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2l**) (68.1 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (108.5 mg, 99% yield) as a brown solid. R_f = 0.31 (hexanes:EtOAc = 10:1). The spectroscopic data for this product matched the literature data.[5]

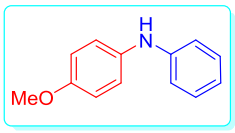


***N*-phenyl-3-(trifluoromethyl)aniline** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2h**) (67.6 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (110.3 mg, 93% yield) as a brown oil. R_f = 0.40 (hexanes:EtOAc = 10:1). The spectroscopic data for this product matched the literature data.[6]

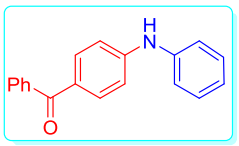


***N*-phenyl-3-methylaniline** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 3-chlorotoluene (**2g**) (59.0 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (88.9 mg, 97% yield) as a brown oil. R_f = 0.57 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.28-7.24 (m, 2H), 7.17-7.14 (m, 1H), 7.07-7.05 (m, 2H), 6.94-6.88 (m, 3H), 6.76 (d, *J* = 7.5 Hz, 1H), 5.64 (brs, 1H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ: 143.5, 143.3, 139.4, 129.5, 129.4, 122.1, 121.1, 118.7, 118.0,

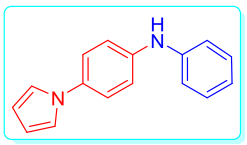
115.1, 21.7. IR (neat): 3395, 3078, 1591, 1515, 1495, 1460, 1410, 1316, 1239, 1167, 1028, 997, 769, 745, 691. HRMS: calcd for $C_{13}H_{14}N$ $[M+H]^+$ 184.1126, found 184.1131.



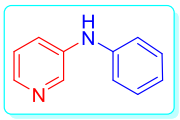
***N*-phenyl-*p*-anisidine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (2.3 mg, 0.025 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-chloroanisole (**2c**) (61.2 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (91.7 mg, 92% yield) as a brown solid. R_f = 0.42 (hexanes:EtOAc = 10:1). The spectroscopic data for this product matched the literature data.[7]



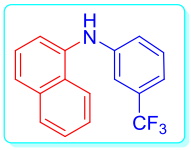
4-Anilinobenzophenone The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (1.15 mg, 0.0125 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-chlorobenzophenone (**2i**) (108.0 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (113.4 mg, 83% yield) as a yellow solid. R_f = 0.56 (hexanes:EtOAc = 10:1). The spectroscopic data for this product matched the literature data.[8]



***N*-phenyl-4-(1*H*-pyrrol-1-yl)aniline** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-(4-Chlorophenyl)-1H-pyrrole (**2m**) (88.9 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (111.3 mg, 95% yield) as a brown solid. Mp 107-108 °C. R_f = 0.55 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.29 – 7.20 (m, 4H), 7.10 – 6.96 (m, 6H), 6.94-6.91 (m, 1H), 6.32 (t, *J* = 2.0 Hz, 2H), 5.63 (brs, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ: 143.2, 141.2, 134.9, 129.6, 122.1, 121.4, 119.7, 119.0, 118.0, 110.1. IR (neat): 3384, 1603, 1596, 1533, 1497, 1315, 1261, 1072, 811, 750, 722, 698. HRMS: calcd for $C_{13}H_{14}N$ $[M+H]^+$ 235.1235, found 235.1239.

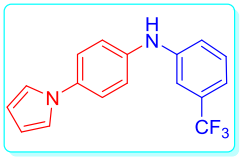


***N*-phenyl-3-aminopyridine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (1.15 mg, 0.00125 mmol), **6a** (54.7 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-chloropyridine (**2b**) (48µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 5:1) to give the product (75.7 mg, 89% yield) as a yellow solid. R_f = 0.29 (hexanes:EtOAc = 5:1). The spectroscopic data for this product matched the literature data.[9]

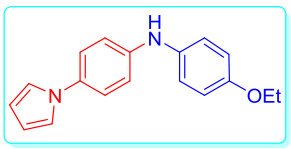


***N*-(3-trifluoromethylphenyl)-1-naphthylamine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), 3-aminobenzotrifluoride **6b** (74.2 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2l**) (68.1 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (129.3 mg, 90% yield) as a brown oil. R_f = 0.53 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.01-7.99 (m, 1H), 7.91-7.90 (m, 1H), 7.68 (d,

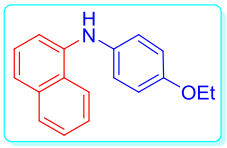
J = 8.1 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.48 – 7.42 (m, 1H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.33-7.30 (m, 1H), 7.18 (s, 1H), 7.12-7.10 (m, 1H), 7.04 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.01 (s, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ: 146.1, 137.6, 135.0, 132.0 (*J* = 31.9 Hz), 130.0, 128.9, 128.7, 126.6, 126.3, 126.2, 124.8, 124.4 (*J* = 270.8 Hz), 122.1, 119.3, 118.4, 116.5 (*J* = 3.8 Hz), 112.9 (*J* = 3.9 Hz). IR (neat): 3396, 1615, 1595, 1576, 1487, 1399, 1336, 1164, 1123, 1069, 779, 698. HRMS: calcd for $C_{17}H_{13}NF_3$ $[M+H]^+$ 288.1000, found 288.1002.



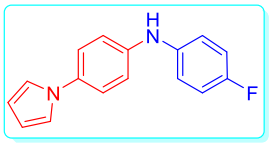
***N*-(4-(1H-pyrrol-1-yl)phenyl)-3-(trifluoromethyl)aniline** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), 3-aminobenzotrifluoride **6b** (74.2 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-(4-Chlorophenyl)-1H-pyrrole (**2m**) (88.9 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (128.5 mg, 85% yield) as a brown solid. R_f = 0.58 (hexanes:EtOAc = 10:1). The spectroscopic data for this product matched the literature data.[10]



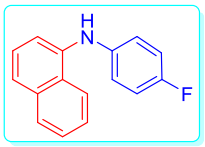
***N*-(4-(1H-pyrrol-1-yl)phenyl)-4-ethoxyaniline** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (1.15 mg, 0.00125 mmol), 4-ethoxyaniline **6c** (77.3 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-(4-Chlorophenyl)-1H-pyrrole (**2m**) (88.9 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (132.2 mg, 95% yield) as a brown solid. Mp 114 – 115 °C. R_f = 0.45 (hexanes:EtOAc = 5:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.22 – 7.12 (m, 2H), 7.05 – 7.02 (m, 2H), 6.97 (t, *J* = 2.2 Hz, 2H), 6.91 – 6.88 (m, 2H), 6.87 – 6.83 (m, 2H), 6.30 – 6.29 (m, 2H), 5.46 (brs, 1H), 4.00 (q, *J* = 7.0 Hz, 2H), 1.40 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ: 155.0, 143.5, 135. 7, 133.7, 122.4, 122.3, 120.0, 116.5, 115.6, 109.8, 64.0, 15.1. IR (neat): 3418, 1522, 1510, 1232, 1116, 1072, 909, 822, 730. HRMS: calcd for $C_{18}H_{19}N_2O$ $[M+H]^+$ 279.1497, found 279.1498.



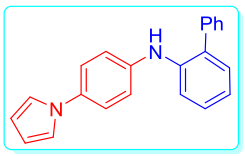
***N*-(4-ethoxyphenyl)-1-naphthylamine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.23 mg, 0.00025 mmol), 4-ethoxyaniline **6c** (77.3 µL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2l**) (68.1 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (127.7 mg, 97% yield) as a brown solid. Mp 55 – 56 °C. R_f = 0.63 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.93 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.80 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.40 – 7.39 (m, 3H), 7.30 – 7.27 (m, 1H), 7.07 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.00 – 6.98 (m, 2H), 6.85 – 6.82 (m, 2H), 5.84 (brss, 1H), 3.97 (q, *J* = 7.0 Hz, 2H), 1.38 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ: 154.7, 141.1, 136.9, 134.8, 128.8, 126.4, 126.2, 126.1, 125.5, 122.1, 121.3, 121.1, 115.6, 111.9, 64.0, 15.1. IR (neat): 3399, 2978, 1578, 1510, 1477, 1402, 1300, 1240, 1173, 1116, 1050, 922, 823, 770. HRMS: calcd for $C_{18}H_{18}NO$ $[M+H]^+$ 264.1388, found 264.1390.



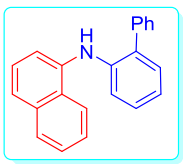
***N*-(4-(1H-pyrrol-1-yl)phenyl)-4-fluoroaniline** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (1.15 mg, 0.00125 mmol), 4-fluoroaniline **6d** (56.8 μL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-(4-Chlorophenyl)-1H-pyrrole (**2m**) (88.9 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 5:1) to give the product (122.4 mg, 97% yield) as a brown solid. Mp 97 – 98 °C. R_f = 0.56 (hexanes:EtOAc = 5:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.32 – 7.29 (m, 2H), 7.09 – 6.02 (m, 8H), 6.39 (t, *J* = 2.1 Hz, 2H), 5.60 (brs, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ: 159.3 (d, *J* = 238.8 Hz), 142.1, 139.1 (d, *J* = 2.5 Hz), 134.6, 122.2, 120.7 (d, *J* = 8.8 Hz), 120.0, 117.9, 116.2 (d, *J* = 22.5 Hz), 110.0. IR (neat): 3384, 1508, 1324, 1260, 1233, 1139, 1075, 908, 814, 726, 613. HRMS: calcd for $C_{16}H_{14}N_2F$ $[M+H]^+$ 253.1141, found 253.1145.



***N*-(4-fluorophenyl)-1-naphthylamine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.23 mg, 0.00025 mmol), 4-fluoroaniline **6d** (56.8 μL, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2l**) (68.1 μL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (111.5 mg, 94% yield) as a brown solid. Mp 70 – 71 °C. R_f = 0.45 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 8.1 Hz, 1H), 7.85 – 7.83 (m, 1H), 7.52 – 7.44 (m, 3H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.22 – 7.19 (m, 1H), 6.96 – 6.94 (m, 4H), 5.87 (brs, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ: 158.5 (d, *J* = 237.5 Hz), 140.7 (d, *J* = 2.5 Hz), 139.8, 134.9, 128.8, 127.2, 126.4, 126.3, 125.9, 122.7, 121.7, 120.1 (d, *J* = 7.5 Hz), 116.2 (d, *J* = 22.5 Hz), 114.6. IR (neat): 3399, 3054, 1594, 1578, 1507, 1403, 1230, 1215, 1154, 1010, 1019, 826, 790, 767. HRMS: calcd for $C_{16}H_{13}NF$ $[M+H]^+$ 238.1032, found 238.1031.

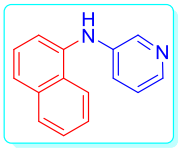


***N*-(4-(1H-pyrrol-1-yl)phenyl)-2-phenylaniline** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), 2-aminodiphenyl **6e** (101.5 mg, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-(4-Chlorophenyl)-1H-pyrrole (**2m**) (88.9 mg, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (153.6 mg, 99% yield) as a brown solid. Mp 94 – 95 °C. R_f = 0.53 (hexanes:EtOAc = 10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.46 – 7.42 (m, 4H), 7.36 – 7.32 (m, 2H), 7.27 – 7.22 (m, 4H), 7.07 – 6.97 (m, 5H), 6.30 (t, *J* = 2.2 Hz, 2H), 5.60 (brs, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ: 141.6, 140.3, 139.1, 135.0, 131.8, 131.2, 129.5, 129.2, 128.5, 127.8, 122.2, 121.5, 119.7, 119.4, 117.6, 110.1. IR (neat): 3460, 3374, 3058, 3025, 1616, 1502, 1483, 1435, 1299, 1286, 1158, 1009, 751, 703, 616, 565. HRMS: calcd for $C_{22}H_{19}N_2$ $[M+H]^+$ 311.1548, found 311.1550.

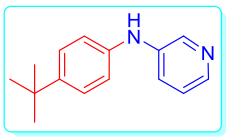


***N*-(2-biphenyl)-1-naphthalenamine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), 2-aminodiphenyl **6e** (101.5 mg, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2l**) (68.1 μL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 10:1) to give the product (146.2 mg, 99% yield) as a brown solid. R_f = 0.50 (hexanes:EtOAc = 10:1). The

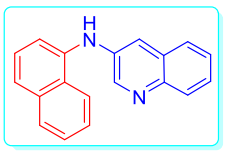
spectroscopic data for this product matched the literature data.[11]



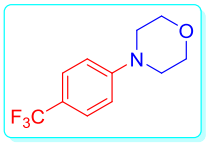
***N*-(1-naphthyl)-3-aminopyridine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (0.46 mg, 0.0005 mmol), 3-animopyridine **6f** (56.5 mg, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2l**) (68.1 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 0:100) to give the product (100.2 mg, 91% yield) as a yellow solid. Mp 122 – 123 °C. R_f = 0.45 (hexanes:EtOAc = 0:100). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 2.5 Hz, 1H), 8.18-8.16 (m, 1H), 8.03 – 8.00 (m, 1H), 7.93 – 7.90 (m, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.37 (m, 4H), 7.24 – 7.13 (m, 2H), 5.96 (brs, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 141.9, 141.5, 139.7, 137.8, 134.9, 128.8, 128.3, 126.5, 126.2, 126.1, 124.4, 123.9, 123.0, 122.1, 117.3. IR (neat): 3237, 3047, 1590, 1573, 1482, 1400, 1321, 791, 776, 707, 631. HRMS: calcd for $C_{15}H_{13}N_2$ $[M+H]^+$ 221.1079, found 221.1089.



***N*-(4-*tert*-butylphenyl)-3-aminopyridine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (1.15 mg, 0.00125 mmol), 3-animopyridine **6f** (56.5 mg, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 4-*tert*-Butyl-chlorobenzene (**2d**) (83.5 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 0:100) to give the product (106.4 mg, 94% yield) as a light yellow solid. Mp 120 – 121 °C. R_f = 0.41 (hexanes:EtOAc = 0:100). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.35 (d, *J* = 2.8 Hz, 1H), 8.12 (dd, *J* = 4.7, 1.2 Hz, 1H), 7.38 – 7.36 (m, 1H), 7.34 – 7.31 (m, 2H), 7.15 – 7.13 (m, 1H), 7.05 – 7.03 (m, 2H), 5.72 (s, 1H), 1.32 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 145.6, 141.6, 140.6, 139.8, 139.3, 126.6, 123.9, 122.9, 118.9, 34.5, 31.6. IR (neat): 3257, 3043, 2958, 1619, 1587, 1536, 1515, 1480, 1402, 1341, 1237, 1195, 1045, 836, 810, 789, 710, 548. HRMS: calcd for $C_{15}H_{19}N_2$ $[M+H]^+$ 227.1548, found 227.1559.

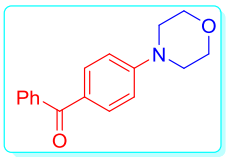


***N*-(1-naphthyl)quinolin-3-amine** The reaction was performed following the General Procedure B with NIXANTPHOS precatalyst **4** (1.15 mg, 0.00125 mmol), 3-aminoquinoline **6g** (86.5 mg, 0.60 mmol), $LiN(SiMe_3)_2$ (100.4 mg, 0.60 mmol) and 1-chloronaphthalene (**2l**) (68.1 µL, 0.50 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 1:1) to give the product (124.4 mg, 92% yield) as a yellow solid. Mp 109 – 110 °C. R_f = 0.35 (hexanes:EtOAc = 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.80 (d, *J* = 2.6 Hz, 1H), 8.03 (t, *J* = 8.7 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 7.0 Hz, 1H), 7.56 – 7.41 (m, 7H), 7.38 (d, *J* = 2.5 Hz, 1H), 6.18 (brs, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 144.7, 143.4, 139.2, 137.7, 134.9, 129.1, 129.1, 128.8, 128.3, 127.1, 126.50, 126.47, 126.3, 126.2, 126.1, 124.5, 122.2, 117.6, 116.6. IR (neat): 3232, 3052, 1607, 1575, 1484, 1399, 1349, 1278, 778, 750, 732. HRMS: calcd for $C_{19}H_{14}N_2Na$ $[M+Na]^+$ 293.1055, found 293.1049.

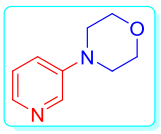


***N*-(4-trifluoromethylphenyl)morpholine** The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 4-chlorobenzotrifluoride (**2h**) (133.6 µL, 1.0 mmol). The crude product was

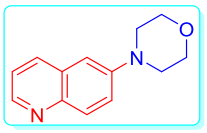
purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 1:1) to give the product (189.6 mg, 82% yield) as a brown solid. R_f = 0.67 (hexanes:EtOAc = 1:1). The spectroscopic data for this product matched the literature data.[12]



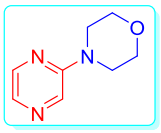
***N*-(4-benzophenyl)morpholine** The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 4-chlorobenzophenone (**2i**) (216.6 mg, 1.00 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 5:1) to give the product (216.5 mg, 81% yield) as a yellow solid. R_f = 0.68 (hexanes:EtOAc = 1:1). The spectroscopic data for this product matched the literature data.[13]



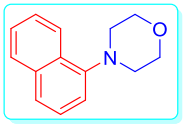
***N*-(3-pyridyl)morpholine** The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 3-chloropyridine (**2b**) (95.1 µL, 1.0 mmol). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc:MeOH = 10:1) to give the product (136.3 mg, 83% yield) as a yellow oil. R_f = 0.45 (EtOAc:MeOH = 10:1). The spectroscopic data for this product matched the literature data.[14]



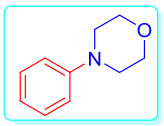
4-(Quinolin-6-yl)morpholine The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 6-chloroquinoline (**2n**) (163.6 mg, 1.0 mmol). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc) to give the product (154.3 mg, 72% yield) as a light yellow solid. R_f = 0.37 (EtOAc). The spectroscopic data for this product matched the literature data.[15]



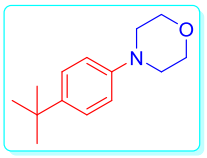
4-(Pyrazin-2-yl)morpholine The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (9.2 mg, 0.01 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 2-chloropyrazine (**2o**) (89.3 µL, 1.0 mmol). The crude product was purified by flash chromatography on silica gel (eluted with EtOAc) to give the product (135.5 mg, 82% yield) as a light yellow solid. R_f = 0.48 (EtOAc). The spectroscopic data for this product matched the literature data.[16]



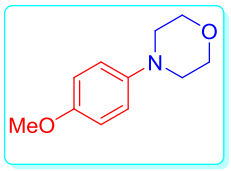
4-(naphthalen-1-yl)morpholine The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (9.2 mg, 0.01 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 1-chloronaphthalene (**2l**) (135.9 µL, 1.0 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 5:1) to give the product (196.2 mg, 92% yield) as a brown solid. R_f = 0.57 (hexanes:EtOAc = 5:1). The spectroscopic data for this product matched the literature data.[17]



4-Phenylmorpholine The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (4.6 mg, 0.005 mmol), **1a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and chlorobenzene (**2a**) (102.0 µL, 1.0 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 5:1) to give the product (114.3 mg, 70% yield) as a brown solid. R_f = 0.52 (hexanes:EtOAc = 5:1). The spectroscopic data for this product matched the literature data.[18]



4-(4-(*tert*-Butyl)phenyl)morpholine The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (9.2 mg, 0.01 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 4-*tert*-Butyl-chlorobenzene (**2d**) (83.5 µL, 1.0 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 5:1) to give the product (133.8 mg, 61% yield) as a yellow solid. R_f = 0.52 (hexanes:EtOAc = 5:1). The spectroscopic data for this product matched the literature data.[19]

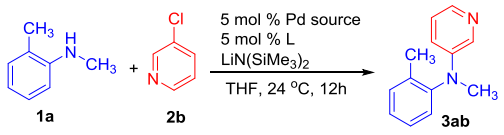


4-(4-Methoxyphenyl)morpholine The reaction was performed following the General Procedure C with NIXANTPHOS precatalyst **4** (23.0 mg, 0.025 mmol), **8a** (102.0 µL, 1.20 mmol), $LiN(SiMe_3)_2$ (200.8 mg, 1.20 mmol) and 4-chloroanisole (**2c**) (122.5 µL, 1.0 mmol). The crude product was purified by flash chromatography on silica gel (eluted with hexanes:EtOAc = 5:1) to give the product (133.8 mg, 61% yield) as a yellow solid. R_f = 0.31 (hexanes:EtOAc = 5:1). The spectroscopic data for this product matched the literature data.[20]

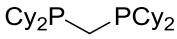
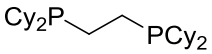
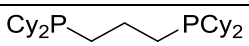
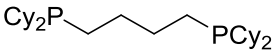
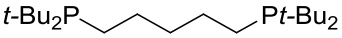
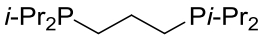
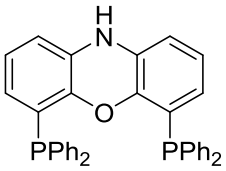
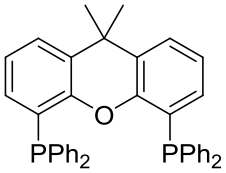
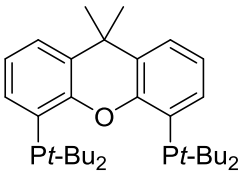
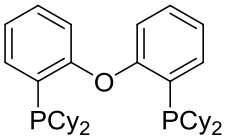
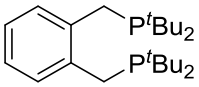
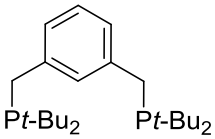
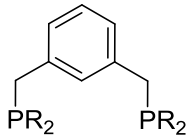
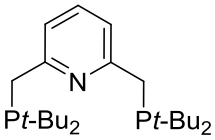
3. Ligand Comparison in C–N Cross-Couplings with Aryl Chlorides

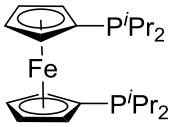
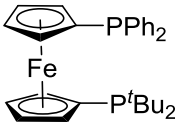
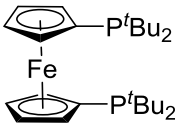
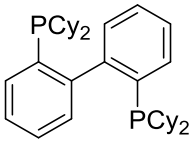
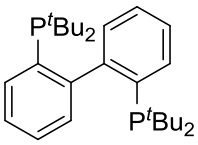
Set up: Experiments were set up inside a glovebox under a nitrogen atmosphere. Two 96-well aluminum blocks containing 1 mL glass vials were predosed with μ-OMs dimer or Pd_2dba_3 (2.5 mol %) and the ligands (5.0 mol % for monodentate ligands and 2.5 mol % for bidentate ligands) in THF. The solvent was removed to dryness using a GeneVac and 1.5 equiv $LiN(SiMe_3)_2$ (15 µmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. 1 Equiv aryl chlorides (10 µmol), 1 equiv amine (10 µmol), 1 equiv biphenyl (1 µmol/reaction) (used as an internal standard) were then dosed together into each reaction vial as a solution in THF (100 µL, 0.1 M). The 96-well plates were then sealed and stirred for 12 h. Work up: Upon opening the plate to air, 500 µL of acetonitrile/DMSO (3/1) was added into each vial. The plates were covered again and the vials stirred for 10 min to ensure good homogenization. Into two separate 96-well LC blocks were added 700 µL of acetonitrile, followed by 25 µL of the diluted reaction mixtures. The LC blocks were then sealed with a silicon-rubber storage mat and mounted on an automated HPLC instrument for analysis.

Results of bidentate phosphine ligand comparison in C-N band formation reactions

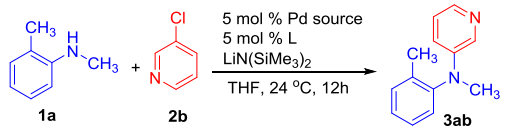


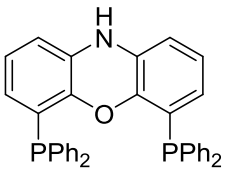
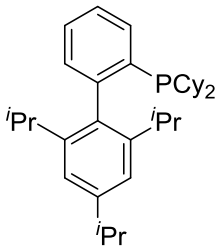
Entry	Ligand	(Prod/IS)	(Prod/IS)

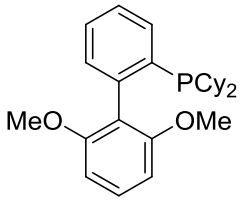
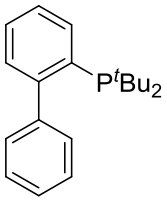
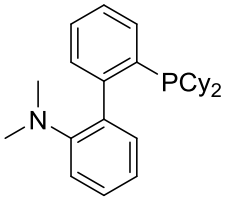
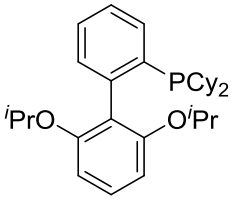
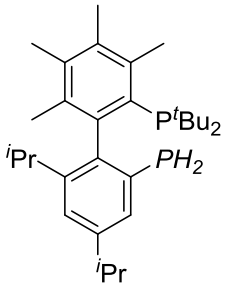
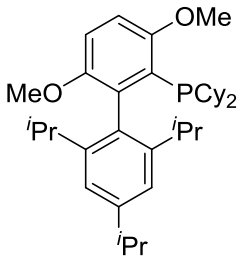
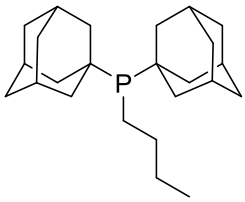
		μ-OMs dimer	Pd_2dba_3
1		0.1	0.2
2		0.2	0.0
3		0.1	0.0
4		0.0	0.0
5		0.1	0.0
6		0.0	0.2
7		8.6	4.5
8		3.1	0.3
9		0.0	0.3
10		1.5	2.1
11		0.0	0.0
12		0.6	0.0
13	 R = Cyclopentyl	0.0	0.0
14		0.0	0.0

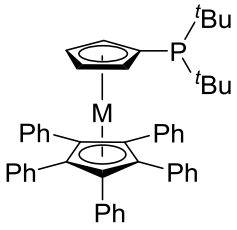
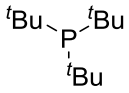
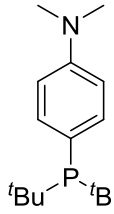
15		1.2	0.2
16		0.9	0.2
17		0.2	0.2
18		0.5	0.0
19		1.0	0.7

Results of comparison of NIXANTPHOS with monodentate phosphines in C-N band formation reactions

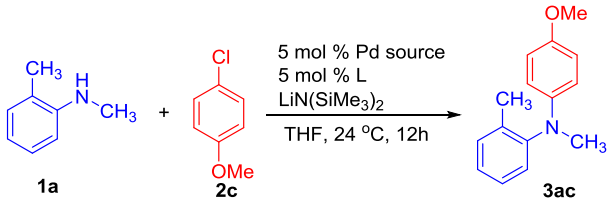


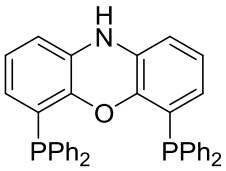
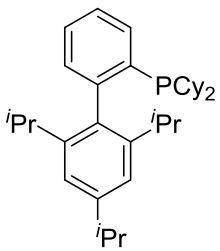
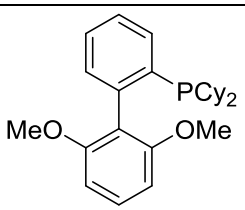
Entry	Ligand	(Prod/IS) μ-OMs dimer	(Prod/IS) Pd_2dba_3
1		8.6	4.5
2		10.1	10.0

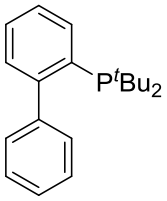
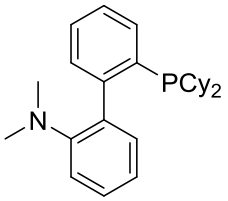
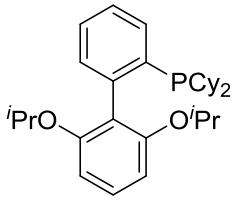
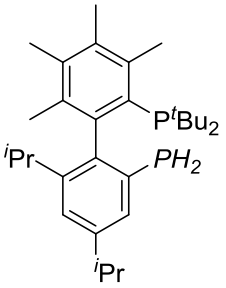
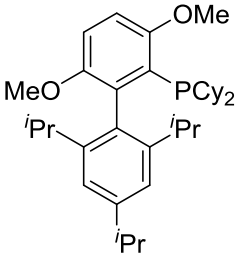
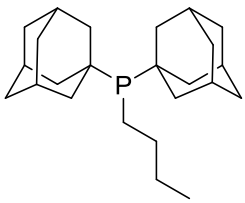
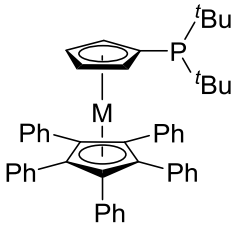
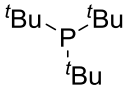
3		8.0	7.3
4		5.7	6.3
5		6.1	6.5
6		7.5	8.4
7		0.3	0.0
8		1.6	1.0
9		0.0	0.0

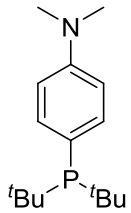
10		0.8	0.2
11		0.1	0.2
12		0.0	0.0

Results of comparison of NIXANTPHOS with commonly used monodentate ligands



Entry	Ligand	(Prod/IS) μ-OMs dimer	(Prod/IS) Pd_2dba_3
1		3.4	0
2		9.3	10
3		7.8	2.1

4		8.3	7.2
5		4.7	1.1
6		7.9	5.7
7		0.1	0.2
8		1.6	1
9		0	0
10		2.1	0
11		0	0

12		0	0

4. NMR Spectrum

***N*-methyl-*N*-phenyl-2-toluidine (3aa)**

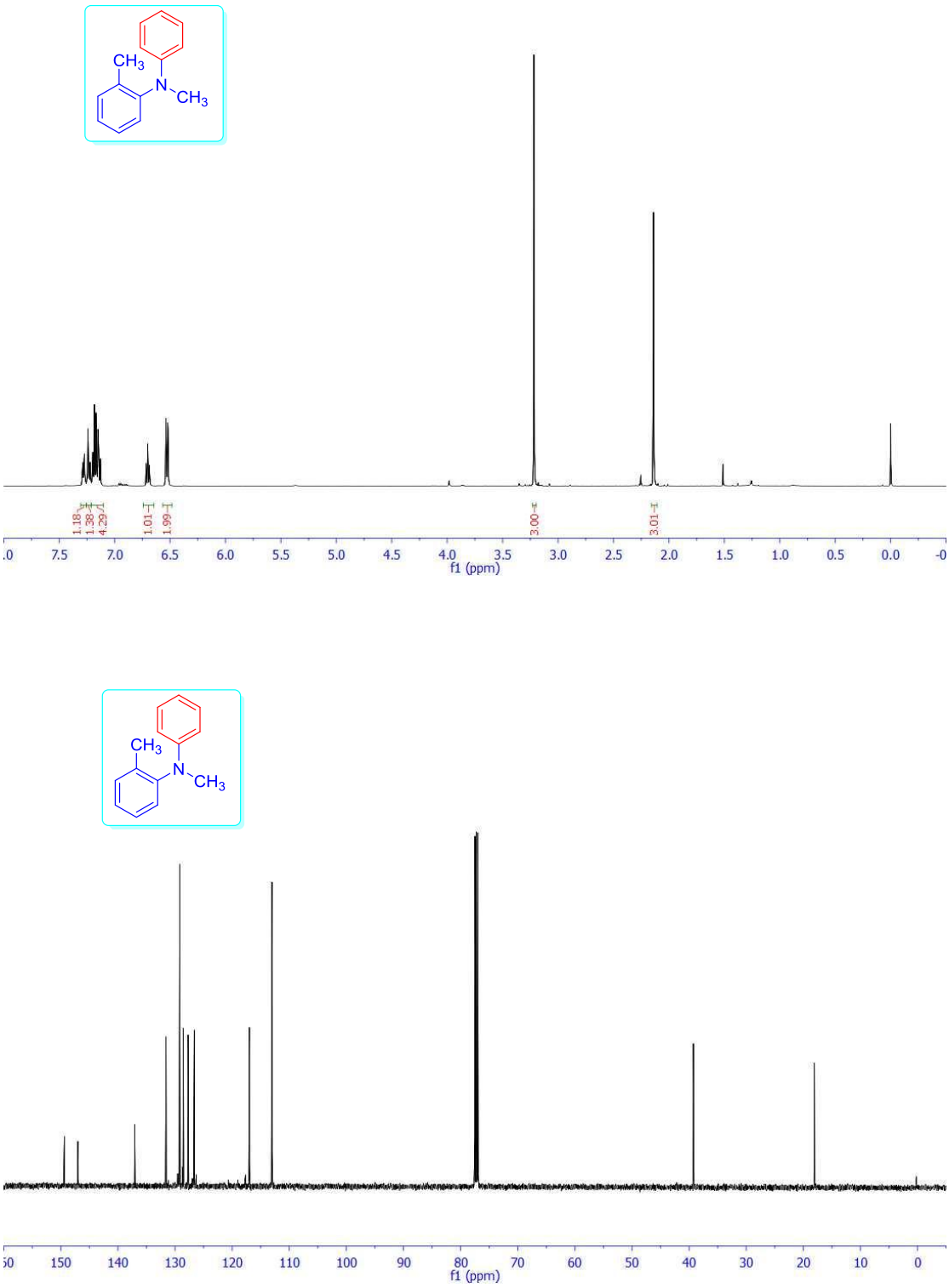


Figure S1. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3aa in $CDCl_3$

***N*-methyl-*N*-(3-pyridyl)-2-toluidine (3ab)**

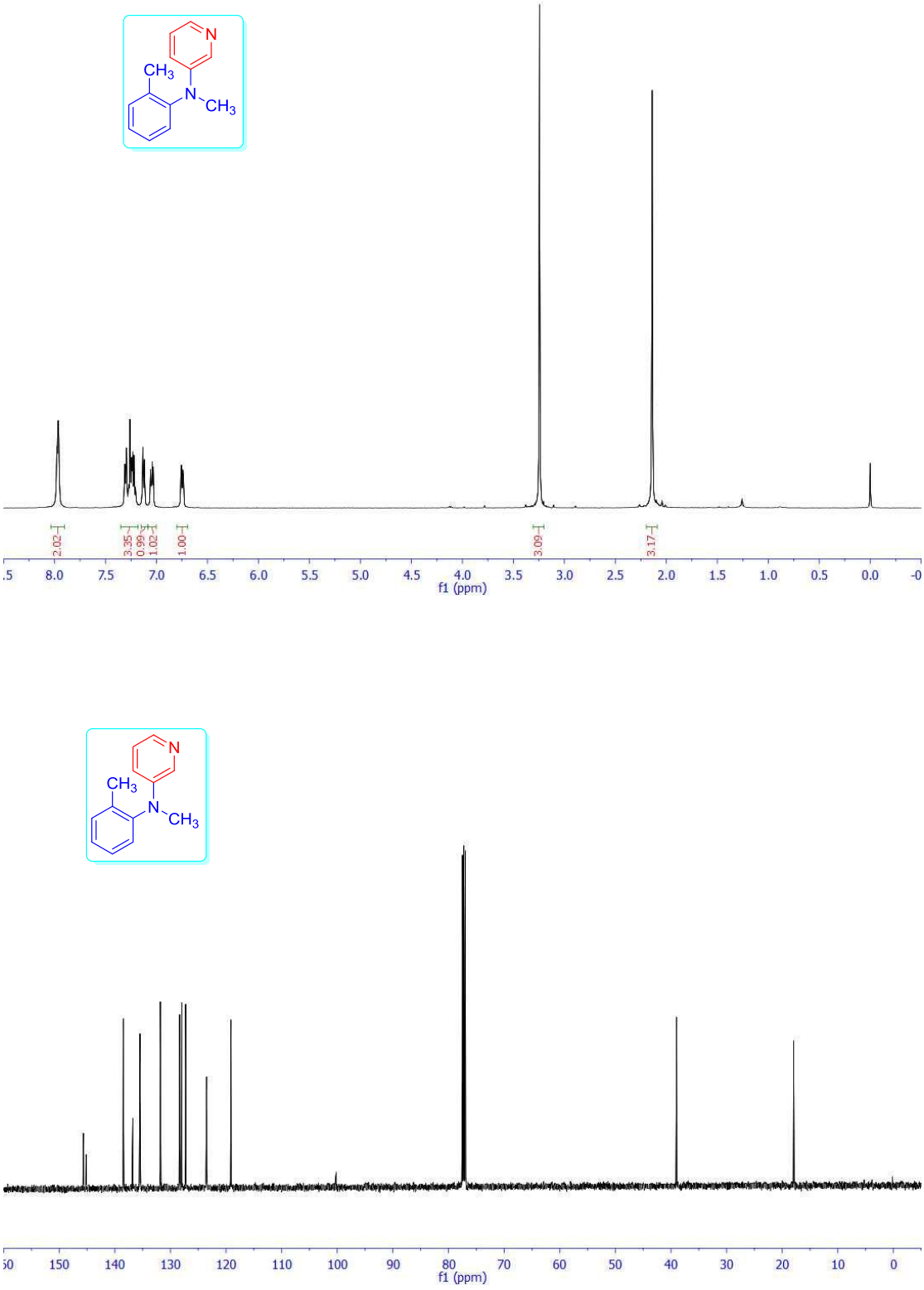


Figure S2. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3ab in $CDCl_3$

***N*-methyl-*N*-(4-*tert*-butylphenyl)-2-toluidine (3ad)**

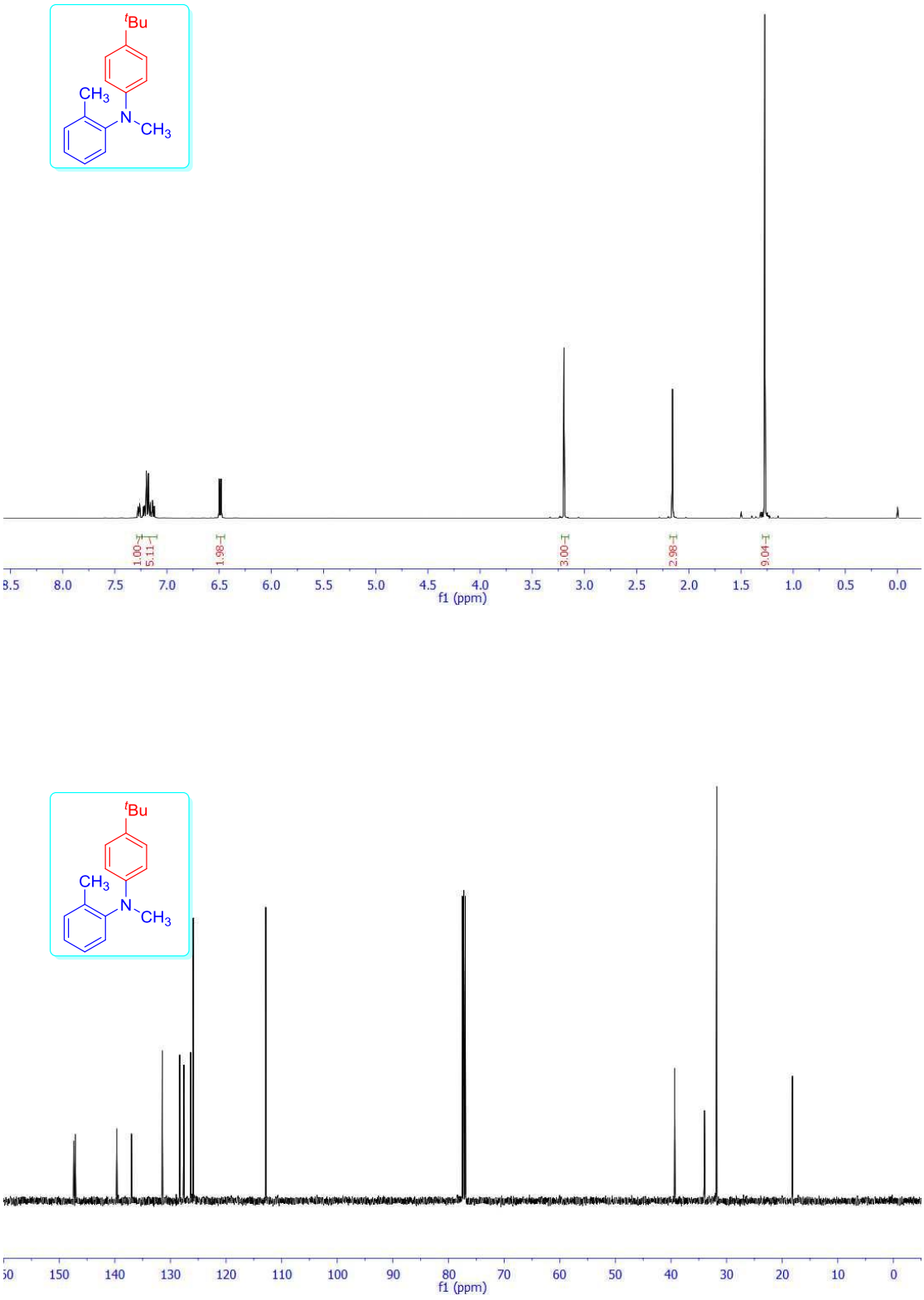


Figure S3. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3ad in $CDCl_3$

***N*-methyl-*N*-(trifluoromethylphenyl)-2-toluidine (3ae)**

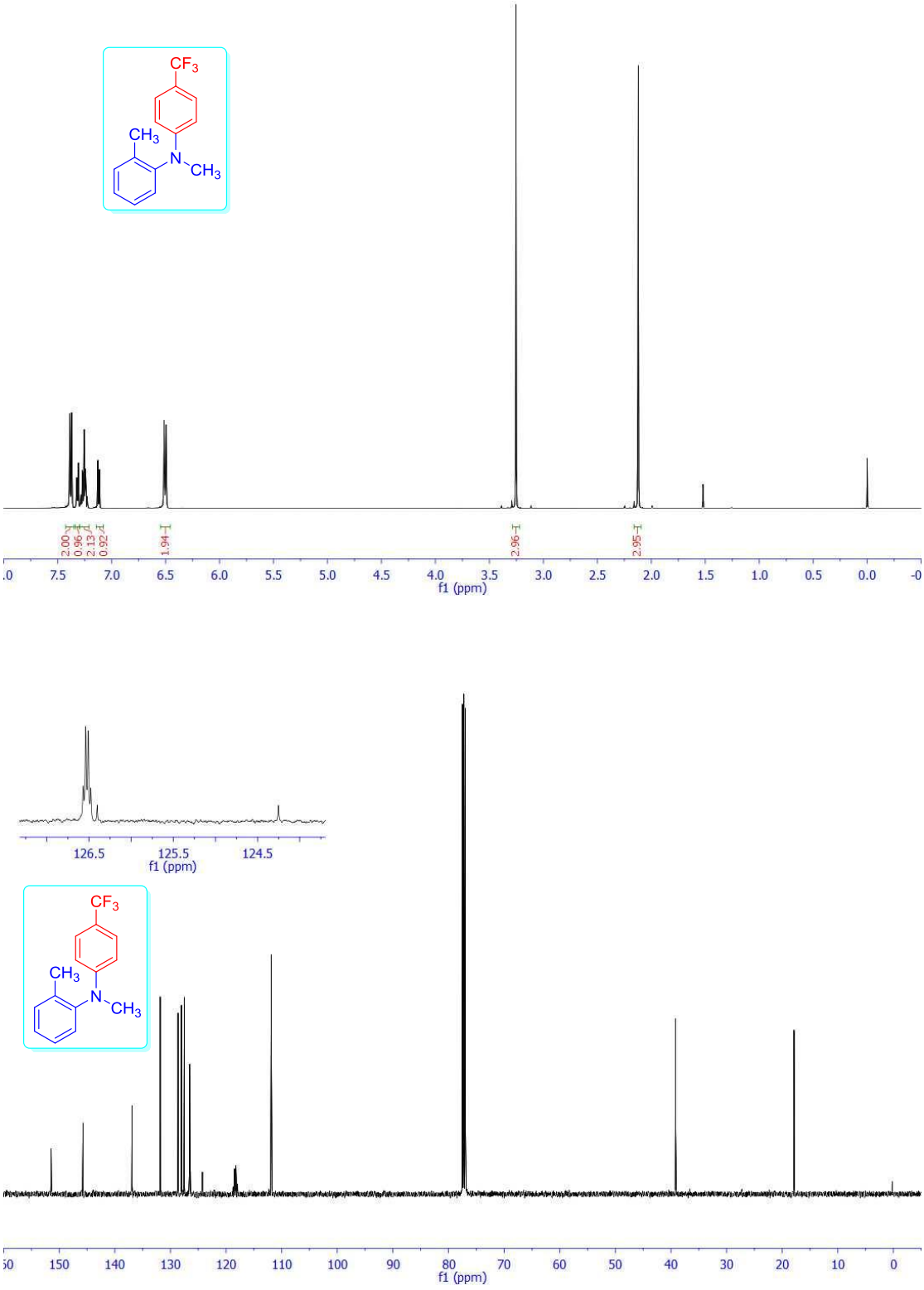


Figure S4. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3ae in $CDCl_3$

***N*-methyl-*N*-(3-methoxyphenyl)-2-toluidine (3af)**

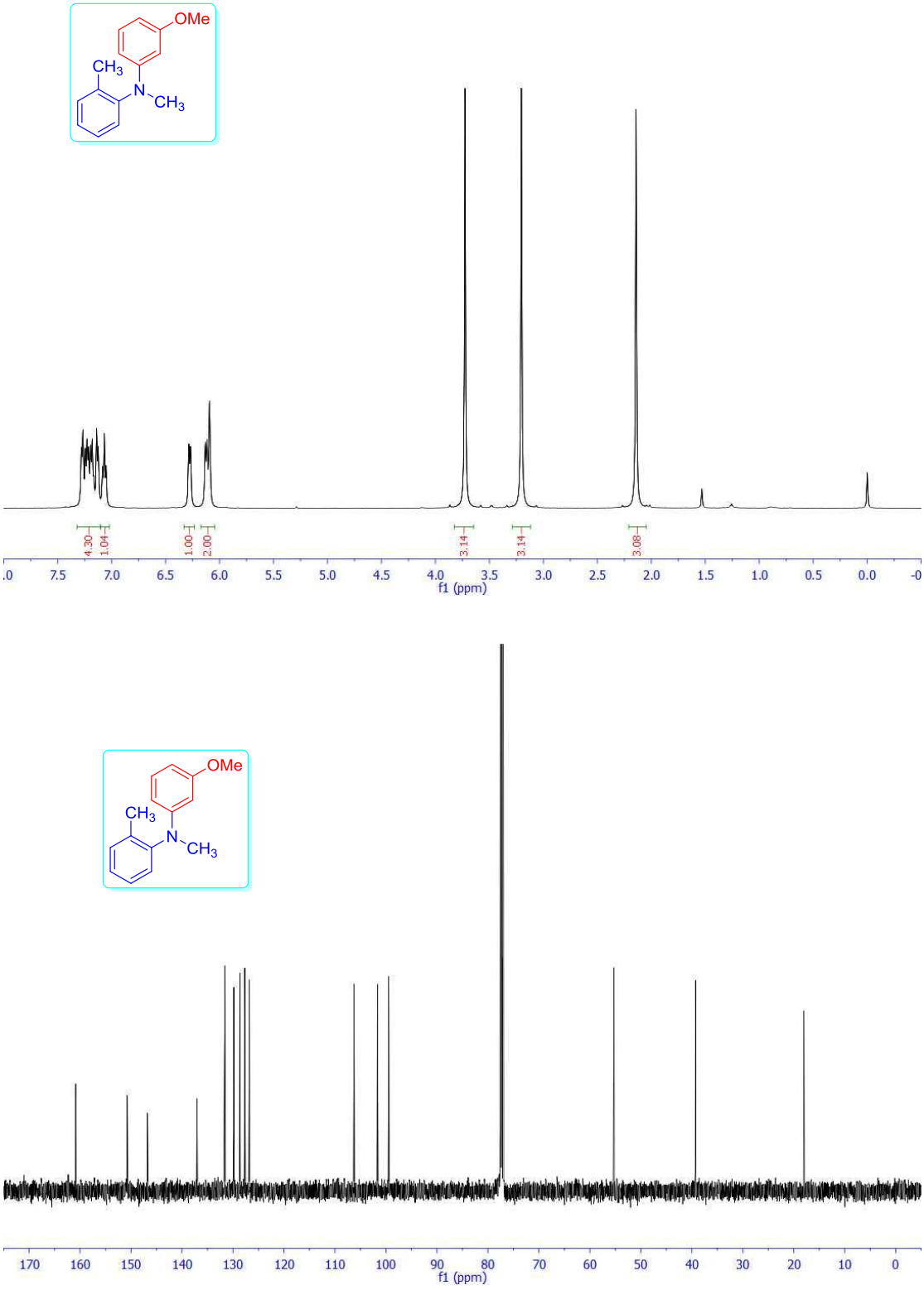
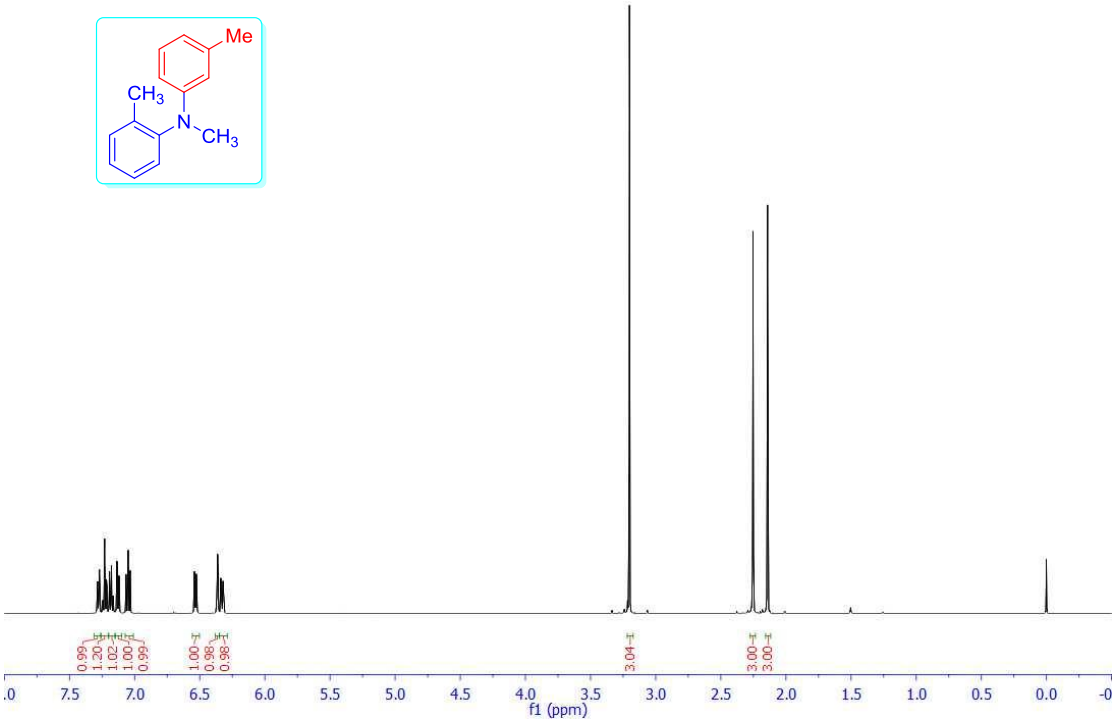


Figure S5. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3af in $CDCl_3$

***N*-methyl-*N*-(3-methylphenyl)-2-toluidine (3ag)**



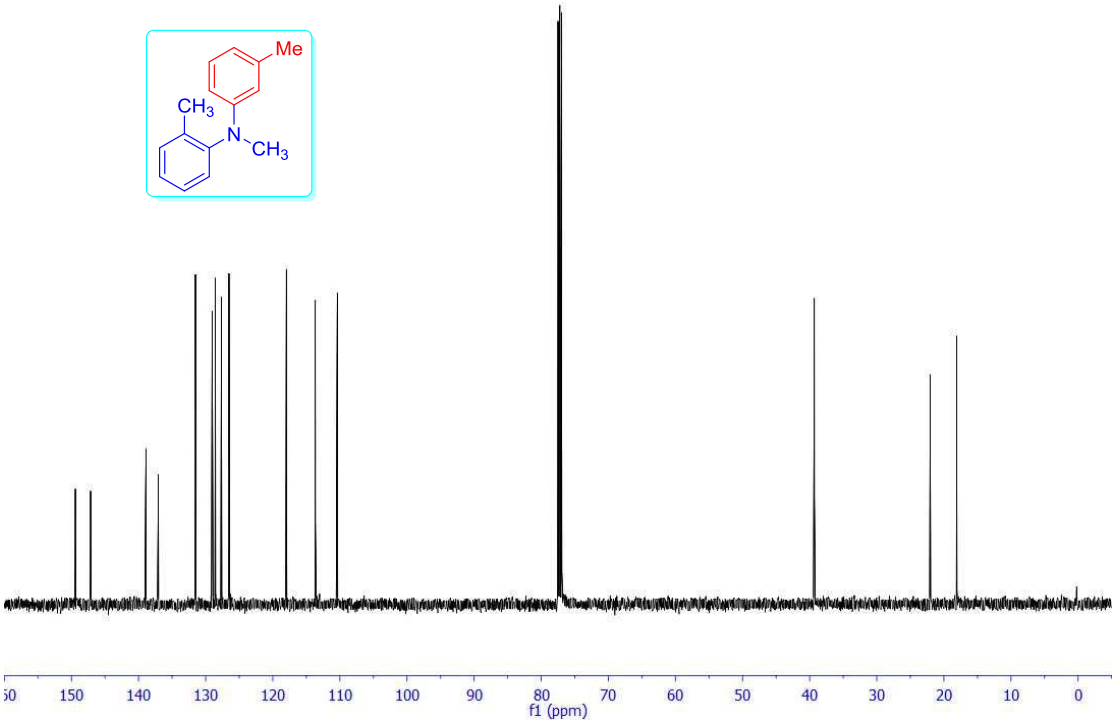


Figure S6. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3ag in $CDCl_3$

***N*-methyl-*N*-(3-trifluoromethylphenyl)-2-toluidine (3ah)**

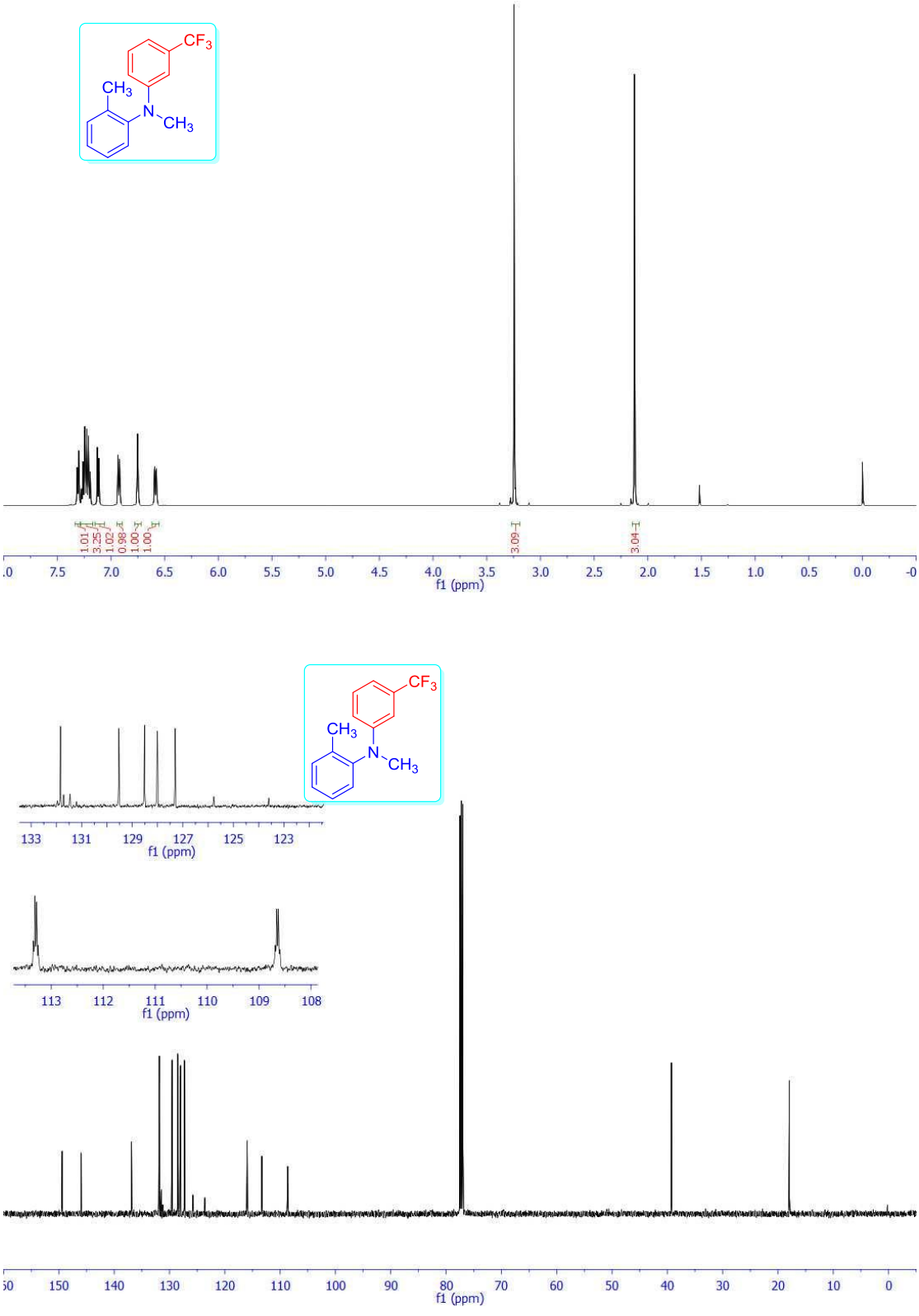


Figure S7. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3ah in $CDCl_3$

***N*-methyl-N-(4-benzophenone)-2-toluidine (3ai)**

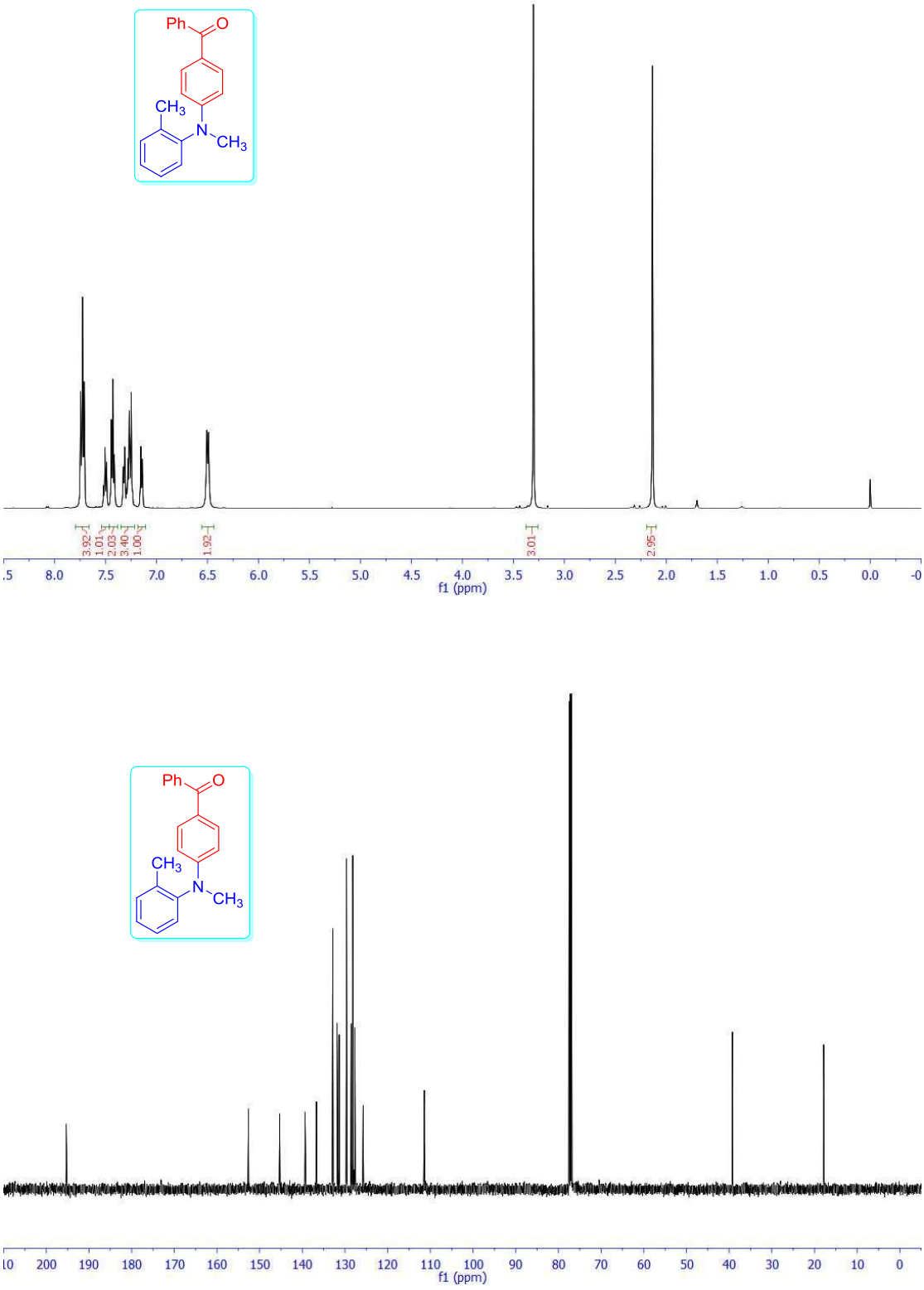


Figure S8. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3ai in $CDCl_3$

***N*-methyl-N-(4-benzophenone)-2-toluidine (3aj)**

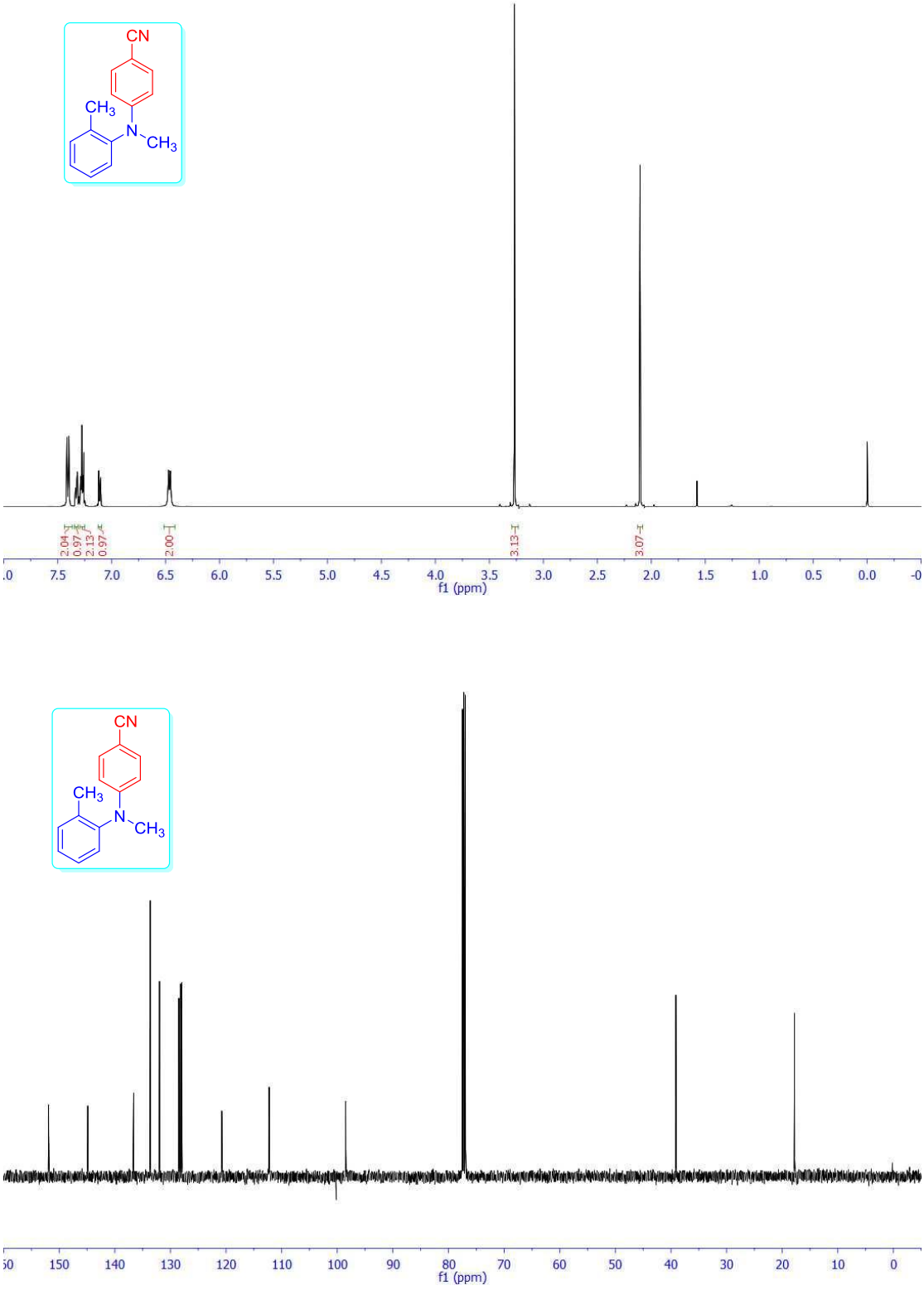


Figure S9. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3aj in $CDCl_3$

***N*-methyl-N-4-benzophenonephenylamine (3bi)**

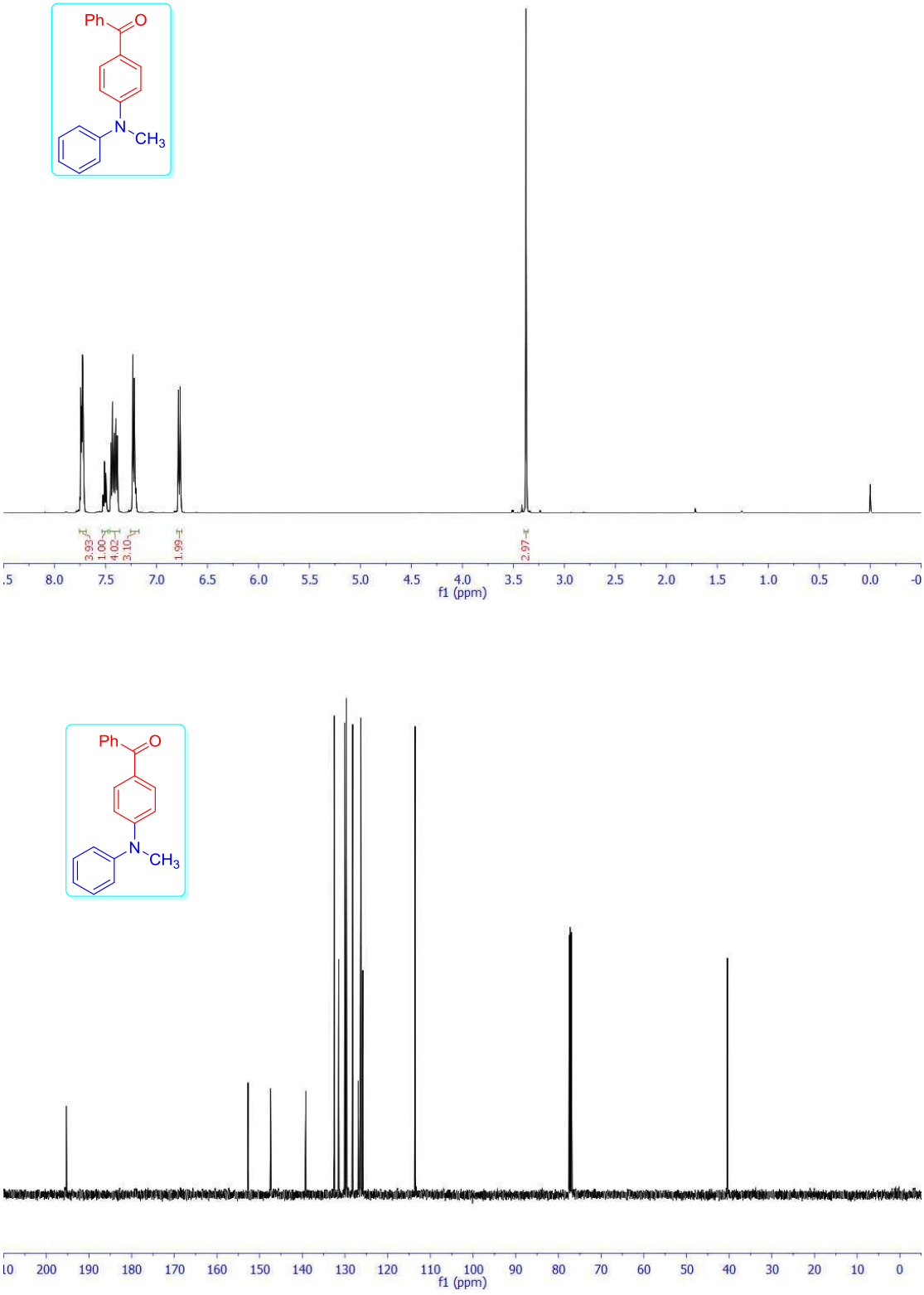


Figure S10. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 3bi in $CDCl_3$

Diphenylamine (7aa)

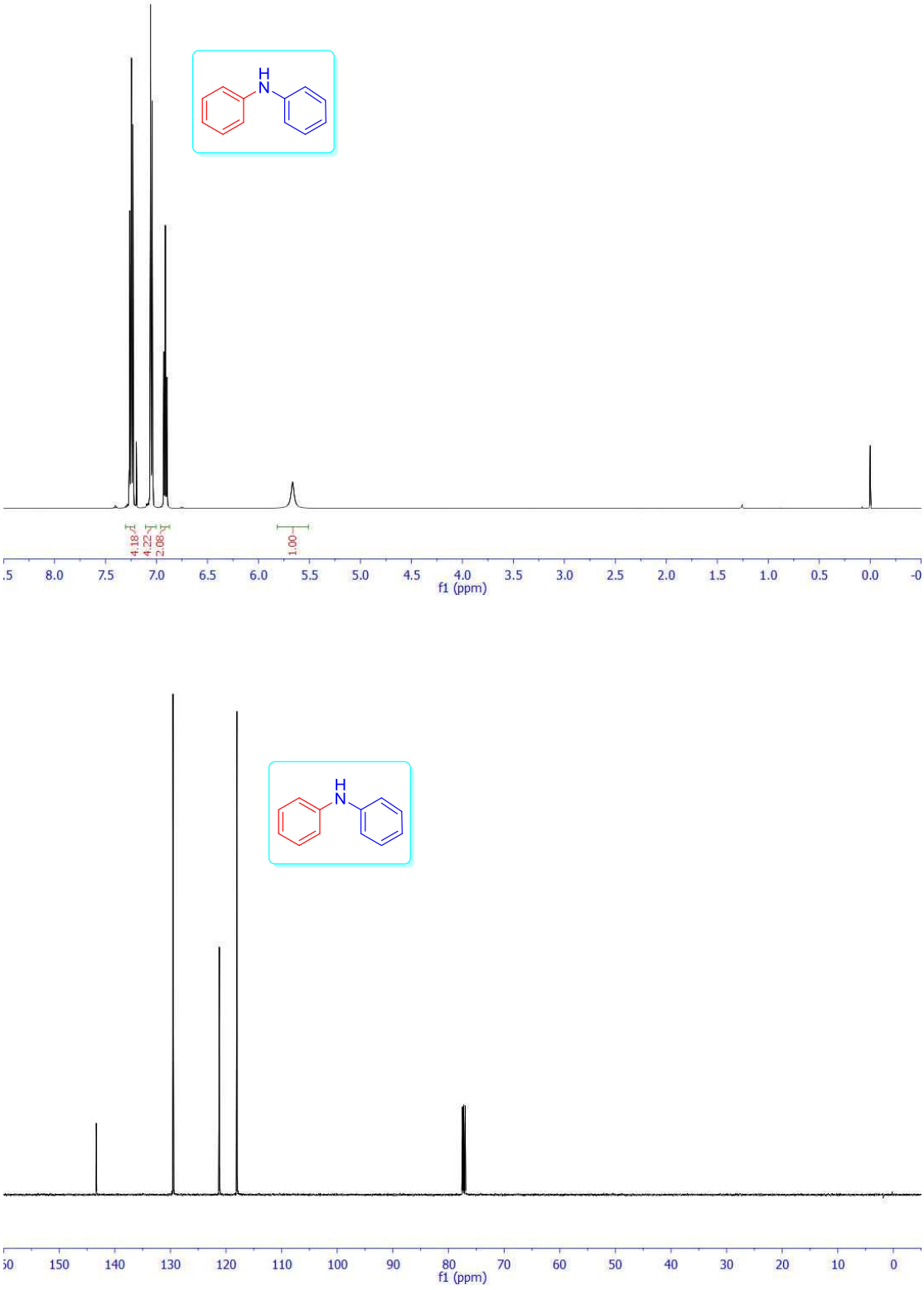


Figure S11. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7aa in $CDCl_3$

2-Methyl-*N*-phenylaniline (7ak)

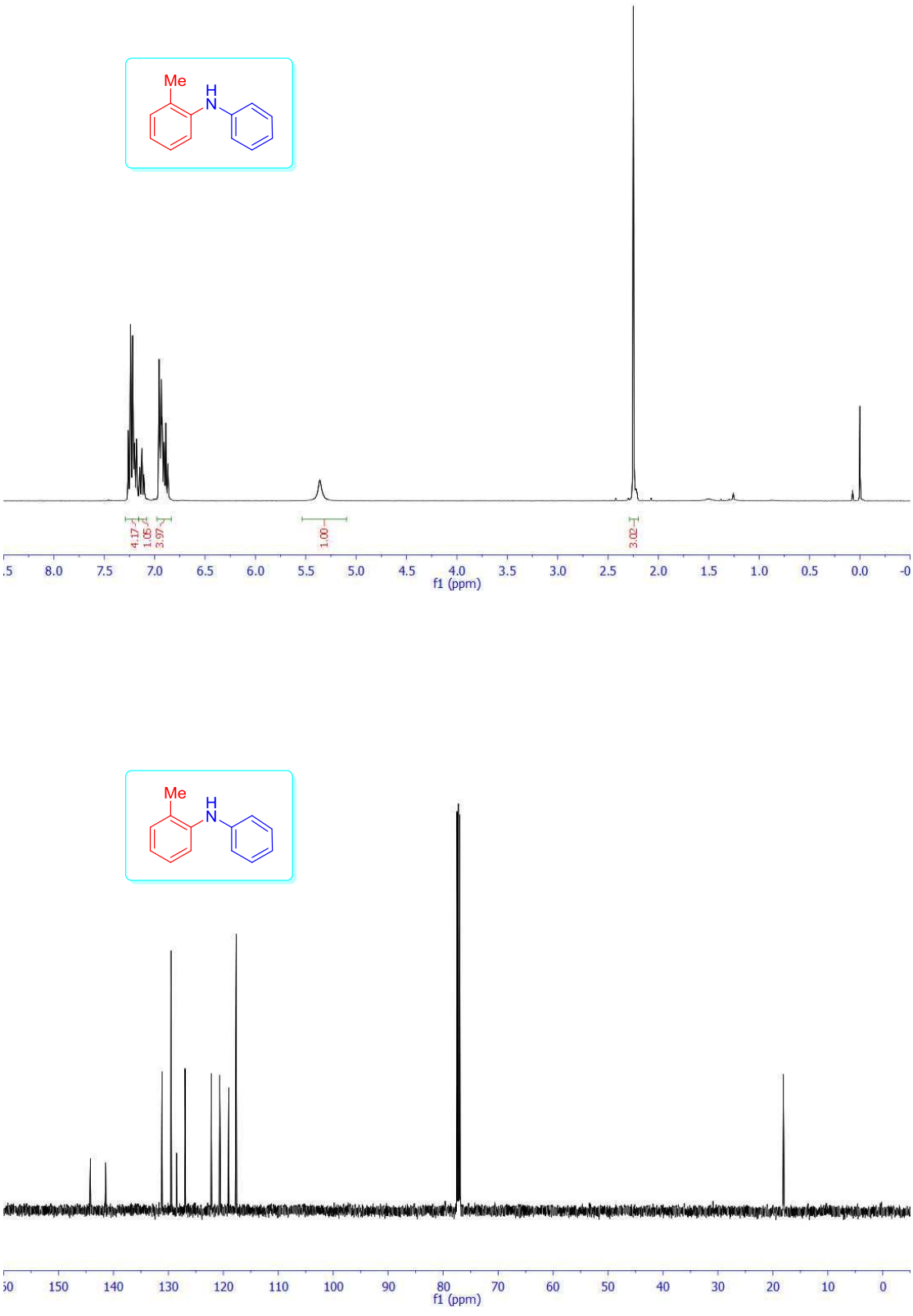


Figure S12. ^{1}H (360 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7ak in $CDCl_3$

4-(*tert*-Butyl)-*N*-phenylaniline (7ad)

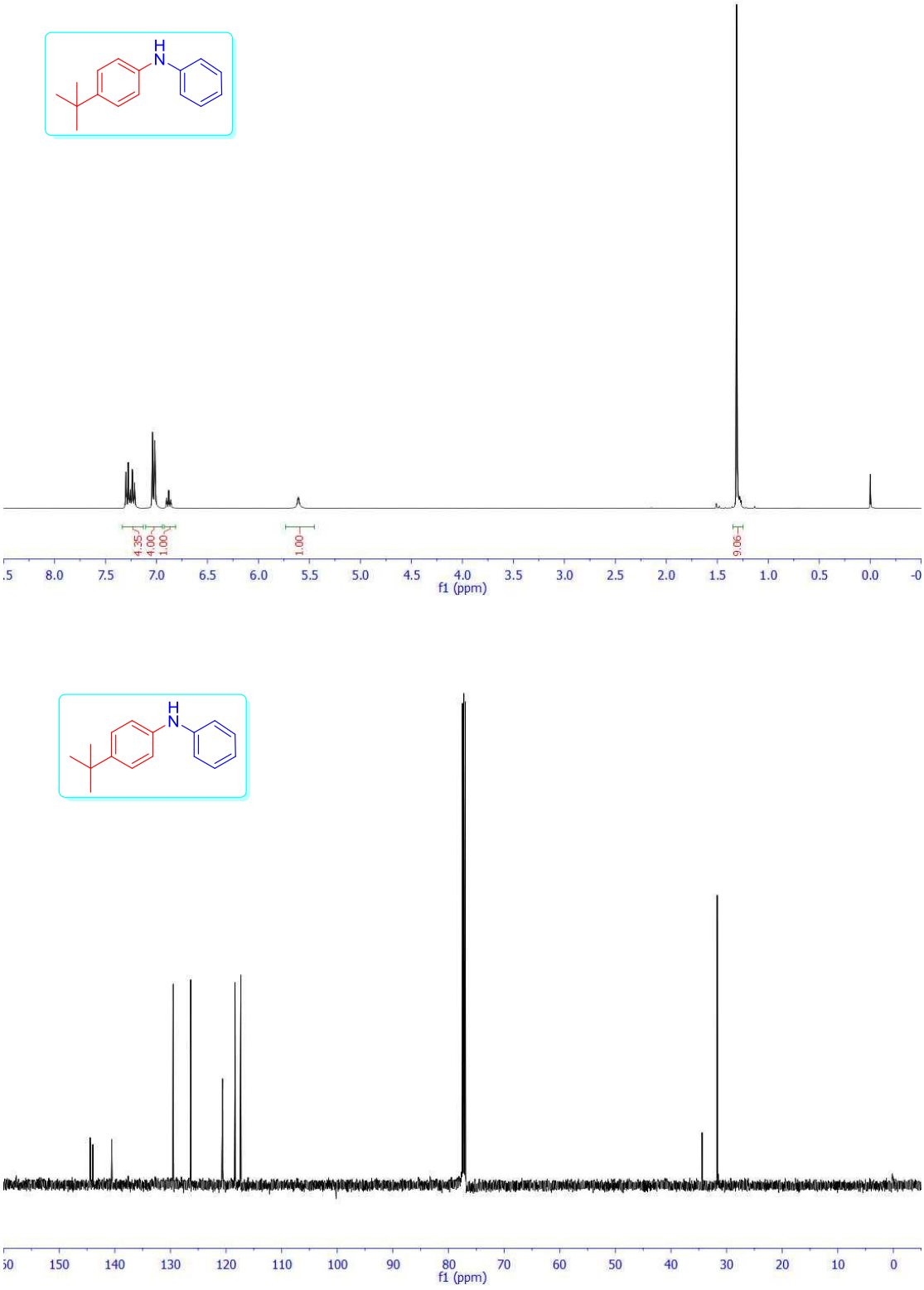


Figure S13. ^{1}H (360 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7ad in $CDCl_3$

***N*-phenyl-1-naphthylamine (7al)**

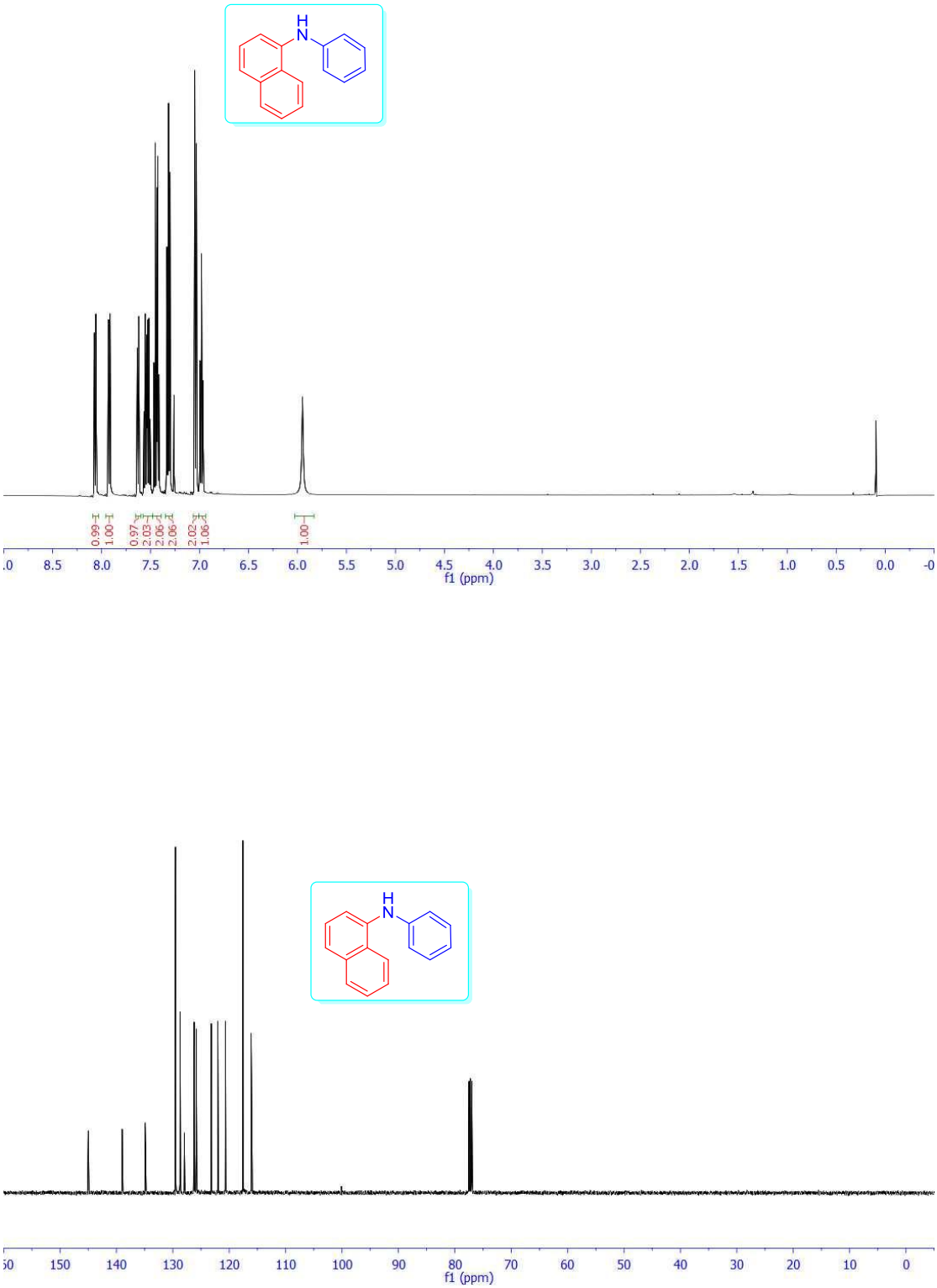


Figure S14. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7al in $CDCl_3$

***N*-phenyl-3-(trifluoromethyl)aniline (7ah)**

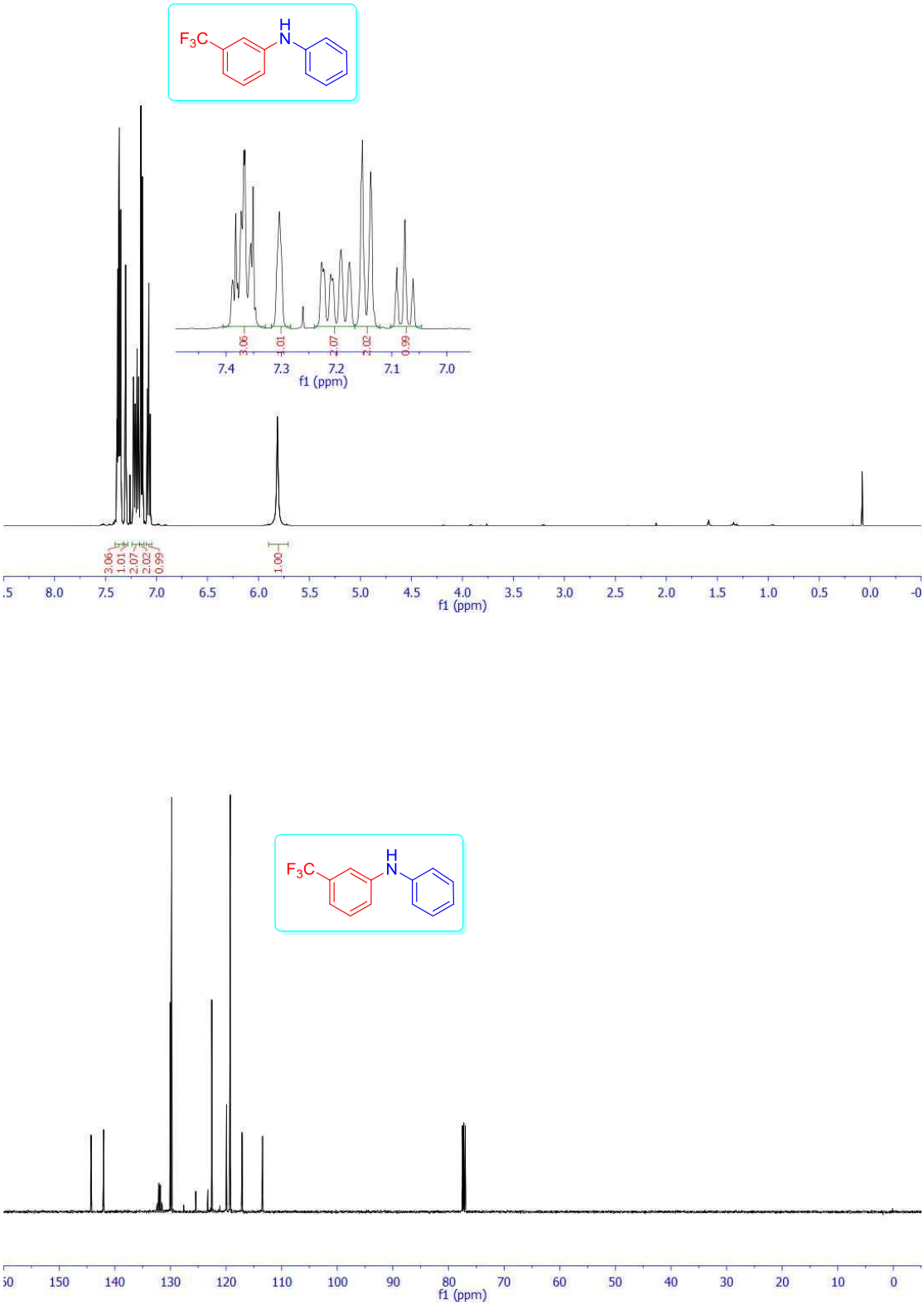


Figure S15. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7ah in $CDCl_3$

***N*-phenyl-3-methylaniline (7ag)**

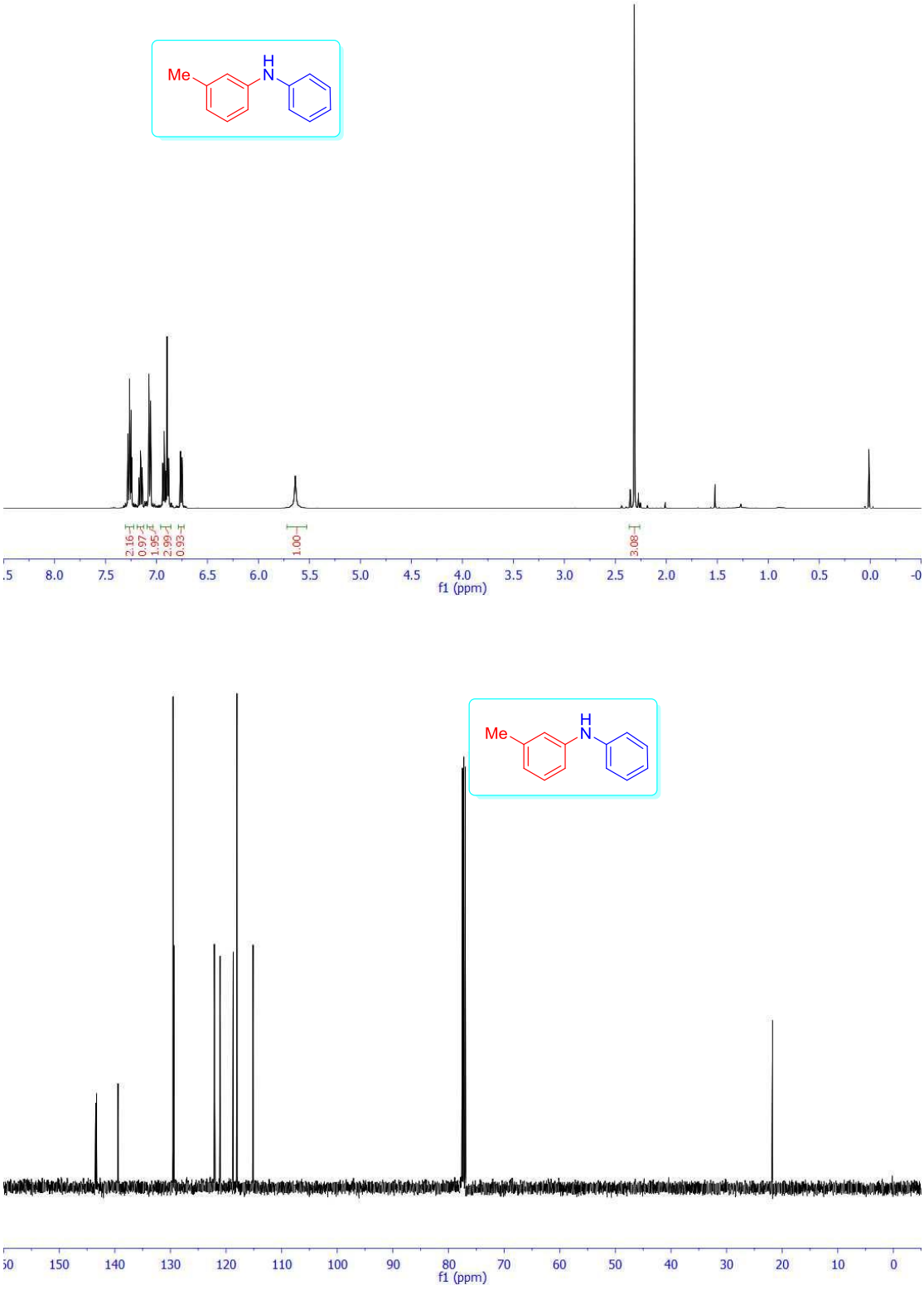


Figure S16. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7ag in $CDCl_3$

***N*-phenyl-*p*-anisidine (7ac)**

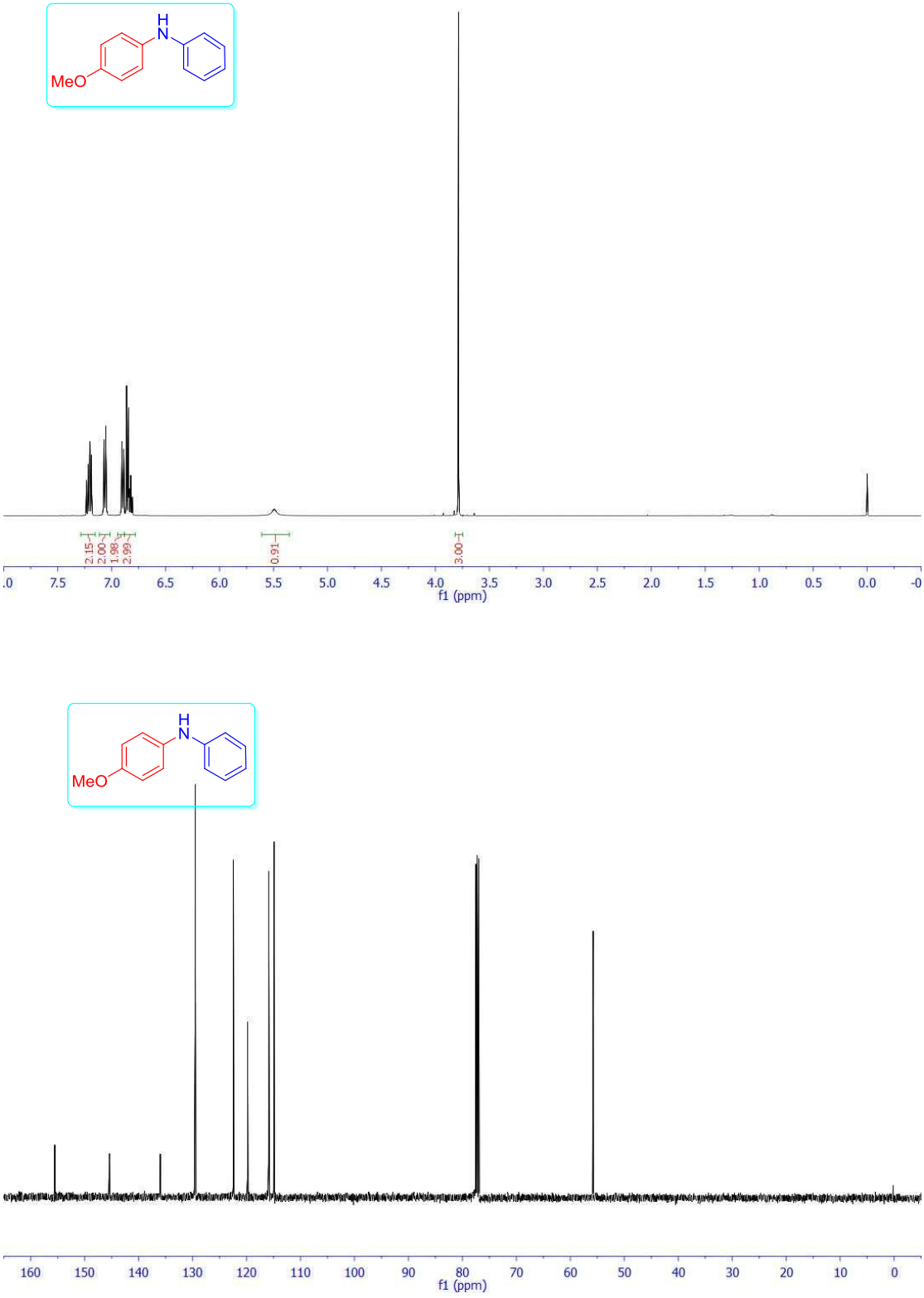


Figure S17. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7ac in $CDCl_3$

4-Anilinobenzophenone (7ai)

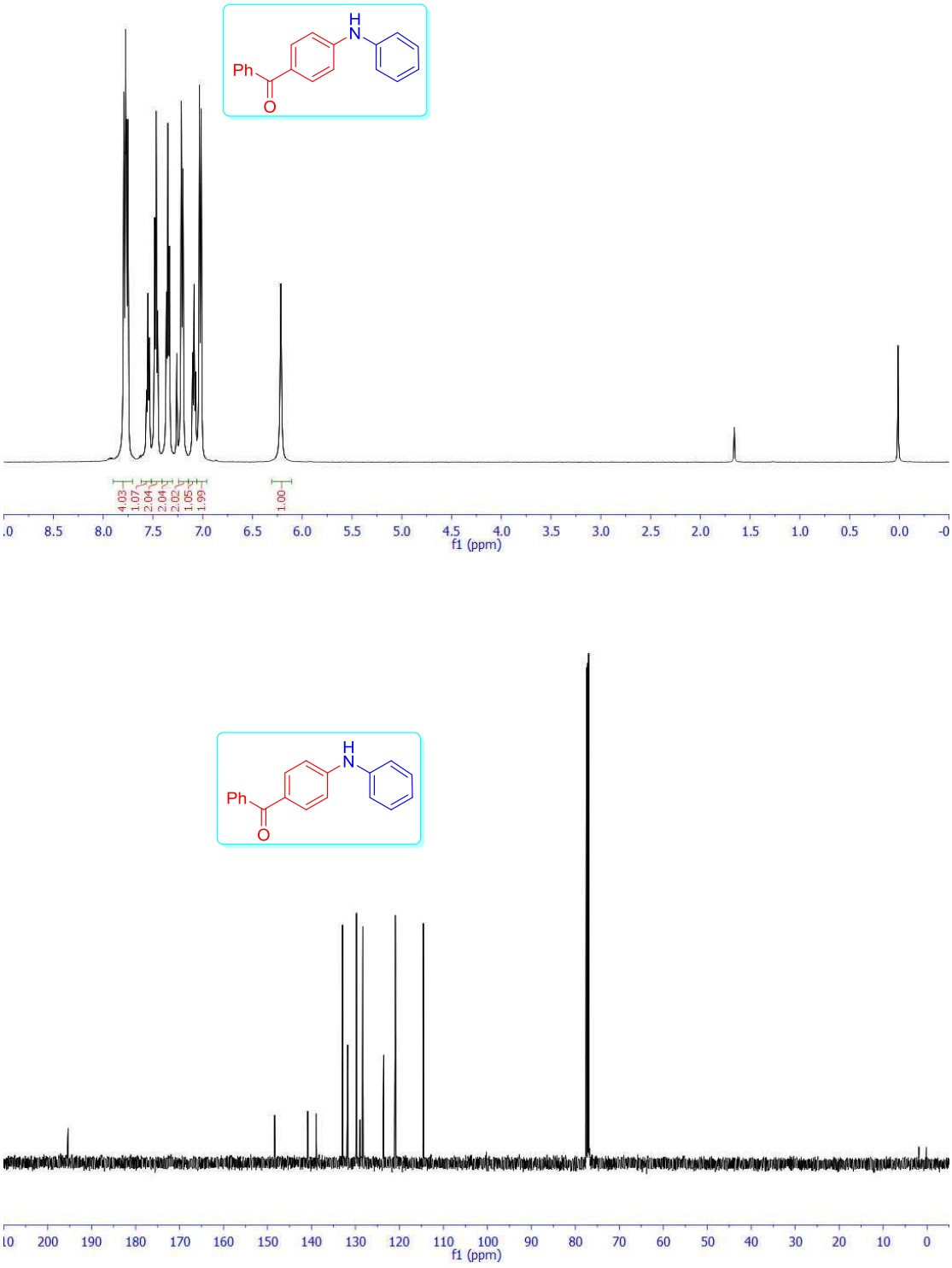


Figure S18. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7ai in $CDCl_3$

***N*-phenyl-4-(1*H*-pyrrol-1-yl)aniline (7am)**

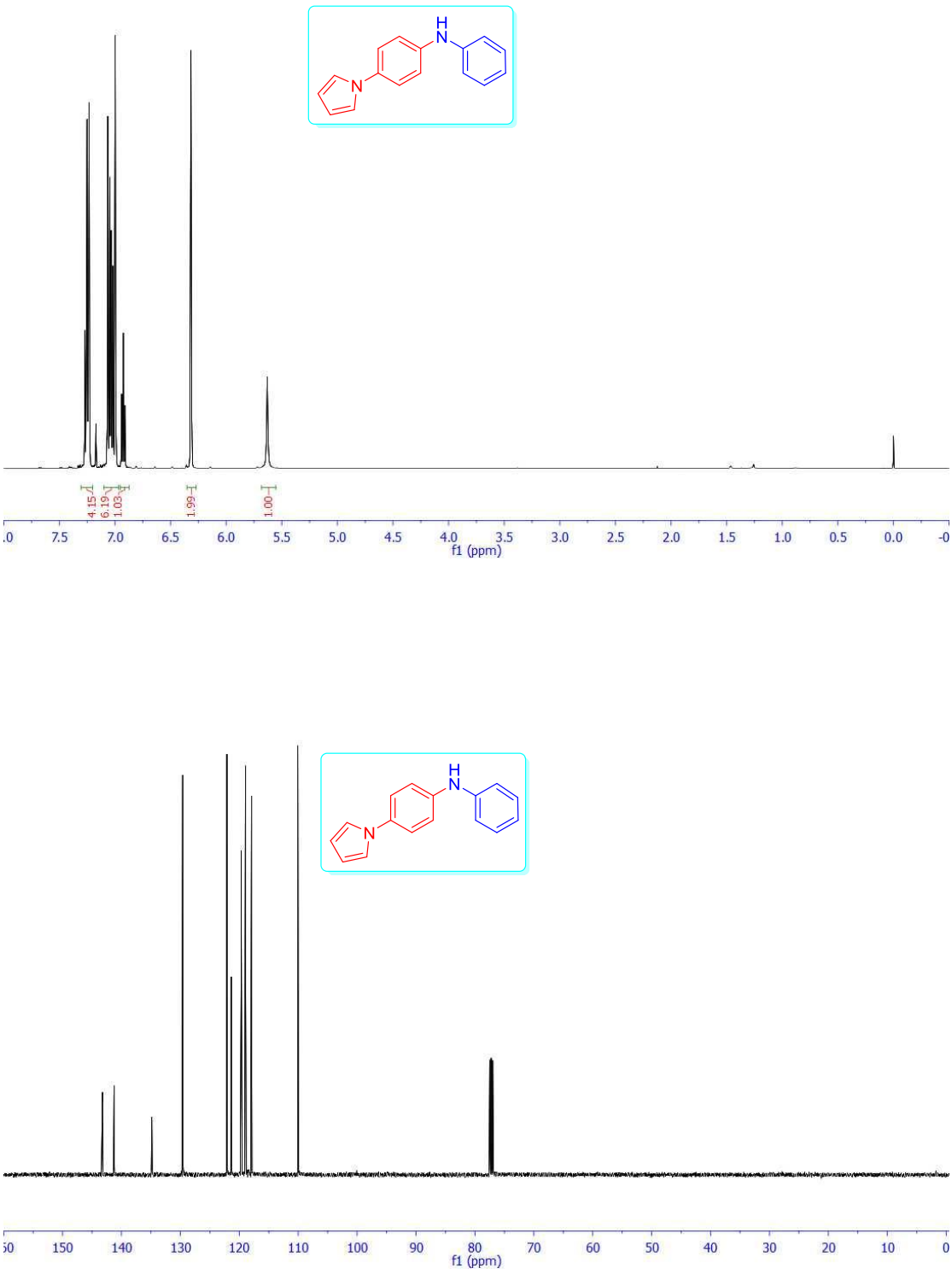


Figure S19. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7am in $CDCl_3$

***N*-phenyl-3-aminopyridine (7ab)**

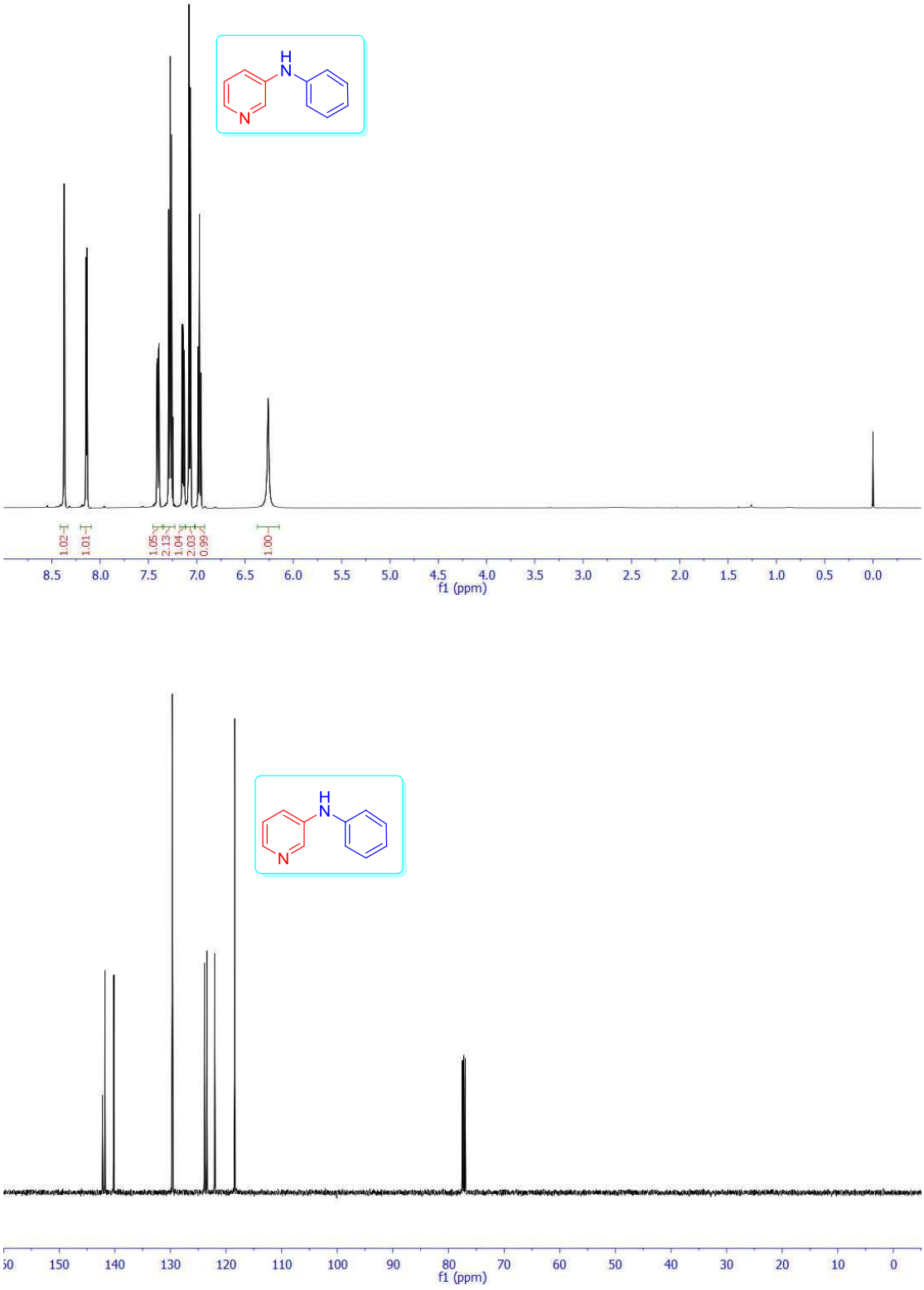


Figure S20. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7ab in $CDCl_3$

***N*-(3-trifluoromethylphenyl)-1-naphthylamine (7bl)**

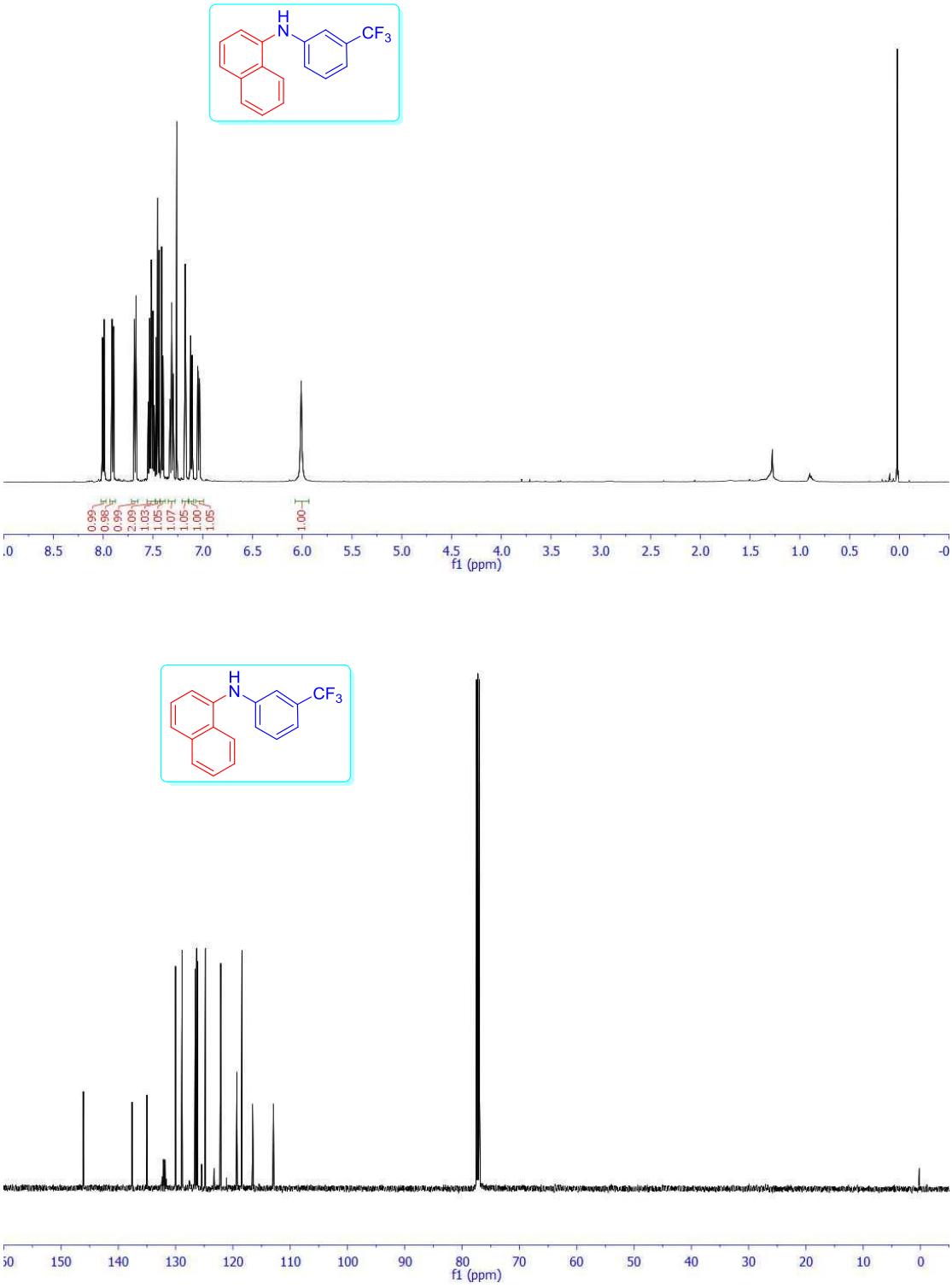


Figure S21. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7bl in $CDCl_3$

***N*-(4-(1H-pyrrol-1-yl)phenyl)-3-(trifluoromethyl)aniline (7bm)**

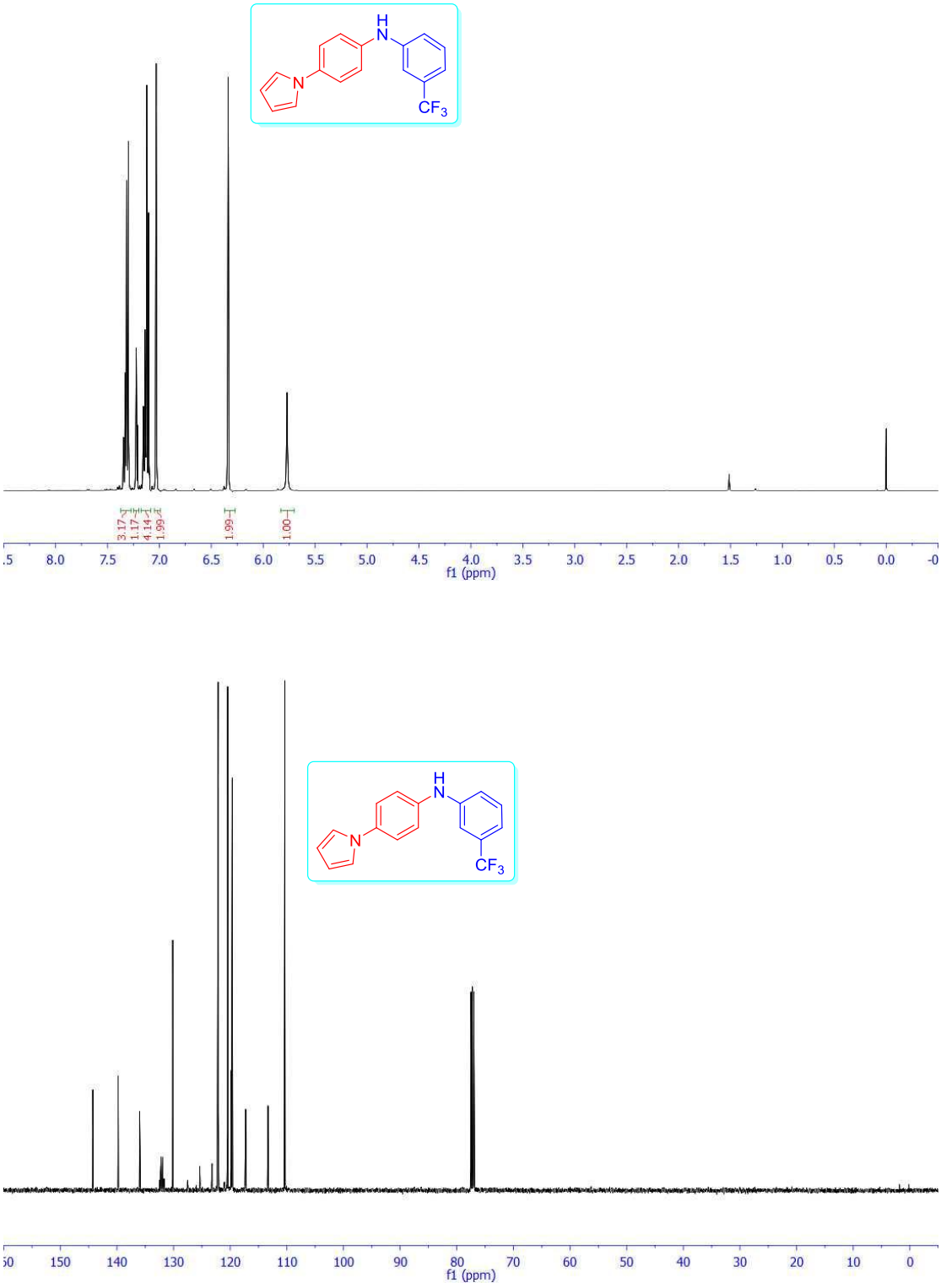


Figure S22. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7bm in $CDCl_3$

***N*-(4-(1H-pyrrol-1-yl)phenyl)-4-ethoxyaniline (7cm)**

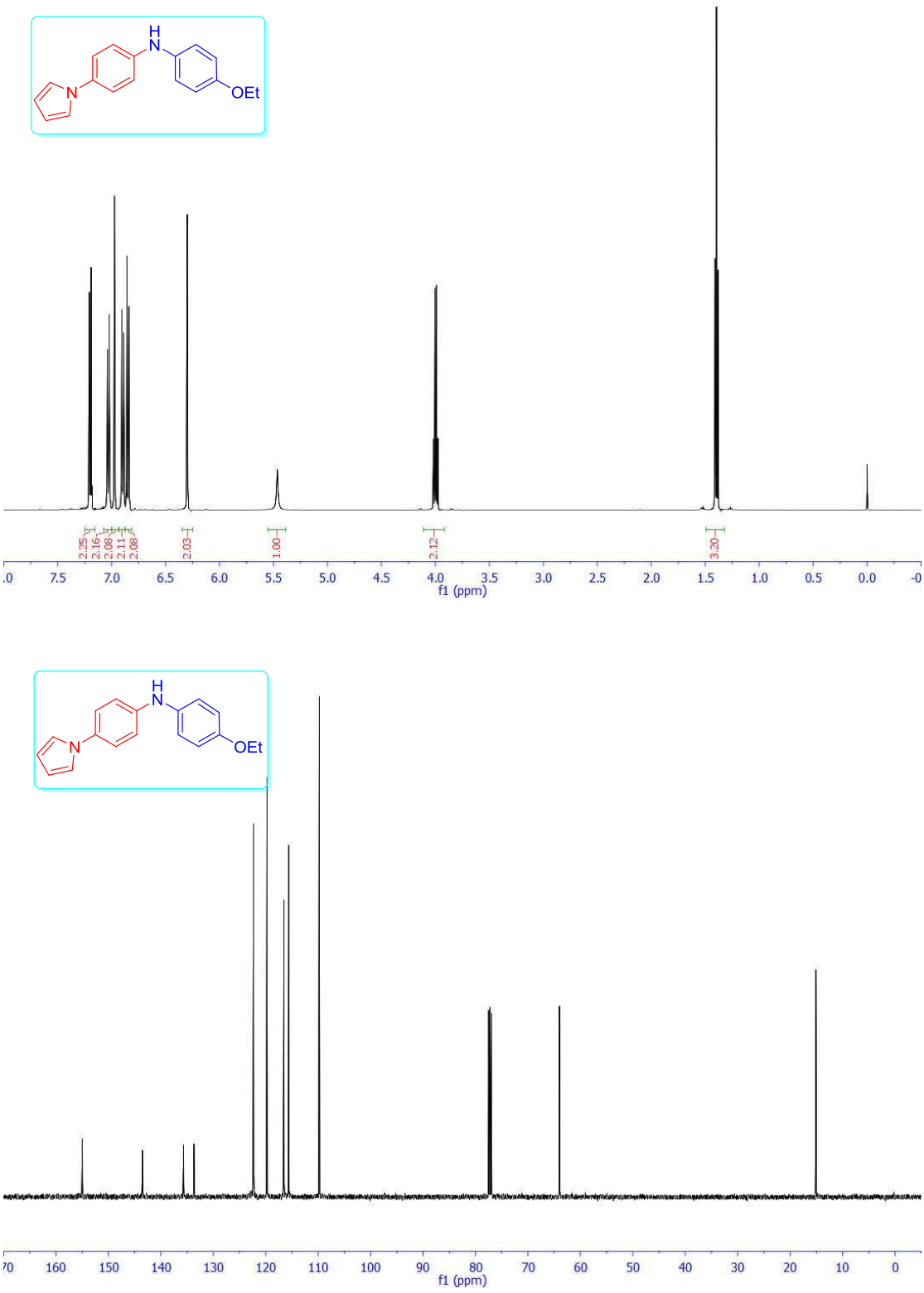


Figure S23. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7cm in $CDCl_3$

***N*-(4-ethoxyphenyl)-1-naphthylamine (7cl)**

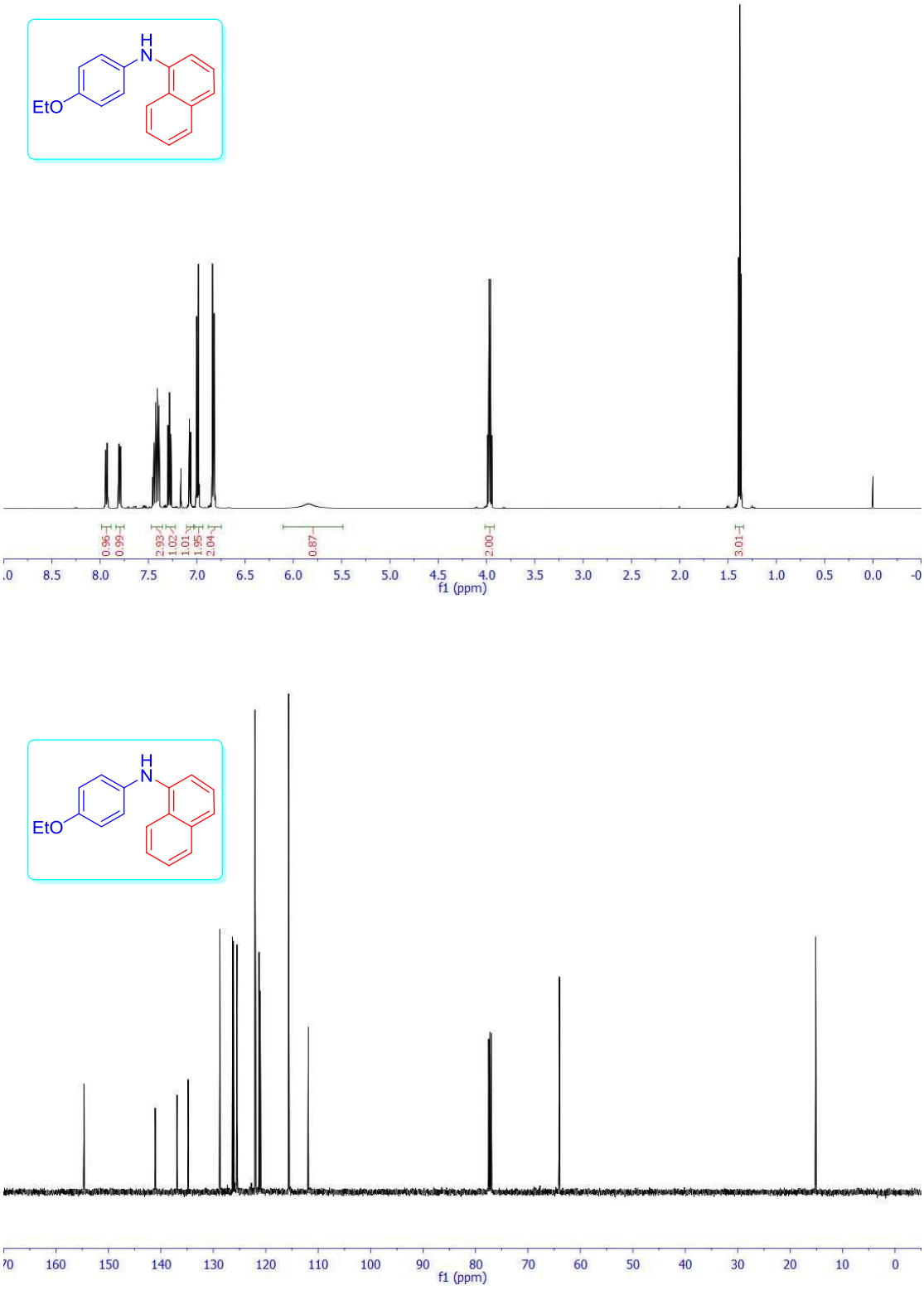


Figure S24. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7cl in $CDCl_3$

***N*-(4-(1H-pyrrol-1-yl)phenyl)-4-fluoroaniline (7dm)**

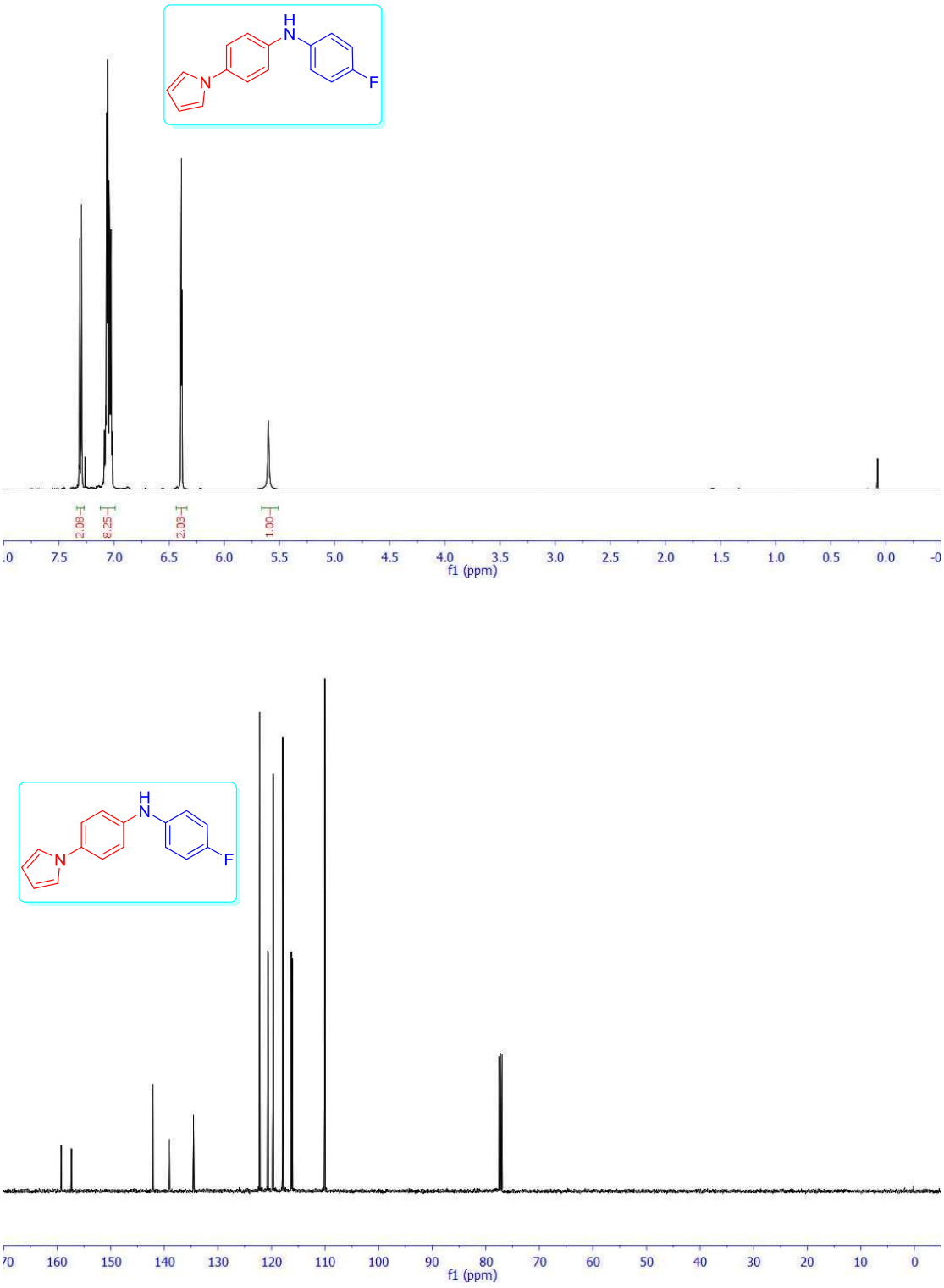


Figure S25. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7dm in $CDCl_3$

***N*-(4-fluorophenyl)-1-naphthylamine (7dl)**

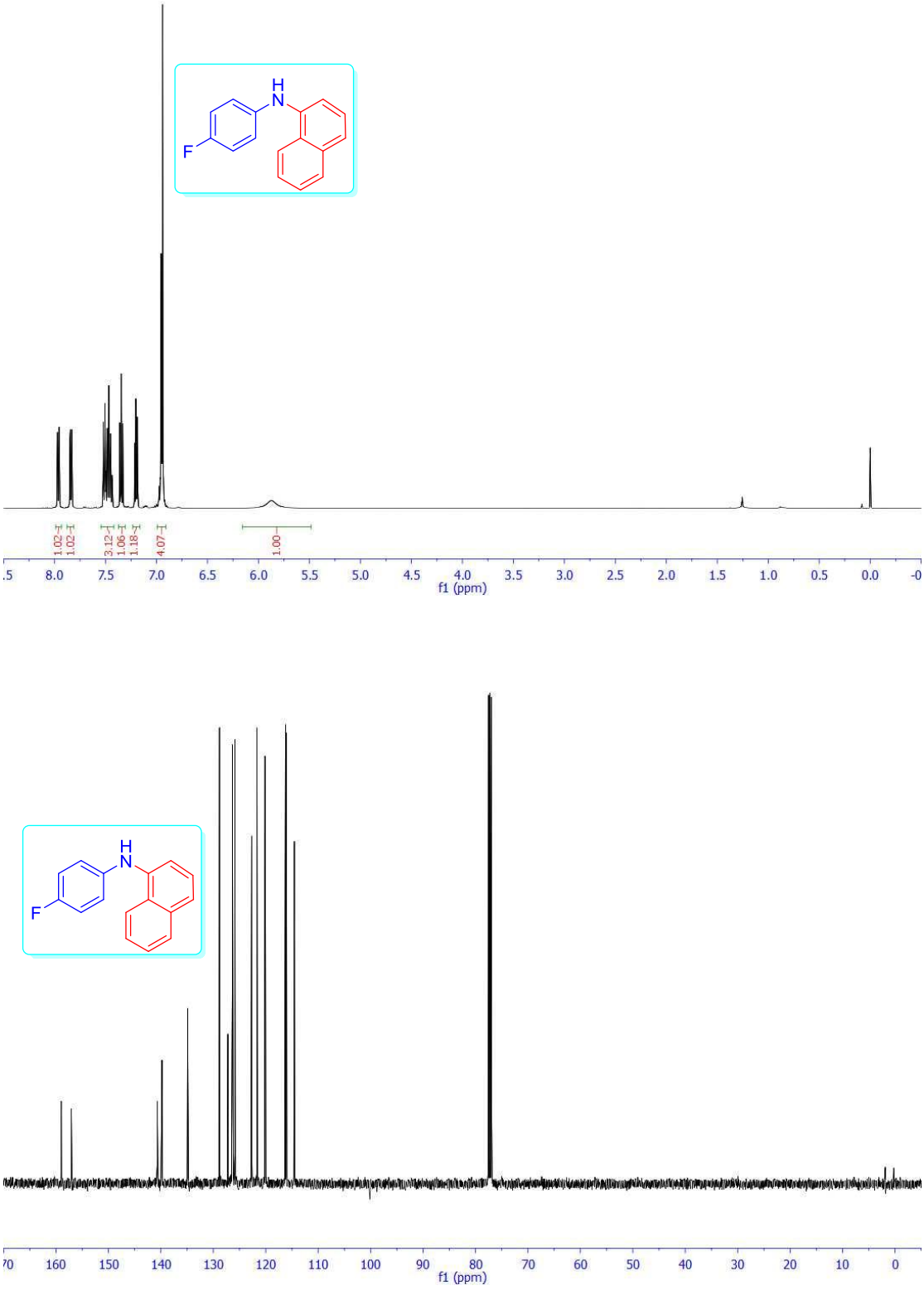


Figure S26. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7dl in $CDCl_3$

***N*-(4-(1H-pyrrol-1-yl)phenyl)-2-phenylaniline (7em)**

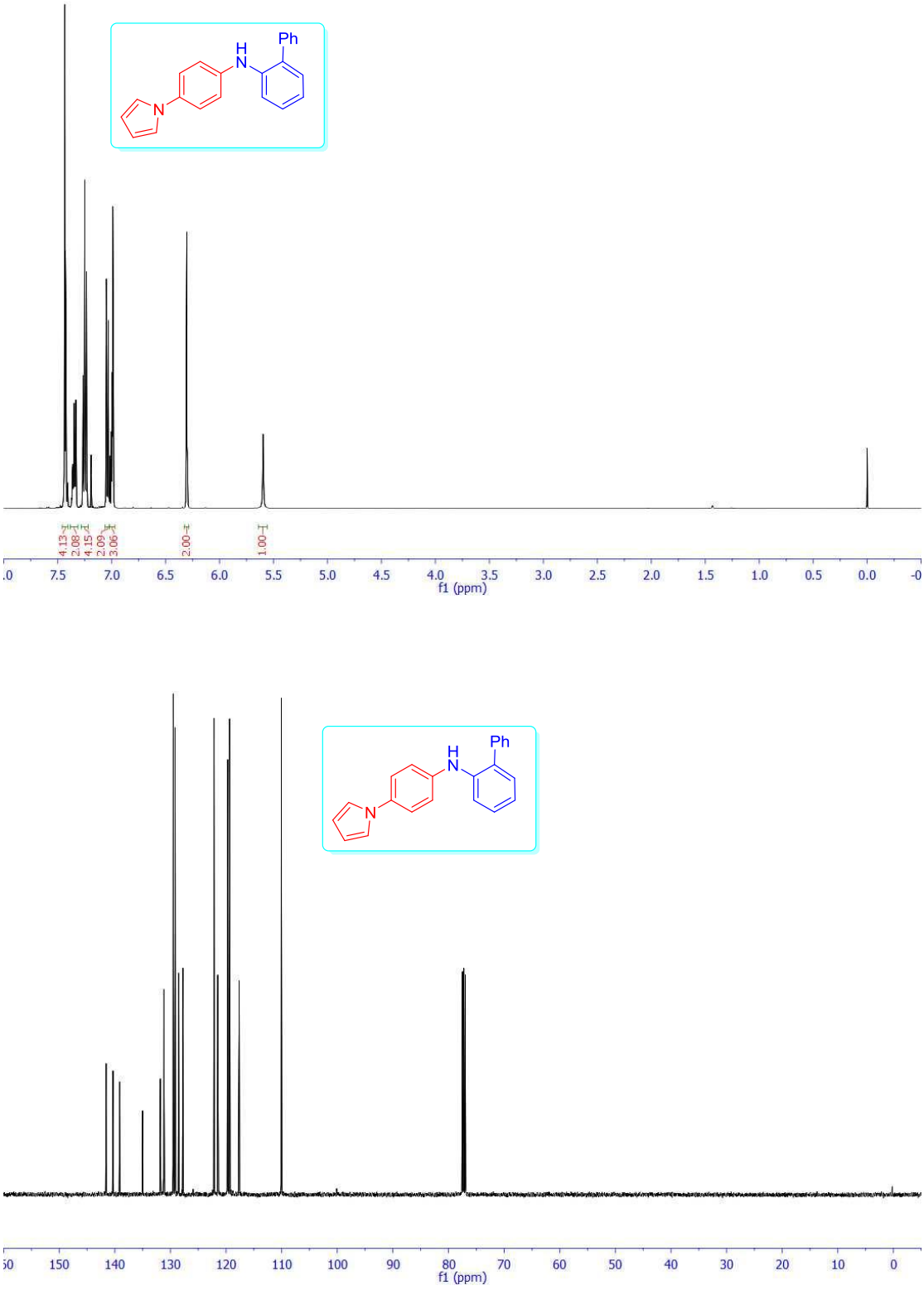


Figure S27. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7em in $CDCl_3$

***N*-(2-biphenyl)-1-naphthalenamine (7el)**

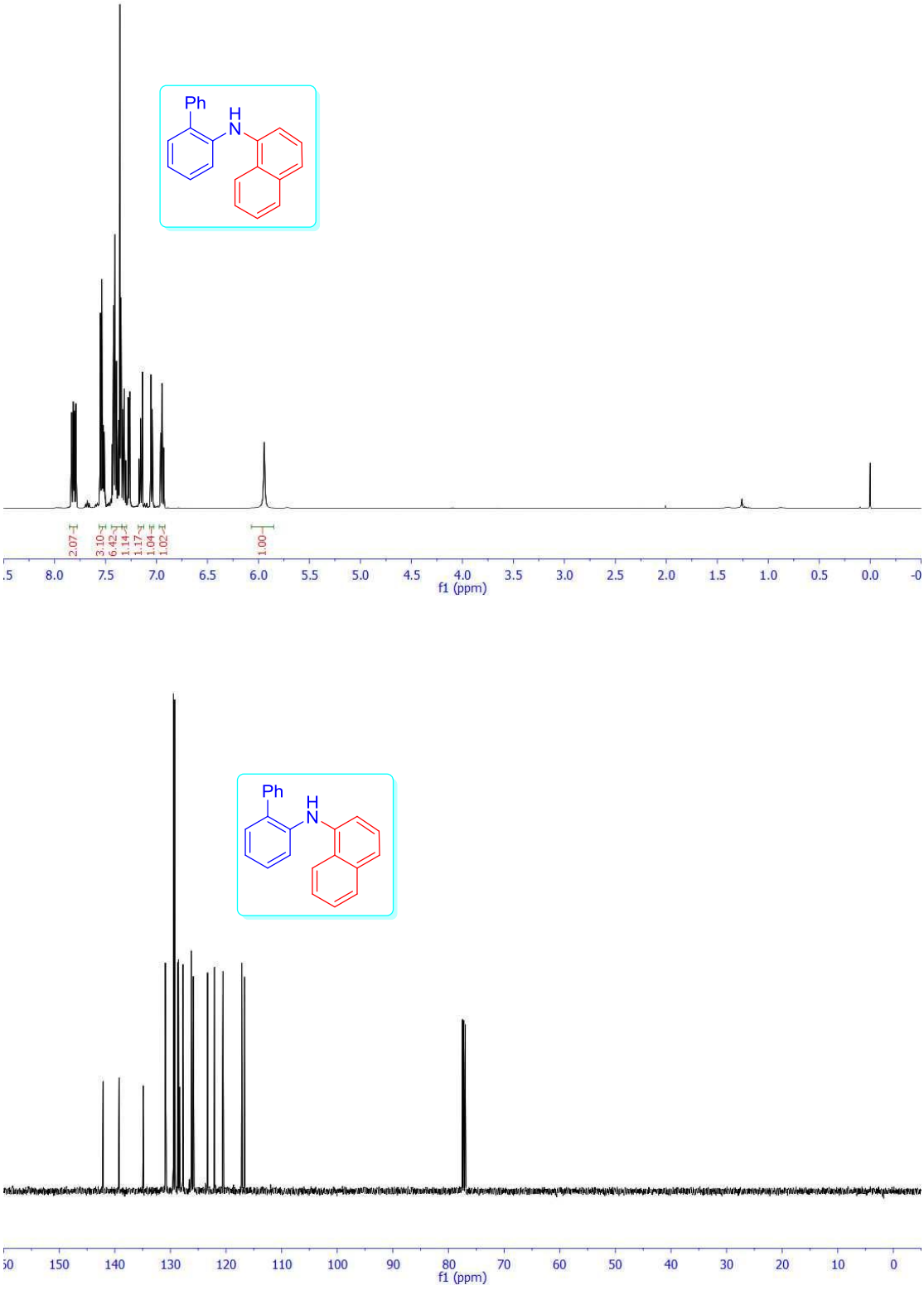


Figure S28. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7el in $CDCl_3$

***N*-(1-paphthyl)-3-aminopyridine (7fl)**

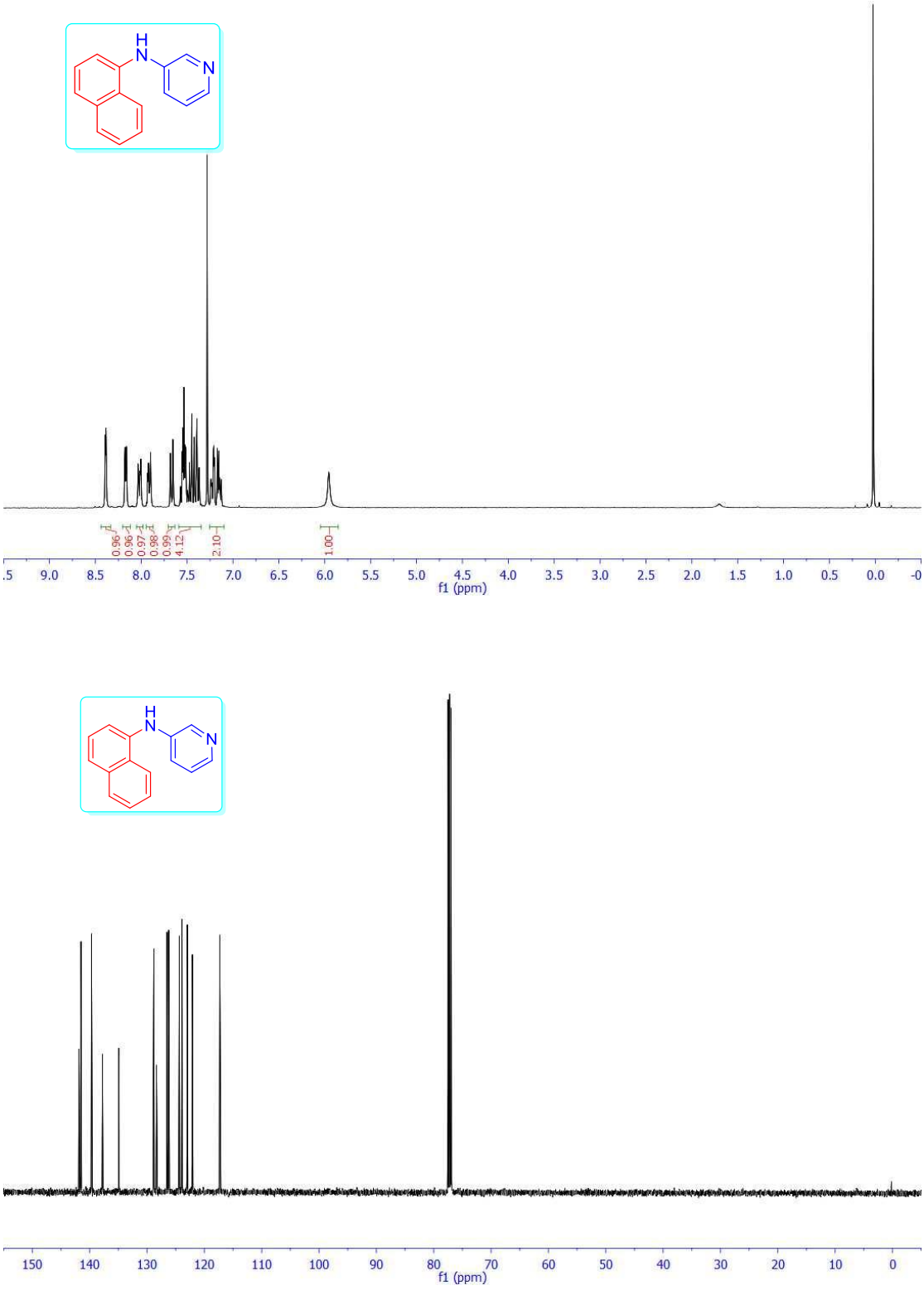


Figure S29. ^{1}H (300 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7fl in $CDCl_3$

***N*-(4-*tert*-butylphenyl)-3-aminopyridine (7fd)**

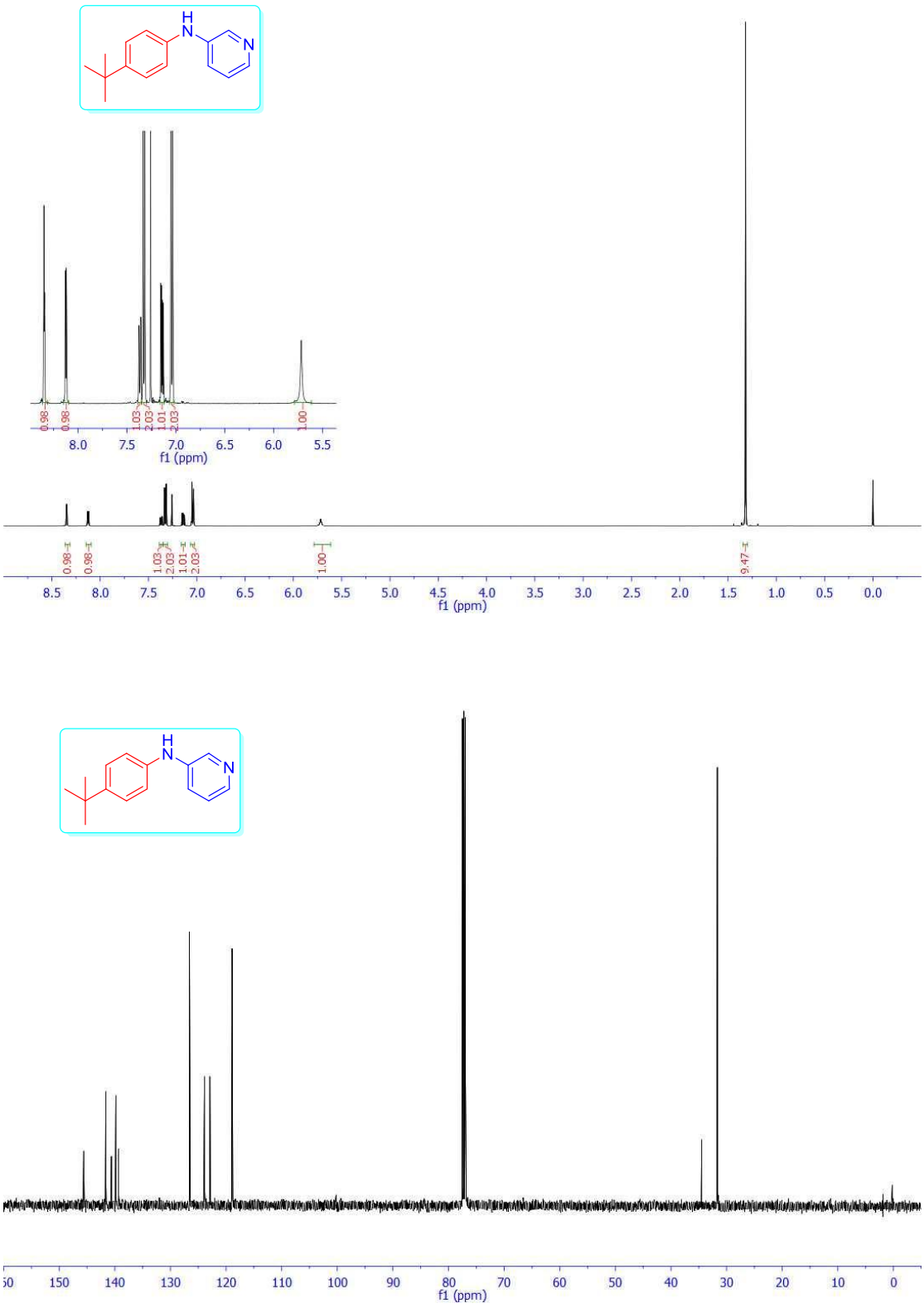


Figure S30. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7fd in $CDCl_3$

***N*-(1-naphthyl)quinolin-3-amine (7gl)**

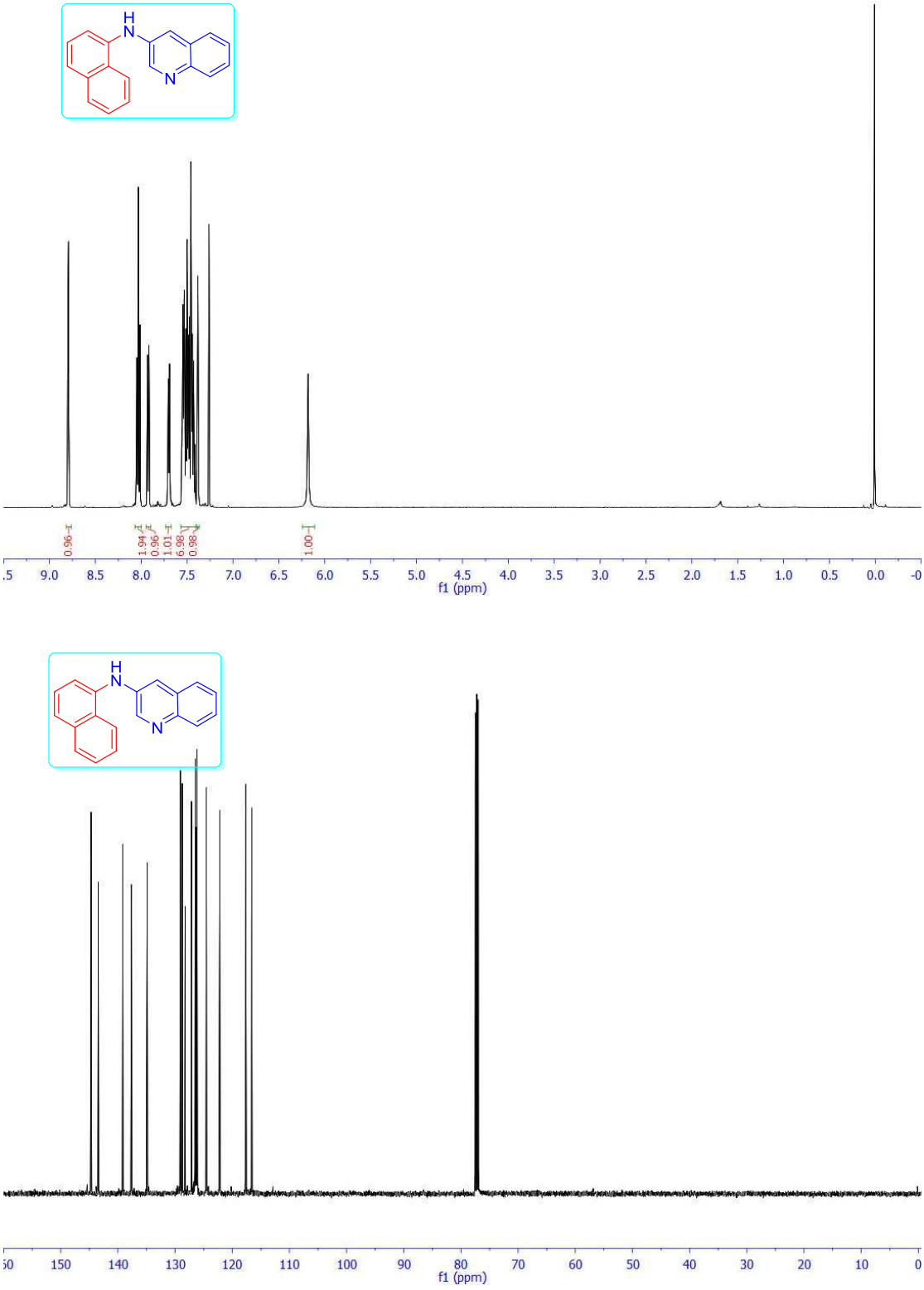


Figure S31. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 7gl in $CDCl_3$

***N*-(4-trifluoromethylphenyl)morpholine (9ah)**

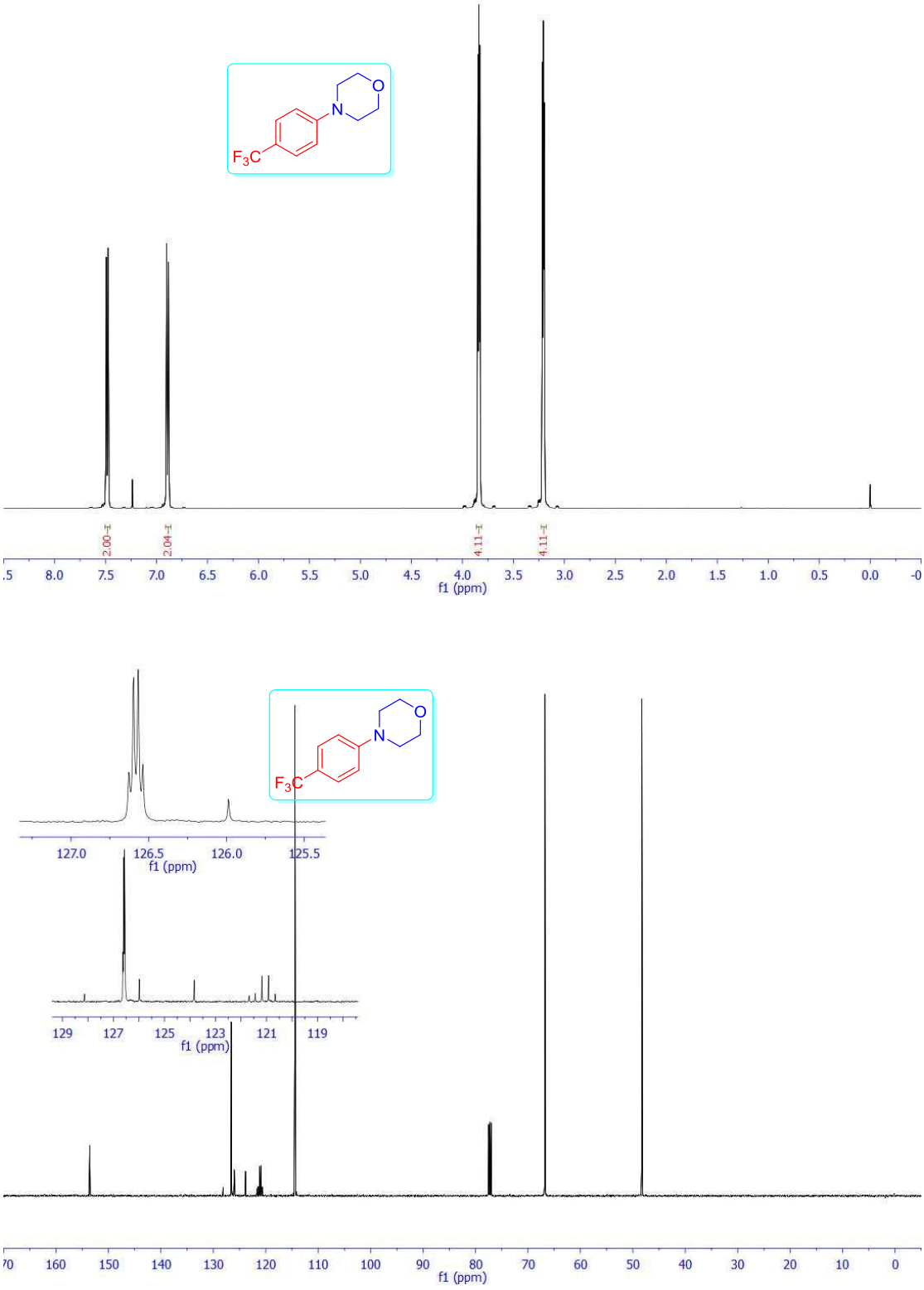


Figure S32. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9ah in $CDCl_3$

***N*-(4-benzophenyl)morpholine (9ai)**

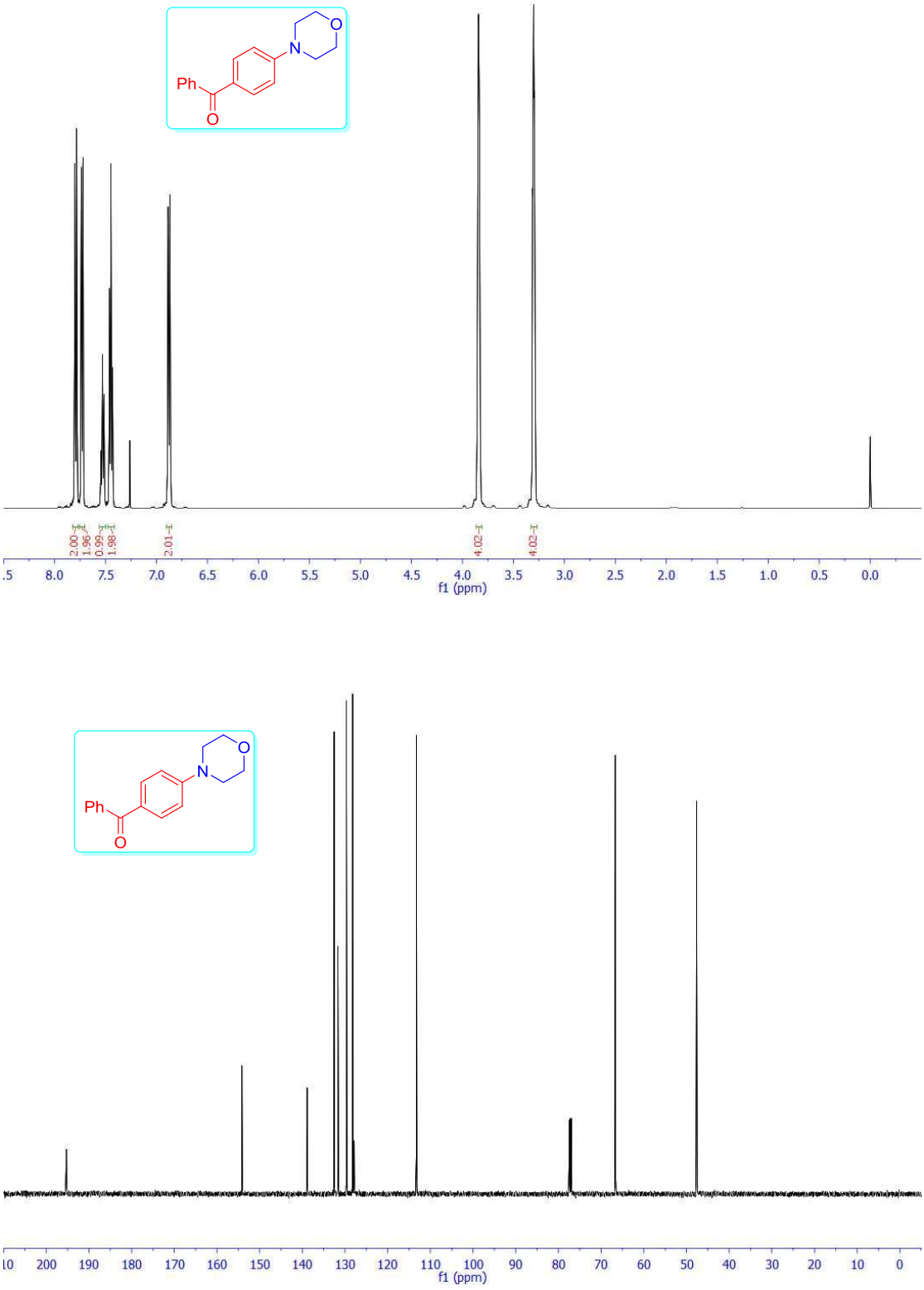


Figure S33. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9ai in $CDCl_3$

***N*-(3-pyridyl)morpholine (9ab)**

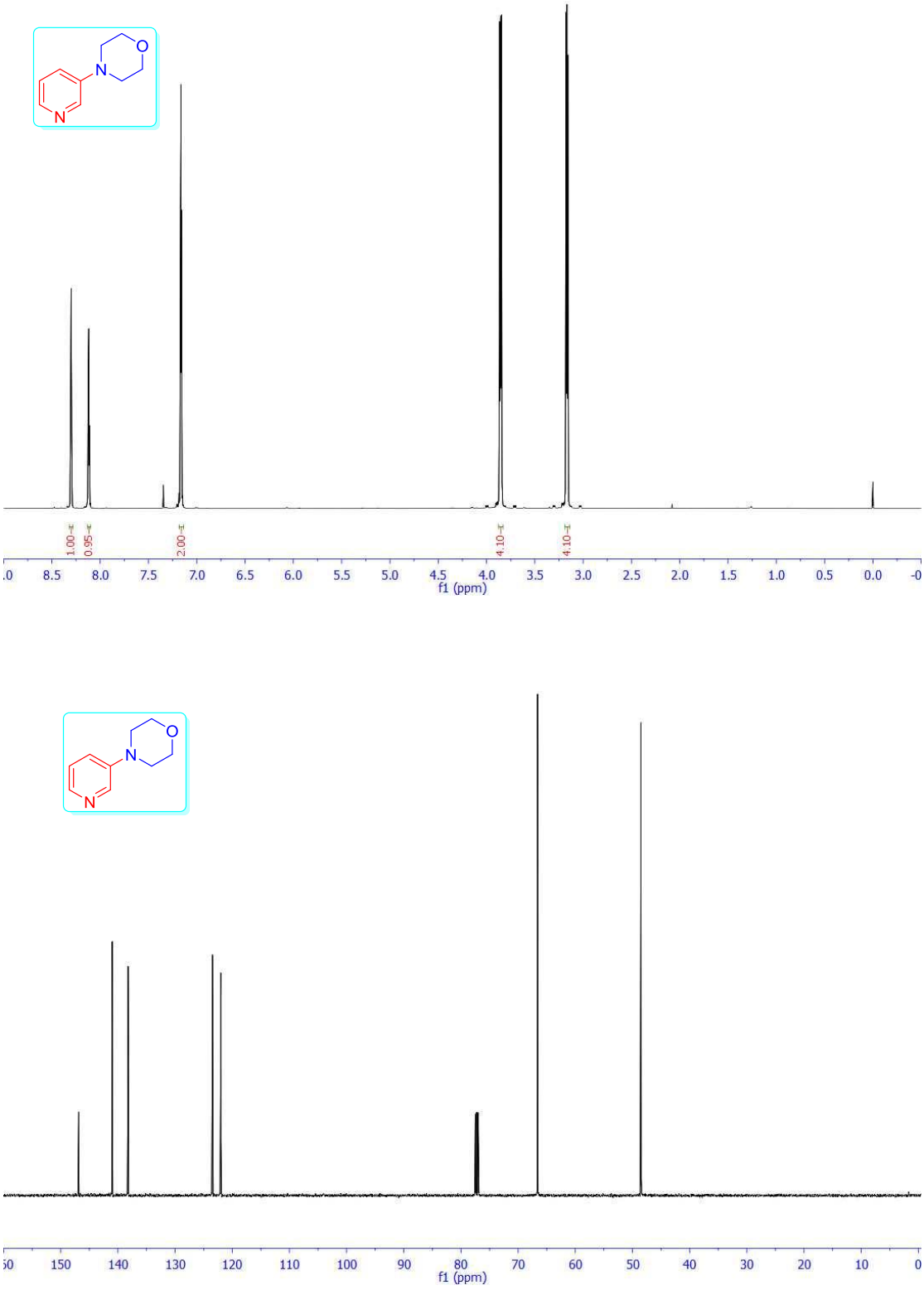


Figure S34. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9ab in $CDCl_3$

4-(Quinolin-6-yl)morpholine (9an)

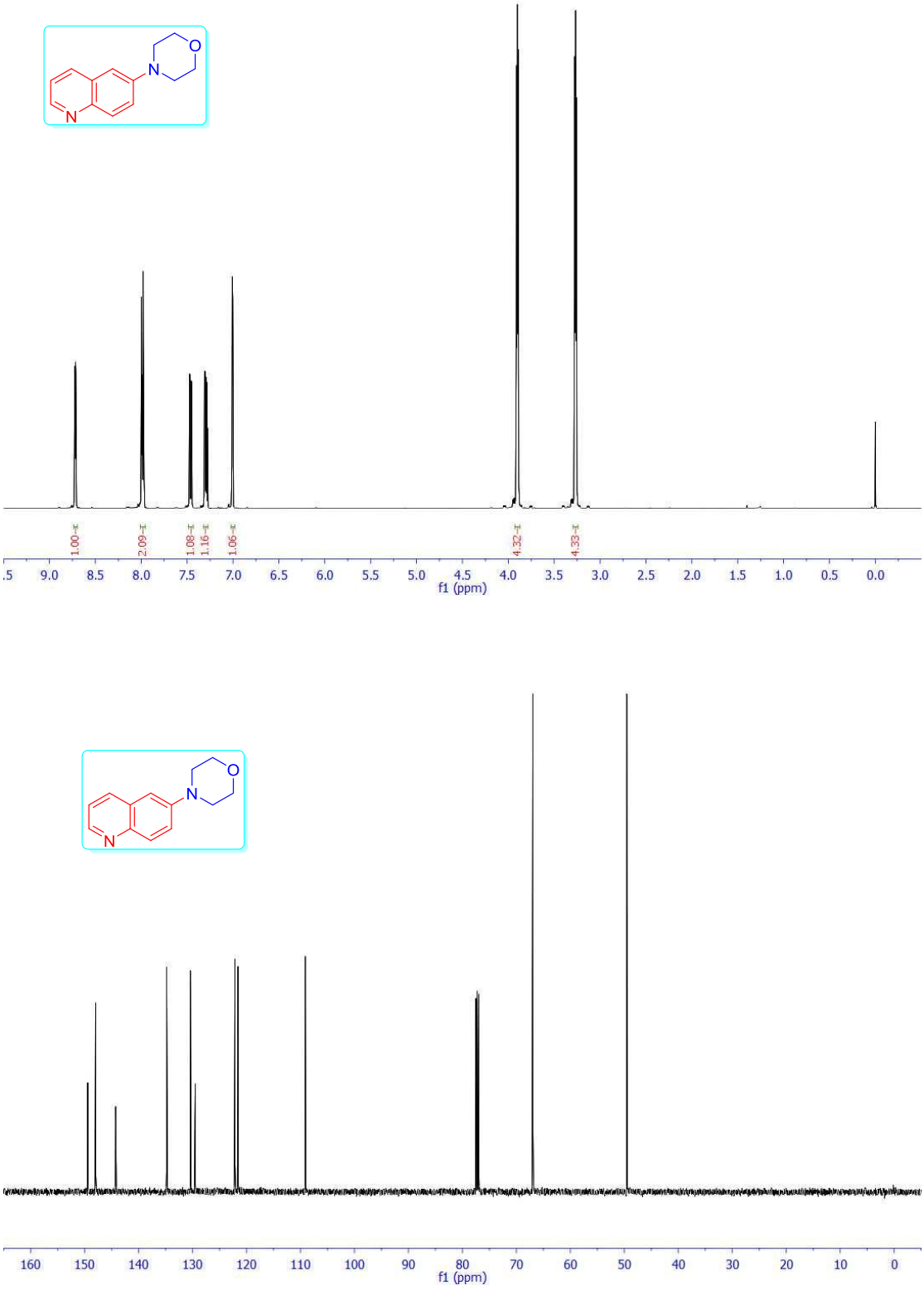


Figure S35. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9an in $CDCl_3$

4-(Pyrazin-2-yl)morpholine (9ao)

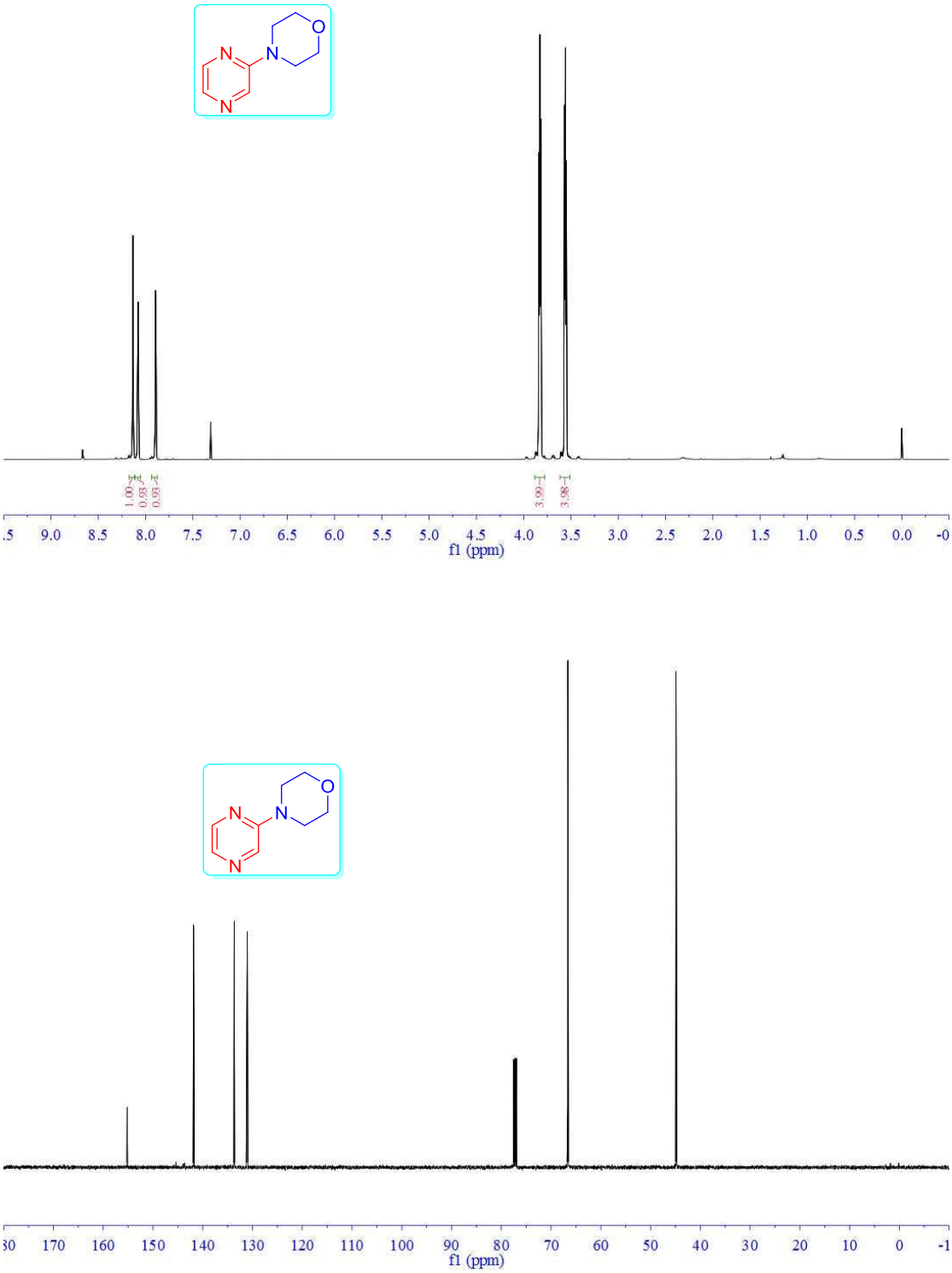


Figure S36. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9ao in $CDCl_3$

4-(Naphthalen-1-yl)morpholine (9al)

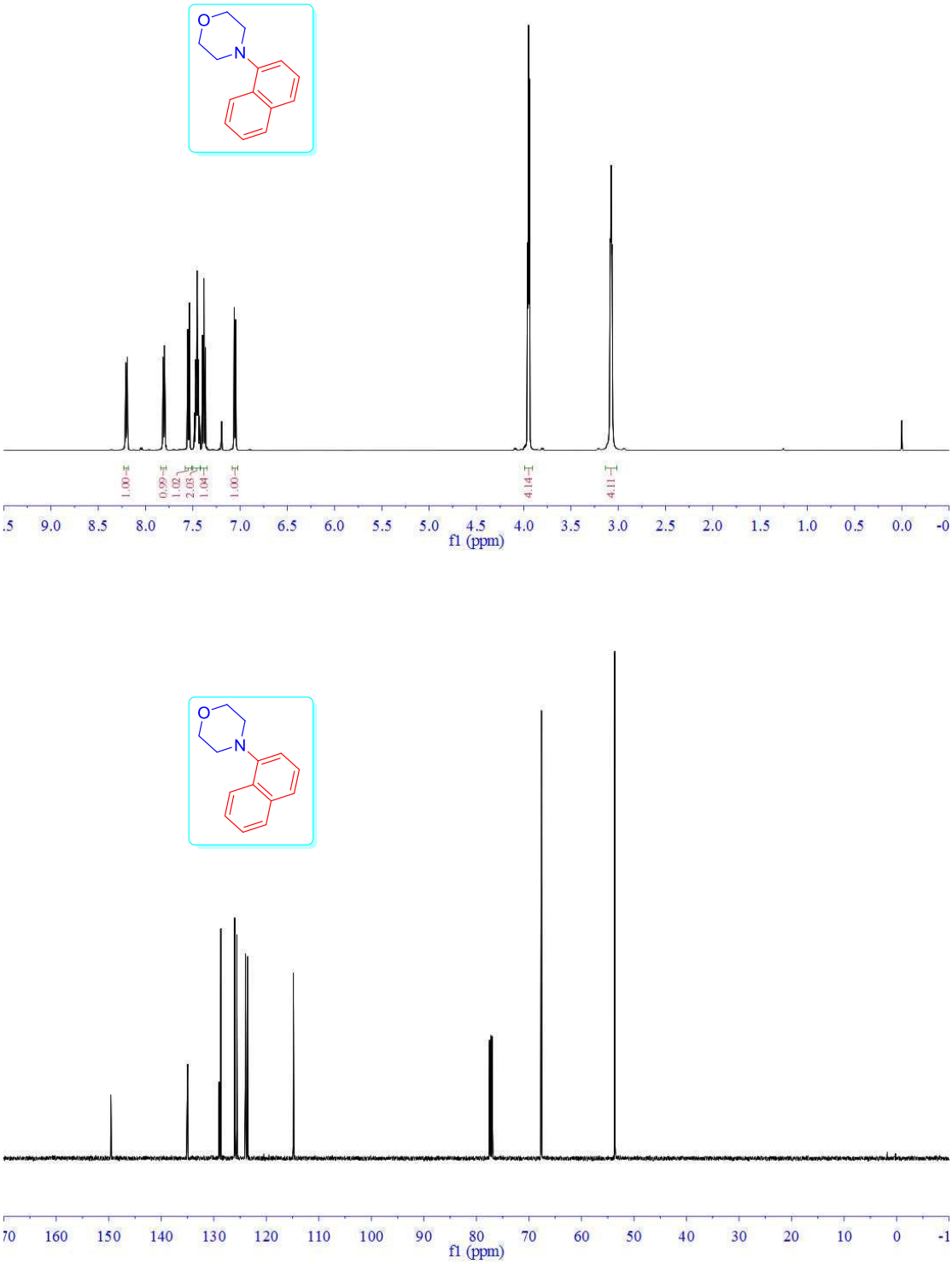


Figure S37. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9al in $CDCl_3$

4-Phenylmorpholine (9aa)

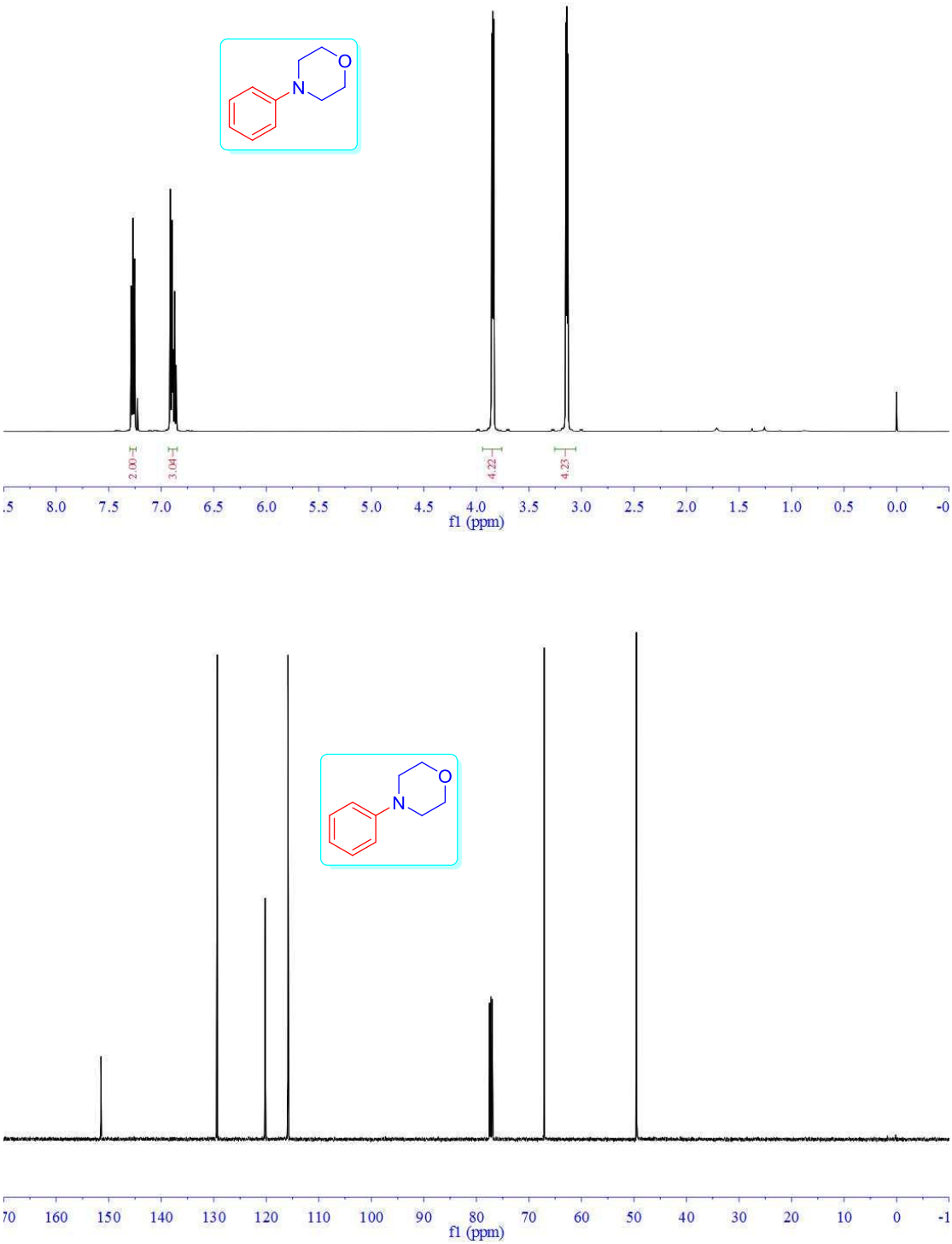


Figure S38. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9aa in $CDCl_3$

4-(4-(tert-butyl)phenyl)morpholine (9ad)

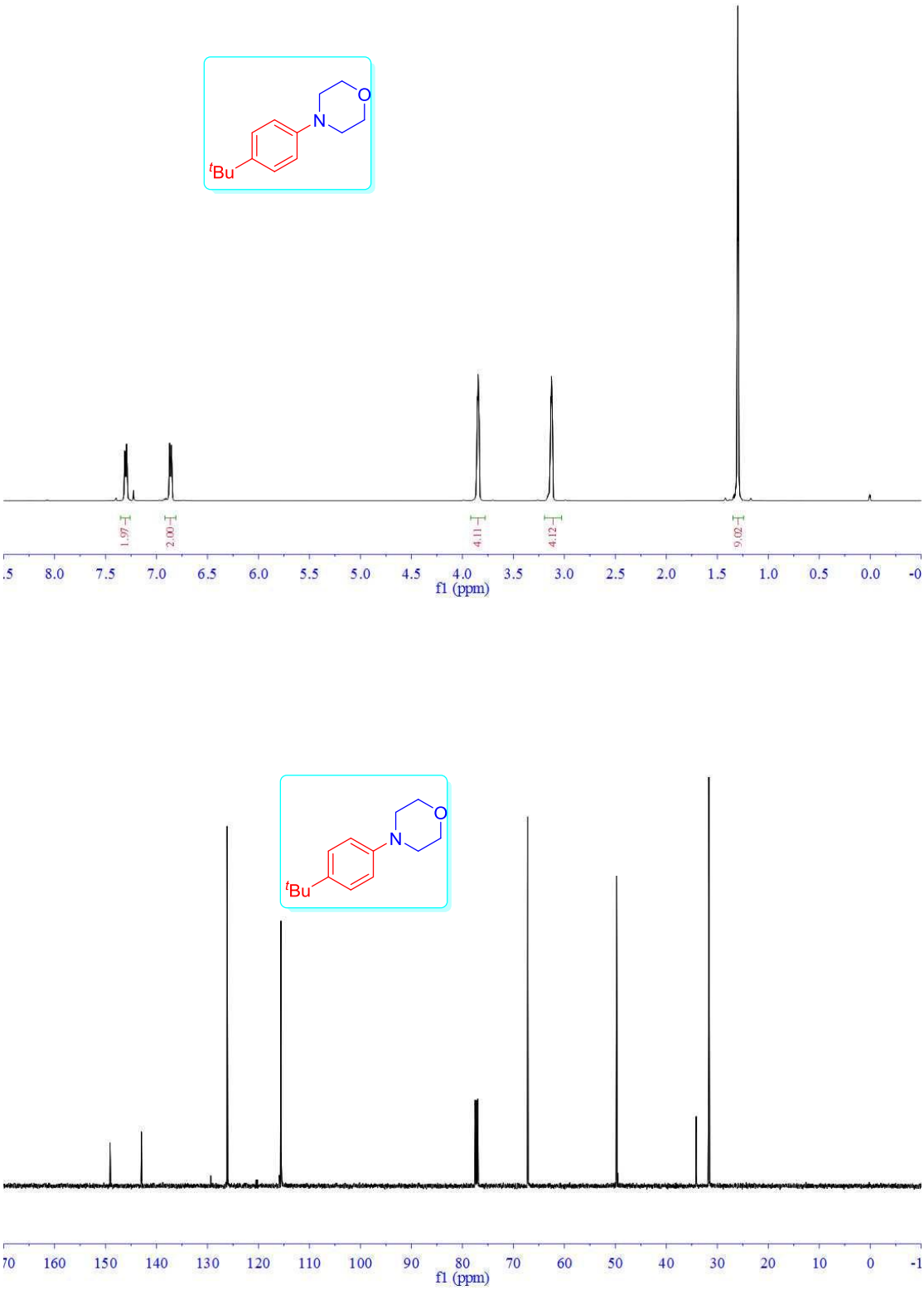


Figure S39. ^{1}H (500 MHz) and ^{13}C {^{1}H} (125 MHz) NMR spectra of 9ad in $CDCl_3$

4-(4-Methoxyphenyl)morpholine (9ac)

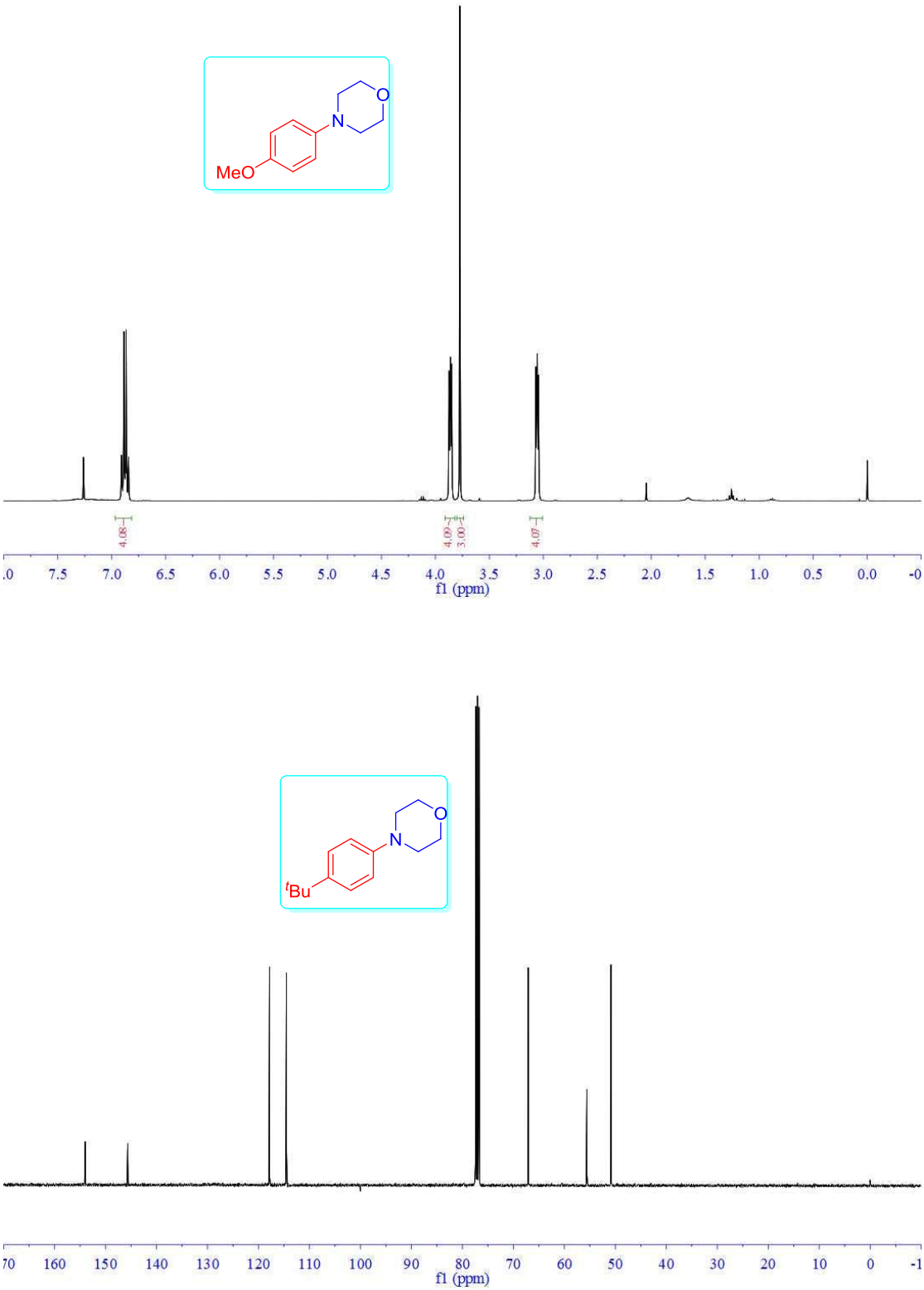


Figure S40. ^{1}H (400 MHz) and ^{13}C {^{1}H} (100 MHz) NMR spectra of 9ac in $CDCl_3$

5. References

[1] J. L. Krinsky, A. Martinez, C. Godard, S. Castillon, C. Claver, *Adv. Synth. Catal.* **2014**, *356*, 460-474.

[2] R. J. Lundgren, A. Sappong-Kumankumah, M. Stradiotto, *Chem. - Eur. J.* **2010**, *16*, 1983-1991.

[3] R. Singh, B. K. Allam, D. S. Raghuvanshi, K. N. Singh, *Tetrahedron* **2013**, *69*, 1038-1042.

[4] Y. Nakamura, L. Ilies, E.-I. Nakamura, *Org. Lett.* **2011**, *13*, 5998-6001.

[5] S. S. Kampmann, A. N. Sobolev, G. A. Koutsantonis, S. G. Stewart, *Adv. Synth. Catal.* **2014**, *356*, 1967-1973.

[6] T. Sugahara, K. Murakami, H. Yorimitsu, A. Osuka, *Angew. Chem., Int. Ed.* **2014**, *53*, 9329-9333.

[7] L. Ackermann, R. Sandmann, W. Song, *Org. Lett.* **2011**, *13*, 1784-1786.

[8] R. Yamasaki, H. Ikeda, H. Masu, I. Azumaya, S. Saito, *Tetrahedron* **2012**, *68*, 8450-8456.

[9] Z.-J. Liu, J.-P. Vors, E. R. F. Gesing, C. Bolm, *Adv. Synth. Catal.* **2010**, *352*, 3158-3162.

[10] M. Pompeo, J. L. Farmer, R. D. J. Froese, M. G. Organ, *Angew. Chem., Int. Ed.* **2014**, *53*, 3223-3226.

[11] S. M. Raders, J. N. Moore, J. K. Parks, A. D. Miller, T. M. Leissing, S. P. Kelley, R. D. Rogers, K. H. Shaughnessy, *J. Org. Chem.* **2013**, *78*, 4649-4664.

[12] A. R. Martin, Y. Makida, S. Meiries, A. M. Z. Slawin, S. P. Nolan, *Organometallics* **2013**, *32*, 6265-6270.

[13] A. R. Martin, D. J. Nelson, S. Meiries, A. M. Z. Slawin, S. P. Nolan, *Eur. J. Org. Chem.* **2014**, *2014*, 3127-3131.

[14] W. A. Carole, J. Bradley, M. Sarwar, T. J. Colacot, *Org. Lett.* **2015**, *17*, 5472-5475.

[15] J. Kwak, M. Kim, S. Chang, *J. Am. Chem. Soc.* **2011**, *133*, 3780-3783.

[16] M. N. Gandy, C. L. Raston, K. A. Stubbs, *Org. Biomol. Chem.* **2014**, *12*, 4594-4597.

[17] Y. Zhang, G. Lavigne, V. Cesar, *J. Org. Chem.* **2015**, *80*, 7666-7673.

[18] Q. Xiao, L. Tian, R. Tan, Y. Xia, D. Qiu, Y. Zhang, J. Wang, *Org. Lett.* **2012**, *14*, 4230-4233.

[19] P. G. Alsabeh, M. Stradiotto, *Angew. Chem., Int. Ed.* **2013**, *52*, 7242-7246.

[20] A. Winkler, K. Brandhorst, M. Freytag, P. G. Jones, M. Tamm, *Organometallics* **2016**, *35*, 1160-1169.